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SUPPLEMENTAL ENTERAL NUTRITION AS MAINTENANCE TREATMENT FOR PAEDIATRIC PATIENTS WITH CROHN’S DISEASE; A TREATMENT OPTION FOR A SUB-GROUP OF PATIENTS

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Objectives and Study: Exclusive Enteral Nutrition (EEN) is now considered first line treatment for active Crohn’s Disease (CD) in many centres. Once remission is achieved the main choice of maintenance treatment is immunosuppression. There is limited amount of research suggesting that ongoing maintenance enteral nutrition (MEN) can be beneficial in terms of optimising nutritional status plus maintaining disease remission. Aim - To assess if MEN post induction of remission is achievable and if so, if it helps prolong remission with follow up to a year post diagnosis.

Methods: All patients newly diagnosed with CD in 2010 and 2011 who were commenced on EEN for 8 weeks to induce remission were studied. Once clinical remission was achieved all patients were encouraged to continue on MEN. Data was collected from departmental notes at diagnosis, end of EEN period at 6 months and 1 year post diagnosis. Relapse was defined as needing a further course of EEN/steroids in the follow up period. Categorical variables were compared using chi–square/Fischer’s exact test.

Results: 59 patients (34 male, median age 11.07 years, range 2.5-16.33 years) were diagnosed and commenced on an 8 week course of EEN. 11/59 (18%) had a poor response to EEN and were switched to steroids. 48/59 patients completed 8 weeks EEN and achieved clinical remission/response. 46/48 patients received Modulen IBD®, 1 patient received Frebini Energy® supplements and 1 patient received Neocate Advance®. 29/48 (60%) consumed EEN orally, 19/48 patients (40%) received EEN via NGT. 15/48 (31%) patients were able to continue MEN post achieving remission via EEN. The drinks were consumed for a mean of 10.8 months, (range 4-14 months). 10/15 patients drank Modulen IBD®, 4/15 drank Fortisip® and 1/15 had Neocate Advance® via NGT. Mean quantity MEN consumed was 398ml (range 240-1000ml). Mean energy intake was 420 calories (range 200-1000 calories). Of the patients that had relapsed at 1 year and had been taking MEN 2/6 (33%) continued to take MEN at relapse the remaining patients had discontinued MEN. Maintenance treatment over the 1st year (n= 48)

<table>
<thead>
<tr>
<th>Treatment option</th>
<th>No. pts</th>
<th>Remission at 6 months</th>
<th>Remission at 1 year</th>
<th>p-value cf. others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplements &amp; Azathioprine</td>
<td>9</td>
<td>8/9 (88%)</td>
<td>6/9 (67%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Supplements only (no Azathioprine)</td>
<td>6</td>
<td>6/6 (100%)</td>
<td>3/6 (50%)</td>
<td>0.66</td>
</tr>
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<td>---------------------</td>
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<td>------</td>
</tr>
<tr>
<td>No Supplements, no</td>
<td>13</td>
<td>2/13 (15%)</td>
<td>2/13 (15%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Azathioprine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azathioprine only</td>
<td>20</td>
<td>16/20 (80%)</td>
<td>13/20 (65%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Conclusion:** A sub group of patients can continue MEN post induction of remission with EEN as a maintenance treatment and this seems a useful strategy especially in those who are not commencing azathioprine. A randomised controlled trial would help clarify these findings.

**Disclosure of Interest:** H. Duncan: None Declared, E. Buchanan Conflict with: Recieved honorarium from Nestle Nutrition, T. Cardigan: None Declared, V. Garrick Conflict with: Recived Honorarium from Nestle Nutrition, L. Curtis: None Declared, A. Barclay: None Declared, P. McGrogan Conflict with: Recieved Honorarium from Nestle Nutrition, R. Russell Conflict with: Recieved Honorarium from Nestle Nutrition
OUTCOMES OF A PAEDIATRIC NAFLD SERVICE: WORKING TOWARDS A THINNER FUTURE
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Objectives and Study: Non Alcoholic Fatty Liver Disease (NAFLD) is a growing problem amongst the paediatric population, largely as a result of childhood obesity. Weight control, the cornerstone of management, can be challenging. Our aim was to audit the outcomes of children attending a tertiary paediatric liver unit with NAFLD and to observe features specifically associated with a change in body mass index (BMI).

Methods: Clinical and anthropometric data on 91 children (59 boys) who attended with a diagnosis of NAFLD were reviewed and details of any interventions were recorded. Specific outcome measures were change in BMI z-score, transaminases and spleen size. Diagnosis was made histologically in 68 children, in the remainder other diagnoses were excluded and the diagnosis was made on clinical grounds. Investigations included liver biopsy, oral glucose tolerance test and routine investigations for chronic liver disease. SPSS v20.0 was used for statistical analysis.

Results: The median age of presentation in the group was 12.68 years (IQR 11.65, 13.83) with a median BMI z-score at presentation of 2.8 (IQR 2.34, 3.13). When the diagnosis was established, children and their parents received lifestyle advice and education about the condition. Median time of follow-up was 24 months (IQR 12, 37). There was an improvement in median BMI z-score change at each time point. BMI z-score change from presentation to 6 months was -0.03 (IQR -0.18, 0.08); from presentation to 12 months was -0.07 (IQR -0.26, 0.1) and from presentation to furthest time point was -0.07 (IQR -0.31, 0.2). The median number of dietetic reviews was 2.6 (IQR 1, 3), while median number of clinic attendances was 7 (IQR 5, 10). Five patients reported attending weight loss groups, 13 had other dietetic input and 1 had tried Orlistat. Proxy outcome measures for liver disease included transaminases and spleen size. Median AST at presentation was 45IU/L (IQR 36, 61); this decreased to 32IU/L (IQR 25, 45) at last follow up. Median ALT at presentation was 61IU/L (IQR 39, 86), decreasing to 48IU/L (IQR 26, 70) at follow up. Spleen size increased in 6 children over the study period. There was no correlation between number of dietetic or clinic visits, age, sex or initial BMI z-score and change in BMI z-score over time. There was a close correlation between improvement in ALT and greater decrease in BMI z-score at both 12 months (p=0.02) and last follow up (p=0.008).

Conclusion: In our experience patients have shown a positive change in their BMI over the study period. However BMI at time of furthest visit still remains high, indicating the vital need to focus on the issue of weight management in this challenging group. We now see children in a dedicated multidisciplinary clinic to address their multifactorial needs with the aim of improving outcomes further.

Disclosure of Interest: None Declared
THE QUALITY OF LIFE OF CHILDREN WITH FOOD PROTEIN INDUCED GASTROINTESTINAL ALLERGIES
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Objectives and Study: The impact of food allergy on quality of life (QoL) has been well studied in children with IgE-mediated food allergies, however much less is known on how non-IgE-mediated food protein-induced gastrointestinal allergies (FPGIA) impact on QoL. These children typically experience debilitating gastrointestinal and extra-intestinal symptoms in addition to having to exclude multiple foods that parents report as impacting on their day to day lives. We therefore set out to explore in families with young children that suffer from FPGIA.

Methods: Parents of children at Great Ormond Street Hospital NHS Foundation Trust, newly diagnosed with FPGIA allergies, were prospectively recruited to take part in the study. FPGIA was diagnosed following an exclusion diet with confirmed symptom improvement. As the majority of children were below 2 years of age, we used the validated PedsQL™ Family Impact Module Questionnaire, which was completed by parents. Data on QoL from a historical paediatric cohort with chronic pain (i.e. musculoskeletal pain, pain secondary to trauma) using the same questionnaire was used as control group.

Results: Fifty parents of eligible children (34 male) filled out the questionnaire. The median age was 21.6 months (3.6-190.8). The most common combination of foods excluded were cow’s milk, hen’s egg, soya, wheat and other targeted foods (38.6%); cow’s milk, hen’s egg, soya, and wheat (18.2%); cow’s milk, hen’s egg and soya (18.2%); and cow’s milk and soy (15.9%).

All QoL questionnaires were filled in by the mothers of the children. There was a statistical difference (p=0.003) in the mean total impact score for children with FPGIA: 54.55 compared to the control 64.68. Although this study indicated that families with children with this type of allergy and those with chronic pain had similar low QoL for “Worry”, “Family Relationships” and “Emotional Functioning”, families of children with FPGIA had a lower QoL in all other categories. These include: physical functioning (53.23, p=0.003), social functioning (58.00, p=0.000), cognitive functioning (65.2, p=0.043), communication (65.6, p=0.000) and daily activities (46.00, p=0.000).

Conclusion: This study suggests that the impact on QoL on families with children with FPGIA is significantly worse than for those with chronic pain disorders. This was seen in particular for physical, social and cognitive functioning and day to day living. Intestinal and extra-intestinal manifestations, in addition to dietary elimination may provide a possible explanation for the high impact seen in this group of families. However, further research is needed with a larger cohort and comparisons with other disease groups when these become available.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

AHP-0004

NUTRITIONAL CONTROVERSIES IN PAEDIATRIC CYSTIC FIBROSIS (CF) CARE; RESULTS OF A EUROPEAN SURVEY

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Objectives and Study: Nutrition is a key aspect to CF care. Use of oral nutritional supplements (ONS) and tube feeding (TF) in CF remain controversial due to scarcity of randomised control trials. European guidelines on nutrition in CF give some broad direction on these aspects but are open to interpretation. Overnutrition and obesity although historically given little attention in the context of CF are now emerging concerns for which there is limited data in the literature. Our aim was to identify and compare the prevalence of 3 key nutritional aspects (ONS, TF and overweight status) in CF patients across Europe.

Methods: A questionnaire was developed and the content agreed with the chairs of the European Cystic Fibrosis Nutrition Group (ECFNG). This was circulated as a personalised email to all members of the group via the members email database. Questionnaires were then returned via email and the data was exported into spreadsheets and tabulated manually. Data collection took place over a 6 month period (February - August 2012). The questionnaire asked about demographic data on the responder's clinic population looking at % prevalence of the following: use of ONS, use of TF and overweight status (defined as BMI >91st centile).

Results: 63 emails were sent out and a total of 39 dietitians responded. The 39 responding dietitians were responsible for a total of 7333 patients (5163 adult, 2170 paediatric). 7 countries were represented providing paediatric data from 20 dietitian responses. Not all responders were able to give data for every section. Medians were used as histograms indicated uneven data distribution for several categories. Median prevalences for the full representative data (n=2170) were 4.4% tube feeding, 20% use of ONS and 1.5% overweight.

<table>
<thead>
<tr>
<th>Country</th>
<th>Contributing patients numbers (n)</th>
<th>No. of Dietitian responses</th>
<th>% Tube feeding</th>
<th>% Use of ONS</th>
<th>% &gt;91st centile</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>1226</td>
<td>10</td>
<td>5</td>
<td>19.5</td>
<td>5</td>
</tr>
<tr>
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<td>285</td>
<td>3</td>
<td>1</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Sweden</td>
<td>110</td>
<td>2</td>
<td>10</td>
<td>30</td>
<td>0.5</td>
</tr>
<tr>
<td>Denmark</td>
<td>89</td>
<td>1</td>
<td>1</td>
<td>44</td>
<td>0</td>
</tr>
<tr>
<td>Germany</td>
<td>85</td>
<td>1</td>
<td>2</td>
<td>20</td>
<td>*</td>
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<tr>
<td>Netherlands</td>
<td>70</td>
<td>2</td>
<td>10</td>
<td>19.6</td>
<td>0</td>
</tr>
<tr>
<td>Norway</td>
<td>55*</td>
<td>1</td>
<td>9</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* No data submitted
Conclusion: This is the first European survey reporting differences in controversial feeding practices and emergence of obesity in CF. TF (range 1-10%) indicates wide variation in use of this type of nutritional support across EU countries. Use of ONS (range 15-44%) emphasises their more routine use across patient populations. Overweight status (median 1.5%) is currently a small but emerging area which requires vigilance to identify risk factors for vulnerable patients. This data provides a collaborative overview of practice and is an encouraging foundation for future projects.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

AHP-0005

NUTRITIONAL ASSESSMENT OF HOSPITALISED INFANTS
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Objectives and Study: Accurate assessment of nutritional status is vital for the management of hospitalised infants; however, there is currently no gold standard method. Traditionally, anthropometric measures have been used although these fail to detect risk of developing malnutrition secondary to hospitalisation. The Paediatric Subjective Global Nutrition Assessment (PSGNA) tool may be more accurate for the assessment of nutritional status in hospitalised infants as it includes assessment of recent changes in anthropometry as well as a broad range of additional nutrition focused variables.

This study aimed to determine the nutritional status of hospitalised infants using both the PSGNA and Body Mass Index (BMI)-for-age z-score cut offs. Secondarily, this study aimed to determine the ability of a series of Malnutrition Screening Questions (MSQ), administered by nursing staff on admission to hospital, to identify infants at risk of malnutrition.

Methods: Infants aged 31 days to 24 months (corrected for gestational age) who were inpatients during September and October 2012, with a length of stay greater than 24 hours, were invited to participate in the study. Bare weight was measured using infant scales and length was measured using a flexible measuring matt. A single observer administered the PSGNA and MSQ. Statistical comparisons were made using Cohen's k statistic and interpreted according to the tables by Landis & Koch.

Results: A total of 23 infants were enrolled in the study, 57% male with an average length of stay of 24 days. The most common reason for admission was infection (40%) followed by neurological (22%) and gastrointestinal (22%). The PSGNA categorised 61% of infants as well nourished and 39% as moderately malnourished. BMI-for-age z-scores categorised 74% as well nourished, 17% as mildly malnourished and 9% as moderately malnourished. Agreement between the two methods was poor (k=0.13±0.20; 95%CI 0.27, 0.53). The MSQ was able to identify the majority of infants considered malnourished according to the PSGNA and was 100% accurate for identifying infants considered to be well nourished. Statistical agreement between the two methods was very good (k=0.91±0.09; 95% CI 0.74, 1.08).

Conclusion: Although nutritional status as determined by the PSGNA differed from the BMI-for-age z-scores, the comprehensive nature of the PSGNA ensured that a more precise classification of the malnourished infant could occur. The MSQ was able to accurately identify 90% of infants considered to be malnourished according to the PSGNA and is suitable for use in the clinical setting. Further research is required to determine sensitivity and specificity of this tool.

2. Secker DJ. JAND 2012;112:424-31
Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

AHP-0006

DIETARY INTAKE ASSESSMENT IN PEDIATRIC HOSPITALIZED PATIENTS USING THE VISUAL PLATE WASTE METHOD
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Objectives and Study: Hospitalization often comes with undernutrition and inadequate food intake. Currently there is not a uniform procedure for recording every patient’s actual intake. Various methods have been introduced for meal observation, in order to early detect patients with inadequate food intake and to apply nutrition therapy as soon as possible. The present study aimed to assess dietary intake of pediatric hospitalized patients in a Greek ward, using the Visual Plate Waste (VPW) method in a single meal, namely lunch.

Methods: One hundred and thirty pediatric hospitalized patients participated in the study (80 boys, 50 girls) aged 2-15 years (mean age=6.76±3.97 years). Dietary intake of lunch was assessed using the VPW scale in four levels (full meal, half, quarter, eat nothing). Energy needs of all patients were calculated with adjustment according to clinical status. Hospital meals were analyzed using Food Processor v.7.4 software. Body weight and height were measured and weight for age z score (WAz) was calculated, using WHO Anthro software. Undernutrition was defined as WAz <2 SD. Factors affecting dietary intake and adequacy were investigated using questionnaires, through interview with the child and the parent/caregiver being present.

Results: The daily hospital menu provided 88 kcal/kg (mean=2218 kcal), 1.2 g of protein/kg and 40.3% of fat, amounts adequate for the patients needs (82.4 kcal/kg, mean=2077 kcal), 0.9-1.2 g protein/kg, 30-35% fat respectively). According VPW records, only 20.8% of the pediatric patients, consumed fully their meal, 34.6% consumed half portion, whereas 27.7% consumed nothing from the provided lunch in the hospital. According patients’ answers, the main reasons for inadequate intake were poor appetite (31.1%), consumption of smaller food portions normally (23.3%), hospital food dislikes (13.6%) and symptoms such as nausea and vomit (9.7%). The majority of the pediatric patients (69.5%) consumed foods except hospital menu such as fruits (32.8%), homemade food (23.3%), junk food (13.7%), cakes/pastries/confectionery (15.1%), and dairy (15%). Increased energy intake from lunch, correlated with greater WAz values (p<0.05).

Conclusion: In the majority of participants (79.2%) inadequate dietary intake during lunch was observed. This situation can result to malnutrition in the long run. Meal observation using VPW tool provides an easy applicable method concerning food consumption and dietary intake. The routine use of VPW in pediatric wards can contribute to an accurate nutrition assessment and to early identification of patients with inadequate intake and therefore candidates for provision of more appealing meals or oral supplements.

Disclosure of Interest: None Declared
THE EXPRESSION OF EPITHELIAL JUNCTION PROTEINS IS DECREASED ALREADY IN EARLY DEVELOPING COELIAC DISEASE AND NEGATIVELY CORRELATES WITH DIARRHEA

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Objectives and Study: The small bowel mucosal damage in coeliac disease develops gradually from normal morphology to moderate villous shortening with crypt elongation and finally into severe villous atrophy and crypt hyperplasia. The expression of epithelial junction proteins is altered in the small intestine of untreated coeliac disease patients with flat lesion but information about their expression level during early developing disease is not currently available. Therefore, we investigated whether alterations in the expression of epithelial junction proteins are present already during early developing coeliac disease with normal mucosal morphology. We also studied the correlation between the junction protein expression and signs of inflammation and clinical symptoms.

Methods: Twenty coeliac patients and twenty control individuals were included in the study. All patients were studied during overt disease and after gluten-free diet. Ten patients were also studied during early developing disease. The expression of junction proteins (Claudin-3, occludin, ZO-1, E-cadherin) was studied in small bowel biopsies with immunofluorescence stainings and western blotting. Their expression level was correlated to mucosal morphology (villus height crypt depth ratio; Vh/CrD), serum and mucosal antibodies, the number of intraepithelial lymphocytes (IELs) and to gastrointestinal symptoms (measured with gastrointestinal symptom rating scale; GSRS).

Results: The expression of all junction proteins was decreased already during early developing coeliac disease. Their expression further declined in overt coeliac disease and improved during a gluten-free diet. Interestingly, the expression of all junction proteins correlated with Vh/CrD, and negatively with the number of IELs, intensity of small intestinal autoantibody deposits and serum autoantibodies. Moreover, the expression of claudin-3 negatively correlated with diarrhea sub-dimension score of GSRS.

Conclusion: We conclude that the expression of junctional proteins is decreased in the small-intestinal epithelium already during early developing coeliac disease with normal mucosal morphology. In addition, the expression of junctional proteins correlates with mucosal damage and negatively with different indicators of inflammation. Claudin-3 expression also negatively correlates with the presence of diarrhea. Therefore, our data suggests that junctional disintegrity likely plays a role already in the early phases of coeliac disease.

Disclosure of Interest: None Declared
EVOLUTION AND HLA-ASSOCIATION OF THE EARLY INFANTILE GLIADIN ANTIBODY RESPONSE IN A HIGH-RISK COHORT FOR COELIAC DISEASE WITH GLUTEN INTRODUCTION FROM 4 OR 6 MONTHS OF AGE
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Objectives and Study: To characterize the outcome of serum antibody positivity to native (AGA) and deamidated (DGP) gliadin observed in infancy.

Methods: During 2007-2010, 1324 infants with a 1st degree relative with coeliac disease (CD) were recruited in 8 countries shortly after birth (EU-PreventCD project www.preventcd.com) and 931 HLA DQ2 and/or DQ8 positives were randomised double-blind to 100 mg of gluten suspension/day or placebo from 4 months of age. From 6 months all children consumed gluten-containing foods and serum samples were collected at 4, 6, 9, 12, 18, 24 and 36 months. Small bowel biopsies were performed based on symptoms suggestive of CD and/or anti-tissue transglutaminase (TG2A) or AGA antibodies.

Results: As of 11/2012, 814 children have been followed till 3 years and CD diagnosis was obtained in 56. At least 5-fold transient increase over baseline in AGA-IgA without TG2A occurred in 134 infants at 6 months, median 16.7 U/ml (range 6-100); the antibodies recognised also DGP. This early response was associated with the duration of exclusive breast feeding. A smaller AGA peak was observed in 35 children (p<0.0001) at 9 months who were stationary at 6 months, median 8.2 U/ml (range 6-100, p<0.001). Both these groups had in 41% HLA DQ2.2 (with or without DQ2.5) compared to 14.4% in children without an AGA or DGP peak. Evaluating the children with complete sets of follow-up samples, the outcome was:

<table>
<thead>
<tr>
<th>At 2 years of age (n=723)</th>
<th>At 3 years of age (n=588)</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>C</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>AGA &gt;5x baseline at 6 months</td>
<td>11</td>
</tr>
<tr>
<td>AGA &gt;5x baseline at 9 months</td>
<td>21</td>
</tr>
<tr>
<td>AGA not &gt;5x baseline during first year of life</td>
<td>52</td>
</tr>
<tr>
<td>Other pattern</td>
<td>63</td>
</tr>
</tbody>
</table>

OR *0.62, **1.80, ***2.79

**Conclusion:** Both AGA and DGP had low predictive value for CD in these children. An early IgA AGA response at 6 months of age or earlier seems to be beneficial while at 9 months or later is associated with higher CD risk.

**Disclosure of Interest:** None Declared
ANTHROPOMETRIC CHARACTERISTIC AND METABOLIC CONTROL OF PAEDIATRIC PATIENTS WITH TYPE 1 DIABETES MELLITUS AND COELIAC DISEASE.

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Objectives and Study: Coeliac Disease (CD) concurs with many other autoimmune conditions, markedly Type 1 diabetes mellitus (T1DM). In patients with T1DM, CD commonly presents without overt clinical symptoms and the use of serological screening in T1DM patients remains controversial considering the extra psychological burden an additional disease imposes. This study looked at the impact of a gluten free diet (GFD) on growth, symptoms and disease control in T1DM patients with CD.

Methods: In the present study parameters of growth (weight, height, BMI z-scores) and disease management (Hba1c) were analysed two year prior and two years post CD diagnosis in T1DM paediatric patients routinely screened for CD and tissue transglutaminase (tTg) to assess dietary compliance in all patients with CD. 23 CD+T1DM patients were matched for age, sex, T1DM duration, age at CD diagnosis and T1DM age of onset with 23 CD and 46 T1DM control.

Results: BMI, height and weight z-scores were normally distributed in each group. There were no statistical differences between the T1DM+CD patients and CD and T1DM controls for any mean growth parameters at any time points, nor difference in the number of children classified as underweight or of short stature. At CD diagnosis short stature was observed in 13% of CD patients but not in T1DM or T1DM+CD, 2 years post CD diagnosis short stature was observed in no T1DM or CD patients but 11% of T1DM+CD patients. One year prior to CD diagnosis the change in BMI z-scores (representing growth velocity) was significantly lower in CD+T1DM group than the T1DM group (-0.168±0.4 vs 0.136±0.5, p=0.009). After CD diagnosis and GFD initiation height and BMI z-score change was comparable in all three groups. No differences were observed in median or mean glycosylated haemoglobin A1c (HbA1c) between the T1DM patients with or without CD before or after CD diagnosis, nor did level of dietary compliance to a GFD assessed by tTg levels affect the ability of T1DM to maintain normal (<7%) HbA1c levels.

Conclusion: In this study no differences were observed in the metabolic control of T1DM patients before or after the onset of CD. The level of compliance to a GFD did not affect metabolic control or the ability to maintain HbA1c below 7%. The significant reduction in growth velocity observed in T1DM+CD patients one year prior to CD diagnosis may indicate the true onset of coeliac disease prior to diagnosis and further deterioration of growth might have been prevented with routine screening.

Disclosure of Interest: None Declared
CLINICAL SPECTRUM OF UNSELECTED NEWLY DIAGNOSED COELIAC DISEASE PATIENTS – DATA FROM THE OBSERVATIONAL MULTI-CENTER STUDY PROCEDE

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Objectives and Study: The Prospective Coeliac Disease Diagnostic Evaluation (ProCeDE) study aims to validate the new ESPHGAN diagnostic criteria for coeliac disease (CD) in a large cohort of at least 600 newly diagnosed CD children. An interim analysis was performed after the first 200 recruited patients to recalculate the sample size. Here we describe the clinical presentation at diagnosis of consecutive unselected CD patients diagnosed at the different centers.

Methods: Since 11/2011, 38 centres in 23 countries started to collect data of paediatric patients aged 0.5 to 18 years who undergo duodenal biopsies for suspected CD. Patients are included if 1) they are positive for tissue transglutaminase type 2 (TG2) IgA-antibodies (IgG in case of IgA-deficiency) at any antibody level, 2) report symptoms or are at high risk for CD, 3) eating a normal gluten-containing diet, and 4) parents have given written informed consent. Detailed data on medical and family history, physical examination and basic lab tests are collected at the day of endoscopy. Serology, HLA-typing and histopathology will be repeated centrally.

Results: Until the end of June 2012, clinical data on 200 CD patients were available from 18 centers. Median age was 6.3 years (range: 1.1 to 18.6), 66% were female, 33.0% belonged to a high risk group for CD. Stool frequency was normal in 82%, while 60.0% reported normal stool consistency. The most frequent symptom was abdominal pain (44%) followed by abdominal distention (26%), diarrhea (25%), weight loss (23%), fatigue (22%), moodiness (21%), anorexia (17%), flatulence (16%), growth failure (15%), constipation (14%), and vomiting (6%). Malabsorption syndrome was present in 17%. Median z-score for height was -0.51 (min -4.8; max 2.9) and for BMI -0.18 (-3.2; 3.1) (N=198). Hemoglobin was below normal value for sex and age in 14.2% (N=197), ferritin was reduced in 37.1% (N=167), and albumin in 4.3% (N=138), ALT was elevated in 7.7% (N=155). All patients initially had positive TG2-IgA (by inclusion criteria), with very high TG2-IgA levels (≥ 10fold cut-off,) in 64% (N=200) and positive EMA-IgA in 88% (N=192). CD was proven by histology in 84.5% of the patients, however, in 7.0% the diagnostic work-up was incomplete (N=200). Patchy villous atrophy was identified in 7.2% of patients where Marsh staging was available from both, pars descendens and duodenal bulb (N=153).

Conclusion: The interim analysis of the first 200 study patients confirms that the cohort is representative for pediatric CD patients with the majority having no or unspecific symptoms and with malabsorption syndrome in only a small proportion. Our results support that screening for CD specific antibodies should be also performed in patients with minor gastrointestinal signs and/or symptoms.

Disclosure of Interest: None Declared
Endoscopic efficacy of two regimens of maintenance therapy in patients with Crohn disease aged 7-17 years - multicenter randomized study


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Objectives and Study: REACH study demonstrated the efficacy and safety of induction and maintenance therapy of infliximab with concurrent immunomodulator in children with Crohn disease (CD), whereas SONIC study revealed that combined maintenance therapy is more efficient vs. infliximab and immunomodulator alone in adults. However it is healing of mucosal lesions which seems to be most important endpoint in assessment of treatment for Crohn's disease with biological agents. The aim of this study was to compare the endoscopic efficacy of two regimen of maintenance therapy (1. Infliximab with immunomodulator and 2. Infliximab alone) in children aged 7-17 years with moderate to severe CD.

Methods: 99 patients with PCDAI>30 pts and endoscopic evaluation performed were involved to the study and received induction therapy with infliximab 5 mg/kg at weeks 0, 2, and 6. Clinical (PCDAI score) and endoscopical (using Simple Endoscopic Score for Crohn's Disease (SES-CD)), evaluations were performed at week 10 and patients with clinical response (decrease of PCDAI≥15 AND PCDAI<30) were randomized to Group I receiving infliximab 5 mg/kg every 8 weeks with immunomodulator until Week 54 (n=45) or Group II receiving infliximab 5 mg/kg every 8 weeks with immunomodulator stopped at Week 26 (n=39). Endoscopical assessment was performed at week 54 in both groups. Primary endpoint was relapse of mucosal response defined as increase of SES CD score, and the secondary endpoint was number of patient in mucosal remission defined as SES CD=0.

Results: At Week 10, after induction therapy, 84 out of 99 (85%) pts had clinical response, and 78 out of 84 (93%) pts with clinical response had also mucosal response defined as decrease of SES CD score. 26 out of 84 (31%) had mucosal remission. At Week 54 mucosal deterioration (increase of SES CD score) was found in 13 out of 45 pts in Group I (29%) and 11 out of 39 pts in Group II (28%) (NS). Mucosal remission was observed in in 22 out of 45 pts in Group I (49%) and in 16 out of 39 pts in Group II (41%) (NS).

Conclusion: Both regimens of maintenance therapy (1. Infliximab with immunomodulator and 2. Infliximab alone) are endoscopically equally efficient in children aged 7-17 years with moderate to severe CD.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PA-G-0033

INTERACTIONS BETWEEN DNA VARIANTS IN THE CYP4F3 GENE AND THE CONSUMPTION RATIO OF Ω-3/Ω-6 FATTY ACIDS CAN ENHANCE RISK FOR CROHN’S DISEASE IN CHILDREN

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Objectives and Study: An imbalance in dietary consumption of polyunsaturated fatty acids (PUFA) has been implicated in the pathogenesis of inflammatory diseases such as Crohn’s disease (CD). In particular a low ratio of ω-3/ω-6 PUFA in the diet has been shown to be relevant. Similarly inherited variations in genes involved in PUFA metabolism were recently shown to confer risk for CD. We hypothesized that interactions between PUFA metabolic genes such as CYP4F3 and the ratio of ω-3/ω-6 fatty acids could mediate the pathogenesis of CD in children.

Methods: We carried out a case-control study including patients newly diagnosed with CD (<=19 yrs of age at diagnosis) recruited from 3 pediatric clinics across Canada. Controls included children with minor trauma and their siblings. The study was restricted to children of Caucasian ancestry. Diagnosis of CD was confirmed using standard methods. Usual dietary consumption during the 12 months prior to the diagnosis was ascertained using a validated food-frequency questionnaire. DNA from blood samples was genotyped for single nucleotide polymorphisms (SNP) in the CYP4F3 gene using the Sequenom genotyping platform. Based on the consumption of ω-3 (DHA and EPA) and ω-6 (arachidonic acid) the ratio of ω-3/ω-6 was calculated. Children in the lower two quartiles were classified as consuming a low ratio and those in the higher 2 quartiles were classified as consuming a higher ratio. Interactions between the CYP4F3 gene and ω-3/ω-6 ratio were analyzed by fitting an interaction term in the logistic regression model that was adjusted for age, gender and caloric intake. Interaction odds ratios (IOR), OR corresponding 95% confidence intervals (95% CI) were estimated. P values <0.05 were considered significant.

Results: A total of 158 new CD cases and 156 controls were studied. The mean (±SD) age of the cases was 13 (±3.0) and was similar to that of the controls: 12.8 (±3.1). About 54% of the CD patients were male. CD patients had a higher mean caloric intake (2517±804) in comparison to the controls (2234±583). Of the 5 SNPs, significant interactions between 2 SNPs (rs1290617 and rs2283612) and the ratio of ω-3/ω-6 were observed (IOR=0.24, 95% CI=0.10-0.56, p=0.002 & IOR=0.30, 95% CI=0.11-0.78, p=0.038 respectively). For both these SNPs, associations with CD were evident only among children who consumed a low ratio of ω-3/ω-6 fatty acids (OR=2.58, 95% CI=1.4-4.74, p=0.002; OR=2.0, 95% CI=1.0-4.0, p=0.046 respectively). No significant interactions involving the 3 other CYP4F3 SNPs were observed.

Conclusion: Our findings suggest that inherited variation in genes involved in the metabolism of fatty acids can enhance susceptibility for CD in children with a lower consumption ratio of ω-3/ω-6 fatty acids.

Disclosure of Interest: None Declared
Efficacy and Safety of Adalimumab in Children with Crohn’s Disease Previously Treated with Infliximab

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Objectives and Study: Adalimumab (ADA) is effective in the treatment of Crohn’s disease (CD) in children naive to infliximab (IFX) (1). The objective of this study was to evaluate the efficacy and safety of ADA in children with CD refractory or intolerant to IFX.

Methods: This retrospective study included all children with CD recorded in a paediatric-onset cohort through a population-based registry. They received ADA before the age of 18 years because of failure or intolerance to IFX. Response to treatment was assessed using the Physical Global Assessment score (PGA). The effectiveness of ADA was defined as clinical remission (PGA=1) or clinical response defined by a decrease of at least 2 points of PGA 6 months after the introduction of ADA. Following parameters were recorded from ADA initiation to maximal follow-up: growth (height/age Z-score), nutritional status (BMI/age Z-score), inflammatory biomarkers (CRP, orosomucoid). Adverse effects due to ADA were also detailed.

Results: Twenty-seven CD patients were included. Median age at CD diagnosis and at ADA initiation were 11 years [Q1=10-Q3=12] and 15 years [13-15], respectively. Indication of ADA was primary failure to IFX in 4 cases (14%), loss of response to IFX in 16 cases (60%) and intolerance to IFX in 7 cases (26%). Median duration of ADA treatment was 10 months [6-18]. After a follow-up of 9 months, ADA was efficient in 19 patients (70%). Eight patients experienced primary failure (30%) and 5/19 (26%) experienced secondary failure. Optimizing therapy (increase of ADA dose and/or decrease of intervals between ADA injections) was required in 14 patients. Eleven patients (40%) experienced a total of 19 adverse effects but no allergic reaction was observed. The main adverse events were: 1) cutaneous (xerosis; n=6, depigmentation; n=3, acne; n=2 and psoriasis: n=1); 2) local reactions (pain, inflammatory reaction) at the injection site (n=3) and 3) impermanent arthralgia and/or myalgia (n=4). None of these adverse effects resulted in ADA discontinuation. There was no significant change in growth and nutritional status over the study period but we found a significant decrease of median CRP from the ADA initiation to the maximal follow-up (18 mg/L [5-39] vs 7 [3-19]; p=0.026) and median orosomucoid (1.64 g/L [1.50- 2.56] vs. 1.17 [0.88-1.89]; p<0.001).

Conclusion: In this cohort of paediatric-onset CD patients previously treated with IFX, treatment with ADA was safe and efficient in 70% of patients after a median follow-up of 9 months.

References: (1) Hyams JS et al. Gastroenterology 2012

Disclosure of Interest: None Declared
COMPARISON OF DIFFERENT TESTS FOR DETERMINATION OF INFliximab LEVELS AND ANTIBODIES AGAINST INFliximab IN PEDIATRIC IBD PATIENTS

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Objectives and Study: Infliximab (IFX) is increasingly used in pediatric IBD patients. Determination of IFX trough levels and antibodies to IFX (ATI) is gaining more importance to identify at an early stage loss of response and potential side effects. Reliable assays are urgently needed to improve quality of care.

Methods: Serum samples (125 IFX exposed and 77 IFX naïve) of pediatric patients were analysed using two newly developed Enzyme-linked Immunosorbent Assays (EIA) for determination of ATI and IFX levels (both: Immunodiagnostik, Bensheim, Germany). Sera of IFX exposed patients were obtained on the day of IFX infusion (trough) or in-between - if side effects occurred - and were simultaneously analysed with an established radioimmunoassay (RIA) for ATI and a reference EIA for measurement of IFX concentrations (both: Sanquin Diagnostic Services, Amsterdam, Netherlands). To establish a correlation between IFX concentrations of the two different test systems and ATI levels respectively a non-parametric Spearman’s rho correlation as well as kappa value were applied.

Results: In IFX-naïve patients one sample each was false positive with the EIA new for ATI and IFX (specificity 98.7%). In IFX-exposed patients, 25 of 125 samples had IFX levels below the respective detection limits of the two tests (<0.002 µg/ml for EIA ref and <0.8 µg/ml for EIA new). In 87 samples results were concordantly positive (range 0.1-484 µg/ml for EIA ref and 1.0-126 for EIA new). In the remaining 11 samples with discordant results IFX was only detected by EIA ref (range 0.1-2.3 µg/ml). For ATI measurements concordant negative results were found in 88 samples and discordant positive results in 27 samples (range for RIA and EIA new: 49-7600 AU and 0.030-3.858 OD, respectively). In 10 samples low levels of ATI were detected by RIA only (range 17-61 AU). IFX levels analysed by EIA ref and EIA new were highly correlated (r=0.889, p<0.01). Inter-rater reliability (kappa value) was 0.792.

Conclusion: The new EIAs for determination of IFX levels and ATI revealed a very good specificity. Compared to the reference methods the test is less sensitive to detect IFX and ATI at low concentrations. Improving the sensitivity for ATI detection is desirable, because the positive ATI at low levels should lead to dose adaptation or shortening the infusion interval.

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EFFECT OF EXCLUSIVE ENTERAL NUTRITION ON THE COURSE OF CD AND INTESTINAL MICROBIOTA

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Objectives and Study: Nutritional therapy has a well-established place as induction therapy in pediatric Crohn’s disease (CD). Exclusive Enteral Nutrition (EEN) can be as efficacious as steroids in inducing remission without having the numerous adverse effects, and achieves mucosal healing, whereas corticosteroids do not. The molecular mechanisms that could account for the effectiveness of EEN are only sparsely understood and an indirect effect of EEN via the modification of intestinal microbiota might be one of these mechanisms.

The aim of this work was to study the anti-inflammatory effects of EEN by Modulen® IBD (Nestlé, Vevey, Switzerland) in active CD as compared to steroids and to assess the associated modifications of intestinal microbiota.

Methods: Nineteen patients with active CD (Harvey Bradshaw index HBI> 5), aged from 6 to 17 years were included in the study and randomized in two groups: treatment with Cortancy® (n=6) or EEN (n=13). The nutritional formula used in the EEN group was exclusively Modulen® IBD. Patients were assessed at Week 0 and 8 using clinical parameters HBI, endoscopic findings (CDEIS score) and analysis of biopsies and fecal microbiota by both fingerprinting and pyrosequencing technologies.

Results: At 8 weeks, clinical remission (HBI<5) was achieved in 13/13 patients on EEN and 5/6 patients on steroids. Mucosal healing (CDEIS≤3) was more frequently achieved in EEN patients (89%) than in steroid group (17%). There were no statistically significant differences between groups regarding biological markers. Interestingly the intestinal microbiota profile clearly distinguished patients with EEN-induced remission from patients with steroid induced remission (p=0.049) (fig1).

Conclusion: Both steroids and EEN induce clinical remission, however, patients with EEN-induced remission showed a markedly higher rate of mucosal healing and this was associated with a different gut microbiota composition shift in these children.
Disclosure of Interest: None Declared
NEONATAL ANTIBIOTIC PROPHYLAXIS MODULATES INTESTINAL IMMUNITY AND IMPROVES RESISTANCE AGAINST NECROTIZING ENTEROCOLITIS IN PRETERM PIGS

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Objectives and Study: Preterm birth, bacterial colonization and formula feeding predispose to development of necrotizing enterocolitis ( NEC). It remains unclear how prophylactic use of antibiotics may affect NEC resistance and intestinal immunity, both short and long term. We hypothesized that oral and systemic treatment with broad-spectrum antibiotics just after preterm birth would improve short term NEC resistance and intestinal structure, function and immunity.

Methods: Caesarean-delivered preterm pigs received 3 days of parenteral and enteral nutrition followed by 2 days full formula feeding. Antibiotics (AB: gentamycin, ampicillin, metronidazole, n=11) or control treatment (CON, n=13) were given twice daily from birth to tissue collection at 5 days of age. NEC-lesions, intestinal villi heights, digestive enzyme activities, microbial density and immune and metabolism parameters (myeloperoxidase activity, goblet cell density and gene expression analyses) were recorded. Additional preterm pigs (AB, n=6; CON, n=9) were kept up to 10 days to investigate NEC sensitivity after the initial 5 d of prophylactic AB use.

Results: None of the AB and 85% of the CON pigs developed NEC by d 5 (0/11 vs. 11/13, P<0.05). Moreover, AB pigs had higher intestinal villi (+60%), digestive enzyme activities (+53-73%), goblet cell density (+110%), and lower myeloperoxidase (-51%) and colonic microbial density (10⁵ vs. 10¹⁰ CFU, all p<0.05). Micro array analyses showed marked up-regulation of genes in AB pigs related to amino acid metabolism, in particular threonine, glucose transport systems and cell cycle, and strong down-regulation of genes related to immune response, including the inflammatory pathways and the Type-1 interferon related genes on d 5. Formula feeding after d 5, caused all CON pigs (9/9) to be euthanized with NEC before d 10, while all (6/6) AB pigs survived without NEC until d 10 (P<0.05).

Conclusion: AB prophylaxis during the first 5 days after preterm birth prevents formula-induced intestinal atrophy, dysfunction, inflammation and NEC. The short term beneficial effect of neonatal AB treatment was associated with enhanced expression of gut function genes and suppression of inflammatory genes. More long term effects of neonatal AB prophylaxis on NEC resistance, gut development and immunity in preterm neonates remain to be investigated.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GI INFECTIONS

PA-G-0048

SURVEY ON EUROPEAN LOCAL SETTINGS FOR THE MANAGEMENT OF ACUTE GASTROENTERITIS IN CHILDREN

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Objectives and Study: Acute gastroenteritis (AGE) is a major pediatric public health problem. We aimed at exploring differences in clinical management and health policies in Europe as a preliminary survey of a project of e-learning based clinical practice guidelines (CPGs) implementation for AGE by ESPGHAN (TEEN-AGE).

Methods: Key-informants experts in PedGI from 13 European countries were asked to describe the care provided to children < 5 years with AGE in in- and out-patients settings: a) organization of care; b) common violations to CPGs; c) oral rehydration. Scores from 1 to 3 were given based on ranking of behaviors and percentages were derived. Comparisons were assessed by chi-square test and linear regression.

Results: Children with AGE were firstly seen by a Pediatrician in 7 countries (Ped-Countries) and by general practitioner in 6 (GP-Countries). In 8 countries, children had free access to health care services (free HCS). According to estimates, 15% of children with AGE were managed by parents, 8% by non-physicians, 11% in telephone consultation, 30%, 27% and 9% seen in outpatients' clinic, ED and in regular admission, respectively. A higher rate of ED admissions were reported in GP-Countries than in Ped-Countries (37% vs 21%; p=0.019). In free HCS countries, with respect to others, children with AGE were mostly seen in ED (33% vs 14%; p=0.002), outpatients clinic (32% vs 24%; p=0.047) and were rarely managed by family (9% vs 30, p=0.0003). The most common violations to CPGs in Europe were inappropriate nutritional interventions (29%), antibiotic use (25%), rehydration (24%), hospitalization (10%). Changes in diet (35% vs 19%; p=0.0164) and use of not recommended drugs (11% vs 0%; p=0.0007) were perceived as more frequent in Ped-countries than in GP-countries, unlike unnecessary hospitalizations (Ped-countries 3% vs GP-countries 19%; p=0.0004). In East Europe (6 countries) inappropriate antibiotic use was more common than in West Europe (7 countries) (38% vs 10%; p<0.0001), unlike the use of antiemetics (0% vs 7%; p=0.014). The informants estimated that early ORS was not administered in 8% and rarely given in 23% of children.

Conclusion: The organization of care for AGE varies among European countries and CPGs implementation interventions should address these differences.

Disclosure of Interest: None Declared
EFFICACY AND SAFETY OF AZATHIOPRINE IN PEDIATRIC CROHN’S DISEASE IN A FRENCH REFERRAL CENTER (1993-2012)
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Objectives and Study: Azathioprine (AZA) is increasingly used to maintain in remission in pediatric Crohn’s disease (CD). The aim of our study was to evaluate efficacy and safety profile of AZA and to assess the evolution of treatment modalities in pediatric CD according to two study periods (before and after 2007).

Methods: Eighty five consecutive CD children were included in a cohort study from a French referral center from July 1993 to July 2012. All children were treated with AZA. Remission was defined as Harvey-Bradshaw Score (HBS) <5. Treatment failure treatment was defined by the need for surgery and/or the need to initiate other CD-related medications (methotrexate, corticosteroid, and/or anti-TNF therapy).

Results: Average dosage was 1.67 mg/kg/day in the 1993-2007 period and increased to 2.43 mg/kg/day in the 2007-12 period. During the same study periods, AZA was introduced earlier in the disease course: median time decreased from 3.8 months to 0.7 month, respectively. Treatment modalities also evolved during study period, with less steroids use and (85% in the 1993-2007 period versus 51% in the 2007-12) and an increased use of exclusive enteral nutrition (Modulen®: 15% in the 1993-2007 period versus 48% in the 2007-12). Steroid-free clinical remission rates were respectively 76%, 57%, 44% and 35% at 6, 12, 18 and 24 months, with median azathioprine dosage of 1.8 mg/kg/day at 6 months. By survival analysis, a dosage lower than 1.1 mg/kg/day at 6 months was associated with an increased risk of relapse (p<0.0001, HR, 3.0; CI 95%, 1.74 to 5.3). A dosage lower than 1.7 mg/kg/day at 6 months was associated with an increased risk of hospitalisations (p<0.0074, HR, 4.2, CI 95%, 1.48 to 12.1). Surgery was associated with stricturing phenotype (p=0.02, HR, 9.7; CI 95%, 1.4 to 69). Thirty one percent (n=27) of patients experienced a side effect, leading to AZA withdrawal in 15/85 patients (17%): pancreatitis, hepatic cytolysis, general weakness, nausea, lymphopenia and thrombopenia, and one medullar aplasia (homozygous for a mutated TPMT gene). AZA dosage had no impact on drug safety profile.

Conclusion: Overall, after one year, half of CD patients remain in steroid-free remission. Treatment modalities have evolved, with earlier introduction of AZA and the use of higher dosage. Lower AZA dosage significantly increased the risk of treatment failure and hospitalisation rates.

Disclosure of Interest: None Declared
Objectives and Study: Cyclic vomiting syndrome (CVS) is a chronic disorder characterized by recurrent, stereotypical episodes of nausea and vomiting interspersed with symptom-free periods. In a subgroup of children, both acute and prophylactic standard treatments remain unsatisfactory. Aprepitant, a neurokinin-1 receptor antagonist, is efficacious in preventing chemotherapy-induced nausea and vomiting in adults and older children; its role in other disorders remains to be defined. In this study we assessed the efficacy of aprepitant as a prophylactic/acute treatment in CVS children refractory to standard therapies.

Methods: Thirty-eight children (16 males; median age 11 years) fulfilling Rome III criteria for CVS and treated acutely or prophylactically with aprepitant were identified through retrospective chart review. The prophylactic schedule (Regimen A, RA) was: 40 mg twice/week in children <40 kg, 80 mg in children >40<60 kg, 125 mg in children >60 kg. The acute schedule (Regimen B, RB) was: 125 mg at day 1 (prodromic phase), followed by 80 mg at day 2 and 3 in children >20 kg, 80 mg for 3 consecutive days for those <20 kg, 80 mg at day 1, 40 mg at day 2 and 3 for those <15 kg. Primary outcome was defined as: 1. complete response, no attacks; 2. partial response, ≥50% decrease in attack frequency and intensity; 3. no response, <50% decrease. Secondary outcomes were: no. of episodes/year, episode length (days), symptom-free interval length (days), and % of school attendance.

Results: [median (25th–75th)]. During a follow-up period ranging between 12 and 58 months, 37 children were still on treatment. One child discontinued the treatment due to headache. Thirteen children were on RA, while 24 on RB. 30 children (81%) had response to the treatment. Among them, 6 (16%) showed a complete response, while 24 (65%) a partial response. At follow-up there was a significant decrease in no. of episodes/year [6 (2.8-12) vs 12.9 (10-20), p<0.001] and in episode length (days) [2.5 (0.5-4) vs 5 (4-5), p<0.001], as well as a significant increase in symptom-free interval length (days), [60 (30-127.5) vs 28 (18.5-36.2), p<0.001] and % of school attendance [80 (80-100) vs 63 (50-67.5), p<0.001]. In the subgroup analysis, no difference was found between RA and RB in the proportion of children showing either complete response (3/13 vs 3/24 respectively, NS) and partial response (8/13 vs 16/24 respectively, NS) as well as for all secondary outcomes. No other side effects were recorded.

Conclusion: Aprepitant is effective and well tolerated for acute and prophylactic management of CVS refractory to standard therapies. However, larger randomized studies are needed to confirm our findings.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GERD, PEPTIC DISEASE AND HELICOBACTER PYLORI

PA-G-0055

MUCOSAL CYTOKINES PATTERNS IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS
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Objectives and Study: EoE is a chronic inflammatory condition defined by symptoms of esophageal disfunction with an eosinophil infiltrate in the esophagus epithelium. Key cytokines such as interleukin (IL)-4, IL-5, and IL-13 stimulate the production of eotaxin-3 in the esophageal mucosa. Corticosteroids used topically (fluticasone and budesonide) are a mainstay of EoE treatment and first-line agents in many cases. They can improved patients symptoms but the recurrence is frequent. Few studies, in a small number of adult patients with EoE, have shown the behaviour of cytokine pattern on esophageal mucosa after topical steroid treatment. The aim of our study was to evaluate the expression of IL-5 and IL-13, eotaxin-3/CCL26 on esophageal mucosa and modifications after treatment with topical steroids in children with EoE.

Methods: We recruited 10 children (M/F= 8/2; median age 11.4 ± 9) with EoE at the first diagnosis with biopsy sampling (a total of 4 biopsies) from proximal and distal esophagus and after 8-weeks treatment with topical budesonide delivered orally and swallowed (Aircort® inhalation suspension 400 µg/d twice daily if weight < 15 Kg or 800 µg/d twice daily if weight > 15 Kg). IL-5, IL-13, and eotaxin-3/CCL26 levels were measured by enzyme-linked immunosorbent assay (ELISA) in esophageal mucosa. The Control Group was consisted in 10 children (M/F=6/4; median age 10.5 ± 9) that performed endoscopy for other symptoms. Statistical significance comparing 2 different groups was determined by the Student t test (normal distribution, equal variance).

Results: In all patients with EoE was detected a high expression levels of IL-5 (P < 0.0001) compared to control samples. More significant levels reduction, after 8 weeks of treatment, were observed in the proximal esophagus biopsies (108 UI/ml ± 45.6 vs 70.4 UI/ml ± 42.5, P < 0.0001). These changes were less significant at the level of the distal esophagus (83.7 UI/ml ± 48.2 vs 61 UI/ml ± 45.1, P < 0.0001). Similar results were obtained from analysis of IL-13 levels even if the average values are lower compared to IL-5 (distal esophagus 15.5 UI/ml ± 19.9 vs 9.3 UI/ml ± 11, P = 0.02; proximal esophagus 21.6 UI/ml ± 20.8 vs 7.7 UI/ml ± 3.2, P < 0.0001). No significative modifications have been demonstrated about Eotaxin-3/CCL26 levels (distal esophagus 70.4 UI/ml ± 66.3 vs 63.4 UI/ml ± 73.3, P < 0.52; proximal esophagus 85 UI/ml ± 78 vs 64.3 UI/ml ± 82.2, P < 0.08).

Conclusion: Our results have confirmed the over expression of mucosal levels of IL-5, IL-13 and Eotaxin-3/CCL26 in EoE. IL-5 can be considered the principle cytokine responsible for regulating of eosinophilic activation. Topical steroid therapy can be useful as first-line therapy to control symptoms but with limited capacity to reduce the overall eosinophilic inflammation.

Disclosure of Interest: None Declared
EFFICACY AND SAFETY OF THE LOCAL APPLICATION OF MITOMYCIN C TO RECURRENT ESOPHAGEAL STRICTURES IN CHILDREN
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Objectives and Study:

Purpose: Experience with mitomycin C in recurrent esophageal stenosis remains limited. The aim of this study was to assess efficacy and safety of the application of mitomycin in recurrent esophageal strictures in children.

Methods: We performed a retrospective study including 39 patients (17 girls) aged 37.5 months (range: 2.4 to 196 months) at the time of mitomycin application. Etiologies of strictures were esophageal atresia (n=25), caustic (n=9), congenital esophageal stenosis (n=3) and other causes (n=2). The stricture was single in 35 patients, multiple in 4. Before mitomycin application, patients undergone multiple repeated dilations varying from 2 to 26 per children (median: 3) during a period varying from 2.6 to 49.3 months (median: 7 months).

Results: Mean follow-up after mitomycin was 3.1 years (ranges: 0.6-8.5 years). For 26 patients (67%) the application of mitomycin was considered as a success defined by a reduction in the number of dilations over the same period of time comparing before and after application of mitomycin (102 versus 17). Sixteen patients (41%) never required a new dilation after mitomycin with a follow-up of 0.4 to 8.5 years (median 3.1). However 8 patients (20%) finally needed surgical treatment for recurrence of stricture. Digestive symptoms improved in 80% of patients. No complication were observed. Biopsies at the site of mitomycin application were performed in 15 patients and revealed no dysplasia. Only 3 factors were found to be associated with success of mitomycin: uniqueness of the stenosis (p < 0.05), short stenosis (p=0.02) and esophageal atresia type III (p=0.05).

Conclusion: Despite its limitation (retrospective and not controlled), this study is the largest series even reported showing that topical application of mitomycin is an efficient treatment for recurrent esophageal strictures. Long-term monitoring of these patients is however necessary considering the risk of complications, particularly neoplasia.

Disclosure of Interest: None Declared
DIAGNOSTIC AND THERAPEUTIC UTILITY OF DOUBLE BALLOON ENTEROSCOPY IN CHILDREN
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Objectives and Study: The diagnostic and therapeutic benefits of double-balloon enteroscopy (DBE) have now been largely documented in the adult population with as yet little published in the paediatric population. We aimed to evaluate the diagnostic and therapeutic utility of DBE in the setting of a paediatric tertiary-referral centre.

Methods: Prospective assessment of consecutive children younger than 18 years undergoing DBE for a variety of suspected small bowel disorders from Jan 2008 to August 2012 in a single paediatric tertiary referral centre was carried out. All the children had undergone prior upper GI endoscopy, ileo-colonoscopy, and in the majority wireless capsule endoscopy. The clinical and histological findings/treatment by DBE was followed by active treatment or followed up without any treatment.

Results: 113 DBE were performed in 58 children (M=36, F=22, median age 12.7 years, range 1-18 years). 61 (54%) procedures were performed via the trans-oral approach with a median time of 90 minutes (range 26-245), and 47 (42%) procedures via the trans-anal approach (4 via ileostomy) with a median time of 45 mins (range 15-100), and 5 (4.5%) were with laparoscopic assistance. The median estimated insertion length of the small bowel distal to the pylorus (DTTP) was 230 cm (range 80-450), and proximal to the ileo-caecal valve (PICV) was 80 cm (range 5-275). The overall diagnostic yield for relevant lesions in the small bowel was 67% (n=39). The common indications were polyposis syndromes (n=21, 36%), and obscure GI bleeding (n=16, 28%). The findings included polyps (n=19, 32%), mucosal ulcers and erosion (n=8, 14%), sub mucosal elevations with white nodules (n=4, 7%), and angioma/angiodysplasia (n=2, 4%). In children requiring endo-therapeutic treatment this was performed with a successful therapeutic yield of 48% (n=28) with median duration of 85 min (range 20-245), compared to 69 min (range 20-135) for diagnostic procedures. Therapeutic procedures included polypectomy (n = 19), argon plasma coagulation of vascular lesions (n = 8), stricture dilation (n = 1), endoclip haemostasis (n=1), and small bowel variceal banding (n = 1). The overall usefulness of DBE in contribution to treatment including endoscopic, medical, and surgical was 72.5% (n=42). Three complications (5%) were noted with uneventful recovery.

Conclusion: The diagnostic yield of DBE was comparable to WCE with the added advantage of therapeutic possibility, histological diagnostic yield, and minimal complications and we believe that this technique should serve as a valuable addition to existing endoscopic techniques. The results of DBE had a substantial impact on subsequent management decisions. DBE should be considered as an alternative diagnostic and therapeutic option in the small bowel in children.

Disclosure of Interest: None Declared
CONTROVERSIES IN DIAGNOSING AND TREATING WILSON DISEASE IN CHILDREN: RESULTS OF AN INTERNATIONAL SURVEY

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Objectives and Study: Insufficient evidence guiding the management of children with Wilson disease (WD) may lead to variation in care. We aim to determine consensus and variation in how pediatric hepatologists (PH) diagnose and treat WD patients.

Methods: PH, members of ESPGHAN Hepatology or AASLD Pediatric Liver Special Interest Groups, were invited to participate in this web-based, international survey.

Results: Participation was 43% (104/253 invitations). The majority (67%) of participants have >10 years experience as PH, 64% see 1-10 and 31% see ≥11 WD patients regularly. Guidelines by Roberts and Schilsky¹ and Ferenci et al.² were preferentially used (67% and 22%, respectively). Consensus existed on use of diagnostic first-line tools in patients from unaffected families: serum ceruloplasmin (CER), basal 24-h urine copper excretion (UCE) and liver copper content (LCC). However, interpretation of LCC varied (25% interpreted >50µg/g and 56% >250µg/g as abnormal). Genetic testing (GT) is performed by 50% in all suspected cases and not at all by 12%, although GT is available. Once genotype of an index patient was known, GT was 1 of 3 preferred methods (81%). Penicillamine (PEN) challenge was not preferred, however similarly applied in asymptomatic and symptomatic patients (20% and 26%). Most PH reported to screen a child of an affected parent using CER, UCE and/or GT; however, 24% chose not to screen. Use of low-copper diet was judged diversely with 46% recommending indefinite and 12% not advising any diet. The drug of choice for primary therapy varied significantly. Zinc was preferred in a 4 yo affected sibling with elevated aminotransferases (43%). For older patients with hepatic dysfunction from previously unaffected families, PEN or trientine were chosen, with significant regional preferences: PEN was rejected as primary choice of therapy by 29% of North American PH. Management of a WD patient with acute liver failure varied. Chelators were chosen by 54% and transplantation by 13% as primary treatment. Monitoring disease severity only, without initiating medical therapy or transplantation, was reported by 23%.

Conclusion: The approach of PH to diagnosing and treating WD in children is distinctly variable. The reasons for this may include regional and individual preferences, differences in test and drug availability and clinical variability of WD. Reducing variability may improve standard of care for WD in children.


Disclosure of Interest: None Declared
ANTI-CD20 MONOCLONAL ANTIBODY AS RESCUE TREATMENT IN FUNCTIONAL BILE SALT EXPORT PUMP (BSEP) DEFICIENCY AFTER LIVER TRANSPLANTATION
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Objectives and Study: BSEP deficiency, a form of intrahepatic cholestasis caused by mutations in ABCB11, is characterised by normal-range serum gamma-glutamyltransferase activity (GGT) despite hyperbilirubinaemia. Some patients require liver transplantation (LT). Clinical illness recurrent after LT in a subgroup of patients is difficult to treat, even requiring re-LT. Using anti-CD20 monoclonal antibodies (Rituximab), we successfully treated 2 BSEP-deficient patients with intrahepatic cholestasis and normal-range GGT after LT.

Methods: Case histories are presented.

Results: Female patient A underwent LT (age 4 years) for severe BSEP deficiency (jaundice, liver scarring without BSEP expression; c.2012-8T>G and c.1145_1165del). Cholestasis and pruritus resolved, but recurred and worsened beginning at age 12 years, with normal-range GGT, and resisted corticosteroid/immunoglobulin therapy. Liver biopsy found inflammation and scarring; BSEP and GGT were expressed. At age 13 years she underwent repeat LT. Pruritus and cholestasis recurred, with normal-range GGT. Aged 15 years she received a first course of Rituximab (375 mg/m² once weekly, 4 weeks). Near-complete resolution of clinical and laboratory symptoms and signs ensued but did not persist. A second course (same regimen) 4 years after LT yielded complete resolution with good continuance to date (30 months).

Male patient B underwent LT (22 months) for severe BSEP deficiency (jaundice, liver scarring without BSEP expression, hepatocellular carcinoma; c.2012-8T>G and c.1939delA). Cholestasis and pruritus resolved, but recurred and worsened beginning at age 7 years, with normal-range GGT, and resisted corticosteroid/immunoglobulin therapy. Liver biopsy found inflammation and scarring; BSEP and GGT were expressed. At age 8 years he received a first course of Rituximab (regimen as above). Clinical and laboratory symptoms and signs lessened but did not wholly resolve. A second course (same regimen) 10 months later yielded complete resolution with good continuance to date (18 months).

Conclusion: Rituximab appears beneficial in functional BSEP deficiency after LT.

Disclosure of Interest: None Declared
HEPATOLOGY

PA-H-0030

SEBELIPASE ALFA NORMALIZES TRANSAMINASES AND REDUCES LIVER FAT CONTENT IN PATIENTS WITH LATE ONSET FORM OF LAL DEFICIENCY

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Objectives and Study: Lysosomal acid lipase (LAL) Deficiency is an autosomal recessive disorder that results in abnormal accumulation of cholesteryl esters and triglycerides. Patients present with dyslipidemia, elevated transaminases and hepatomegaly often progressing to cirrhosis and early death. LAL-CL01, the first-in-human study found that 4 once-weekly infusions of sebelipase alfa were well-tolerated across a range of doses (0.35, 1 and 3 mg/kg) in adults with LAL Deficiency.

Methods: Once completing LAL-CL01, subjects enrolled in LAL-CL04, a long term treatment study, and received 4 once-weekly infusions of sebelipase alfa (0.35, 1 or 3 mg/kg) before transitioning to every-other-week infusions (1 or 3 mg/kg).

Serum transaminases and lipids were followed. MRI/MRS of the liver was performed at baseline, 10-12 weeks and 24 weeks.

Results: Re-initiation of sebelipase alfa in LAL-CL04 resulted in rapid, sustained reductions in transaminases similar to those seen in LAL-CL01. Seven of the 8 subjects in LAL-CL04 have 24 week data; the decreases for ALT and AST (mean +/- SD) at 24 weeks were 48 +/- 21 U/L (54%) and 19 +/- 18 U/L (30%), respectively. These subjects had mean decreases in total cholesterol of 69 +/- 52 mg/dL (31%), LDL-C of 62 +/- 36 mg/dL (43%) and triglycerides of 47 +/- 69 mg/dL (22%), p<0.05 for all, and mean increases in HDL of 4 +/- 5 mg/dL (14%) (p=0.09). The mean (+/- SD) hepatic fat fraction was reduced by 34% (+/- 48%) (n=7 at 24 weeks). Most AEs were mild and unrelated to sebelipase alfa. Adverse effects related to infusion were uncommon, were mainly gastrointestinal and of mild severity. Three IRRs (flushing/chills/nausea/throat tightness and paresthesias) were of moderate severity but resolved with standard management. One patient experienced acute cholecystitis and cholelithiasis/elective cholecystectomy; the investigator considered these SAEs to be unlikely related to sebelipase alfa. No anti-drug antibodies were detected in LAL-CL01 (n=9) or those tested to date in LAL-CL04 (n=8).

Conclusion: These results suggest that long term every-other-week dosing with sebelipase alfa normalizes serum transaminases, improves the abnormal serum lipid profile and decreases liver fat fraction in patients with LAL Deficiency.

GENERATION OF HEPATOCYTES FROM ARC PATIENT-DERIVED IPSCS

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Objectives and Study: ARC syndrome is an autosomal recessive multisystem disorder characterised by arthrogryposis, renal dysfunction and cholestasis with low gamma glutamyl transpeptidase activity and abnormal expression of hepatocyte canalicular membrane transporters such bile salt export pump (BSEP). Other common features include severe failure to thrive, absence of platelet alpha granules and ichthyosis. Affected infants usually die in the first year of life although milder cases have recently been described. No specific medical treatment is currently available, hence the need to develop disease specific models. Induced Pluripotent Stem Cell (iPSC) technology can provide such patient-specific disease models since iPSCs have the potential to differentiate into any specialised cell of the body and constitute an almost unlimited source of cells for research purposes.

Methods: Using a single excisable polycistronic lentiviral 'stem cell cassette' vector developed by Somers et al1, efficient reprogramming of skin fibroblasts from ARC patients was achieved. Simultaneous transfer of the four reprogramming factors Oct4, Sox2, Klf4 and cMyc into human skin fibroblasts using this single vector allows derivation of human iPSCs containing a single excisable viral integration that upon removal generates cells virtually free of integrated transgenes.

Results: The iPSCs generated display embryonic stem cell-like morphology and express characteristic stem cell markers.

The genetic mutation present in the patient was identified in the derived iPSCs by Sanger sequencing. Furthermore, ARC patient-derived iPSCs were differentiated into Hepatic Endoderm following a method developed by Sullivan et al2, mimicking liver natural development. The iPSC-derived hepatocyte-like cells generated exhibit hepatic morphology and express hepatic markers such as albumin and alpha-fetoprotein.

Conclusion: This work shows that iPSCs from fibroblasts of infants with rare metabolic diseases such as ARC syndrome can be generated and then differentiated into hepatocyte-like cells, thus providing an in vitro hepatic ARC model for further study of its specific cell phenotype and underlying pathophysiology. The iPSC-derived hepatocyte-like cells will also provide a platform for the identification of potential therapeutic molecules.


Disclosure of Interest: None Declared
HEPATOLOGY

PA-H-0050

BILE SALT KINETICS IN CHILDREN WITH GENETIC CHOLESTASIS AND BILE DIVERSION THERAPY.

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Objectives and Study: Low GGT Progressive Familial Intrahepatic Cholestasis (low-GGT PFIC) comprises cholestatic liver diseases with defects in canalicular bile salt transport due to mutations in ATP8B1 (FIC1) and ABCB11 (BSEP). Partial external bile diversion (PEBD) is first-line therapy for low-GGT PFIC, but its mechanism of action is not well understood. The clinical response and limited studies in these patients suggest improved canalicular bile salt transport, but the kinetics of bile salt homeostasis have not been studied. The objective of our study was to determine the fractional turnover rates (FTR) for cholic acid (CA) and chenodeoxycholic acid (CDCA) in low-GGT PFIC PEBD as compared to low-GGT PFIC with liver transplant (OLT, i.e., anatomic correction of BSEP and hepatobiliary FIC1).

Methods: Oral ingestion of stable isotope labeled bile acids [2H4-CA and 2H4-CDCA] and sampling of serum at 0, 10, 24, 32, 48, and 72 hours post-ingestion permitted computation of FTR using established mathematical modeling based on isotope dilution. Capillary gas-liquid chromatography and mass spectrometry was used to determine the prevalence of the labeled bile acid relative to unlabeled endogenous bile acid. PEBD subjects comprised 4 FIC1, 1 BSEP, and 2 UNKNOWN patients (no identifiable mutation and positive BSEP immunostaining). OLT subjects comprised 1 FIC1, 3 BSEP, and 1 UNKNOWN patient (no identifiable mutation and negative BSEP immunostaining). All subjects had normal serum bile salts and no cholestasis.

Results: PEBD subjects had extremely brisk FTR of CA and CDCA: All PEBD CA = 1.6 ± 1.27 d-1 and CDCA = 2.87 ± 2.5 d-1; FIC1 CA = 1.93 ± 1.6 d-1, CDCA = 1.8 ± 0.9 d-1; BSEP CA = 1.47 d-1, CDCA = 7.73 d-1; Unknown CA = 1 ± 0.7 d-1, CDCA = 2.6 ± 2.6 d-1. Pool sizes were low, but could not be accurately estimated due to the rapid FTR. These results indicate extremely rapid synthesis and efficient excretion of CA and CDCA. In comparison, OLT subjects showed FTR of CA = 0.62 ± 0.31 d-1 and CDCA = 0.35 ± 0.08 d-1, somewhat greater than published normal adults and equivalent to post-cholecystectomy. The pool sizes were relatively normal. These results indicate that OLT corrects faulty bile salt kinetics in FIC1 and BSEP.

Conclusion: PEBD appears to relieve cholestasis in low-GGT PFIC by inducing rapid FTR of CA and CDCA. This implies normalization of hepatic excretion of both hydrophobic and hydrophilic bile salts. The mechanism by which this occurs in BSEP likely involves induction of an alternate excretory pathway, whereas in FIC1 it could involve alteration of the canalicular membrane to accept BSEP insertion or permit better function.

Disclosure of Interest: None Declared
RATIO OF TAUROCHENODEOXYCHOLATE / CHENODEOXYCHOLATE (TCDC/CDC) IN SERUM AS A POTENTIAL DIAGNOSIS BIOMARKER FOR BILIARY ATRESIA (BA)

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Objectives and Study: Biliary Atresia (BA) is a severe hepatobiliary disorder unique to infancy which results from inflammatory destruction of the intrahepatic and extrahepatic bile ducts. Early diagnosis and Kasai operation greatly improve the outcome of BA patients. However non-invasive tests that distinguish BA from other types of neonatal cholestasis are unavailable. In this study, we investigated if serum bile acids could be used as diagnosis makers for BA.

Methods: Using HPLC coupled tandem mass spectrometry, we detected 15 bile acids in serum and livers of BA (before Kasai operation) and neonatal cholestasis infants. Liver expressions of genes involved in synthesis (CYP7A1, CYP27A1, BAT, SULT2A1), transport (BSEP, MDR1, MDR3, MRP2, MRP3, MRP4, NTCP, OATP1B1, OATP1B3, OATP1A2, OATP2B1, OST-α, OST-β), and nuclear receptors (FXR, PXR, CAR, SHP) of bile acids were measured by real-time PCR.

Results: Serum bile acids were detected in 30 BA and 20 neonatal cholestasis infants. TCDC/CDC significantly increased in BA with fold change of 4.1 and p value <0.0001 compared to neonatal cholestasis. The area under receiver operating characteristic curve was 0.99, with sensitivity of 100% and specificity of 95.2%. Bile acids concentrations in liver were measured in 9 BA and 4 neonatal cholestasis. Chenodeoxycholate (CDC) content in liver greatly raised in neonatal cholestasis compared to BA (fold change = 8.7, p=0.009). Furthermore, The liver expression of BESP, Bile acids Export Pump, greatly decreased in BA than neonatal cholestasis.

Conclusion: TCDC/CDC can serve as a biomarker to distinguish BA from other type of neonatal cholestasis and the increase of TCDC/CDC may be caused by the great decrease of CDC in BA liver.

Disclosure of Interest: None Declared
Objectives and Study: Encapsulated human hepatocyte transplantation is an attractive option for the management of acute liver failure in children. Microbeads (MB) can be safely transplanted intraperitoneally without the need for immunosuppression. Optimal hepatocyte function and maintenance of physical integrity of MB are important factors for clinical use.

AIM: To establish an optimised protocol for alginate MB by evaluating the effect of polymerisation time and cell density on physical integrity and hepatocyte-specific function.

Methods: MB were produced using an encapsulator (250µm nozzle) with sterile/clinical grade materials. Empty and human hepatocyte (2.5x10⁶ cells/ml alginate) MB were made using different polymerisation times (10, 15 & 20min). Physical stability of MB was determined using an osmotic stress test. Empty microbeads (EMB) were incubated for 3h in 4 hypotonic (graded dilution with water) and 1 isotonic solutions (transplant medium: CMRL) to establish the osmolarity at which microbeads are stable. MB size (n=100/sample), MTT assay, and viability (FDA/PI) were evaluated. Hepatocyte functions (urea and albumin synthesis) in human hepatocyte microbeads (HMB) were assessed after maintenance in CMRL for 24h. HMB were produced at 4 densities: 2.0, 2.5, 3.0 and 3.5 million cells/ml alginate. HMB were maintained in culture for 3 days. HMB morphology and cell viability were assessed at day 1. Cell functions (MTT, urea and albumin) were evaluated at day 1 and day 3.

Results: MB obtained were of uniform shape and size (mean diameter: EMB 577±SEM 0.89µm and HMB 583±0.64µm). There was a significant increase in EMB diameter in all samples incubated in hypotonic solution compared to control (p<0.001; ANOVA). The 15min polymerisation group tended to resist osmotic shock better than 10 and 20min groups. HMB showed a similar trend with least swelling at 15min polymerisation time compared to control (10min: 14.7%, 15min: 14.0% & 20min: 17.5%). No ruptured MB were observed. HMB maintained their size and functional activities when incubated for 3h and 24h in CMRL compared to control. There was no significant difference in metabolic function between the 3 different polymerisation time groups. Cell density data (MTT, urea and albumin assays) also demonstrated no significant differences between the 4 groups on either day 1 or day 3. However the results for MTT on day 3 (range 0.23-0.28 OD reading) showed a statistically significant decrease (p<0.05) compared to day 1 (0.51-0.70).

Conclusion: An optimised protocol for production of human hepatocyte MB with good cell viability, function, and physical integrity has been established. This protocol is being used for preparation of MB for clinical transplantation.

Disclosure of Interest: None Declared
Objectives and Study: Currently hepatocyte transplantation is limited by the availability of good quality hepatocytes. Mesenchymal stem cells (MSCs) co-culture preserves the morphology and functionality of human hepatocytes in vitro. As MSCs normally reside in a hypoxic niche [1], we hypothesised that hypoxic preconditioning (HPc) could enhance MSCs hepatotrophic effects, and that reactive oxygen species (ROS), a pivotal signalling factor of hypoxia, could be a mediator of the enhanced hepatotrophic effects [2].

Methods: Human adipose tissue-derived MSCs (hADSCs) were subjected to 20%O2 normoxic (NPc) or 2%O2 HPc for 24 hours; 10-mM N-acetylcysteine (NAC) was supplemented into HPc-hADSCs culture to antagonise intracellular ROS. Fresh human hepatocytes were seeded onto media-refreshed hADSCs monolayers; hepatocyte monocultures were used as control. CM-H2DCFDA mean fluorescence intensity (MFI) was measured by flow cytometry to determine intra-hADSCs ROS activity. MTT assay, SRB assay, and albumin ELISA were used to determine hepatocyte mitochondrial activity, cell attachment, and liver-specific synthetic metabolism, respectively. Soluble caspase-cleaved cytokeratin 18 (CCK18) was measured using M30 CytoDeath ELISA to investigate the effect of hADSCs co-culture on hepatocyte apoptosis.

Results: HPc significantly increased ROS activity in hADSCs (HPc vs NPc, 23,251±1,163 vs 9,521±427 MFI units, p<0.01), while the addition of NAC reduced ROS activity in HPc-hADSCs (9,333±367 MFI units, p<0.01). HPc-hADSCs co-culture significantly improved hepatocyte mitochondrial activity up to day 4 (HPc vs NPc vs control, 2.19±0.14 vs 1.27±0.10 vs 1.26±0.07 OD units, p<0.01), attachment up to day 7 (3.46±0.14 vs 3.03±0.12 vs 2.82±0.16 OD units, p<0.01), and albumin synthesis up to day 7 (1.353±86 vs 1.185±54 vs 359±38 ng/mL, p<0.01). hADSCs co-culture significantly reduced hepatocyte soluble CCK18 release (NPc vs control, 7,605±340 vs 10,502±241 U/mL, p<0.01), with a greater effect observed in HPc co-culture up to day 4 (4,324±137 U/mL, p<0.01). ROS antagonisation inhibited hepatotrophic (albumin, 1,113±99 ng/mL, p<0.01) and antiapoptotic effects (7,630±158 U/mL, p<0.01) of HPc-hADSCs co-culture up to day 4.

Conclusion: HPc further augments hepatotrophic and antiapoptotic effects of MSCs co-culture, while increased intra-MSCs ROS activity results in HPc-induced enhancement.


Disclosure of Interest: None Declared
HIGH PREVALENCE OF IRON DEFICIENCY IN HEALTHY YOUNG CHILDREN IN THE NETHERLANDS: RESULTS OF THE IROSTAT STUDY

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Objectives and Study: Background

Young children are particularly vulnerable to the effects of iron deficiency (ID) because of the rapid growth and development of their brain and other organs that occur from birth to the age of three. Increasing evidence suggests that even ID in absence of anemia can have a long-term detrimental influence on mental and psychomotor development.

A food consumption survey in the Netherlands showed that the median iron intake of young children, aged 2 to 3 years, was below the advised adequate intake of 7 mg/day. Since data are not available, we questioned whether this low iron intake results in ID among young children in the Netherlands.

Aim

To investigate the iron status in healthy young children in the Netherlands and to identify risk factors for ID.

Methods: Methods

We conducted a multi centre, observational study in healthy young children aged 0.5 to 3 years. Exclusion criteria were known infection in the last four weeks, use of iron supplementation within the last six weeks, blood transfusion within the last six months, preterm birth before 32 weeks gestational age, known hemoglobinopathies, oncologic disorders, multiple congenital malformations and metabolic diseases.

We measured serum ferritin (SF) and hemoglobin (Hb). We measured C-reactive protein (CRP) to identify infections. Parents were asked to fill in a questionnaire concerning demographic data, average intake of iron containing foods and daycare attendance of their child. Multiple regression analysis with adjustment for age was used to identify risk factors for ID.

Results: Results

We included 400 children. Six children with underlying causes for anemia and 43 children with elevated CRP levels (>5 mg/L) were excluded. ID and IDA were detected in 66 (18.8%) and 30 (8.5%) of the 351 remaining children respectively. The duration of exclusively breastfeeding was positively associated with ID (p 0.00) while birth weight (p 0.01), the current use of formula (p 0.00) and visit of preschool/daycare (p 0.01) were negatively associated with ID. Prenatal risk factors for low iron stores at birth did not influence iron status.

Conclusion: Conclusion

ID is present in 18.8% of healthy young children aged 0.5 to 3 years in the Netherlands.
Birth weight was positively correlated with ferritin concentrations. The use of formula and visit of preschool/daycare protect against ID.

**Disclosure of Interest:** None Declared
Objectives and Study: Low birth weight infants (LBW, <2500g) have increased risk of iron deficiency during their first six months of life and they are recommended iron supplementation since infant iron deficiency is associated with poor neurodevelopment. However, prolonged supplementation in iron replete infants is associated with adverse effects, even on neurodevelopment, and the optimal duration of iron supplementation to LBW infants is unknown. The objective of the current trial was to investigate the long term effect on iron status in marginally LBW (MLBW, 2000-2500g) infants, iron supplemented during their first, but not second half year of life.

Methods: In a randomized, controlled trial, 285 healthy marginally LBW (2000-2500g) infants received 0, 1, or 2 mg/kg/day of iron supplements from six weeks to six months of age. At 12 mo and 3.5 years of life we analyzed hemoglobin (Hb) and serum ferritin. The prevalence of iron deficiency (ID, ferritin < 12µg/L) and ID anemia (IDA, Hb < 110g/L and ferritin < 12µg/L) was calculated.

Results: At 12 months of age, there was a significant difference in ferritin between the groups with a geometric mean (95% CI) of 17.5 (15.6 – 19.5), 20.0 (17.9 – 22.3), and 22.3 (20.1 – 24.6) µg/L in the placebo-, 1mg-, and 2mg-group respectively, p = 0.006. Furthermore, there was a significant difference in the prevalence of ID and IDA (Table). However there was no significant difference in mean Hb. At 3.5 years of life there were no significant differences in mean Hb, mean ferritin, or in the prevalence of ID or IDA (Table).

Table

<table>
<thead>
<tr>
<th>ID at 12 mo, n (%)</th>
<th>Placebo</th>
<th>1 mg/kg/day</th>
<th>2 mg/kg/day</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 (23.7%)</td>
<td>7 (10.6%)</td>
<td>5 (6.8%)</td>
<td></td>
<td>0.009</td>
</tr>
<tr>
<td>4 (5.2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
<td>0.035</td>
</tr>
<tr>
<td>2 (3.3%)</td>
<td>3 (4.9%)</td>
<td>2 (3.1%)</td>
<td></td>
<td>0.898</td>
</tr>
<tr>
<td>0 (0%)</td>
<td>1 (1.5%)</td>
<td>0 (0%)</td>
<td></td>
<td>0.316</td>
</tr>
</tbody>
</table>
**Conclusion:** From this trial we have previously suggested that iron supplementation to marginally LBW infants until 6 months, reduces the risk of IDA at 6 months and the risk of behavioral problems at 3.5 years of age.\(^1\)\(^2\) The current results suggests that the intervention also effectively reduces the risk of ID and IDA at 12 months to levels similar to term infants. At 3.5 years of life MLBW infants have a low risk of ID and IDA and it is not affected by iron supplements during infancy. Iron supplements until 6 months of life may be an optimal duration of iron supplementation to MLBW infants.

**References:**


**Disclosure of Interest:** None Declared
PROTECTIVE EFFECT OF LACTOFERRIN SUPPLEMENTATION ON INTESTINAL BARRIER FUNCTION IN RATS AFTER MASSIVE BOWEL RESECTION

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Objectives and Study: To evaluate the effect of Lactoferrin (LF) on intestinal barrier function in a rat model of short bowel syndrome.

Methods: Thirty three-week old male SD rats were randomized into 3 groups (n=10): Sham operated rats underwent bowel transection and reanastomosis, SBS rats underwent 75% small bowel resection, and SBS-LF rats underwent 75% small bowel resection and were treated with LF(0.5g/kg.d) by intragastric gavage from day 2 throughout day 20 after operation. Body weight was measured serially. On day 21, intestinal permeability (lactulose/mannitol; L/M), and bacterial translocation (BT) to mesenteric lymph nodes (MLNs), liver, spleen and peripheral blood were measured. Secretory immunoglobulin A (sIgA) levels in ileum content and serum total IgG levels were determined by ELISA. Intestinal adaptation was evaluated using villus height and crypt depth. Expression of tight junction protein Claudin-1 was measured by western-blotting. Statistical analysis was performed using the one-way ANOVA test or non-parametric test, with P<0.05 considered statistically significant.

Results: Compared with the sham operated group, both SBS and SBS-LF rats showed significantly lower body weight development, but increased villus height and crypt depth (p<0.05). In contrast to the SBS rats, there was significantly less bacterial translocaton to the MLN in SBS-LF, (40% vs 20% for e.g. Enterococcus fecalis). Enteral Lactoferrin supplementation significantly increased sIgA levels (36.10±25.94 ng/mL, p<0.05), as compared with the SBS and Sham operated group with the latter two having similar sIgA levels in the ileum (16.95±9.26ng/mL and 20.29±7.58ng/mL, respectively). The serum levels of total IgG were lower in SBS-LF group (3.16±1.01μg/mL) compared with Sham and SBS groups (5.05±1.14μg/mL and 4.51±0.96μg/mL, respectively). Claudin-1 expression in SBS-LF group was significantly higher compared with SBS rats (p<0.05), but without significant differences to Sham animals.

Conclusion: Enteral Lactoferrin in SBS up regulates small bowel sIgA and could thus support the protection against bacterial infection or translocation. Furthermore, Lactoferrin may support intestinal barrier integrity after intestinal reanastomosis through up regulating specific tight junction protein expression.

Disclosure of Interest: None Declared
HIGH BETAPALMITATE FAT CONTROLS THE INTESTINAL INFLAMMATORY RESPONSE AND AVOIDS INTESTINAL DAMAGE IN MUCIN MUC2 DEFICIENT MICE

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Objectives and Study: The human mammary gland has evolved specific pathways for acylation of fatty acids into triglycerides for secretion in milk. This stereo-specific positioning of fatty acids in human milk triglycerides involves preferential positioning of the saturated fatty acid palmitic acid (16:0) at the sn-2 position, rather than at the sn-1,3 positions as is typical for vegetable oils used to manufacture infant formula. Palmitic-acid in the sn-1 and sn-3 positions, is hydrolyzed by pancreatic lipase, resulting in free palmitic acid. The latter is poorly absorbed due to its high melting point and forms insoluble calcium soaps causing abdominal discomfort. In contrast, beta-palmitate structured triglyceride fat, with high levels of palmitic-acid in the sn-2 position, is well absorbed and mimics the fat composition and properties of human milk fat. Mucins are the principal components of the intestinal mucus layer, which forms a physical barrier protecting the underlying epithelium against luminal substances and microbes. Muc2 deficient (Muc2+/−) mice lack a protective mucus layer, and spontaneously develop severe colitis. In the present study we aimed to examine the potential protective role of high beta-palmitate fat (HBPF, InFat™, Advanced Lipids AB) in colitis development in Muc2+/− mice.

Methods: Muc2+/− mice, a well-described animal model for colitis, received 3 different synthetic diets: standard AIN-93G diet, diet with control fat (CF, low beta-palmitate) or diet with HBPF (11.1%, 16.7% and 16.8% palmitic-acid, with 6.3% 11.0% and 50.4% palmitic-acid at the sn-2 position respectively), for a period of 5 weeks after weaning. Clinical symptoms, intestinal morphology, and inflammation in the distal colon were analyzed.

Results: Compared with AIN-93G diet, CF diet increased the extent of intestinal erosions and morphological damage, while HBPF diet did not show an effect. In addition, HBPF dietenhanced the immunosuppressive regulatory T cell response as demonstrated by up-regulation of Foxp3, Tgfβ1 and Ebi3 gene expression compared with AIN-93G and CF diets. HBPF diet also increased the gene expression of Pparg and enzymatic antioxidants (Sod1, Sod3 and Gpx1), which are all reported to protect against colitis and to be involved in promoting a regulatory T cell response.

Conclusion: Low beta-palmitate diet increased the incidence of erosions and mucosal damage inMuc2+/− mice. However, high beta-palmitate diet limits the intestinal damage by enhancing the immunosuppressive regulatory T cell response.

BMI BEFORE PREGNANCY AND MATERNAL MICROBIOTA CORRELATE WITH SPECIFIC MICROBES IN THE GUT OF NEONATES
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Objectives and Study: The maternal microbiota is suggested to be an important driver for the development of the infant's intestinal microbiota. A link between maternal microbiota and body weight has been suggested. However, the influence that this may exert on the composition of the developing infant's gut microbiota and on health status later in life is poorly understood. The aim of this study was to investigate the influence of the maternal gut microbiota and body weight on the infant's gut colonisation during the first 6 months of life.

Methods: One hundred forty-three healthy pregnant women were enrolled in an observational study. Two faecal samples from the mother were collected before delivery. Infant's faecal samples were collected at days 0, 3, 7, 30, 90, 180, and one week after the introduction of solid foods. Information about maternal body mass index (BMI) before pregnancy was recorded. The composition of the maternal and infant microbiota was analysed using qPCR and faecal short chain fatty acids were determined. Random coefficients mixed model analysis (for continuous variables) and generalized linear mixed model (for binary variables) were used to study associations between variables in time.

Results: The maternal microbiota composition significantly influenced the infant's gut. Levels of bifidobacteria in infant's faecal samples were positively correlated with maternal levels of bifidobacteria while a negative correlation was observed with the maternal enterobacteria levels. Maternal body mass index (BMI) before pregnancy was found to significantly correlate with the infant's intestinal microbiota. Maternal overweight (BMI>25) was positively associated with the presence of Clostridium coccoides, C. perfringens and Bacteroides in the infant's gut. Higher maternal BMI before pregnancy significantly correlated with a higher probability to detect propionic acid in infant faecal samples over time.

Conclusion: This study has clearly shown the impact of the maternal gut microbiota and body weight on the development of the infant intestinal microbial community, using a sophisticated statistical model incorporating all possible confounding factors measured, including maternal and infant's diet. Our results suggest that dietary interventions during pregnancy, aiming to modulate the maternal microbiota composition may influence the developing gut microbiota of neonates, and therefore offer new nutritional solutions to support health later in life.

POSTPRANDIAL PLASMA LIPID PARAMETERS IN BREASTFED OR FORMULA FED INFANTS

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Objectives and Study: Little is known about postprandial response to either breast- or formula feeding in the neonatal period. We conducted an exploratory observational single-centre study in healthy term infants who were either exclusively breast-fed (BF) since birth or received for at least four weeks prior to testing exclusive formula feeding (FF). Infants in the FF group received the same commercially available cow's milk based infant formula.

Methods: At the postnatal age of 56 ± 4 days, two heel prick samples were collected from each infant at home: one prior to and one at a randomised time after the feeding (the 2nd ad libitum feeding of the test day after 6 am). Postprandial sampling times were randomised to 30, 60, 90, 120, 180, or 240 min after the 1st sample, resulting in a baseline value for all subjects and at least four values at each postprandial time-point (ppTP) for each feeding mode. Based on these data, we created post-meal plasma lipid concentration profiles. These were compared at each ppTP and between feeding mode. Ethical approval for the study was obtained from the ethics committee of the UMCG.

Results: Gestational age, weight and length at birth and at testing were similar between both groups. BF subjects had a 30 min shorter feeding interval prior to the study feeding and BF meal duration lasted approximately 5 min longer than FF. BF subjects consumed on approximately 175 ml milk, as measured by test weighing at testing. The FF subjects consumed 160 ml formula.

The postprandial lipid profiles showed distinct differences between feeding modes: The Triglyceride (TG) baseline concentrations were similar in both groups. However, the difference between ppTP and baseline sample indicated that FF-TG appear earlier in plasma after the meal than BF-TG. In contrast, total cholesterol concentrations (tChol) were different at baseline with BF-tChol concentrations being higher than FF-tChol. However, when corrected for baseline, BF-tChol were below baseline at 30 min and increased steadily thereafter with a peak at 120 min. Conversely, FF-tChol concentrations were above baseline at 30 min and decreased below thereafter.

Conclusion: To our knowledge, this is the first report of postprandial plasma lipid concentration differences between formula and breastfed healthy term infants. These findings may help understand differences in early lipid handling and may provide insights into the reported long-term protective effects of breastfeeding.

DOES HIGH PROTEIN IN INFANT FORMULA INDUCE MUSCLE OR FAT DEPOSITION? RESULTS FROM A RANDOMIZED CLINICAL TRIAL.

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1Abteilung Stoffwechsel- und Ernährungsmedizin, Dr. von Haunersches Kinderspital, Munich, Germany, Munich, Germany, 2CHC st Vincent, Liège-Rocourt, 3Université Libre de Bruxelles, Bruxelles, Belgium, 4Universitat Rovira I Virgili, Tarragona, Spain, 5University of Milano, Milano, Italy, 6Children’s Memorial Health Institute, Warsaw, Poland

Objectives and Study: Infant feeding choices are known to be important modulating factors for infant and child growth. Higher formula protein intake was associated to increased values of weight-for-length at 2 years of age and BMI throughout childhood in a multicenter randomized clinical trial, the Childhood Obesity Project (CHOP). The aim of this study was to assess the effect of the intervention on body fat mass.

Methods: During the first 8 weeks of life 1090 formula fed infants were randomized to receive either higher (2.05 and 3.2 g/dl; HP) or lower (1.25 and 1.6 g/dl; LP) protein content infant and follow-on formulas; 588 breastfed infants were enrolled as a reference group. Anthropometrical measurements included weight, height, triceps and subscapular skinfolds at 2 and 6 years of age. Percent body fat was estimated using the Slaughter equations (based on gender and skinfolds); total body fat mass was calculated by multiplying the estimated percent body fat by body weight.

Results: Complete anthropometrical data was assessed in 921 children at 2 years of age and 649 at 6 years of age. Triceps and subscapular skinfolds were higher at 2 and 6 years of age in the HP than in the LP group. Both, percent body fat and total body fat showed an increase in the higher compared to the lower protein group at 2 and 6 years of age: estimated difference between HP and LP group adjusted for gender and study country 0.47% (95% confidence interval 0.04;0.90) and 0.09kg (0.01;0.16) at 2 years; 0.92% (0.05;1.79) and 0.33kg (-0.01;0.67) at 6 years, respectively. Boys had lower percent body fat at both time points. Compared to HP children breastfed children had a similar body fat mass at 2 years but a significantly lower body fat mass at 6 years.

Conclusion: Body composition up to early school age is affected by early protein intake.


Disclosure of Interest: None Declared
INTESTINAL MICROBIOLOGY OF EARLY LIFE: FACTORS IMPACTING GUT COLONISATION
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Objectives and Study: The intestinal microbiota plays an important role in human physiology which goes beyond gut health. Colonisation during infancy is critical for the development of the gut and potentially linked to diseases later in life. The aim of this observational study was to assess the colonisation dynamics of the infant gut and to identify the key factors influencing this process.

Methods: One hundred forty-three healthy pregnant women were enrolled in this study without any dietary intervention. Infant faecal samples were collected at days 0 (meconium), 3, 7, 30, 90, 180, and one week after the introduction of solid foods. Information about gender, weight, mode of delivery, diet, health condition and medication used was recorded. The composition of the infant microbiota was analysed using qPCR, and faecal short chain fatty acids were determined. Random coefficients mixed model analysis (for continuous variables) and generalized linear mixed model (for binary variables) were used to study associations between variables over time.

Results: Mode of delivery and type of feeding were confirmed to influence the development of the microbiota but also associations were found with e.g. siblings. The probability to detect \textit{Bacteroides fragilis} and \textit{Atopobium} was higher in infants born vaginally than in those born by caesarean. Also, acetic acid and bifidobacteria were found to be higher in infants born vaginally. These differences disappeared after 2 months except the probability to detect \textit{B. fragilis} in vaginally-delivered infants which was still higher at 6 months. Exclusive breastfeeding was associated with higher levels of \textit{Staphylococcus}, an observation that was maintained after weaning. The level of bifidobacteria was also higher after weaning in breast fed infants. Interestingly, specific bifidobacteria species, like \textit{Bifidobacterium animalis} were negatively associated with breast feeding. Introduction of solid foods was associated with the detection of butyric acid and \textit{Clostridium coccoides}. The use of antibiotics was shown to specifically lower the levels of bifidobacteria and staphylococci.

Conclusion: This study has shown that the dynamics of the developing gut microbiota are influenced by many variables. When time is included as a continuous variable in the statistical model, clear insights on the colonisation dynamic of the infant gut can be obtained. Our results suggest that, although mode of delivery and type of feeding are key drivers of the intestinal colonisation, also less expected factors can impact the developing microbiota.

A PROSPECTIVE COHORT AT HIGH-RISK FOR COELIAC DISEASE – THE YOUNG COELIACS OF THE PREVENTCD STUDY.


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Objectives and Study: To characterize the development of coeliac disease (CD) in a prospective cohort of high-risk children at the age of 3y.

Methods: From 2007-2010, 1324 infants with a 1st degree relative with CD were recruited in 8 countries shortly after birth (EU-PreventCD project, www.preventcd.com), to participate in a double-blind intervention study investigating the effect of early gluten introduction on CD development. The analysis is still blinded as to the effect of the intervention. 814 children, HLA-DQ2+ and/or DQ8+, have been followed clinically and serologically until the age of 3y. Small bowel biopsies (SBBs) were performed based on symptoms suggestive of CD, and/or anti-tissue transglutaminase antibodies (TG2A) or anti-gliadin antibodies (AGA).

Results: Mean age 4.3y; 48.5% girls; 89% of the children were DQ2+ (16% homozygous); 52% were breastfed ≥ 6 months. Seventy-four SBBs were performed in 68 children. CD was confirmed by SBBs in 53 children and in another 3 without SBBs (new ESPGHAN criteria). The cumulative incidence (CI) of CD at 3y was 5.2%. The mean age at diagnosis was 2.7y, with 64% being diagnosed under 3y. All 56 children with CD had elevated TG2A, 82% had elevated AGA, and 64% had symptoms. CD was not significantly associated with pregnancy duration, birth weight, duration of breastfeeding, or number/type of relatives with CD. CD developed more frequently in girls (CI 7.2% v.s. 3.3%; p=0.03). HLA genotypes were highly related to the CI of CD (p<0.0001, see table).

<table>
<thead>
<tr>
<th>HLA genotypes</th>
<th>Frequency (%)</th>
<th>CI at 3y (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR3-DQ2/DR3-DQ2</td>
<td>4.9</td>
<td>25.3</td>
</tr>
<tr>
<td>DR3-DQ2/DR7-DQ2</td>
<td>7.9</td>
<td>14.3</td>
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<tr>
<td>DR3-DQ2/DR5-DQ7</td>
<td>11.2</td>
<td>6.9</td>
</tr>
<tr>
<td>Genotype</td>
<td>Prevalence</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>DR7-DQ2/DR7-DQ2</td>
<td>3.2</td>
<td>4.5</td>
</tr>
<tr>
<td>DR3-DQ2/DQX</td>
<td>31.6</td>
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</tr>
<tr>
<td>DR7-DQ2/DR5-DQ7</td>
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</tr>
<tr>
<td>DR7-DQ2/DQX</td>
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</tr>
<tr>
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</tr>
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</table>

**Conclusion:** These preliminary results show that genetically susceptible children from high-risk families develop CD at a very young age and that this is significantly associated with homozygosity for DQ2. Even in very young children, presence of TG2A is a powerful predictor of CD.

**Disclosure of Interest:** None Declared
NEW INSIGHTS FOR MOLECULAR DIAGNOSIS OF CELIAC DISEASE

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Objectives and Study: Celiac disease (CD) is a polygenic and immune-mediated condition, characterized by destruction of small bowel mucosa after gluten ingestion. HLA genes account for only around 35% of the genetic variation. A recent genome-wide association study (GWAS) identified 39 risk variants account for less than 15% of the disease genetic variance. Nonetheless, much more work needs to be done to explain the missing heritability. Despite the progress of technologies for molecular data analysis, the diagnosis of celiac disease is still based on duodenal biopsy. The aim of this study was to explore the gene expression profile of selected candidate genes in peripheral blood monocytes from patients affected by celiac disease as a step towards the molecular diagnosis of the disease.

Methods: We recruited a cohort of 8 active celiac disease patients, 5 CD patient on gluten free diet (GFD), 18 controls and 11 Crohn patients as positive controls of inflammation. We used real-time PCR and TaqMan assays to evaluate the expression of genes found to be associated with CD, namely; \textit{KIAA1109, IL-2, IL-21, c-REL, LPP, RGS1, SH2B3, TAGAP, TNFAIP3} and \textit{TNFRSF14}. The analyses were performed in duodenal biopsies, in monocytes isolated from peripheral blood, and in gliadin-specific T-cell lines obtained from intestinal biopsies.

Results: The expression of candidate genes differed significantly between celiac disease patients and controls in all the three systems analyzed. Using Wilk's lambda distribution we weighed the discriminating capacity of each single gene in the attempt to obtain a single new composite variable. We obtained 5 genes (\textit{TNFAIP3, IL-21, c-REL, RGS1} and \textit{LPP}) selected for discriminating capacity, with a p-value always less than 0.001. We obtained also a clustered Discriminant score (D-score), which results into a probability of membership either to the cases or to the controls without overlap between the groups. D-score values were negative in the celiac disease group, and positive in the two control groups.

Conclusion: Our study provides the first evidence that a non-invasive method has the capability to distinguish patients with celiac disease from controls and from Crohn patients without considering \textit{human leukocyte antigens} and anti-tissue transglutaminase levels.

Disclosure of Interest: None Declared
Impact of Human Leukocyte Antigen-DQ2/DQ8 Genotyping in Children from Coeliac Families

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Objectives and Study: Screening for coeliac disease (CD) is recommended in 1st-degree relatives of diagnosed cases. Human Leukocyte Antigen (HLA) DQ2/8 is found in almost all CD patients and is useful for ruling out CD when negative and for risk determination. The aims were to investigate 1. the parental knowledge of HLA typing and the impact of it on these parents, 2. the effect of HLA typing in their children on perceived health.

Methods: This study took advance of the Dutch, Israëli and German cohort of the European study on prevention of CD in high risk families (www.preventcd.com), in which newborns and their siblings are HLA typed. A questionnaire was developed using validated questionnaires on genotyping for other diseases and addressed parents’ understanding of, and attitude towards HLA-typing, distress related to the results, levels of current stress (min 1/max 5), perceived health of their children (min 5/max 15), and healthcare utilization. The Armitage trend test was used for statistical analysis.

Results: 404 Parents were asked to participate, 68% gave informed consent and returned the questionnaires, representing 252 newborns and 62 siblings. 85% Of children were DQ2/8+ (DQ+). 97% Of the parents had good knowledge on HLA-typing and the risk of CD in general. However, when asked about their offspring, 46% of parents of a DQ2/8- (DQ-) tested child thought their child could still develop CD. Regrets about HLA-typing were not present among parents of DQ- children and only in 5% of parents of DQ+ children (n.s.). In future pregnancy, 94% of all parents would repeat HLA-typing. After hearing the test results, 16% of parents of DQ+ children felt anxious versus 2% of parents of DQ- children (p<0.05). On the other hand, 88% of parents of DQ- children felt relieved versus 13% of parents of DQ+ children (p<0.001). When completing the questionnaire, levels of parental stress were similar (DQ+ and DQ- means 3.2, SD 2.8-3.7 and 2.5-3.9 resp.). The perceived health was similar in the DQ- (mean 13.5, SD 12.1-14.9) and DQ+ children (mean 13.3, SD 11.6-15). Frequent medical consultation (>2 times/month) was found in 8% of DQ- and 10% of DQ+ children (n.s.).

Conclusion: Parents of CD families support HLA-typing in their children for risk determination. Interpretation of DQ-results of their own child can be difficult for parents of high risk CD families, despite good knowledge of CD and HLA in general. HLA-results do not cause health concerns, but DQ+ results may cause temporary negative feelings among parents.

Disclosure of Interest: None Declared
PROBIOTICS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDHOOD; A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives and Study: Functional gastrointestinal disorders (FGID), currently diagnosed according to the Rome III criteria, are a common problem among childhood. Treatment effects are limited, but considering the relationship between alteration of gut microbiota and inflammation, manipulation of gut microbiota by probiotics appears to be an ideal treatment modality for FGID. The aim of this review was to investigate and to summarize the quantity and quality of all current evidence on the effects of probiotics in the treatment of FGID in children and adolescents.

Methods: MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials were searched systematically up to June 2012. Only randomised controlled trials (RCTs) comparing probiotics with placebo in children and adolescents with FIGD were included. Outcomes were treatment success (measured by treatment responders), abdominal pain, defecation frequency and stool consistency. Two reviewers independently judged the eligibility and quality of the studies.

Results: We identified 9 RCTs that met our inclusion criteria, five studies in 464 children with abdominal pain-related FGID and four studies in 282 children with functional constipation. Trial quality was generally good. Treatment success of probiotics in children with abdominal pain related FGID was significantly higher compared to placebo (5 RCTs, n=464, RR 1.50, 95% CI 1.22, 1.84). No significant effect was found for the treatment success of constipation (3 RCTs, n=255, RR 1.16, 95% CI 0.83, 1.62). In children with abdominal pain-related FGID the use of probiotic was associated with a significant decrease in the intensity of abdominal pain compared to placebo (3 RCTs, n=296, SMD -0.49, 95% CI -0.76, -0.22). No effect was found for the frequency of abdominal pain (3 RCTs, n=296, SMD -0.49, 95% CI -1.11, 0.12). Data was limited for constipated children. Pooled continuous data showed no significant effect in favour of probiotic for increasing defecation frequency in children with constipation (3 RCTs, n=270, SMD 0.44, 95% CI -0.35, 1.24). Data for stool consistency in constipated children was conflicting, two studies (n=88) showed a significant improvement, but this was not found in another larger study (n=159). No significant improvement of stool pattern was found in children with abdominal pain-related FGID.

Conclusion: This systematic review suggests the data published to date provide sufficient scientific evidence that probiotics are a promising strategy to treat children with abdominal pain-related FGID. Currently there is no sufficient evidence to support the use of probiotics in the treatment of functional childhood constipation.

Disclosure of Interest: None Declared
TRANSGLUTAMINASE IGA ANTIBODIES IN A CELIAC DISEASE MASS SCREENING AND THE ROLE OF HLA-DQ GENOTYPING AND ENDOMYSIAL ANTIBODIES IN SEQUENTIAL TESTING

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Objectives and Study: To evaluate hypothetical screening strategies in a Swedish celiac disease (CD) mass screening.

Methods: Within the ETICS/PreventCD study, 10041 Swedish sixth-graders born in 1993 were invited to a population-based CD mass screening and 7208 participated. Serological analysis and HLA genotyping was performed as follows; tTG-IgA in all children (n=7208), s-IgA in all possible (n=7161), tTG-IgG if s-IgA <0.5 g/L (n=174), EMA-IgA if tTG-IgA 2-20 U/mL (n=197), EMA-IgG if tTG-IgG 3-6 U/mL (n=10) and HLA genotyping in all children fulfilling serological criteria for small intestinal biopsy and in age and sex matched controls (n=1320). A lower cut-off for tTG-IgA (>4 U/mL) than recommended (>5 U/mL) was applied and children with tTG-IgA 2-4 U/mL were included if EMA-IgA positive (≥1:5). Children with positive serological screening were recommended a small intestinal biopsy resulting in 153 CD cases.

Results: By lowering the cut-off for tTG-IgA, 17 additional cases of CD were identified at the cost of 32 biopsies. All children with tTG-IgA above 50 U/mL (10 times the recommended upper limit of normal) had CD. Area under the ROC curve for tTG-IgA was 0.988. All cases carried HLA-DQ2 or HLA-DQ8, as did 53% of the controls. Sequential testing of HLA risk alleles would have reduced the number of negative small intestinal investigations by 4. Requiring EMA positivity when tTG-IgA <20 U/mL would have reduced the number of negative investigations by 10, but 2 CD cases would have been missed. For different hypothetical screening strategies sensitivity, specificity, positive (PPV) and negative predictive values (NPV) ranged between 87.6-100%, 99.5-99.9%, 79.7-89.7% and 99.7-100%, respectively.

Conclusion: tTG-IgA is a robust marker when used in CD mass screening and its performance can be enhanced by sequential testing for EMA or HLA-DQ genotyping, both with advantages and disadvantages. HLA risk alleles were more prevalent than expected. Prevalence of HLA risk alleles in a population should be considered when deciding upon strategies for a mass screening for CD.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GERD, PEPTIC DISEASE AND HELICOBACTER PYLORI

PL-G-0012

ONE-YEAR OUTCOME OF ESOPHAGEAL ATRESIA: RESULTS FROM THE FRENCH NATIONAL REGISTER


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Objectives and Study: A prospective population based register was initiated in 2008 including all the centres taking care of esophageal atresia (EA) in France.

Methods: All the 38 multidisciplinary French centres taking care of EA participated to the register and returned a specific questionnaire about the one-year outcome of each patient, which was centralized, checked and entered in a database.

Results: From the total population of 309 EA born in 2008 and 2009, data concerning the one-year outcome were obtained from 303 (98%) while 4% were lost for follow-up and 6% died. A complicated issue occurred in 34% of the cases: anastomotic leaks (8%); recurrent tracheo-esophageal fistulas (4%), anastomotic stenosis (23%) needing esophageal dilation in 22% (median 2 dilations/patient ranged from 1 to 9). During the first year follow-up, a new hospitalisation was required for 58% of patients with a median number of hospitalisations of 2/patient (ranged from 1 to 3), for digestive (40%) or respiratory reason (39%). Twelve percent of patients required antireflux surgery at a median age of 134 days (ranged from 20 to 398) and 0.7% aortopexy for severe tracheomalacia. Weight/age Z score was 0.2 (ranged from -5.1 to 5.5) at 6 and -0.8 (ranged from -5.5 to 3.7) at 12 months. Fifteen percent of patients were undernourished at the age of 12 months, while 41% presented respiratory symptoms and 15% food oral disorders.

Conclusion: Although EA survival dramatically improved during the last decades, digestive and respiratory morbidity remains frequent, especially during the first year of life.

Disclosure of Interest: None Declared
EXPERIENCE OF ONE STEP GASTROSTOMY BUTTON IN CHILDREN
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Objectives and Study: Pediatric experience of single-stage perendoscopic gastrostomy (PEG) button or “one-step button” is scarce. Our aims were: 1) to evaluate this technique, using gastropexy with T-bar fixation; 2) to report immediate and mid-term complications and; 3) to analyze our learning curve.

Methods: This is a 3-year prospective, descriptive study. All patients aged less than 18 years for whom PEG was indicated were included. Anthropometric data, underlying disease, indication for PEG as well as operating modalities and outcome were registered. Data are reported as mean and ranges, and influence of experience was analyzed comparing the first half (0-18 months) to the second half (19-36 months) of the study period.

Results: A total of 183 patients were included, with a mean age of 4.5 years (1 month-17 years) and a mean weight of 13.6 kg (2.4-57 kg); 93 % had PEG for nutritional indication, 45 % for swallowing disorders. Underlying disease was: associated neuro-muscular disorder (53 %); gastrointestinal disease including cystic fibrosis (12%); heart or respiratory disease (9%); malignant neoplasia (8%). The procedure failed in 7 children (4%): lack of adequate transillumination (n=5), problem of button measurement (n=1), and insertion of a metallic T-bar of gastropexy (n=1); all of them were converted in PEG using the pull technique. The procedure was not attempted in 2 children (1%) because of a high anesthetic risk and a low weight. Mean duration of the procedure was 19 min (7-67). Any technical difficulty was described in 65 % of cases. The main reported difficulty concerned the dilation of the gastrostomy tract. There were significantly fewer technical difficulties experienced by the operator in patients aged less than 1 year compared to others (26 % vs 43 %, p=0.025). Early complications (occurring during the first 7 days after the procedure) or late complications (occurring between the eighth day following the implantation of the button and its first replacement) were mild, including accidental loss of the button (35 %), peristomial infection (10 %) and gastric heterotopy (24 %).

Duration of the procedure, failure rate and early complications rate decreased significantly between the first and the second half of the study (24 min+/−24.5 vs 14 min+/−5.1 ; 10 % vs 1 % ; 52 % vs 24 %, respectively, all p <0.001). Mean duration between the implantation of the button and its first replacement was 4.4 months (7 days-8 months). In 77 % of the patients, we noticed at X-ray the persistence of at least one metallic T-bar of gastropexy impacted in the stomach at the first replacement.

Conclusion: Perendoscopic one step button is a safe and reliable technique, that it easy to learn. It represents a good alternative to the “Pull” technique by avoiding a second anesthetic session aimed at replacing the tube by a button.

Disclosure of Interest: None Declared
**Objectives and Study:** Despite advances in Immunosuppressant therapies a significant number of patients have therapy-refractory intestinal disease and a poor quality of life following years of aggressive pharmaceutical treatment, surgery and parenteral nutrition (PN).

HSCT has become a well-established therapy for many severe congenital or acquired disorders of the hematopoietic system, autoimmune and metabolic conditions as well as malignancies in children.

**Aim:** To describe the characteristics and outcome of a cohort of patients with severe chronic intestinal inflammation treated with HSCT.

**Methods:** All children with chronic intestinal inflammation who underwent HSCT since 2001 were recruited from the GOSH IBD data base. Data was extracted on demographics, presentation, pathology, genetics, HSCT characteristics and outcome. Patients with unknown genetic cause underwent custom made HaloPlex™ Target Enrichment System or whole exome sequencing.

**Results:** 14 patients had HSCT (11 boys) with median age of onset of 3 months (1-144).

Clinical/histopathological categorization: 7 Autoimmune Enteropathy-like (AIE), 4 Crohn’s Disease-like (CD) and 3 Indeterminate Colitis-like (IC). 5 (36%) with established genetic diagnosis (2 IL10L/R, 2 IPEX, 1 XIAP).

10 children (71%) required two or more immunosuppressants (IS), 7 underwent bowel resection and stoma formation (50%), 8 were on long term PN (57%) pre-HSCT. Average time from onset of symptoms to HSCT: 48 months (10-107). Reduced-intensity bone marrow conditioning: 5 Matched Related Donors, 4 Mismatched Unrelated Donors and 5 Matched Unrelated Donors. 13 patients achieved 100% donor engraftment (93%) while only one child had 50-80% donor chimerism. 7 patients suffered from milder forms of skin and/or intestinal GvHD (50%). 12 children (86%) had complete histological resolution of original disease, 2 demonstrating some improvement. 10 patients (79%) had excellent clinical outcome (off PN and IS). 2 patients (14%) died from infective causes (1 IPEX: 11 months post HSCT; 1 XIAP 24 months post HSCT). 2 patients with unknown underlying disease have continued to require PN and IS.

**Conclusion:** HSCT is a potentially curative treatment option for a selected group of therapy resistant children with severe intestinal inflammation. Early categorization and genetic profiling might enable us to select children
for HSCT early in their disease course and therefore reduce the sequelae of long term chronic inflammation, immunosuppression and invasive surgery.

**Disclosure of Interest:** None Declared
A comprehensive programme of reaudit of >1000 paediatric IBD inpatients identifies both good practice and areas for improvement

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Objectives and Study: The 1st UK IBD audit of paediatric IBD services was performed in 2008. Involvement in the reaudit in 2010 enabled analysis of comparative data for the first time, including adult audit data. Aim: The UK IBD audit seeks to improve quality and safety of care for all IBD patients in hospitals throughout the UK. The aim of this abstract is to summarise the development of the IBD audit and reflect changes noted in paediatric IBD care over a 5-year period.

Methods: 25 specialist paediatric gastroenterology units across the UK (sites), were invited to participate (rounds of audit referred to as 2008 and 2010). 2008–23 sites collected clinical data on consecutive UC and CD inpatients and undertook a one-off assessment of their provision of service (as at 01/09/08). 2010–24 sites collected clinical data on consecutive UC/CD inpatients, all IBD patients newly started on biological therapies and undertook a one-off assessment of their provision of service (as at 01/09/10).

Results: Participation in the 2010 audit was 92% and 96% in the organisational and inpatient care elements respectively. Across 2 rounds of audit, inpatient data was collected on 1119 (424 UC/695 CD) cases. Significant improvements: 1) Inpatients seen by IBD Nurse (306/512 [60%] 2008 and 310/435 [71%] 2010 p=0.001) 2) Collection of stool samples (122/270 [45%] 2008 and 174/318 [55%] 2010 p=0.02) 3) Use of rescue therapy in UC (17/33 [52%] 2008 and 10/38 [26%] 2010 p=0.03) 4) CD patients seen by dietitian (213/297 [72%] 2008 and 229/285 [80%] 2010 p=0.015) 5) Prescription of prophylactic Heparin (11/512 [2.1%] 2008 to 26/435 [6%] 2010 p=0.002). Across the two rounds there was a significant increase in the number WTE IBD/Gastro nurse specialists (median [IQR]) (1[0,1] 2008 to 1.5[0.8,2] 2010 p=0.017). Areas identified for improvement: 1) 59/237 (25%) of CD patients had pubertal status recorded in the previous 12 months in 2010. 2) PUCAI score was recorded on Day 1 in 13/66 (20%) of UC cases in 2010 3) 15/25 (60%) eligible sites have entered data on biologics.

Conclusion: Clear improvements in care and service provision have been shown. The next round of IBD audit is beginning and continued support of the paediatric community is vital to: monitor provision of biological therapies, assess areas of care still known to be deficient eg recording PUCAI scores, pubertal status, inform debate around anticoagulation. Data will be used to assist guideline development (local and national), drive service improvement and address inconsistencies in care.

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HUMAN MILK OLIGOSACCHARIDES AND PREBIOTICS REDUCE THE DURATION OF ROTAVIRUS-INDUCED DIARRHEA IN PIGLETS

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Objectives and Study: Rotavirus (RV) infection is the leading cause of diarrhea in human infants. Breastfeeding reduces the incidence of RV infection in infants. Human milk oligosaccharides (HMO), the third most abundant component in human milk, inhibit RV binding to enterocytes and promote the growth of beneficial gut bacteria in vitro. Herein, the role of HMO in the prevention of RV infection in vivo was evaluated in piglets.

Methods: Colostrum-deprived piglets were fed with formula alone (FF), or formula containing 4 g/L HMO (40% 2'-fucosyllactose, 35% lacto-N-neotetraose, 10% 6'-sialylactose, 5% 3'-sialylactose and 10% free sialic acid) or prebiotics (PRE) (9:1 of short-chain galactooligosaccharides and long-chain fructooligosaccharides) for 15 days. At d 10, approximately half of the piglets were infected with 5x10^6 focus forming units of group A porcine RV strain OSU. Stool consistency was monitored 3 times daily. Serum, small intestinal tissue and colonic contents were collected at 5 d post-infection (PI). Serum RV-specific IgG and IgM were measured by ELISA. The mRNA expression of RV non-structural protein-4 (NSP4), a marker of RV replication, was analyzed in jejunal and ileal mucosa by RT-qPCR. Villus and crypt morphology were measured. Microbial composition of ascending colonic contents was analyzed by 454 pyrosequencing of the v1-v3 region of the 16S rRNA gene.

Results: The onset of diarrhea occurred at 36.3±1.83 h PI in all infected piglets independent of diet, however, the duration of diarrhea was shorter in HMO (48.8 ± 9.8 h) and PRE (53.1 ± 11.1 h) compared to FF (80.6 ± 4.5 h, p=0.038). Serum RV-specific IgG and IgM were increased in infected piglets. PRE (p=0.001) and HMO (p=0.07) groups had higher concentrations of RV- IgM than FF. RV-IgG did not differ among diet groups. RV NSP4 mRNA expression in jejunal and ileal mucosa were significantly increased in the infected piglets with no effect of diet. Jejunal and ileal villus height was decreased in infected piglets; crypt depth was increased. Diet has no effect on small intestinal morphology. Ascending colonic microbiota was significantly different among infection and diet groups. The amount of Bacteroidaceae was significantly increased in the infected groups. HMO increased the amount of Lachnospiraceae, which contains numerous butyrate producing bacteria.

Conclusion: HMO and prebiotics did not prevent the RV infection, but did reduce the duration of diarrhea in piglets, possibly in part by promoting immunoglobulin response to RV infection and modulating the gut microbiota. (Funded by R01 HD061929)

Disclosure of Interest: None Declared
PRO-INFLAMMATORY VΔ2+ T-Cells Populate the Human Intestinal Mucosa and Enhance IFNγ Production by Colonic αβ T-Cells


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Objectives and Study: In non-human primates Vy9Vδ2+ (Vδ2)-T-cells proliferate and accumulate in mucosal tissues following microbial activation. Human Vδ2-T-cells produce pro-inflammatory cytokines in response to bacterial species that colonize the gut, but the role played by Vδ2-T-cells in intestinal immunity is unknown. We hypothesized that circulating Vδ2-T-cells can populate the human intestine and contribute to mucosal inflammation.

Methods: Cell suspensions prepared from peripheral blood and intestinal biopsies were stimulated with microbial phosphoantigen (HDMAPP) and analyzed by flow-cytometry to determine Vδ2-T-cell phenotype, cytokine production and proliferative potential.

Results: Circulating Vδ2-T-cells expressed gut-homing integrin α4β7 (>70%) which was co-expressed with skin-associated cutaneous leukocyte antigen (CLA) by up to 15% of Vδ2-T-cells. Vδ2-T-cell activation with HDMAPP and exposure to retinoic acid (signaling via RARα) increased α4β7 expression and suppressed CLA, generating a committed gut-tropic phenotype. Confocal microscopy of human colonic mucosa identified frequent Vδ2-T-cells that readily migrated out of cultured intestinal biopsies and could be maintained for more than 30 days in vitro. Intestinal Vδ2-T-cells comprised both CD103+ and CD103- subsets that produced TNFα and IFNγ upon phosphoantigen exposure, but cytokine-producing cells were more frequent in the CD103- population. Activated intestinal Vδ2-T-cells expressed CD70 and HLA-DR but were unable to drive the proliferation of allogeneic naïve CD4+ T-cells. Instead, phosphoantigen-activated CD103- Vδ2-T-cells increased T-bet expression and enhanced IFNγ production by autologous colonic qβ T-cells.

Conclusion: These data demonstrate that circulating Vδ2-T-cells display enhanced gut-homing potential upon microbial activation and populate the human intestinal mucosa, generating functionally distinct CD103+ and CD103- subsets that can promote inflammation by colonic qβ T-cells.

Disclosure of Interest: None Declared
EFFICACY AND SAFETY OF STANDARD VS LOW DOSE ADALIMUMAB MAINTENANCE THERAPY AS A FUNCTION OF DISEASE SEVERITY IN PAEDIATRIC PATIENTS WITH CROHN’S DISEASE: SUBANALYSIS OF IMAGINE 1

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Objectives and Study: Adalimumab (ADA) has recently been shown to be an effective treatment for inducing and maintaining clinical remission and/or response in paediatric (ped) patients (pts) with moderate to severe Crohn’s disease (CD). Although the standard adult dose (SD) ADA maintenance therapy exhibited generally greater efficacy than low dose (LD), the influence of baseline (BL) disease severity on outcomes has yet to be determined.

Methods: In IMAGINE 1, pts aged 6-17 years that had a PCDAI score >30 at BL, with CD resistant or intolerant to conventional therapy, including prior infliximab, received open-label induction of ADA at weeks (wks) 0/2 according to body weight (≥40kg, 160/80mg; <40kg, 80/40mg). At wk4, 188 pts were randomised to receive either double-blind SD (≥40kg, 40mg every other wk (eow); <40kg, 20mg eow) or LD (≥40kg, 20mg eow; <40kg, 10mg eow) maintenance therapy. Pts experiencing disease flare or non-response could move to blinded weekly (ew) dosing after wk12. Clinical remission (PCDAI≤10) and response (PCDAI decrease ≥15 points from BL) were measured at wks 26 and 52. Subgroup analyses were performed by disease severity based on the median of BL PCDAI observed for the study population (less severe CD, PCDAI<40; more severe CD, PCDAI≥40). Non-responder imputation was used for missing data or after switch to ew therapy. Treatment-emergent adverse events (AE) were reported for any pt that received at least one dose of ADA.

Results: Greater clinical remission and response was achieved with SD ADA therapy compared to LD at wk52 in pts with more severe disease. For pts with less severe CD, SD ADA resulted in greater remission at wk26 than with LD ADA (Table). The overall rate of AEs was similar between dosing groups for either pt population. Serious AEs were slightly higher in less severe CD pts receiving SD than LD ADA. No malignancies, TB, congestive heart failure or deaths were reported.

Image:

<table>
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<th>Less severe CD (PCDAI&lt;40)</th>
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<tr>
<td></td>
<td>ADA LD 20/10mg N=41</td>
<td>ADA LD 20/10mg N=54</td>
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<tr>
<td>Remission Wk 26, %</td>
<td>29.3</td>
<td>27.8</td>
</tr>
<tr>
<td>Response Wk 26, %</td>
<td>51.3*</td>
<td>53.7</td>
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<tr>
<td>Remission Wk 52, %</td>
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<tr>
<td>Response Wk 52, %</td>
<td>41.5</td>
<td>38.9*</td>
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*p<0.05 SD vs LD
**Conclusion:** At wk52, SD maintenance ADA was a more effective therapy than LD for ped pts with more severe CD, whereas pts with less severe disease benefitted equally from both doses. The safety profile was similar for SD and LD ADA treatment.


INCIDENCE OF MITOCHONDRIAL DISEASE IN CHILDREN PRESENTING WITH ACUTE LIVER FAILURE UNDER 2 YEARS OF AGE.

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Objectives and Study: Acute liver failure (ALF) in early life has a very poor outcome without liver transplantation (LT). ALF may be the initial presentation of a systemic mitochondrial disease where LT is contraindicated. It is important to recognise mitochondrial disease as quickly as possible to avoid futile LT without denying this life-saving option to those who would benefit. The best approach to investigate mitochondrial disease in the presence of ALF in young children is unclear.

Aim. To determine the incidence of recognised mitochondrial disease in a group of children presenting with ALF under two years.

Methods: Methods. Consecutive children less than 2 presenting with ALF to a single centre from 2009-11 were studied. Where possible, mitochondrial DNA (mt DNA) copy number was assessed in liver; sequencing of the POLG, MPV17, DGUOK and TRMU genes were undertaken.

Results: Results. 40 children (20 male) presented over the study period of whom 26 survived. 11 underwent LT with 8 early survivors. The underlying diagnosis was; infection (n=12), unexplained (n=10), mitochondrial disease (n=7), metabolic disorders (n=5), neonatal haemochromatosis (n=4) and other (n=2). Five of the children with mitochondrial disease had pathogenic detected: DGUOK (n=2), POLG (n=2) and MPV17 (1). Four of these children died from progressive multisystemic disease while one recovered and remains well 3 years later. The remaining 2 children with mitochondrial disease had mt DNA depletion in liver and muscle tissue but no detected pathogenic mutations. One underwent LT but died later with evidence of progressive systemic disease. The other underwent successful LT and remains well with no evidence of systemic disease three years later. An additional 4 children had evidence of mt DNA depletion in liver tissue only. One of these was proven to have neonatal haemochromatosis and underwent successful LT. The other 3 had unexplained liver failure. One underwent successful LT while the other 2 recovered. None of these children have developed evidence of systemic disease following follow-up of up to 4 years.

Conclusion: Mitochondrial disease is an important cause of ALF in children less than two years old.

Where the genetic defect leading to mt DNA depletion can be characterised, inappropriate LT can be avoided.

Evidence of mt DNA depletion in liver in the absence of a recognised genetic defect may be secondary to liver failure.

Conclusion. Screening mt DNA maintenance gene mutations may be the most efficient way to exclude mitochondrial disease in ALF in the first two years of life.

Disclosure of Interest: None Declared
HEPATOLOGY

PL-H-0041

BIDIRECTIONAL CELLULAR SUPPORT IN THE COCULTURE OF HEPATOCYTES WITH MESENCHYMAL STEM CELLS IN ACUTE LIVER FAILURE SERUM: IMPLICATIONS FOR CELLULAR THERAPY

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Objectives and Study: Human hepatocyte (HC) transplantation has promise as a bridge to organ transplantation or spontaneous recovery in acute liver failure (ALF). Intraperitoneal transplantation of alginate encapsulated HC is an exciting new approach though the function and viability of transplanted hepatocytes is a concern. There has been interest in mesenchymal stem cells (MSCs) in ALF therapy as support for coencapsulated HC in addition to their anti-inflammatory/anti-apoptotic properties. We have previously shown trophic effects of MSCs on HC in standard coculture. The aim of this study was to investigate this coculture system in the presence of human ALF serum to assess the potential of this cellular therapy in ALF.

Methods: Human HC were isolated from donor organs and MSCs from donated umbilical cord. Cells were plated in monoculture or in direct coculture at a ratio of 6:1 (HC:MSCs). After 24 hr, serum from patients with ALF, normal controls or fetal calf serum (FCS) was added in increasing concentrations. 24 hr later, serum was replaced by standard culture medium following washing. Cytotoxicity was measured using the sulforhodamine B and MTT assays at 24 and 48 hrs of culture. Specific HC toxicity was estimated using the soluble Keratin (K)18 M65 cell death assay. Albumin production was measured using ELISA. Experiments were repeated in triplicate.

Results: At 24 and 48 hrs, MSC monoculture demonstrated higher cytotoxicity (>50% reduction in metabolic activity) in ALF serum versus FCS control (p<0.001). HC monoculture maintained metabolic activity and cell survival in ALF serum versus FCS at both time points. Cocultured HC and MSCs demonstrated better metabolic activity in ALF serum compared to HC or MSC monoculture (p=0.04). At 48 hrs, specific HC death in coculture versus monoculture was increased by a factor of 2.3 in FCS and by 1.3 in normal serum. This adverse effect was allayed culture with ALF serum with no increase in HC death in this condition. Albumin production at 48 hrs was greatly increased in cultures which had previously been exposed to human serum versus FCS. This effect was seen best in cocultured HC with albumin production 7.5 times greater following ALF serum versus FCS exposure (p=0.02).

Conclusion: ALF serum has toxic effects on MSCs but when cocultured with HC, cytotoxicity appears to be reversed, suggesting a possible protective effect of HC on MSCs in this context. This is a novel finding as previous work has described the trophic effects of MSCs on hepatocytes. This bidirectional cellular support may have an important role in cellular therapy of ALF.

Disclosure of Interest: None Declared
ANTIINFLAMMATORY PROPERTIES OF THE NOVEL ANTIINFLAMMATORY INTERLEUKIN-1 HOMOLOGUE IL-37 IN ISOLATED LIVER KUPFFER CELLS
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Objectives and Study: Interleukin-37 (formerly IL-1 family member 7) is a natural suppressor of innate immune responses. We recently reported that the in vivo expression of human IL-37 in mice reduces local and systemic inflammation in ConA-induced hepatitis. To gain more insight into its pathophysiological role in liver disease, we chose to investigate the functionality of isolated Kupffer cells (KC) from wildtype (wt) and IL-37tg mice. KCs are resident macrophages in the liver and constitute 20% of non-parenchymal cells. KCs produce a variety cytokines and chemokines, play diverse roles in inflammatory conditions and are involved in the production of extracellular matrix in the fibrotic liver.

Methods: We isolated murine KC from wt C57/BL6 (n=13) and IL-37tg (n=8) mice by density centrifugation. After sedation with phenobarbital the portal vein of mice was identified, cannulated and the liver was flushed with cold RPMI to remove blood cells. Subsequently, the livers were removed, minced in Gey’s Balanced Salt Solution containing DNase and strained through filter membranes. The resulting cell suspension containing hepatocytes, KC and hepatic stellate cells was applied to a 17.2% Nycodenz solution followed by gradient centrifugation. The mononuclear cells from the interface (>95% KC according to immunohistochemistry with Kupffer and stellate cell specific markers CD163 and GFAP, respectively) were harvested and stimulated with different concentrations of LPS (E. coli 055:B59 0.1, 1, 3 mg/ml) for 18 hrs. Cytokines in the supernatants were measured by Elisa and Bioplex assay.

Results: Supernatants of non-stimulated KC from wt and IL-37tg mice contained minor concentrations of IL-6 (<50 pg/ml). LPS at 0.1 mg/ml induced the release of a variety of pro-inflammatory cytokines from KC. LPS at higher concentrations (1, 3 mg/ml) did not further increase cytokine expression. IL-6, IL12 (p40, p70), Eotaxin, G-CSF, KC, MCP-1, MIP1a, MIP1b, and RANTES were significantly reduced (40-70%) in the supernatant of KC from IL-37tg in comparison to wt mice. There was no difference in anti-inflammatory IL-10 or IL-13 before and after LPS-stimulation. IL-1b, IL-2, IL-4, IL-5, IL-17, IFNg and TNFa were not detected in the supernatant of either wt or IL-37tg KC.

Conclusion: Transgene expression of human IL-37 in mice results in a significantly reduced secretion of pro- but not anti-inflammatory cytokines from isolated KC after LPS-stimulation in comparison to wt KC. These data suggest that IL-37 has anti-inflammatory effects on liver cells and could potentially reduce liver injury. IL-37 mechanism of action may represent a therapeutic target for the treatment of inflammatory liver disease.

Disclosure of Interest: None Declared
HEPATOLOGY

PL-H-0043

POTENCY OF ADULT DERIVED HUMAN LIVER STEM/PROGENITOR CELLS (ADHLSC) TO CORRECT GALACTOSE-1-PHOSPHATE URIDYLTRANSFERASE (GALT) DEFICIENCY

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Objectives and Study: Classic Galactosaemia (CG) is characterized by deficient Galactose-1-phosphate uridyltransferase (GALT) activity leading to hepatic, renal and cerebral damage due to the accumulation of toxic galactose, galactose-1-phosphate, galactitol and galactonate and to the reduced galactosylation of glycoproteins and glycolipids. Diagnosis of CG is confirmed by assaying GALT activity in erythrocytes as described by Schutgens et al (1978) (normal range of 18.5-32.9 µmol/hour. g Hb). Treatment is limited to strict galactose free regimen. However, due to endogenous galactose production, specific diet is not sufficient to reduce the galactose burden and its toxic metabolites. As previously demonstrated in our lab, adult derived human liver stem/progenitor cells (ADHLSC) can be easily isolated and expanded in vitro. These cells are of hepato-mesenchymal phenotype and exhibit hepatic features after in vitro hepatogenic differentiation. Objective: The aim of this study was to i) evaluate the feasibility of in vitro GALT assay in ADHLSC and ii) compare its level to that of mature hepatocytes. Erythrocytes from healthy and CG patients were used as controls.

Methods: We used the GALT spectrophotometric two-step protocol, and adapted it to cell lysates from hepatocytes and ADHLSC. In this assay cell lysates were incubated with specific GALT substrates. GALT activity was expressed in µmoles/hour. g proteins. Two different healthy hepatocytes and ADHLSC donors were evaluated in this study. Feasibility of the assay was first tested with increasing incubation times with the specific substrates in order to maximize GALT activity in ADHLSC. Limit of detection was also evaluated after incubation with different ADHLSC concentrations.

Results: Preliminary results: Incubation kinetic of ADHLSC lysates with the specific substrates demonstrated a linear GALT activity until 60 minutes. However, undifferentiated ADHLSC demonstrated lower GALT activity when compared to hepatocytes.

Conclusion: Our results demonstrate that undifferentiated ADHLSC exhibit GALT activity in vitro, although much lower than mature hepatocytes. These promising results may offer new future possibilities in the context of hepatic cell therapy research for galactosemia patients.

Disclosure of Interest: None Declared
PROTEOMIC IDENTIFICATION OF NOVEL BIOMARKERS OF PAEDIATRIC NON-ALCOHOLIC FATTY LIVER DISEASE

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Objectives and Study: Identification of biomarkers that could aid in the early clinical diagnosis and accurate disease staging of non-alcoholic fatty liver disease (NAFLD) is a current research priority. The objectives of these experiments were to first identify candidate protein biomarkers of non-alcoholic steatohepatitis (NASH) in mice and then assess protein expression in biopsies from paediatric patients with NAFLD.

Methods: Apolipoprotein E knockout mice (ApoE-/-) and wild type animals fed normal chow or high fat diet (HFD) for 12 weeks. Membrane and cytosolic liver protein fractions were analyzed in a relative quantitative proteomic approach utilizing isobaric tags for relative and absolute quantitation (iTRAQ) labeling combined with nano-liquid chromatography and tandem mass spectrometry (nLC-MS/MS). Protein identification and quantitation was done using Scaffold 3.0 Q+S software. Differential expression was confirmed independently by western blotting and immunohistochemistry first in mouse sections and then in biopsies from paediatric NAFLD patients.

Results: After 12 weeks of HFD, ApoE-/- animals had clearly developed the histological features of NASH. Across biological replicates, an average of 249 cytosolic and 343 membrane proteins were identified with high stringency (0.05 FDR; ≥2 peptides), and quantified by Scaffold. Of these, 83 cytosolic and 80 membrane proteins were found significantly differentially expressed by both randomized permutation and ANOVA tests. Liver fatty acid binding protein and fatty acid synthase, both previously found down-regulated in NASH patients, were among those found significantly down-regulated (-1.2; P=4.3E-15 and -0.9; P=7.9E-11) in the HFD-fed ApoE-/- animals. Pathway analysis demonstrated enrichment in the RXR-dependent regulation of lipid metabolism (P=6.55E-05) and several lipid metabolic networks (4/10). Two novel candidate biomarkers for NAFLD, identified by proteomics were independently examined in clinical biopsy samples from paediatric patients with NAFLD. Sterol carrier protein x and glyoxalase 1 were both confirmed as down regulated in 7 of 7 and 6 of 7 NASH biopsies examined to date.

Conclusion: ApoE-/- animals fed a HFD for 12 weeks is a valid animal model of NASH. Sterol carrier protein x and glyoxalase 1 are altered in the liver of paediatric NASH patients. Proteomics offers the potential to identify protein biomarkers of clinical significance to NAFLD.

Disclosure of Interest: None Declared
COMMON ESPGHAN TOPICS
TRANSPLANTATION

PL-H-0045

LONG TERM OUTCOME OF CHILDREN FOLLOWING LIVER TRANSPLANTATION
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Objectives and Study: To evaluate survival and outcome of patients > 15 years following liver transplantation.

Background: Liver transplantation (LT) is a successful treatment for end stage liver disease. There are little data on the long term outcome of patients who underwent LT during childhood.

Methods: We retrospectively reviewed all patients who underwent LT more than 15 years ago. We reviewed their medical notes and patients who lived locally were interviewed personally during their routine outpatient appointments. We contacted physicians looking after those patients who had been referred elsewhere in order to complete the data collection. We collected data on liver & renal function, hypertension, dyslipidemia, bone disease, recurrent disease, rejection, de Novo Autoimmune Hepatitis, psychological disorders, compliance and social adaptation.

Results: 116/181 patients who underwent LT between 1985 and 1995 in BCH were alive more than 15 years after transplantation (median post-transplantation time was 19.5 years, range: 16 to 27 years). Median age at LT was 25 months (range: 15 days to 16 years) and the main indication for transplantation was extrahepatic biliary atresia (51%). 23/116 were re-transplanted. The majority of re-transplantations occurred during the first year post LT. 7 patients required a second transplant 5 to 11 years after their first LT due to chronic rejection. At > 15 years 89% had normal functioning grafts; 43% were on steroid immunosuppression and 54% were on monotherapy mainly with Mycophenolate/Tacrolimus or Cyclosporin. The main causes of graft dysfunction were chronic rejection (66%) and graft fibrosis (33%). Long term complications included renal dysfunction (22% had calculated Glomerular Filtration Rate (cGFR) or GFR < 60 ml/min/1.73 m² and 3 patients required a renal transplant), 39% required antihypertensive treatment, 9% had had post transplant lymphoproliferative disorders/lymphoma/leukaemia. 54% were compliant with treatment and appointments. 28% went to university; 43% to college; 29% were still at school. 50% are still in education and 50% are employed. 20% are unemployed and not in education. 51% are married or in a relationship and 13% have had children.

Summary: The survival rate of LT recipients more than 15 years after LT is 64%. Most have normally functioning grafts, are in employment or education and are married or in a relationship. The main reasons for graft loss were chronic rejection and graft fibrosis. The complications of long term immunosuppression include high blood pressure, renal dysfunction and lymphoproliferative disorders. Non-adherence was present in 46% of the group.

Conclusion: The long term outcome of LT is excellent allowing patients to have normal social adaptation and functioning.

Disclosure of Interest: None Declared
SUPPLEMENTATION OF THE MATERNAL DIET WITH ALPHA-LINOLENIC ACID MODIFIES PIGLET GUT IMMUNE SYSTEM EDUCATION TOWARDS LPS
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Objectives and Study: N-3 polyunsaturated fatty acids (PUFA) have many beneficial health effects, especially in neonates. We recently demonstrated that supplementation of the maternal diet with alpha-linolenic acid (C18:3 n-3) increases intestinal permeability at the end of the suckling period in piglets1. Education of the gut immune system towards the colonizing microbiota, and particularly towards lipopolysaccharides (LPS) is intense during this period. We hypothesized that the increased intestinal permeability observed with maternal n-3 PUFA would lead to increased transepithelial passage of LPS and modification of the gut immune system education towards this bacterial component.

Methods: Two groups of sows were fed either a flaxseed-based (n-3 group) or a sunflower oil-based diet (n-6 group) during gestation and lactation. Piglets suckled their dam until post-natal day (PND) 28 when they were weaned on a regular weaning diet. From PND 14 to 28, a sub-group of piglets in each litter received an anti-gram negative bacteria antibiotic per os daily. At PND28 and 52, FITC-labeled LPS passage across the jejunum was evaluated ex vivo in Ussing chambers. Cultures of jejunal explants were used to evaluate cytokine secretion in response to LPS. Mononuclear cells were also isolated from mesenteric lymph nodes (MLN) and cultivated with LPS or concanavalin A.

Results: At PND28, passage of FITC-LPS across the jejunum was increased in n-3 piglets (P<0.05), as well as in piglets receiving the antibiotic (P<0.05). Pro-inflammatory cytokines (IL-8, TNF-α) secretion by jejunal explants was not altered by the maternal diet nor antibiotic administration. However, TNF-α secretion by MLN cells in response to LPS tended to be decreased in n-3 piglets (P=0.06) without modification of IL-10 or IFN-γ secretion. Antibiotic treatment tended to reduce this TNF-α secretion (P=0.08). Maternal diet effects were specific to LPS since no difference between groups was noticed in response to concanavalin A. Later in life (PND52), transepithelial passage of LPS was similar in both groups. TNF-α secretion by jejunal explants was reduced while IL-10 secretion by MLN cells was increased in response to LPS in n-3 piglets (P=0.01 and 0.04, respectively), irrespective of the antibiotic treatment during the suckling period.

Conclusion: Supplementing the maternal diet with alpha linolenic acid during gestation and lactation orientated the gut immune system response to LPS towards an anti-inflammatory profile which lasted beyond the suckling period. This long-lasting anti-inflammatory response seems independent of microbiota composition during the suckling period.

References: 1 de Quelen et al. J Physiol. 2011, 589:4341-52

Disclosure of Interest: None Declared
SACCHAROMYCES BOULARDII IN THE PREVENTION AND TREATMENT OF ANTIBIOTIC-ASSOCIATED DIARRHEA IN CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT INFECTIONS

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Objectives and Study: To determine whether Saccharomyces boulardii (S. boulardii) can prevent and treat antibiotic-associated diarrhea (AAD) in children.

Methods: A total of 333 children (aged 6 months to 14 years) with acute lower respiratory tract infection were enrolled in an open randomized controlled trial. This was a 2-phase study: 1st phase all children received intravenous (IV) antibiotic treatment and were randomized in two groups: group A (S. boulardii + IV antibiotics, n =167) and group B (IV antibiotics alone, n =166). The children in group A received 500 mg of S. boulardii for the duration of the antibiotic treatment. They were followed for 2 weeks. Analyses were based on allocated treatment and included data from 283 patients. The second phase of the study patients in group B who developed diarrhea during the antibiotic treatment: they were randomized in two sub-groups: group B1 (S. boulardii + oral rehydration solution (ORS)) and Group B2 (ORS alone).

Results: Patients from Group A had a lower prevalence of diarrhea than group B [11 of 139 (7.9%) vs. 42 of 144 (29.2%); relative risk (RR): 0.271, 95% confidence interval (CI): 0.133–0.553]. S.boulardii also reduced the risk of AAD compared with group B [6 of 139 (4.3%) vs. 28 of 144 (19.4%), relative risk: 0.22 ; 95%CI: 0.089–0.555]. When children in group B developed diarrhea, S. boulardii treatment (group B1) resulted in lower stool frequency and better recovery than single ORS (P<0.05). After 5 days, the recovery rate in group B1 (91.3%) was significant higher than in group B2 (21.1%) (χ²=21.314 , P<0.001). The mean duration of diarrhea in group B1 was shorter than in group B2 (2.31±0.95 vs 8.97±1.07, t=21.359 , P<0.001). No adverse events related to S. boulardii were observed.

Conclusion: S. boulardii is effectively in the prevention and the treatment of AAD in children with acute lower respiratory tract infection.

CAESAREAN SECTION AND RISK OF OBESITY IN CHILDHOOD: RESULTS FROM THE LONGITUDINAL LISAPLUS BIRTH COHORT

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Objectives and Study: The gut microbiome is considered as modifying factor for obesity. Data from a birth cohort of 1255 US children suggested that caesarean section (c-section) compared to vaginal delivery increases the risk for obesity at 3 years of age (n = 1255) (ref.1). We used longitudinal data from a German birth cohort to examine whether the findings can be replicated and whether the effect persists into school age.

Methods: Data were analyzed from the ongoing study LISAplus (Influences of Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood). Height and weight were measured at age 2, 6, and 10 years (n =1734, 1244, and 1170, respectively), BMI and BMI z-scores were calculated using WHO macros. Overweight and obesity were defined according to WHO age- and sex-specific BMI cut-offs (overweight: 85th to < 95th percentile; obesity: ≥ 95th percentile). Potential influencing factors such as duration of gestation, birth weight, head circumference, maternal pre-pregnancy BMI, maternal smoking during pregnancy, breastfeeding initiation, exclusive breastfeeding duration, and timing of solid food introduction were included in the multivariable models. Multivariable linear and logistic regression models were used to evaluate the association between c-section and BMI z-scores, being overweight, or obese.

Results: C-section was the mode of delivery in ~17.0% of the children. Mothers who delivered by c-section had higher pre-pregnancy BMI (23.7 kg/m² vs. 22.5 kg/m², p<0.05), higher gestational weight gain during pregnancy (15.3 kg vs. 14.5kg, p<0.05), and shorter exclusive breastfeeding duration (3.4 vs. 3.8 months, p<0.05) compared to those who had a vaginal delivery. Rates for obesity at 2 years of age were higher after c-section compared to vaginally delivered children (13.6% vs. 8.3%, p<0.05). The significance was lost at 6 and 10 years of age. Crude and adjusted hazard ratios identified c-section as risk factor for obesity at age 2 years (HR_{crude} = 1.78, 95% CI: 1.10 to 2.61 vs. HR_{adj} = 1.74, 95% CI: 1.12 to 2.70). Hazard ratios for obesity at age 6 and 10 years lost significance and were attenuated after adjustment (HR_{crude} = 2.15, 95% CI: 0.92 to 5.01 vs. HR_{adj} = 1.60, 95% CI: 0.58 to 4.36) and ten years (HR_{crude} = 1.58, 95% CI: 0.88 to 2.84 vs. HR_{adj} = 1.30, 95% CI: 0.64 to 2.64).

Conclusion: Caesarean delivery may increase the risk for obesity during early, but not later childhood. Our results do not support the hypothesis that the increasing rates of c-section contribute to the epidemic of childhood obesity.


Disclosure of Interest: None Declared
ORAL ZINC SUPPLEMENTATION REDUCES MORBIDITY AND MORTALITY OF VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED, PLACEBO-CONTROLLED STUDY.

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Objectives and Study: To investigate the efficacy of zinc in reducing morbidity and mortality of preterm neonates.

Methods: Prospective, double-blind, randomized controlled study enrolling very low birth weight neonates randomly allocated at 7 days of life to “active treatment” (oral zinc supplementation at 10 mg/Kg/d, in a multivitamin preparation) or to “placebo” (similar multivitamins preparation without zinc). The main endpoint was morbidity, defined by the presence of at least one of the following conditions: late-onset sepsis, necrotizing enterocolitis, bronchopulmonary dysplasia, intraventricular hemorrhage, periventricular leucomalacia and retinopathy of prematurity. Secondary outcomes were mortality and growth at discharge.

Results: We enrolled 97 neonates in the active treatment group and 96 in the placebo group. Morbidity was significantly reduced for the neonates receiving oral zinc supplementation (44.3%) compared with placebo (61.5%, p=0.017). Occurrence of necrotizing enterocolitis was higher in the placebo group (6.3%) compared with active treatment group (0%, p=0.014). Mortality risk was increased in neonates receiving placebo compared to those supplemented with zinc (2.37, 95%CI 1.08-5.18, p=0.006). Body-weight at discharge was higher in the zinc-group (2208 ± 501g) compared with placebo-group (1889 ± 639g, p=0.001).

Conclusion: Zinc reduces morbidity and mortality and improves body growth in preterm neonates.

Disclosure of Interest: None Declared
PREVENTION OF FUNCTIONAL Gastrointestinal DISORDERS IN THE FIRST THREE MONTHS OF LIFE WITH PROBIOTIC SUPPLEMENTATION: AN ITALIAN MULTICENTRIC STUDY

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Objectives and Study: Colic, regurgitation and constipation are common feeding problems in infants. The onset of these disturbances in the neonatal period not only required a over load work for pediatrician but also could act as a n early traumatic experience that might influence the onset of gastrointestinal tract disturbances late in life. The aim of this prospective study was to evaluate the effects of probiotic supplementation reduce the onset of these “minor” gastrointestinal disorders.

Methods: A double blind placebo controlled multicentre study was performed among 8 Pediatric and Neonatology Centre over Italy. Both formula fed-infants and breast fed-infants a term were enrolled in the study at the 3rd day of life from October 2010 to December 2011. The infant were randomly assigned in a double-blind manner to receive either L. reuteri at dose of 1x10^8 CFU a day (5 drops of an oil suspension) or placebo for 90 days. Parents were given a structured diary to record daily episodes of colic, regurgitation and number of stools.

Results: Of the 589 infants enrolled, 468 completed the study. At one month follow up The newborns receiving probiotics had a significant decrease in mean of minute of crying time per day (45,07 ± 12,34 vs 96,36 ± 34,67 p<0.01) and a larger number of stools per day compared to the placebo group. (4.01± 1.1 days vs 2.8±0.6 p<0.01). At three months follow up evaluation out of 468, 435 infants showed the following clinical outcome: the newborn receiving probiotics maintain the significant decrease in mean of minute of crying time per day (37,7 ± 33,8 vs. 70,9 ± 51,9) p<0,01) and the larger number of stools per day compared to the placebo group (4,2 ± 1,8 vs 3,6 ± 1,7) p<0,01). Moreover, also the number of regurgitation per day show a statistical significance difference between the two groups (2,9 ± 1,1 vs 4,6 ±3,2, p<0,01). The results did not change even though the analysis was stratified for type of feeding and type of delivery. No infant showed any adverse effect related to the trial.

Conclusion: These findings show that supplementation with L. reuteri DSM 17938 prevents the onset of colic and constipation in the first month of life. In the third month of life the probiotic supplementation also reduce the number of regurgitation. This could represent a new therapeutical strategy for preventing these potential harmful condition

References:

Disclosure of Interest: None Declared
THE EARLY NUTRITIONAL FACTORS EPA AND DHA EXERT A DIRECT BENEFICIAL EFFECT ON HUMAN PRIMARY ADIPOCYTES

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Objectives and Study: The rising obesity epidemic requires novel approaches. Early postnatal nutritional factors may benefit healthy weight development in adult life. Early dietary supplementation with n-3 series long-chain polyunsaturated fatty acids (LC-PUFAs) like eicosapentaenoic acid (EPA) and docohexaenoic acid (DHA) has been shown to reduce adipogenesis and adipose tissue inflammation later in life in mice. The effects of these LC-PUFA’s on human adipocytes remain largely unknown. Adiponectin is one of the best known adipokines with anti-inflammatory, vasculoprotective and anti-diabetic effects. Thus, profiling of the adipocyte secretome in response to early nutritional factors may help to identify novel preventive strategies. Therefore, the aims of this study were to assess the impact of EPA, DHA and arachidonic acid (ARA) on adipokine secretion and to determine their effect on TNFα-induced activation of the pro-inflammatory nuclear factor (NF)-κB in human adipocytes.

Methods: Human primary adipocytes were isolated from subcutaneous adipose tissue. Primary human adipocytes represent a unique cellular model to study the impact of early nutritional factors on human cell physiology and function, such as the human adipokine secretome. Differentiated adipocytes were characterized by immunofluorescence and adipogenesis was assessed by Oil Red staining. Adiponectin and leptin secretion were assessed by ELISA and adiponectin protein levels, Akt phosphorylation and NF-κB activation were measured by Western blot.

Results: DHA and EPA (50 µM and 100 µM) significantly upregulated adiponectin secretion without affecting leptin secretion. Importantly, DHA (100 µM) inhibited NF-κB inflammation induced by 5 ng/ml of TNFα (43,0±15,7 % vs. TNFα-induced NF-κB activation levels). Although EPA showed a trend towards inhibition, DHA demonstrated to be the most potent inhibitor of TNFα-induced NF-κB activation. In contrast, ARA had no impact whereas a high ARA/high oleic acid mixture did even upregulate TNFα-induced NF-κB activation. Furthermore, EPA, DHA and ARA did not impair insulin sensitivity as Akt phosphorylation levels did not differ as compared with the untreated control.

Conclusion: DHA and EPA arise as promising nutritional factors able to upregulate adiponectin secretion, thus modulating adipokine secretion in human adipocytes towards a more beneficial cardiometabolic profile. Moreover, DHA can significantly reduce TNFα-induced NF-κB activation in human adipocytes suggesting a direct protective role of this n-3 PUFA in pathological conditions where TNFα levels are upregulated, such as obesity.

GASTROENTEROLOGY
GI MOTILITY AND FUNCTIONAL GI DISORDERS

SP-G-0013

GASTRIC ELECTRICAL STIMULATION FOR TEENAGE CHILDREN WITH CHRONIC UNEXPLAINED NAUSEA AND VOMITING (CUNV)
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Objectives and Study: Gastric electrical stimulation has been shown in clinical trials in adults to be safe and effective in drug refractory nausea and vomiting, with long term studies showing statistically significant improvement in gastroparetic symptoms.
Objective: We performed a pilot study in 5 teenagers who had been referred after unsuccessful drug treatment. To assess the utility of gastric electrical stimulation (GES) in reducing the symptoms of chronic nausea and vomiting.
Methods: Patients: Their median age was 15.5 (range 14-18 years). All were female. Two had presented with cyclic vomiting syndrome unresponsive to medication, one of which had three fundoplications for GORD with no improvement. One on TPN with severe erosive oesophagitis and had numerous admissions, and one on long term enteral n/j feeds. They all had gastric emptying studies which showed delayed gastric emptying. None were diabetics. Electrogastrography showed gastric dysrhythmias in all five, with increased episodes of tachygastria in 3 and mixed dysrhythmias in 2. The surgical approach was via laparotomy in two patients; while the other three had laparoscopic surgery (two had robotic assisted laparoscopic surgery). There were no complications following surgery.
Main Outcome Measurements: All patients were evaluated at baseline for the primary outcome parameters associated with GI symptoms, gastric physiology and electrophysiology, and hospital admissions and patient diaries and compared to evaluate the long-term effect of GES. Patients were evaluated at baseline and at follow-up visits (3, 6 and 12 months and thereafter twice yearly in 4 patients).
Results: Results- The median follow up time was 9.5 months (range 4 - 50 ). There was a significant reduction of nausea and vomiting in three patients in 6 months, marginal improvement in one and none so far in the patient with the shortest time to follow up of 4 months. Two patients who had assisted feeding (1 TPN, 1 NJ feeding) are now able to eat normally.
Conclusion: GES has been shown effective in adults but has been done infrequently in children. This study and one other recent abstract presented at DDW (1), show that GES can be effectively applied to the pediatric population. GES is an effective and safe treatment in children with intractable nausea and vomiting. However, these results are limited by the small number of the patients and relatively short follow up period. Nevertheless, their clinical improvement in symptoms warrant further study of this new modality of treatment in children.
References: 1. Lu P et al. Improvement of Quality of Life and Symptoms After Gastric Electrical Stimulation in Children With Gastroparesis and Functional Dyspepsia.DDW Abst;Gastroenterol May 2012.

Disclosure of Interest: None Declared
PREVALENCE OF SUBTYPES OF IRRITABLE BOWEL SYNDROME IN CHILDREN AT DIAGNOSIS AND CHANGES OF THESE SUBTYPES AT FOLLOW-UP

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Objectives and Study: Irritable bowel syndrome (IBS), as described by the Rome III criteria, includes weekly symptoms of abdominal pain or discomfort accompanied by changes in bowel patterns: constipation (C-IBS), diarrhea (D-IBS) or alternating C and D (A-IBS). In adults, it is fundamental to identify subtypes of IBS in order to establish the most appropriate treatment. Aim of the present study was to evaluate the prevalence of childhood IBS-subtypes at diagnosis and any change at follow-up.

Methods: This is an observational, prospective, multicenter study. Consecutive patients with IBS were enrolled within one year. Parents received a diary to record weekly stool frequency and consistency, the presence of specific behaviours during the evacuation and of any possible gastrointestinal symptom. A score of the stool consistency was then obtained, according to the Bristol Stool Form Scale. Children were prospectively evaluated at three time points. Two months after enrolment children underwent clinical examination and all the weekly diaries were collected. After 3 and 6 months from the enrolment, they and/or their parents were asked to complete again the IBS symptoms questionnaire.

Results: We enrolled 100 children with diagnosis of IBS (mean age: 9.5 yrs; range: 4.2 to 16.7 yrs; F52/M48). At time of enrolment (T0), C-IBS was the most prevalent subtype, presented in 45 out of 100 children (45%), with a prevalence of females of 62% (28/45; p<0.005); D-IBS was reported in 26/100 (26%) children, with a prevalence of males of 69% (18/26; p<0.005); A-IBS was described in 29/100 children (29%). Forty percent of patients had difficulty falling asleep, 46.5% of patients reported absences from school and/or interruption of their activities. At two month-follow up (T1), 10 out of 100 (10%) patients presented changes in IBS subtypes: 3 from C-IBS to D-IBS, 3 from A-IBS to C-IBS and 4 from A-IBS to D-IBS. At 3 month-follow up (T2), 9 out of 99 (9.1%) patients presented changes in IBS subtypes: 3 from A-IBS to C-IBS, 3 from C-IBS to D-IBS and 3 from A-IBS to D-IBS. At 6 months-follow up (T3), 7 out of 95 patients (7.4%) presented changes in IBS subtypes: 4 from A-IBS to C-IBS, 2 from C-IBS to D-IBS and 1 from A-IBS to D-IBS. Twenty out of 95 (21%) patients changed IBS subtype between T0 and T3.

Conclusion: This survey on the prevalence of IBS subtypes in children shows that C-IBS is the most prevalent subtype overall the time points considered, with a significant higher frequency in females. In contrast, in males D-IBS is the most common subtype. Therapeutic strategies should be tailored according to the prevalent bowel pattern and abdominal pain.

Disclosure of Interest: None Declared
IMMUNE DYSREGULATION AND FOXP3+ REGULATORY T CELLS IN PATIENTS WITH GENETIC DEFECTS IN PTEN

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Objectives and Study: The Phosphatase And Tensin Homolog Deleted On Chromosome10 (PTEN) regulates the phosphoinositol-3-kinase (PI3K)-AKT-mTOR signaling pathway. Patients with mutations in PTEN develop a tumor syndrome (Cowden syndrome, Bannayan Riley Ruvalcaba syndrome) as well as immune dysregulation in the intestine and extraintestinal sites. Reduced activity of PTEN affects homeostasis of human germinal center B cells by increasing PI3KAKT signaling via mammalian target of rapamycin as well as antiapoptotic signals (Heindl et al. 2012). Mouse models suggest a role of PTEN for controlling the AKT pathway in regulatory T cells. We proposed that a lack of PTEN in humans would affect regulatory T cell function and might contribute to intestinal and extraintestinal immunopathology.

Methods: We investigated a series of 73 patients with pathogenic PTEN mutations for immune dysfunction. Peripheral blood lymphocytes were investigated (26 patients and 216 controls). Lymphocyte subsets in particular FOXP3+ regulatory T cells were investigated by FACS as well as intestinal tissue by immunofluorescence microscopy in a subset of patients. Induction of regulatory T cells was investigated in vitro in the absence or presence of the PTEN inhibitor SF1670.

Results: Gastrointestinal lymphoid hyperplasia, extensive hyperplastic tonsils, thymus hyperplasia, autoimmune lymphocytic thyroiditis, autoimmune hemolytic anemia, and colitis was found in patients with pathogenic PTEN mutations. Gastrointestinal lymphoid hyperplasia was associated with peripheral blood lymphopenia. In contrast to CD5+ and CD10+ B cell subsets, T cell subsets were not different between patients and controls. PTEN mutations were not associated with impaired FOXP3 level or reduced CD4+CD25+CD127lowFOXP3 cell numbers. Inhibition of PTEN did reduce the induction of FOXP3+ T cells only marginally.

Conclusion: Despite of the known negative role of activated AKT-mTORC1 pathway for induction of FOXP3 for CD4+ regulatory T cells, we did detect normal Foxp3+ T cell numbers and distribution and did not detect activated mTORC1 signalling in PTEN deficient patient regulatory T cells. We show that FOXP3+ regulatory T cells are largely protected from negative effects of overactivated AKT signalling allowing to compensate the loss of PTEN.

Disclosure of Interest: None Declared
NEW INSIGHTS INTO CONGENITAL TUFTING ENTEROPATHY BROUGHT BY ELECTRONIC MICROSCOPY ANALYSIS ACCORDING TO RECENT GENE IDENTIFICATION

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Objectives and Study: Recent identifications of EPCAM1 and SPINT2 genes as responsible for Congenital Tufting Enteropathy (CTE) have brought new perspective in the understanding of the pathophysiology of this rare and severe disease. In this study, we analyzed by electronic microscopy (EM) the anomalies of duodenal biopsies of children suffering from CTE and mutated for one or the other gene. We then correlated the differences using the molecular data of proteins EPCAM and SPINT2 known to date.

Methods: Six children's duodenal biopsies have been obtained during endoscopic procedures after informed consent in our reference center for rare digestive diseases, followed by analysis by EM of the intestinal epithelium. EPCAM and SPINT2 genes sequencing analysis of the included CTE patients had been performed: two children were mutated for EPCAM and two for SPINT2. Biopsies of these children were compared to two controls: one from a child suffering from Microvillous Inclusion Disease (MVID), and another biopsy from a child with no known enteropathy.

Results: All CTE patients’ enterocytes displayed specific anomalies, compared to controls, of the brush border, junctional complexes, mitochondria, endoplasmic reticulum, intracytoplasmic material and of the nucleus with different characteristics. We could correlate these anomalies’ specificities with each gene. Moreover, the EPCAM mutated patients harbored particular anomalies that were not found in the case of SPINT2 mutations with dilatation of the intercellular space.

Conclusion: CTE’s enterocytes displayed specific anomalies common to both genes, compared to controls. Moreover, we analyzed the differences that could be highlighted in the two genetic groups of CTE using molecular data known to date about the two proteins. We propose a hypothetical mechanism involving a common pathway for this particular disease.

References:

Disclosure of Interest: None Declared
TRANSORAL INCISIONLESS FUNDOPLICATION USING ESOPHYX FOR THE TREATMENT OF GASTRO-OESOPHAGEAL REFLUX DISEASE IN CHILDREN: 36 MONTHS’ RESULTS OF A FEASIBILITY EVALUATION

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Objectives and Study: Transoral Incisionless Fundoplication (TIF) allows an endoluminal approach for the treatment of gastroesophageal reflux disease (GERD) with success in adult series reported.

Objective: To evaluate the safety and efficacy of TIF for pediatric GERD using prospective subjective and objective outcomes.

Methods: Design: Prospective cohort evaluation.
Setting: Tertiary pediatric endoscopy center.
Patients: TIF was attempted in 23 children. In 3 oesophageal intubation was not feasible due to abnormal anatomy. Therefore TIF occurred in 20 (14 male): age 12.9(8.8-17.9) years; weight 47(24-91) kg.
Interventions: TIF was used between December 2008 and May 2011. Exclusion criteria: >18 years; dysphagia; esophageal stricture; BMI >30; previous upper intestinal surgery; hiatus hernia > 2cm.
Main outcome measures: 24-hr oesophageal pH, validated Quality of Life in Reflux and Dyspepsia (QOLRAD), and proton pump inhibitor (PPI) daily dose. Follow up assessments occurred at 6, 12, 24, and 36 months.

Results: Follow up of 39 (12-44) months, in 17/19 (89.5%) (1 lost to follow up) Significant improvement in all parameters was observed (including 2 with neurological compromise). 2/19 patients remained symptomatic at 12 months post-procedure and underwent laparoscopic fundoplication (LF), which also failed. TIF duration: 56.5 (28-80) minutes. With C0₂ insufflation no complications occurred, and no adverse events noted during follow up.

Limitations: small study; selected population.

Conclusion: TIF is feasible and safe in children. Sustained subjective/objective outcomes occurred at median 39 months. PPIs use ceased in 84%. 2/19 proceeded to LF. Further studies are required to assess long term outcomes and efficacy.

Disclosure of Interest: None Declared
RNA-BINDING PROTEIN CUGBP1 REPRESSIONS TRANSLATION OF E-CADHERIN AND MODULATES EPITHELIAL BARRIER FUNCTION

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Objectives and Study: E-cadherin, the primary component of adherence junction (AJ), is critical in directing formation of junctional complex thus maintaining epithelial barrier function. CUG-binding protein 1 (CUGBP1) primarily binds to GU-rich elements located in the 3'-untranslated regions (UTRs) of its target transcripts and regulates mRNA stability and translation. Due to the predicted CUGBP1-hits in the E-cadherin 3'UTR, this study sought to determine if CUGBP1 regulates E-cadherin expression, thus modulates the barrier function.

Methods: Caco-2 cells was used in these studies. The binding of CUGBP1 with E-Cadherin mRNA was examined by biotin pull-down assays and ribonucleoprotein/IP analysis. E-cadherin mRNA stability was examined by measuring its half-life with real-time PCR analysis, and its translation was examined by chimeric luciferase- E-cadherin 3'UTR reporter assays. CUGBP1 function was investigated by its gene silencing and overexpression. Barrier function was detected by paracellular tracer flux assay and trans epithelial electric resistant.

Results: CUGBP1 bound to the E-cadherin mRNA by directly interacting with the E-cadherin 3'UTR rather than its 5'UTR and coding region. Ectopic overexpression of CUGBP1 by transient transfection increased [CUGBP1/ E-cadherin mRNA] complex, repressed E-cadherin translation (by~75%), and decreased its protein level (by~65%), but it failed to alter E-cadherin mRNA stability and total E-cadherin mRNA level. In contrast, silencing CUGBP1 decreased CUGBP1/ E-cadherin mRNA association, enhanced E-cadherin translation, and increased its protein abundance without affecting the stability and level of E-cadherin mRNA. CUGBP1 silencing also promoted the epithelial barrier function as indicated by a decrease in paracellular permeability. Decreased E-cadherin translation by CUGBP1 overexpression disrupted the barrier function and increased paracellular permeability.

Conclusion: These results indicate: 1) E-cadherin mRNA is a target of CUGBP1; 2) increased CUGBP1/ E-cadherin mRNA association represses E-cadherin mRNA translation; and 3) CUGBP1 plays an important role in the regulation of intestinal epithelial barrier function.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

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THERAPEUTIC STRATEGY AND PATIENT OUTCOME DURING THE FIRST 2 YEARS OF PEDIATRIC CROHN'S DISEASE.
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UZBrussels, 4 Pediatric, UCL St Luc, Brussels, 5 UZ Gent, Gent, Belgium

Objectives and Study: BELCRO was initiated in 5/2008. The aim of the registry is to prospectively study a cohort of pediatric CD patients. We here report therapeutic strategy and outcome after the first 2 years of disease.

Methods: Data from the BELCRO database were evaluated at inclusion (M0), after 6 (M6), 12 (M12) and 24 (M24) months. All analyses were performed using SAS 9.3 (SAS Institute, Cary NC) and hypothesis were tested at 5% level of significance. Mixed models via Procedure Mixed were used to analyze the effect of treatment on growth related variables allowing, for patient-specific random effects. Wilcoxon signed ranked test was used to compare individuals at M0 and M24.

Results: Data from 98 newly diagnosed patients were available at M0, 6 were lost to follow up at M24.

Disease severity scores decreased over time: for inactive/mild/moderate-severe were respectively at M0 4.26%,24.47%,71.28%; at M6 53.73%,38.81%,7.46%; at M12 60.00%,35.71%,4.29% and at M24 77.14%,21.43%,1.43%.

Changes in therapeutic strategy at M0 and M24: mono 5ASA:7.14 and 7.61%; immunomodulatory(IM): 1.02 and 19.57%; exclusive enteral: 1.02 and 1.09 %; steroids: 19.39 and 0%; mono biologicals: 0 and 10.87%; combinations with 5ASA: 30.61 and 22.83%; with IM: 38.78 and 52.17%; with enteral supplements 12.24 and 6.52%; with steroids: 37.76 and 16.30%; with biologicals 1.02 and 39.13%.

Treatment and growth showed significant associations only for better height z scores and conversely decreasing BMI z scores on mono IM treatment between M6 and M24 (p =0.0221 and p=0.0057).

Individual comparisons at M0 and M24 show that patients with z score for height <2 at M0 do not improve their z score at M24. Patients on mono IM treatment improve their z scores for height at M24 (p=0.0353).

Disease severity at M0 influences therapeutic strategy at M24 only for the prescription of IM treatment as ‘mono’ in patients with mild disease at M0 (p=0.0384) but ‘in combination’ for patients with moderate to severe disease at M0 (p=0.0398). Disease location L3 is inversely related to the prescription of mono IM therapy (p=0.027). Patients with moderate to severe disease at M0 are more likely to be on a combination with biologicals at M24 (p=0.0176). Disease severity at M0 is correlated with a lower z score for BMI (p=0.0116). BMI z score improves significantly at M24 (p=<0.0001).

Conclusion: Disease course is well controlled in the BELCRO cohort as severity scores decrease. Current therapeutic strategy appears satisfactory at M24. Predictors for treatment type are disease severity at presentation. Patients with growth retardation deserve more attention.
“CHARACTERISTICS, GENOTYPES AND CLINICAL OUTCOME OF A COHORT OF CHILDREN WITH VERY EARLY ONSET IBD”
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Objectives and Study: For infants and toddlers presenting with inflammatory bowel disease a diagnostic label is of limited benefit. Infants present with more varied symptoms and histological heterogeneity than children with later onset disease. In 2009 Glocke r et al established that defects in the IL10 pathway can be solely responsible for an IBD-like phenotype in very young children. Early onset of symptoms, high percentage of consanguinity and rapid, severe disease progression supports the probability of an underlying monogenic disorder.

Aim: To describe the characteristics and outcome of a cohort of children with very early onset IBD

Methods: All children with onset of GI symptoms under the age of three years and histological evidence of chronic intestinal inflammation from 1997-2012 were recruited from the GOSH IBD data base. Data was extracted on demographics, clinical presentation, pathology, genetics (IL10L/R, XIAP, FOXP3) and outcome. Children with no known genetic cause identified underwent custom made HaloPlex™ Target Enrichment System or whole exome sequencing.

Results: 39 patients met inclusion criteria (24 boys (62%), median age of onset: 4 months [1-36]). 12 patients (31%) were from consanguineous families. Clinical/histopathological categorization into three groups: CD-like, UC/IC-like, Autoimmune Enteropathy (AIE)-like (15 AIE 38%; 16 CD 41%; 8 IC/UC 21%). 10 underwent bowel resection and ileostomy formation (26%). 21 patients required two or more immunosuppressant agents (54%) and 17 required prolonged parenteral nutrition (44%). 8 genetic diagnoses were established (1 XIAP, 2 IPEX, 5 IL10R/L). 14 patients (36%) were treated with Haematopoietic Stem Cell Transplantation (HSCT) for severe disease progression and treatment failure or following diagnosis of HSCT-responsive disease (IL10 pathway deficiency/IPEX): 11/14 HSCT patients had excellent clinical outcome, 1/14 with protracted disease and 2 deaths from infective complications.

Key features of the subgroup analysis revealed that 14/15 AIE-like patients presented with non-bloody diarrhoea (93%) and the majority required PN (73%). The 16 CD-like patients mostly presented with bloody diarrhoea (81%), 44% required surgery and this group included all 5 children with IL10L/R deficiencies.

Conclusion: This study highlights the heterogeneity and complexity of very early onset IBD. The majority of children remain without genetic diagnosis (80% in our cohort). Establishing a firm diagnosis early in the disease course is important for management and successful outcome.

Disclosure of Interest: None Declared
AZATHIOPRINE AND 6-MERCAPTOPURINE FOR MAINTENANCE OF SURGICALLY-INDUCED REMISSION IN CROHN'S DISEASE: A SYSTEMATIC REVIEW

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Objectives and Study: There is no standard therapy for the prevention of postoperative recurrence or relapse in Crohn's disease (CD). Purine analogues, such as Azathioprine (AZA) and 6-mercaptopurine (6-MP), have been extensively used in the maintenance of remission of Crohn's disease. It is unclear whether AZA/6MP are more effective than other interventions or placebo. We performed a systematic review to investigate the use of AZA/6MP for prevention of post-operative relapses in CD.

Methods: Randomised controlled trials (RCTs), published between 1966 and August 2012, which compared AZA or 6MP with either placebo or other interventions were included. Data sources were MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane inflammatory bowel disease and functional bowel disorders Specialised Register and reference lists of retrieved articles. Data extraction and assessment of methodological quality were performed independently by two reviewers. Data was analysed according to the intention to treat principle.

Results: 5 RCTs met the inclusion criteria. 1 study compared AZA with Placebo (all patients received metronidazole), 3 studies compared AZA with 5-ASA and 1 study compared 6MP with 5-ASA and placebo.

Meta-analysis of 4 studies with 390 participants comparing AZA/6MP with 5-ASA showed no significant difference in rates of relapse (Odds Ratio (OR) 1.49, 95% confidence interval (CI) 0.97 to 2.30). Serious adverse events that required medication to be discontinued were significantly more common in the AZA/6MP groups (OR 2.49, 95% CI 1.38 to 4.50).

An analysis of 3 studies that just compared AZA with 5-ASAs found a statistically significant reduction in relapse in the 5-ASA group (OR 1.86, 95% CI 1.13 to 3.06). There was still a statistically significant higher risk of serious adverse events requiring discontinuation of AZA (OR 3.00, 95% CI 1.46 to 6.06).

Meta-analysis of 2 studies with 168 participants comparing AZA/6MP with placebo showed a significant difference in rates of relapse favouring AZA (OR 0.41, 95% CI 0.20 to 0.85). There was significant clinical and methodological heterogeneity between these two studies, regarding the use of concomitant medications and the choice of purine analogue.

Conclusion: There is some evidence to suggest benefit of AZA/6MP over placebo. There is no evidence that purine analogues have superiority over 5-ASA agents. It appears that 5-ASA agents may be more efficacious than AZA/6MP to maintain remission of CD post-operatively. However, individual studies were small and of varying quality. The side effect profile of AZA/6MP is significantly worse when compared to 5-ASA.

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INTERGENIC SNP BETWEEN SHIP1 AND IL12A IS ASSOCIATED WITH EARLY ONSET COELIAC DISEASE
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Objectives and Study: Coeliac disease (CD) is a systemic autoimmune complex genetic disease. The clinical presentations of CD differ depending on the patients’ age. Children younger than 2-3 years of age in most cases suffer from the classical CD, whereas children older than 8-9 years and adults usually suffer from the atypical CD. The pathomechanism of this diversity remains unknown. The most important and best-understood genetic risk factors are HLA-DQ2 and HLA-DQ8 molecules. Recent large scale genome wide association studies confirmed strong association to HLA and revealed further 57 non-HLA loci, within 39 distinct regions, to contribute to CD. In this study for the first time we correlate the genetic background with the age of onset of coeliac disease.

Methods: We analyzed 57 single nucleotide polymorphisms (SNPs) previously found to be associated with CD, as well as all DQ2 and DQ8 haplotypes in two age groups, early onset (621 children diagnosed with CD below 3 years of age) and late onset (6674 children and adults diagnosed after age of 12 years). Patients originated from five European countries (Polish, Spanish, British, Dutch and Italian). Data were analyzed using a Cochran-Mantel-Haenszel test with clustering for populations in PLINK (v.1.07, 2009) and for HLA analysis we used stepwise logistic regression in SPSS (v.15.0.1, 2006). For robustness of our approach additional analysis using bootstrap method was performed.

Results: All together 7295 patients with CD were included in the analysis. We found significant association for three SNPs: rs76830965 in an intergenic region between SCHIP1 and IL12A (p=0.00108, OR=1.42), rs990171 within IL18R1/IL18RAP region (p=0.0034, OR=1.3) and rs61579022 within intron 10 of ARHGAP31 gene (p=0.0145, OR=0.81). Using bootstrap we established strong association of the SCHIP1 and IL12A (p= 0.000027, OR=1.98) loci with early onset of CD. We found two haplotypes within HLA region, DQ2.2/DQ2.2 and DQ2.2/DQx, that associated with early onset of CD (p=0.02, OR=2.90 and p=0.000001; OR=2.47, respectively).

Conclusion: Here we report that the genetic background vary between early and late onset of CD. We show that of the 39 previously established loci, three have an effect on the age of onset, including SCHIP1/IL12A where associated SNP increases by almost two times the risk of developing CD below 3 years of age.

Disclosure of Interest: None Declared
INTERPLAY BETWEEN TYPE-1 IFNS AND IL-15 IN THE CONTEXT OF CELIAC DISEASE

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Objectives and Study: Celiac disease (CD) is characterized by a gluten specific T cell response in the lamina propria (LP) and an expansion of activated intraepithelial lymphocytes (IEL) in the small intestinal mucosa. IL15 is involved in the induction of both responses, nevertheless an aberrant up-regulation of IL15 alone is not sufficient to trigger CD and other factors may contribute to its development.

Type-1 IFNs are cytokines induced upon viral infections. Intriguingly, genetic risk factors related to viral responses were shown to be associated with CD by GWAS and viral infections were found to promote CD. Moreover long-term recombinant IFN-α and IFN-b treatments have been reported to elicit the development of CD in few subjects. Furthermore, an increase in IFN-α transcripts in active CD biopsies has been shown. All together these observations suggest a potential role of Type-1 IFNs in the pathogenesis of CD. Our hypothesis is that Type-1 IFNs could substitute or act synergistically with IL15 to induce CD development.

Methods: IL15 and MxA (a protein specifically induced upon type-1 IFNs signaling) immunohistochemistry (IHC) staining was performed on duodenal paraffin-embedded sections from 43 active CD patients and 9 Controls (CTR). RNA was isolated from whole biopsies from at least 20 CD and 20 CTR; real time qPCR (Taqman) was performed for the following genes: Mx1, IFN-α, IFN-β.

Results: IHC data showed that MxA expression is significantly increased both in the epithelium (EP) and in LP of CD patients. In particular 51% of active CD patients had high MxA levels in the LP (70% of whom were IL15 negative) vs 20% of controls. Increased MxA expression was observed in the EP of 58% of active CD patients (60% of whom were IL15 negative) vs only 11% of controls (p=0.01). Moreover high levels of Mx-1, IFN-a and IFN-b transcripts (qPCR data) were found in patients with active CD compared to CTR (p<0.01). Functionally, we showed that Type-1 IFNs are able to induce lymphokine activated killer activity in IEL from active CD patients in a dose-dependent manner. Preliminary data show that IFN-b oral feeding can promote the loss of oral tolerance in wild type mice.

Conclusion: These results allow us to infer that the EP and the LP cells are likely to be important targets of type-1 IFNs signaling in CD. A better understanding of the different pathways involved in CD pathogenesis will allow us to categorize patients based on IL-15 and MxA expression to establish individualized therapies for CD patients.

Disclosure of Interest: None Declared
Objectives and Study: Coeliac Disease (CD) is a chronic inflammatory disease caused by the immunological response to the oral ingestion of dietary gluten, a protein found in wheat, rye and barley in genetically susceptible individuals. Differences in gut microbiota populations, diversity and metabolic activity have been identified in previous studies in people with CD (Collado, Calabuig et al. 2007) compared to healthy controls but the evidence is contradictory and it is not clear whether these changes have a causative role in the pathogenesis of the disease or are the result of the latter.

Methods: 38 treated CD (mean age 9.5 y, range 2-18 y), 14 healthy siblings of children with CD (mean age 9.1 y, 2-14 y) and 18 healthy controls (HC), (mean age 5.8y, 2-10 y). Faecal samples were collected, stabilised with 1M NaOH and stored at -20°C within 6 hours of passage. Samples were freeze dried and SCFA (C2-C8 and BCFA iC4, iC5, iC6) were analysed by gas-liquid chromatography. Disease activity was assessed by Immunoglobulin a tissue transglutaminase measured by ELISA.

Results: There was a significant difference between the median level of SCFAs in CD children compared to siblings and HC. The median concentrations (µmol/g) of acetic acid (137.51±59.33 vs 102.02±36.42 vs 127.37±60.23, p<0.001), butyric acid (54.16±38.17 vs 43.15±23.08 vs 84.85±52.42, p=0.003), n-valeric (10.39±4.90 vs 18.21±5.65 vs 18.77±6.27, p<0.001), n-caproic (2.41±2.08 vs 9.33±6.77 vs 7.30±6.27, p<0.001), enanthic acid (0.14±0.53 vs 0.38±0.96 vs 0, p=0.034), caprylic acid (2.38±3.32 vs 0.76±4.02 vs 8.31±19.58, p=0.006) iso-butyric (9.26±4.60, 15.51±3.99, 16.54±4.62, p<0.001) and iso-valeric (12.34±7.42, 23.46±6.95, 25.23±4.62, p<0.001) per dry faecal material were all significantly lower in the CD children than siblings and HC. There was no correlation in the levels of individual or total SCFAs and age of subject in all groups. No correlation was seen between the duration of treatment or disease activity and SCFA levels in CD patients.

Conclusion: Children with CD have an altered faecal profile of SCFAs than siblings and HC. The variations in SCFA production may be indicative of altered microbiota profile and activity in children CD. Genetic influences in faecal SCFA content can be eliminated as siblings had similar SCFA to HC. Variation in diet, particularly low intakes non-digestible carbohydrates subjected to CD patients on a gluten free diet, along with persistent intestinal inflammation and malabsorption may be factors influencing the SCFA profiles observed.


Disclosure of Interest: None Declared
MICROBIOTA PROFILING IN HEALTHY CHILDREN: ANALYSIS OF SHORT-TERM AND MEDIUM-TERM STABILITY AS MEASURED WITH IS-PRO

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Objectives and Study: The intestinal microbiota is considered to have major functions in maintaining human health, including nutrient digestion, protection against pathogens, stimulation of angiogenesis and regulation of host metabolism and immune system. The study of the role of microbiota in paediatric diseases such as allergy and IBD requires better insight into the composition and stability of the intestinal microbiota in healthy children. The aim of this observational study is to analyse and describe the composition of the intestinal microbiota of 60 healthy children in time. Studies concerning stability of intestinal microbiome in children between 2 years of age and adulthood is lacking. In view of the fact that the intestinal microbiota composition in healthy adults remains stable in time, we hypothesised that the intestinal microbiota in healthy children show a stable pattern as well.

Methods: Sixty healthy children collected faecal samples once weekly for 6 weeks. 10 children collected an additional sample after 3 months. All samples are analysed by IS-pro, a recently validated PCR-based, high-throughput profiling technique, providing virtually complete insight in the composition of the human intestinal microbiota. Identification is possible both at the level of the main phyla (Firmicutes, Bacteriodetes, Acinobacteria and Proteobacteria) as well as on species level. For each phylum, we analysed the correlations between succeeding samples.

Results: So far, samples of 6 children have been analysed (mean 9,6 years, range 5,3-15,2), showing variable results for the stability of the three main phyla. Firmicutes seem to remain relatively stable over the period of 6 weeks, with R median 0,64, Q1 0,49 and Q3 0,73. Bacteriodetes remained stable, with R median 0,82, Q1 0,71 and Q3 0,87. Proteobacteria, however, showed considerable variation over time. Short-term results of all 60 children and results on medium-term stability of 10 children will be presented at the congress.

Conclusion: IS-pro is a recently validated, PCR-based high throughput profiling method providing unrestricted insight in the highly complex composition of intestinal microbiota. First results of our study investigating short-term stability of microbiota composition in healthy children suggest that composition of the phyla Firmicutes and Bacteriodetes remain stable in time, Proteobacteria show a more variable pattern.


Disclosure of Interest: None Declared
IDENTIFYING INCIDENCE OF INHERITED METABOLIC DISORDERS IN PATIENTS WITH INFANTILE LIVER DISEASE

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Objectives and Study: The incidence of liver disease due to rare inherited metabolic disorders, including Niemann Pick type C (NPC), Citrin Deficiency (CD) and Progressive Familial Intrahepatic Cholestasis (PFIC), is unknown. New sequencing methods, including next generation sequencing (NGS), permit analysis of multiple genes simultaneously, reducing time to molecular diagnosis and cost. Accurate timely diagnosis is essential to optimise clinical management, improve targeted therapy for liver disease in infants, and avoid inappropriate liver transplantation. To identify the incidence of inherited metabolic disorders, in patients with infantile liver disease, and make this molecular information available early on in the diagnostic pathway.

Methods: A prospective study from 13 centres worldwide recruiting infants under 2 years presenting with cholestasis, acute liver failure or splenomegaly, using targeted NGS, for mutations in 6 genes (NPC1, NPC 2, ATP8B1, ABCB11, ABCB4 (PFIC 1-3), and SLC24A13 (CD)).

Results: 204 patients have been recruited, and DNA sequenced in 87. Of those sequenced 66 presented with cholestasis, 12 acute liver failure, 7 isolated splenomegaly, 19 isolated hepatomegaly and 24 hepatosplenomegaly. Diagnosis was confirmed (homozygous, or compound heterozygous, pathogenic mutations) in 9 patients (10%): NPC1 (1); PFIC1 (ATP8B1) (2); PFIC2 (ABCB11) (3); PFIC3 (ABCB4) (2); and in 1 patient two pathogenic mutations were identified in both PFIC1 and PFIC3 causing genes (ATP8B1/ABCB4). 4 patients had single heterozygous pathogenic mutation identified. 29 variants of unknown significance were detected. There were no mutations detected in 55 of the 87 tested. Of these patients 12 had idiopathic cholestasis, 7 biliary atresia, 7 neonatal hepatitis, and 3 congenital cytomegalovirus infection.

Conclusion: Summary: This unique study has recruited 204 patients with infantile liver disease, and successfully sequenced DNA in 87. Genetic diagnosis was confirmed in 9 patients, and a heterozygous pathogenic mutation in a further 4. 29 novel variants were detected, of currently unknown pathogenicity. There were no mutations detected in 55/87 sequenced.

Discussion/Conclusion: These data show promising results for this sequencing method as a screening tool. Further analysis will allow us to establish the true prevalence of these disorders among patients with infantile liver disease, correlation between phenotypes and genotypes and clarify clinical indications for screening for these disorders.

Disclosure of Interest: None Declared
NATURAL HISTORY OF EARLY ONSET LYSOSOMAL ACID LIPASE (LAL) DEFICIENCY (WOLMAN DISEASE)
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Objectives and Study: Lysosomal Acid Lipase (LAL) Deficiency is a rare autosomal recessive disorder caused by mutations in the gene encoding a key enzyme responsible for lysosomal processing of cholesteryl esters and triglycerides. Markedly reduced LAL activity leads to the early onset form of LAL Deficiency also called Wolman disease, a progressive disorder which manifests in the first few months of life and leads to death usually before the child’s 1st birthday. These patients typically develop malabsorption, hepatosplenomegaly, liver failure, adrenal calcifications, cytopenias, and growth failure due to the accumulation of lysosomal lipids in tissues. Case reports describing the hallmark features of Wolman Disease have been published, but no systematic study of this phenotype has been undertaken. This is the first natural history study of a large group of patients with early onset LAL Deficiency.

Methods: Demographic and clinical information on patients with Wolman disease were collected utilizing clinical chart data abstractions and summarized to date from this ongoing study.

Results: This report includes 19 patients (12 males, 7 females) with Wolman disease defined by growth failure by 6 months of age. Thirteen of the 19 patients (68%) were from Europe and 10 patients of the 19 were Caucasian. The median age (range) at first symptom, at diagnosis, and at death were 1.00 month (0.23 – 3.0), 2.17 months (1.05 - 7.07), and 3.44 months (1.45 – 37.37), respectively. Six of these patients had hematopoietic stem cell (n=5) or liver transplants. Excluding these 6 patients, the median age (range) of death was 2.95 months (1.45 – 5.72). Of the 6 transplanted patients, 5 died before 9 months of age, while the 6th, the liver transplant recipient, died at 37.4 months. Six out of 18 patients (33%) did not have adrenal calcifications.

Conclusion: Early onset LAL Deficiency/Wolman disease is a rare inherited metabolic disease with a rapidly progressive clinical course and nearly universal mortality during the first year of life.

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BONE MINERALIZATION IN OBESE CHILDREN AND ADOLESCENTS WITH NONALCOHOLIC FATTY LIVER DISEASE
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Objectives and Study: Nonalcoholic fatty liver disease (NAFLD) has been recently suggested as a cause of low bone mineral density (BMD) in obese children. However, mechanisms explaining these relations are not completely understood. Obesity-induced chronic inflammation, a key component in the pathogenesis of insulin resistance and NAFLD, may negatively influence bone health. Thus we examined the associations of adipose-secreted molecules (leptin and adiponectin) and high-sensitivity C reactive protein (HSCRP) levels with BMD in a group of obese children and adolescents with NAFLD.

Methods: Ninety obese [body mass index (BMI) above the 95th percentile for age and gender] children [50 boys and 40 girls; mean age 12.5 (SD 1.8) years] were included in the study. According to the threshold of 5% for hepatic fat fraction (WJG 2011;17: 3012-3019) as established by hepatic Magnetic Resonance Imaging, NAFLD was identified in 44 of the 90 obese children. Whole body (WB) and lumbar spine (LS) BMD were assessed by dual energy X-ray absorptiometry. BMD Z-scores were calculated using race and gender specific LMS curves (JCEM 2011;96:3160-3169).

Results: Children with and without NAFLD did not differ with respect to gender, age, pubertal status, and BMI-SD score. Children with NAFLD had significantly higher fasting insulin and HOMA-IR (Homeostasis model assessment of insulin resistance) values, and HSCRP levels, but lower adiponectin values. The two groups did not differ in leptin concentrations. Children with NAFLD had a significantly lower LS BMD z-score than those without NAFLD [mean, 0.55 (95% confidence intervals, 0.23-0.86) vs 1.29 (0.94-1.63); P< 0.01]. WB BMD z-score was also decreased in children with NAFLD compared to those without liver involvement, though borderline significance was observed (P= 0.06). In univariate analysis, NAFLD, alanine aminotransferase and HSCRP concentrations were identified as variables that correlated negatively with LS BMD z-score, while BMI and leptin were positively associated with BMD. After including in the model all the significant variables, NAFLD remained significantly and independently associated with LS BMD z-score (standardized beta coefficient, -0.272; P <0.01), along with HSCRP.

Conclusion: This study reveals that NAFLD is associated with low BMD in obese children and adolescents, and that systemic, low-grade inflammation may play a role in such association independently of adiposity.

Disclosure of Interest: None Declared
EXCHANGEABLE COPPER: A NEW PROMISING BIOMARKER FOR THE DIAGNOSIS OF WILSON'S DISEASE (WD)

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Objectives and Study: Background: WD diagnosis can be challenging and is based on several clinical and biological features. Measuring of the serum exchangeable copper (CuEXC) seems to be a promising tool. A recent preliminary study showed that relative exchangeable copper (REC), defined by ratio CuEXC / Total serum copper (CuT), > 18.5% had a sensitivity (Se) and a specificity (Sp) of 100% for the diagnosis of WD. To date, there is no data regarding exchangeable copper levels in cohorts of patients suffering from hepatic (non wilsonian) diseases.

Methods: Aim and Methods:
The aim of our study is to determine the sensitivity and specificity of REC for the diagnosis of WD among a group of patients suffering of WD at diagnosis or who fail to respond to treatment (group 1, n=6), a group of Wilsonian patients on stable condition with medical treatment (group 2, n=31), and 2 groups of patients followed for non wilsonian hepatic diseases in an adult hepatology unit (group 3, n=46) and a pediatric hepatology unit (group 4, n=25). Measuring of ceruloplasminemia (Cp), CuEXC and CuT levels was performed for all patients.

Results:
Underlying diseases of the non wilsonian patients were as followed. In group 3: ASH (n=8), NASH (n=11), HCV (n=7 with one HIV-HVC coinfected), HBV (n=8), cryptogenetic (n=8), miscellaneous (n=4). In group 4: HCV (n=5), HBV (n=3), Biliary atresia (n=4), AIH (n=1), cryptogenetic (n=7 with one fulminant hepatitis), miscellaneous (n=5). Six patients of group 3 and two of group 4 had a Cp <0.16g/L, whereas one patient of group 2 had a Cp=0.19 g/L. Exchangeable copper level (N : 39-73 µg/L) was significantly higher in group 1 (mean 142 +/- 43 µg/L) compared to the other three groups: group 2 = 48 +/- 18 µg/L, group 3 = 66 +/- 19 µg/L, group 4 = 63 +/- 16 µg/L (p<0.05). REC >18.5% had a Se/Sp of 100% for the diagnosis of WD (group 1 vs groups 3 and 4). REC>14% had a Se/Sp of 100% for all wilsonian patients (groups 1 and 2 vs groups 3 and 4)

Conclusion: Conclusion:
Our study confirms that exchangeable copper and particularly the determination of REC is a highly valuable tool for the diagnosis of WD.

Disclosure of Interest: None Declared
HUMAN ADULT LIVER PROGENITOR CELLS (HALPCs) IS A PROMISING TOOL TO RESTORE PEROXISOMAL DYSFUNCTION AS INFANTILE REFSUM’S DISEASE.
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Objectives and Study: Infantile Refsum’s disease is a peroxisome dysfunction caused by peroxisomal biogenesis/assembly defect. This liver metabolic disease leads to phytic acid accumulation in plasma and severe neurologic disorders. At this time, orthotopic liver transplantation is the gold standard treatment to restore this metabolic liver disease but is limited by the cost, surgery complications and organ shortage. Recently, human Adult Liver Progenitor Cells (hALPCs) isolated from parenchymal liver fraction has demonstrated similar phenotypic characteristics to hepatomesenchymal cells including expression of CD73, CD90, CD105 but also ASMA and albumin. We also previously demonstrated the acquisition of hepatic functions when submitted to hepatogenic differentiation medium (urea synthesis, CYP3A4 activity and Glucose 6 Phosphatase activity). Objective: The aim of this study was to investigate the ability of hALPCs to metabolize phytic acid and to compare with hepatocytes.

Methods: Phytanic content measured by Gaz Chromatography analysis was performed using supernatant from undifferenciated/differenciated hALPCs and hepatocytes, both incubated with 1µM phytanic acid for 24 hours. As negative control, hepatocytes from Infantile Refsum’s patient were used in this study.

Results: After 24 hours incubation with 1µM phytic acid, we observed an important decrease of phytic acid concentration in cell culture supernatants from 1µM to 0.4µM and 0.16 µM with respectively hALPCs and hepatocytes. We also demonstrated higher decrease in phytic acid concentration from 1µM to 0.06µM after differentiation of hALPCs into hepatocyte-like cells. No decrease in phytic acid concentration was noted using hepatocyte culture supernatant from Infantile Refsum's patient. To exclude spontaneous degradation of phytic acid in IMDM, we also measured phytic acid concentration using same protocol but in absence of cells.

Conclusion: hALPCs isolated from parenchymal liver fraction and in vitro expanded are able to metabolize phytic acid and could thus represent an attractive alternative to orthotopic liver transplant to restore metabolic function as peroxisomal disorders.

Disclosure of Interest: None Declared
CAN TAUROLIDINE-BASED CATHETER LOCKS REDUCE CENTRAL VENOUS CATHETER RELATED BLOOD STREAM INFECTIONS IN CHILDREN ON LONG-TERM HOME PARENTERAL NUTRITION?

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Objectives and Study: The objective of the study was to compare the incidence and characterise the type of catheter-related blood stream infections (CRBSIs) in children with intestinal failure on long-term home parenteral nutrition (PN), using heparin-saline based catheter locks versus those using taurolidine-based catheter locks.

There is growing body of evidence that taurolidine-based catheter locks, which have a broad-spectrum antimicrobial and antifungal action, is associated with a decreased incidence of CRBSIs children on home PN.

Methods: All children referred to a tertiary paediatric gastroenterology service with temporary or on-going intestinal failure requiring long-term PN or preparation for home PN between 2005 and 2011 were identified and included. Central venous catheters were all tunnelled Hickmann catheters aseptically inserted either surgically or radiologically. All children were given a single bag system of PN with each infusion. Parents were formally trained in aseptic techniques to connect and disconnect the PN transfusion. Parents were then taught to instil heparin-saline or taurolidine-based (TauroLock™) solution into the catheter after completion of each PN infusion.

CRBSIs were defined as a laboratory-confirmed blood stream infection from with a peripheral or central venous sample. Results were excluded if evidence that the source of infection was from a second site. All blood cultures results were confirmed through the microbiology database and clinical records.

Research ethics committee approval was sought, but ethical review was not deemed necessary.

Results: 32 children (18 boys, 14 girls) were identified who required PN for intestinal failure for combined total of over 12,500 PN days. 9 children had no positive blood cultures. There were 126 positive blood cultures (27 organisms isolated) in the remaining 23 children. Of the 21 children who used a heparin-saline based catheter lock, 86% had one or more CRBSI. 11 children used a taurolidine-based catheter lock, with only 45% having one or more CRBSI.

Conclusion: There was a significant reduction in the incidence of CRBSIs in those children using taurolidine-based catheter locks (TauroLock™) compared to heparin locks. There was an absolute risk reduction of 40.3% (95% CI 7.25 – 73.3%) with a numbers needed to treat (NNT) of 3 (95% CI 1.4-13.8). The use of taurolidine locks on all children on long-term home PN could both reduce morbidity and morality, and have a significant impact on the associated costs of CRBSIs. Taurolidine-based catheter locks should be considered for all children on long-term PN.

Disclosure of Interest: None Declared
FINANCIAL IMPACT OF TAUROLIDINE-CITRATE LOCK SOLUTION (TAUROLOCK®) DURING LONG TERM PARENTERAL NUTRITION

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Objectives and Study: Evidence suggests that use of Taurolidine-citrate lock solution (Taurolock®) has a major impact on central venous catheter (CVC) related blood stream infection (CRBSI) during long term parenteral nutrition (PN); Taurolock® may also prevent catheter occlusion. The aim of this study was to evaluate the cost implications of using Taurolock® in a group of PN-dependant patients.

Methods: Out of 16 home PN patients, five received daily Taurolock® because of previous recurrent CVC sepsis, and one because of frequent CVC occlusion necessitating catheter replacements. A retrospective case note review identified the number of CRBSI/1000 catheter days and the number of CVC changes. Based on projections from pre-Taurolock® experience, we estimated the theoretical cost savings from reduced hospital admissions and antibiotic usage observed in our patients over one year post-Taurolock®.

Results: 13,028 catheter days (8371 pre- and 4657 post- Taurolock®) were evaluated. Pre-Taurolock®, CRBSI/1000 catheter days for patients 1 - 6 were 0, 0.87, 4.4, 5.26, 8.7, and 10.9; post-Taurolock®, there were no episodes of CRBSI. In 2 patients with recurrent CVC occlusion, patency was maintained during Taurolock® use. The total number of antibiotic days one year pre-Taurolock® was 387 and one year after the introduction of Taurolock® had reduced to 79. The number of inpatient hospital days pre-Taurolock® was 816 (approximate cost £489108) and one year post-Taurolock® 136 (approximate cost £68000). Expenditure on antibiotic treatment for CRBSI pre-Taurolock® was £14088 compared with £2146 post-Taurolock®. The total expenditure (antibiotics, hospital in patient stay and Taurolock®) was calculated as £503196 pre- and £94236 post-Taurolock®, representing a total cost saving of £408960. No adverse effects related to use of Taurolock® were seen.

Conclusion: The use of Taurolock® during cyclical PN was associated with a dramatic reduction in CVC sepsis rates in a small group of children with long term PN dependency. Taurolock® also appeared to lower the rate of CVC occlusion. The reduction in sepsis has large cost saving implications for the National Health Service, and if used widely, Taurolock® might reduce intestinal failure associated liver disease, venous thrombosis and need for intestinal transplantation.

Disclosure of Interest: None Declared
LONG TERM INTESTINAL FAILURE AND HOME PARENTERAL NUTRITION IN CHILDREN: CHANGES AND PERSPECTIVES

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Objectives and Study: The aim of the study was to focus on the children discharged on Home Parenteral Nutrition (HPN) for underlying primary digestive disease (PDD) over the 2000-2010 decade, and to compare their outcomes and prognosis factors for weaning off PN.

Methods: Retrospective study of the medical data of 251 patients on HPN between 01.01.00 and 31.12.09, and comparison with the reference group of children on HPN between 1980-2000 in the same center, including survival and disease outcome. Statistical analysis was performed with Cox model (R-Software) and Kaplan Meier curves for survival. The patients with non primary digestive disease and those patients who need HPN for the second time in life were excluded of the study.

Results: 151 patients with PDD received HPN during the period, and 2/3 of them for a short bowel syndrome (SBS) including 6 Hirschsprung’s disease. Other subgroups were: motility disorders (MD) (11%), congenital mucosal disorders (CMD) (9%), inflammatory bowel diseases (9%) and others (5%). Probability of weaning off PN was 73% the patients of the whole cohort, and also for the SBS group. The survival, close to 100%, was the most dramatical improvement compared to the 1980-2000 period, and no liver failure associated with HPN caused death. In the SBS group, 9% of the patients underwent transplantation (intestinal +/- associated liver). The residual bowel length (over 40cm), the presence of the ileo-caecal valve (ICV) and more than 50% of the colon, but also the daily caloric PN intakes (over 70% of the needs) were prognosis factors for the univariate analysis, whereas in the multivariate, only the bowel length was a (very significant) prognosis factor (p<0.001). For the whole cohort, including all PDD, the median duration until weaning off was 21 months. MD and CMD appear as poor prognosis factors for weaning off in both statistical analysis (p= 0.048 and p= 0.002).

Conclusion: HPN appears as safe treatment of intestinal failure in children. Very long HPN could be an alternative to intestinal transplantation. However the statistical analysis highlighted risk subgroups for definitive intestinal failure : SBS < 40 cm, MD and CMD. This perspective should lead to a multidisciplinary evaluation in a reference care center.


Disclosure of Interest: None Declared
Objective and Study: Maternal obesity in early pregnancy increases risk of childhood overweight and obesity, likely through genetic and pre- and postnatal environment factors. Breastfeeding represents the gold standard for infant health and formulas are being developed to mimic the physiological response to human milk intake. High protein intake observed with infant formula feeding, in excess of metabolic requirements, may predispose to increased obesity risk in later life. The study investigated the effect of low (LF) or high (HF) protein formula (LF 1.5 g/100 kcal, HF 2.4 g / 100 kcal) on the metabolism of term infants from overweight and obese mothers.

Methods: The study is a double blind, controlled, randomized, single site clinical trial of 2 parallel groups (LF/HF, n=64 each) with a breastfeeding group (n=56) as reference. From birth to 3 months, infants received exclusive breast feeding or starter formula (1.8 g protein /100 kcal). From 3 to 6 months, infants received exclusive assigned study formula (LF or HF) or breast-feeding. From 6 to 12 months, infants received mixed feeding. Metabonomic using 1H NMR spectroscopy was conducted on urines and stools collected at the age of 3, 6 and 12 months.

Results: Infants receiving any formula had higher faecal concentrations of short chain fatty acids (SCFAs, propionate, butyrate, acetate, 5-amino-valerate) and free amino acids. The changes in faecal SCFAs were correlated with urinary metabolites suggesting a functional link between bacterial processing of dietary protein and host amino acid/protein metabolism. A dose dependent metabolic response was observed according to the protein content in formula fed infants, which were still metabolically very different from breast-fed infants. Changes in lipid metabolism were highlighted in formula fed infants, suggesting different β-fatty acid oxidation, ketogenesis, and ω-oxidation. Additional differences in the concentrations of intermediates in the NAD pathway suggest modulation of energy production associated to differential protein/lipid metabolism.

Conclusion: Non-invasive application of metabolomics to urine and stool profiling enables the monitoring of the metabolic response and nutritional requirements of infants receiving different types of feeding during the first year of life. The development of system biology approaches in neonatology will subsequently lead to novel mechanistic hypotheses that could be targeted with new nutritional personalized concepts.

Disclosure of Interest: F.-P. Martin Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, I. Montoliu Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, S. Collino Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, L. Da Silva Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, S. Moco Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, J. Inostroza Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, R. Prieto Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula, P. Steenhout Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula.
commercializes infant formula, J. Inostroza : None Declared, R. Prieto : None Declared, P. Steenhout Industry of: Nestec SA, part of the Nestlé Food and Beverage Company that commercializes infant formula
INFANT FORMULA COMPOSITION AFFECTS ENERGETIC EFFICIENCY FOR GROWTH: A RANDOMIZED CONTROLLED TRIAL
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Objectives and Study: Protein source, macronutrient composition and content of long chain polyunsaturated fatty acids (LC-PUFA) of infant formulae may influence infant growth. We aimed to assess the effect of a modified infant formula on growth.

Methods: Healthy term infants were randomly allocated to one of two isocaloric (67 kcal/100 mL) study formulae during the first month of life. Infants received a protein reduced formula (IF, 1.89 g protein/100 kcal) containing alpha-lactalbumin (ALAB) and LC-PUFA (10.7 mg arachidonic and 10.7 mg docosahexaenoic acid/100 kcal) or a control formula (CF) providing 2.30 g protein/100 kcal, standard whey and no LC-PUFA. Infants were fed with study formulae from postnatal age of 30 until 120 days. A group of breastfed infants served as a reference. Anthropometry and dietary intake were assessed at the ages of 30, 60, 90 and 120 days. A venous blood sample was obtained on day 120.

Results: Of the 107 infants randomized to IF and 106 to CF, 85 and 82, respectively, completed the study according to protocol. The subjects in both formula groups were similar in birth anthropometrics and demographic data. Both formulae were well accepted without significant differences in health related observations. Weight gain was not statistically different between formula groups (IF: 30.2 ± 6.3 vs. CF: 28.3 ± 6.5 g/day, mean ± SD, P=0.06). Length gain was significantly higher in IF (0.11 ± 0.02 vs. 0.10 ± 0.02 cm/day, P=0.02), while head circumference gain was not different. Non randomized breastfed infants had a weight gain of 26.7 ± 6.4 g/day and length gain of 0.10 ± 0.02 cm/day. Energy intake from formula was higher in CF at 90 and 120 days (IF: 509 ± 117 and 528 ± 123 vs. CF: 569 ± 152 and 617 ± 169 kcal/day, P<0.01). Protein intake in CF was significantly higher at each assessment. Growth per energy intake was higher in IF compared to CF for weight (6.45 ± 2.01 vs. 5.67 ± 2.21 g/100 kcal, P=0.02) and length (0.23 ± 0.08 vs. 0.20 ± 0.08 mm/100 kcal, P=0.04). While the concentration of 14 amino acids differed significantly between groups, blood urea and albumin did not differ. Plasma arachidonic acid and docosahexaenoic acid percentages were significantly higher in IF infants but did not correlate with weight and length gain.

Conclusion: We consider the increased energetic efficiency of the new infant formula, in spite of the lower protein content, to result from improved protein composition by added ALAB, whereas a relevant contribution of LC-PUFA seems less likely. Although both formulae appear safe in respect to infant growth, apparently minor differences in composition can markedly affect energetic efficiency for growth. Thus, a major modification of infant formula composition should be generally evaluated by a growth study.

Disclosure of Interest: None Declared
DOES GENETIC SENSITIVITY TO BITTER TASTE INFLUENCE BODY WEIGHT IN CHILDREN?

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**Objectives and Study:** Genetic predispositions to food preferences may be of great importance to the health status, particularly in children, where the innate tasting sensitivity has a strong influence on the feeding behaviour. 6-propyl-2-thiouracil (PROP) sensitivity, genetically mediated by the bitter receptor TAS2R38, has been considered as a general marker of taste acuity able to influence food selection and body weight, but the relationship with dietary habits is still conflicting.

The aim of this study is to refine the role of TAS2R38 and Gustin, a taste buds trophic factor, on taste perception and food preferences, specially in children with high BMI, where a controversial association between obesity and PROP responsivity has been documented.

**Methods:** Bitter perception of 373 children, including 99 mildly or severe obese kids and 439 adults was assessed by means of PROP suprathreshold test; allelic variations in TAS2R38 and Gustin genes were determined on genomic DNA collected from saliva; food preferences were recorded through a food frequency questionnaire investigating the weekly consumption of vegetables and legumes.

**Results:** The allelic variants of the TAS2R38 receptor predict well the taste phenotype, explaining from 60 to 80% of the trait variance, whereas the polymorphism of Gustin gene seems not to be associated with any specific taste phenotype. A significant relationship was found between PROP sensitivity and age, with a progressive increase of responsivity from infants to adolescents and a progressive decrease with age in adults, without gender discrepancies. Regarding the food selection, no significant differences in bitter or non-bitter vegetables intake was found according to tasting phenotype or diplotype. The vegetables consumption increases with age among children and between child and mother, irrespective of the PROP phenotype. Taste acuity is very similar among normal weight and obese children, but the latter group appear to consume more non bitter vegetables if PROP sensitive (tasters) or hypersensitive (supertasters), compared to the same phenotype in the non-obese ones.

**Conclusion:** PROP sensitivity in children is strongly age-related, increasing from infants to adolescents, but no effect on food preferences was observed according to taste phenotype or genotype. No differences of taste acuity were observed among normal weight and obese children, but in obese children PROP sensitivity appears to be associated to increased vegetables consumption. Overall these data suggest that we would not expect a direct effect of PROP sensitivity on food preferences or adiposity: many factors, genetic and environmental, as the sociocultural context or the eating environment, can mediate the acceptance or rejection of food in childhood, in addition to taste.

**Disclosure of Interest:** None Declared
TWO YEARS RESULTS AFTER LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING “LAGB” IN ADOLESCENTS: THE FRENCH EXPERIENCE.

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Objectives and Study: Because the success rate of lifestyle interventions is modest in severely obese adolescents, surgical treatments are now proposed. LAGB represents an attractive treatment with minimal morbidity and reversible procedure.

Since 2008 bariatric surgery is considered for adolescents with severe obesity enrolled in multidisciplinary program after failed one year lifestyle intervention at least.

Methods: All adolescents were included in prospective longitudinal data collection.

Patients undergo an initial screening process for medical, social and psychiatric history then these evaluations were repeated at 6, 12 and 24 months. The technique of AGB was by "pars flaccida dissection" in all patient.

Results: 26 patients have undergone LAGB, the mean age was 16.6 ± 0.9 years. Pre operative body mass index (BMI) was 45.8±5.7.

Base line comorbidities data demonstrated a high incidence of insulin resistance (IR), and 75% of metabolic syndrome.

The group had 21 months of follow up (range 1-51 months) and an average of 14 visits in the first year for behavioural and nutritional assessment.

Thirteen patients (50% of all patients) had more than two years follow up (range 28-51 months).

At two years mean weight loss was 43 ± 14.4 kg corresponding to mean excess weight loss (EWL) of 74.8± 14.3 %.

The BMI decreased below 35 in all patients ( 29.7±2.5).

An improvement in metabolic status was demonstrated (with HOMA-IR decreasing from 5.55±3.5 to 1.94±0.92, p< 0.005).

Three of them were considered as a failure (failure rate of 23%),

The gastric band was removed in one patient due to a band slippage (after 1 year), and 2 patients had failure of weight loss (36 and 37 % of EWL after 24 and 48 months respectively).

Conclusion: At two years, 77% of patients have successful bariatric results (EWL>50%).

LAGB is a restrictive procedure, who requires a high degree of patient cooperation and professional support. However this technique appears to be a primary choice for bariatric surgical procedure in adolescents on the basis of its good weight loss, with low complication rate, and potential reversibility.

Disclosure of Interest: None Declared
RETROSPECTIVE SPANISH MULTICENTRIC STUDY TO VALIDATE THE ESPGHAN 2012 COELIAC DISEASE DIAGNOSTIC CRITERIA


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Objectives and Study: The main objective is to determine whether in certain circumstances a diagnosis of celiac disease (CD) can be safely established without performing a small bowel biopsy (SBB), as proposed in the new ESPGHAN guidelines 2012 which establishes that the SBB could be avoided in HLA DQ2/DQ8 symptomatic patients with positive endomysial antibodies (EMA) and anti-transglutaminase antibodies (TTG) whenever the title is 10 times the upper limit of normal (TTG> 10xULN). Besides challenge is not longer recommended to be mandatory in all cases with a SBB performed before the age of 2 at the time of diagnosis.

Methods: Histological, serologic, clinical and genetic data were retrospectively collected in paediatric patients with a SBB performed between the years 2000 to 2009 and a minimum follow-up period of 2 years. Same data were collected from all children who underwent a gluten challenge.

Results: 33 centres and 12 regions were involved, 16 of them contributing with more than 60 cases each. 2647 patients were included, with 440 (16.7%) children under 2 years at the 1st SBB. In 95.9% of the cases (2537 patients) a CD diagnosis was firmly established, the remaining patients (4.1%) are non CD or unclear cases. In 845 patients data for TTG, EMA and HLA were available, 729 of them being symptomatic. 383 out of these were HLA DQ2/DQ8 positive, had positive EMA and TTG> 10xULN, and thus in these latter a SBB could have been avoided applying the ESPGHAN 2012 recommendations i.e 52.5%. Four patients also positive for HLA, EMA and with TTG > 10xULN had a Marsh 1 lesion but they were asymptomatic. Gluten challenge was carried out in 71 patients younger than 2 at the 1st SBB; all but 8 did relapse: in 6 no serological data were available at diagnosis or the histological findings were not conclusive, thus CD diagnosis was doubtful. The other two are still on follow-up.

Conclusion: Application of the new CD ESPGHAN criteria in our population would have avoided a SBB in 50% of the cases, without the risk of overdiagnosis as in asymptomatic patients regardless of serology SBB is still mandatory. Our data support challenge should be restricted to selected cases independently of the age at first biopsy as recommended in the new ESPGHAN guidance.

Disclosure of Interest: None Declared
FISH OIL INTAKE DURING PREGNANCY AND THE RISK FOR COELIAC DISEASE IN A NORWEGIAN BIRTH COHORT
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Objectives and Study: Fish oil (cod liver oil and omega-3-enriched fish oil) is a commonly used supplement in the Norwegian diet, rich in vitamin A, D and n-3 unsaturated fatty acids. These dietary elements have been shown to have immunological effects in vitro and in animal studies, and some epidemiological evidence for a reduced risk of autoimmune mediated diseases like type 1 diabetes and multiple sclerosis exists. The aim was to study if maternal intake of fish oil during pregnancy was associated with the risk for coeliac disease in the offspring.

Methods: In a prospective birth cohort study including 107 000 children born from 1999-2009, cases of coeliac disease were identified through reporting by parental questionnaires (age 7 and 8) and by linkage to the Norwegian Patient Registry (NPR). This registry contains all diagnoses from public inpatient and outpatient paediatric clinics in the country. The ESPGHAN diagnostic criteria from 1991 were required for diagnosis during this period. Detailed questionnaires regarding use of supplements on week 17 and 30 and a food frequency questionnaire at 22 weeks of pregnancy were completed by the mothers. Use of fish oil was classified in four groups according to the duration of use.

Results: A total number of 396 cases of coeliac disease (245 females, 62%) with the diagnosis recorded at a minimum of two occasions in NPR or indicated from parental questionnaire were identified from 106 917 live births. The mean age of the cohort at analysis was 5.9 years (median 6.0, range 2-12 years).

After exclusion of cases with insufficient information, 333 cases and 86 909 controls were retained in the analysis. Intake of fish oil as supplement from week 0-30 of pregnancy was reported for all months by 27 % whereas 29 % reported no use. The proportion of offspring with coeliac disease among regular fish oil using mothers was 2.98/1000 as compared to 4.29/1000 of non-users (p=0.007).

After adjustments in a multiple logistic regression model for possible confounding effects of child age and sex, maternal coeliac disease, age, parity and education, only the child’s age and sex and maternal coeliac disease (p<0.001 for all) were significant predictors. In the adjusted model, no significant effect of fish oil intake remained (OR 0.89, CI 0.65-1.23, p=0.49). Comparing the lowest to the highest quartiles of estimated intake of vitamin D, total n-3, EPA and DHA from the food frequency questionnaire from week 22 of pregnancy showed a non-significant difference on the risk of subsequent coeliac disease in the offspring.

Conclusion: No significant effect of maternal intake during pregnancy of fish oil, n-3 fatty acids and vitamin D on the risk of coeliac disease in childhood was found.

Disclosure of Interest: None Declared
TOWARDS NON-INVASIVE DIAGNOSIS AND MONITORING OF CELIAC DISEASE: A PROSPECTIVE STUDY TO THE USEFULNESS OF I-FABP

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Objectives and Study:

Introduction

Our retrospective studies showed the differentiating property of intestinal fatty acid binding protein (I-FABP), a sensitive marker for enterocyte damage, in patients with positive CD autoantibodies (IgA-tTG) with and without celiac disease (CD). The new CD guideline emphasizes the need for a non-invasive marker. This study evaluates the usefulness of plasma I-FABP in diagnosing CD in children with positive IgA-tTG titres and for monitoring disease activity in patients on a gluten-free diet (GFD).

Methods:

In a prospective, multicentre study all children presenting with positive CD autoantibodies in 2010 and 2011 were included. Patients fulfilling the ESPGHAN criteria for CD, villous atrophy at duodenal biopsy and/or IgA-tTG >10x cut-off level, started a GFD. Plasma I-FABP and IgA-tTG were determined at presentation and after 3, 6, 12 and 26 weeks of GFD in 61 children (mean age 6.9 years). The control group consisted of 90 children (mean age 7.9 years) with a clinical suspicion of CD but normal CD autoantibody titres.

Results:

Plasma I-FABP levels were significantly elevated at presentation in children with CD (775 pg/ml, IQR 438-1354 pg/ml) compared to the control group (207 pg/ml, IQR 123-288 pg/ml, p<0.001) and correlated with Marsh grade (R=0.37, p<0.05, n=61). The positive and negative predictive values of I-FABP for CD were 95.2% and 77.0%, respectively. I-FABP levels decreased significantly to 444 (n=18), 378 (n=57), 258 (n=50) en 221 (n=52) pg/ml after 3, 6, 12 and 26 weeks GFD, respectively. Median IgA-tTG titers did not normalize in 26 months of GFD and recovery was significantly slower.

Conclusion: An elevated I-FABP level confirms the diagnosis of CD in 91.7% of all patients with positive autoantibody titres. I-FABP analysis could reduce the need for a duodenal biopsy with almost 75%. I-FABP levels recovered after 6-12 weeks of GFD to values in the control group, significantly faster than the currently used indirect marker IgA-tTG. Plasma I-FABP is a reliable additional marker for CD diagnosis and provides actual insight in intestinal damage in children with CD on a GFD.

Disclosure of Interest: None Declared
EARLY FEEDING AND RISK OF COELIAC DISEASE IN A PROSPECTIVE BIRTH COHORT STUDY

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Objectives and Study: Early introduction of gluten as well as a high dose at introduction has been suggested to increase the risk of coeliac disease in young children. The effect of gluten introduction on the risk for coeliac disease with onset later in childhood is less clear. We aimed to study the effect of age of gluten introduction on the risk of coeliac disease, adjusting for continued breastfeeding in a population where <10 % of paediatric cases are diagnosed before two years of age.

Methods: In a prospective birth cohort study including 107 000 children born from 1999-2009, all cases of coeliac disease were identified through reporting by parental questionnaires at age 7 and 8 and by linkage to the Norwegian Patient Registry (NPR). This registry contains all diagnoses from inpatient and from public outpatient paediatric clinics in the country. The ESPGHAN diagnostic criteria from 1991 were required for diagnosis during this period. Exposures regarding weaning diet and breastfeeding were reported in detailed questionnaires at 6 and 18 months of age.

Results: A total number of 396 cases of coeliac disease (245 females, 62%) with the diagnosis recorded at a minimum of two occasions in NPR or indicated from parental questionnaires were identified from 106 917 live births. The mean age of the cohort at analysis was 5.9 years (range 2-12). After exclusion of cases with insufficient information up to 18 months, 285 cases and 67 643 controls were retained in the analyses. Gluten was introduced before or at 4 months in 8%, 4-5 months in 17.9%, 5-6 months in 27.3% and after 6 months in 46.6%. However, there has been a trend to introduce gluten at a later age during the recruitment period with introduction within 6 months in 62 % for the cohort born in 2000 as compared to only 16 % in 2008. Continued breastfeeding at 6 months was stable at around 80 % during the period.

Coeliac disease was diagnosed in 3.62/1000 of the infants who had been exposed to gluten before 6 months of age as compared to 3.98/1000 with later gluten introduction (OR 1.10, p=0.47). The adjusted model included confounding effects of the child’s age and sex and maternal coeliac disease and showed a significantly increased risk for coeliac disease in the group introduced to gluten after 6 months (aOR 1.37, 95 % CI 1.05-1.78, p=0.02). Including duration of breastfeeding (aOR 1.35) and iron intake (aOR 1.39) as confounders had minimal impact on the effect estimates of delayed gluten introduction, and maternal age, parity and education were not included in the final model due to small changes in the estimated effects.

Conclusion: We found a significantly increased risk of coeliac disease in children where gluten introduction had been delayed to after 6 months of age.

Disclosure of Interest: None Declared
IRON INTAKE DURING PREGNANCY AND RISK OF COELIAC DISEASE IN THE OFFSPRING

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Objectives and Study: Iron is a frequently used supplement during pregnancy in iron deficiency anaemia with effects on pregnancy outcome. In latent iron deficiency states, the benefits of iron supplementation are less clear, and supplement to all pregnant women is not recommended. Iron is important in innate and adaptive immune responses, and alters the host's microflora. The aim was to study if iron intake during pregnancy was associated with the risk for coeliac disease in the offspring.

Methods: In a prospective birth cohort study including 107 000 children born from 1999-2009, cases of coeliac disease were identified through reporting by parental questionnaires (age 7 and 8) and by linkage to the Norwegian Patient Registry (NPR). This registry contains all diagnoses from public paediatric clinics in the country. The ESPGHAN diagnostic criteria from 1991 were required for diagnosis during this period. Questionnaires including use of iron containing supplements on week 17 and 30 of pregnancy were completed. From a food frequency questionnaire the total average daily iron intake from week 0 to 22 of pregnancy was calculated.

Results: After exclusion of cases with insufficient information, 360 cases and 92 627 controls (mean age 5.9 years, range 2-12) were retained in the analysis. A total of 56.3 % of the expecting mothers reported use of iron supplements < 30 weeks, and a minimum haemoglobin value of less than 10.5 g/dL was found in 14.4% before week 30 of pregnancy. Anaemia was reported before (2.1%) or during (1.8%) the first four months of pregnancy or both in a total of 3.1 % of the participants.

Coeliac disease was diagnosed in 4.40/1000 of the children exposed to iron supplementation compared to 3.20/1000 of those without (p=0.003). In a multiple logistic regression adjusting for age and sex of the child, maternal parity, education, age and maternal coeliac disease, iron supplementation during pregnancy remained a significant predictor with an OR of 1.048 per month use (95 % CI 1.007 – 1.09, p=0.021) and OR for use vs non-use OR 1.23 (0.99-1.53). The total estimated iron intake at week 22 was found to correlate with the risk of coeliac disease in the offspring (p for trend=0.04). Anaemia before or in early pregnancy was associated with an increased risk of coeliac disease in the offspring (unadjusted OR 1.64, p=0.01), whereas hgb < 10.5 g/dL was not. Adjusting for maternal anaemia in the final analyses did not materially change the estimated OR for association of iron supplements use in pregnancy and risk of celiac disease in the offspring.

Conclusion: We found an increased risk of coeliac disease in childhood with iron supplementation during pregnancy.

Disclosure of Interest: None Declared
DIFFICULTIES WITH DUODENAL BULB BIOPSY IN THE DIAGNOSIS OF COELIAC DISEASE.
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Objectives and Study: Recent studies suggest that villous atrophy in coeliac disease may be found only in duodenal
bulb. We here investigated potential pitfalls and specificity of bulb biopsies in the diagnosis of coeliac disease in children.

Methods: Coeliac disease serology and duodenal biopsies were obtained from 40 consecutive children with a suspicion
of coeliac disease. Villous height to crypt depth ratio was evaluated by two independent observers. Further, densities of
CD3+, αβ and γδ intraepithelial lymphocytes (IELs) were assessed from frozen biopsy sections. The disease control
group comprised 18 celiac antibody-negative children endoscoped because of gastrointestinal symptoms. All children
underwent routine investigations for other gastrointestinal diseases.

Results: Twenty-two out of the 40 children were found to have coeliac disease based on positive serology and villous
atrophy in duodenum. None of the cases presented with villous atrophy solely in the bulb. The quality of bulb biopsies was
unsatisfactory for accurate morphometric villous height to crypt depth ratio analyses in 25 out of 40 patients even after
recutting. The mean villous height in bulb was 128 µm in coeliac patients and 262 µm in disease controls (p=0.101); in
duodenum the heights were 135 µm and 315 µm (p=0.006), respectively. The corresponding crypt depth values were 375
µm and 290 µm (bulb, p=0.205) and 422 µm and 280 µm (duodenum, p=0.005). The mean bulb villous height crypt depth
ratio was 0.5 (n=7, range 0.2-1.4) in coeliac disease patients and 1.1 (n=8, range 0.1-2.7) in controls showing marked
architectural changes also in the latter group. In the control patients the major findings or final diagnoses were H. pylori
(n=2), dyspepsia (n=1), chronic diarrhea (n=1), abdominal pain (n=1), giardia (n=1), entamoeba histolytica (n=1) and
malnutrition (n=1). Even though the disease controls showed marked morphological changes in bulb, the mean density of
γδ IELs was significantly (p=0.004) lower than in coeliac patients.

Conclusion: In our series the bulb specimens were often of poor quality and difficult to interpret in morphometric
analyses. Further, other conditions may cause bulb injury similar to coeliac disease. These results indicate that bulb
biopsies alone should be evaluated with caution in the diagnosis of coeliac disease.

Disclosure of Interest: None Declared
CANCER AND MORTALITY SURVEY IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE


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Objectives and Study: Incidence of paediatric Inflammatory bowel disease (PIBD) has risen during the past two decades. The severe phenotype of PIBD combined with intensified medical treatment may increase the risk of malignancy and mortality. The Porto IBD working Group of ESPGHAN conducted a European survey of cancer and mortality in PIBD.

Methods: A survey among paediatric gastroenterologists of 19 European countries and Israel was undertaken. One representative from each country repeatedly contacted all paediatric gastroenterologists from each country for reporting retrospectively PIBD patients (diagnosed < age 19 years) diagnosed with any cancer and/or mortality after diagnosis of IBD, during the period of 2006-2011.

Results: We identified 44 cases (18 cancers and/or 32 deaths). Median age at diagnosis of IBD was 10 year (59% male). Type of IBD was Crohn’s disease (n=19; 43%), ulcerative colitis (n= 22; 50%) and IBD unclassified (n=2). Causes of mortality were infectious (n=15; 47%), uncontrolled disease activity of IBD (n=6), cancer (n=6), other non-IBD related diseases (n= 3) and unknown (n=2). The most common malignancy was hematopoetic tumors (n=11; 61%), of which 3 were hepatosplenic T cell lymphoma and 2 EBV-associated lymphomas. Medications used in the three months preceding the mortality cases included steroids (n=19; 59%), thiopurines (n=18; 56%), biologics (n=8; 25%) and calcineurin inhibitors (n=7; 22%). Combination therapy (defined as thiopurines and biologics) was used in 5 (16%). Medications used in the 3 months preceding the cancer cases included steroids (n=4; 22%), thiopurines (n=12, 67%), biologics (n=2) and calcineurin inhibitors (n=1). Combination therapy was used in only one patient.

Conclusion: Cancer and mortality in PIBD are rare but the cumulative rates are not insignificant. Mortality is primarily related to infections. Uncontrolled disease activity and cancer were both responsible for 19% of deaths. The lack of a control group makes it impossible to elucidate how many of the cancer cases are disease-specific but at least 5 lymphomas were likely treatment-associated, by virtue of their phenotype. A minority of patients had been treated with combination therapy.

Disclosure of Interest: None Declared
Objective and Study: Measurement of 7 alpha-hydroxy-4-cholesten-3-one (C4) in serum is a semiquantitative test for bile acid malabsorption (BAM). The C4-test has been recently established by our group for pediatric patients. BAM indicated by high C4 values has been found to be an underestimated problem in adults with Crohn’s disease (CD). Here we used the C4-test to investigate pediatric patients with CD and ulcerative colitis (UC) in order to distinguish diarrhea caused by BAM or inflammation requiring treatment escalation.

Methods: C4 was measured using high performance liquid chromatography in fasting serum samples of 41 selected patients with CD (mean age 15.1±2.5; range 7-19 years; 73% with disease location in the terminal ileum, 22% with resection of terminal ileum) and 12 with UC (mean age 14.7±4.4; range 4-18 years). Disease activity was assessed by scores (PDCAI, PUCAI) plus serum and fecal inflammatory markers. C4 results of CD and UC patients were compared to values obtained in a healthy control population (HC, n=100; 0-18 years; upper limit of normal for C4: 54 ng/ml).

Results: The mean C4 values in 41 CD patients were higher compared to HC (49.3 ± 49.1 ng/ml vs. 22.8 ± 15.8 ng/ml; p<0.0001), with 29% of CD-patients having C4-values above 54 ng/ml, indicating BAM. C4 values in UC patients were not significantly different from HC (31.2 ± 23.1 ng/ml vs. 22.8 ± 15.8 ng/ml). CD patients with non-bloody diarrhea (n=9) had higher mean C4-levels compared to those without diarrhea (n=31; 100.4 ± 68.7 ng/ml vs. 32.8 ± 21.3 ng/ml; p<0.0001). C4 levels in CD patients with previous ileal resection were significantly higher than in patients with no resection (72.1 ± 27.3 vs 40.3 ± 47.8; p=0.001). No significant correlation was found in CD patients between C4 values and C-reactive protein in serum or fecal calprotectin. All 7 patients in clinical remission but with persistent diarrhea showed elevated C4 values >54 ng/ml, indicating BAM as the cause of their symptoms.

Conclusion: In contrast to UC patients, C4 values CD patients are elevated compared to HC. In our selected group of CD patients, elevated C4 levels are not related to disease activity and markers of inflammation, but to presence of diarrhea and to previous resection of the terminal ileum. The C4-test allows identifying a subgroup of CD patients with persistent diarrhea in spite of clinical remission which may benefit from bile acid binding therapy.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PD-G-0086

WHEN ARE YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE READY FOR TRANSFER TO ADULT CARE?

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Objectives and Study: Transition is the planned move of adolescents and young adults with long-term physical conditions from child-centred to adult-orientated health care. The need for a well planned transition process has become increasingly recognized, guidelines have been produced to aid health care professionals through this process. The Inflammatory Bowel Disease Transition to Adult Health Care Guidance for Health Professionals was produced by British Nursing, gastroenterology and Crohn's societies in 2008 to facilitate transition.

we studied transition of Inflammatory Bowel Disease (IBD) patients in a tertiary paediatric gastroenterology unit to provide a baseline on our current performance and to further understand this process.

Methods: We prospectively assessed the Paediatric Gastroenterology department transition process against the Inflammatory Bowel Disease Transition Guidance. Parents and young adults were provided with a questionnaire in the IBD transition clinic. The questionnaire addressed the stages of transition and readiness for transfer.

Results: 36 questionnaires were completed. Patients seen in clinic were 14-17 years old. The mean age at diagnosis was 12 years 3 months (Range: 4-16 years). The mean age of discussing transition with young adults was 15 years (Range: 13-16). Despite all patients meeting the adult gastroenterology consultant at least once in the paediatric transition clinic only 55% of patients and 39% of parents felt the young adults were ready for transfer. There is a significant association between young adults being responsible for taking their medications and feeling ready to be transferred to adult follow up care (p=0.0015), furthermore most patients who were able to discuss their symptoms and management in the absence of their parents were happy to be transferred to adult care (p=0.04).

Conclusion: Well planned transition is considered a standard element of care for young adults with IBD. Young adults need to be encouraged early to participate in their medical care. They may be ready to be transferred to adult services once they are able to discuss their own symptoms and management without parental support and are responsible for taking their own medications.

Disclosure of Interest: None Declared
SERUM ADIPOKINE LEVELS DURING INFLIXIMAB THERAPY IN PEDIATRIC CROHN’S DISEASE
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Objectives and Study: Crohn’s disease (CD) is an inflammatory disorder of the intestine and the visceral adipose tissue, characterized by adipocyte hyperplasia and increased fat tissue concentrations of TNFα, leptin and adiponectin. In experimental models TNFα suppresses the expression of leptin and the anti-inflammatory mediator adiponectin. We aimed to investigate the early effect of anti-TNFα therapy with infliximab (IFX) on visceral adipose tissue and assessed serum adipokine levels in pediatric CD.

Methods: Serum concentrations of adipokines (leptin, adiponectin and resistin) were retrospectively measured with commercially available ELISAs before the 1st, 2nd and 4th IFX infusion (week 0, 2 and 14). Results of 18 CD patients were compared with 15 weight/BMI matched healthy controls (HC). We recorded the mathematically weighted Pediatric Crohn’s Disease Activity Index (wPCDAI), laboratory parameters, anthropometric data and treatment response. Wilcoxon signed-rank test was applied to analyze differences between patients and HC and changes during IFX therapy at the 3 time points.

Results: The IFX treated patients included 10 males and 8 females (median age 14.9 years, range 12.2-17.5). The wPCDAI decreased from 26.3 (7.5-72.5) to 15 (0.0-35.0) and 8.8 (0.0-45.0) after 2 and 14 weeks, respectively (p<0.01). Baseline resistin levels were higher in patients than in HC: median 14.7 ng/ml (range 5.1-50.5) vs 7.3 ng/ml (0.5-14.5), respectively (p<0.001), and decreased with IFX at both time points (p<0.01 compared to baseline, n.s. to HC). At baseline leptin levels did not differ from HC, but leptin levels were significantly higher in girls compared to boys (p<0.0001). In girls, leptin levels increased after 2 weeks from 9.5 ng/ml (7.6-30.1) to 16.0 ng/ml (7.9-35.2) (p<0.05). In boys, leptin increase showed only a trend from 2.0 ng/ml (0.6-12.9) to 2.8 ng/ml (1.7-8.6) (n.s.). Adiponectin baseline levels in patients were not different from HC: 7765 ng/ml (4591-11897) vs 8660 ng/ml (5029-10795) (n.s.). Adiponectin notably peaked 2 weeks after 1st IFX infusion to 9200 ng/ml (4075-20706), (p<0.01) but thereafter fell to 6470 ng/ml (2956-12681), which was lower compared to values in HC (p<0.05), at baseline (p<0.05) or at 2 weeks (p<0.001).

Conclusion: TNFα blockade by IFX effectively reduced disease activity and inflammatory markers including resistin in CD and led to an early increase of leptin and adiponectin. Leptin parallels weight gain. We speculate that successful induction therapy with IFX is partially mediated by the anti-inflammatory properties of released adiponectin.

Disclosure of Interest: None Declared
**GASTROENTEROLOGY**  
**INFLAMMATORY BOWEL DISEASE**  

**PD-G-0088**

T300A VARIANT OF AUTOPHAGY ATG16L1 GENE IS ASSOCIATED WITH DECREASED ANTIGEN SAMPLING AND PROCESSING BY DENDRITIC CELLS IN PEDIATRIC IBD

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**Objectives and Study:** Intestinal dendritic cells (DC) sample luminal antigens by protruding dendrites through the epithelial cell layer. The single nucleotide polymorphism (SNP) T300A (rs2241880) of ATG16L1, which has been associated with Crohn’s disease (CD), is responsible for a decreased autophagic activity. The aim of this study was to elucidate the role of autophagy in DC uptake and processing of antigens and in the interaction between DC and intestinal epithelium in pediatric IBD patients.

**Methods:** We recruited CD paediatric patients that homozygously carry either the protective (wt, n=7) or risk allele (var, n=13) of ATG16L1, as well as heterozygous patients (het, n=13). DC obtained from peripheral blood monocytes were studied after 2-hours of incubation with bacteria particles, 4-hour of incubation with DQ-Ovalbumin (DQ-OVA), or 24-hours of co-culture with Caco2 epithelial cells and bacteria particles in transwell culture. DC phenotype, antigen sampling and processing were measured by flow cytometry. The capability of DC to form transepithelial protrusions was determined by confocal microscopy.

**Results:** DC generated from wt patients showed significant higher bacterial sampling and initial antigen processing compared to var patients (p=0.01 and p=0.03, respectively). Additionally, after exposure to either bacterial particles or the model antigen DQ-OVA, wt DC showed a significant increase in the expression of the activation markers HLA-DR and CD86 when compared to var DC. Interestingly, also het patients showed an impairment in bacterial uptake and expression of activation marker compared to wt, except for DQ-OVA processing that, though it was reduced the difference did not reach a statistical significance. This latter finding suggested a dose dependent effect of the T300A allele on DC functionality. To model antigen sampling in the intestine, DC were co-cultured with colonic Caco-2 cells in a transwell system. In this set-up, formation of transepithelial protrusions by DC was less efficient in var DC compared to wt. In accordance, antigen uptake and processing by DC derived from var patients was decreased significantly in the in vitro model of antigen sampling through the intestinal barrier.

**Conclusion:** DCs of pediatric CD patients showed a marked impairment of bacterial uptake and antigen processing, as well as a decreased maturation. Moreover autophagy is involved in the proper interactions between DC and intestinal epithelium. Our results indicate that an autophagy defect is associated with an impairment of intestinal innate immunity in pediatric CD.

**Disclosure of Interest:** None Declared
Objectives and Study: The pathogenesis of Crohn’s disease (CD) involves complex genetic and environmental components. Over 100 loci are associated with CD risk, but all have modest odds ratios. To date, little is known about tissue-specific transcription of these genes in CD and healthy individuals. Differential risk-allele expression in heterozygotes has been implicated in a variety of other disorders, but is largely unexplored in CD. We hypothesized that heterozygotes do not express risk and non-risk alleles equally, and that heterozygotes with CD preferentially express the risk allele. We chose the ATG16L1 autophagy gene for proof of concept because of its high prevalence, its plausible centrality in multiple crucial pathways, and its relatively strong association with disease.

Methods: Children between the ages of 6 and 21 undergoing colonoscopy at St. Louis Children’s Hospital from November, 2010 to November, 2011 were prospectively enrolled and consented. Blood and ileal biopsies were collected. Subjects were genotyped for the ATG16L1 rs2241880 single nucleotide polymorphism (SNP). RNA was extracted from the biopsies, and cDNA was synthesized. A 393 base pair sequence surrounding the SNP was amplified by PCR, transformed into TOP10 E. coli, and sequenced using Sanger sequencing.

Results: 64 subjects were enrolled. All 9 heterozygous CD patients and 8 age-matched controls were sequenced. 404 high-quality (HQ) reads were obtained from CD patients. 345 HQ reads were obtained from non-IBD controls. The G (risk) allele constituted 51.5% of HQ reads from cases, and 53.0% from controls (NS). Splice variants outnumbered the full length transcript in both groups: the full length transcript for exons 7-11 constituted 23.0% of CD reads and 22.9% of control reads (NS). The predominant transcript was isoform 2, which contains a complete deletion of exon 8. Previously undescribed isoforms were also identified, but were rarely produced. No association was found between the expression of the rs2241880 allele and the splice variant.

Conclusion: RNA splice variants are common in ATG16L1 risk allele heterozygotes, regardless of disease status. Categorical presence/absence associations between risk alleles and disease occurrence might be modified by differential expression of isoforms and alleles in newly diagnosed childhood CD. While we did not find evidence of this effect with the ATG16L1 risk allele in the ileum, differential expression in other risk loci may yield important insights into the pathogenesis of IBD. Furthermore, transcripts in the host and affected tissues cannot be assumed to be of uniform size and functionality, and should be considered when correlating host genotype to disease expression.

Disclosure of Interest: None Declared
PROLONGED CLOSTRIDIUM DIFFICILE DIARRHOEA AMONG CHILDREN IN A TERTIARY CARE HOSPITAL: A 10 YEAR RETROSPECTIVE STUDY

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Objectives and Study: To determine the frequency of Clostridium difficile (CD) associated diarrhoea in our Hospital during the last 10 years and the role of this pathogen among infants.

Methods: A retrospective analysis of 244 faecal specimens from 176 children hospitalized in Niguarda Hospital, over a period of 10 years (January 2002-December 2011) was carried out. The inclusion criteria were the presence of diarrhoea (≥3 liquid stool within 24 hours, persisting for more 7 days) or muco-hematic diarrhoea, in pediatric patients aged 0-18 years. The stool samples were cultured for common infective causes of diarrhoea (Salmonella, Shigella, Yersinia, E. Coli Enteroemorragica, Campylobacter) and analyzed for CD toxins (using enzyme immunoassay detection of glutamate dehydrogenase as initial screening and then the polymerase chain reaction real time as the confirmatory test). Other causes of prolonged diarrhoea were excluded. We considered as risk factors for Clostridium difficile infection (CDI): prematurity, solid organ or stem cell transplant, malignancies, chemotherapy, immunodeficiency, cystic fibrosis, gastrointestinal disease, prior hospitalization, antibiotics in past 4 weeks, G or J tube. We compared the incidence of CDI between 2001-2006 and 2007-2011 periods. Between 2007 and 2011 (years of greater incidence) we divided patients into 3 groups: children with CDI and risk factors, children with CDI without risk factors and children without CDI; then we compared symptoms between groups. Statistical analysis was performed using Fisher’s exact test.

Results: Between 2002 and 2006, 2 of 52 children (3.84%) had CD toxins; between 2003 and 2011, 22 of 124 children (17.74%) had CD toxins. The frequency of CD-positive children increased, especially in the last years, from 5.8% in 2007 to 20.68% in 2011; 37.5% of CD-positive children had no risk factors. All children with CDI had a community-acquired infection. There was no difference between clinical presentation, age and gender in the 3 children groups. Fever and abdominal pain were the most common symptoms associated with diarrhoea. Antimicrobial treatment (metronidazole or vancomycin) was successfully used in 21 of 24 children with CDI; only 3 patients didn’t request medical therapy (1 child had cow’s milk allergy and 2 children for a spontaneous resolution of symptoms). 33.33% of CD-positive children aged< 2 years and most of them required antimicrobial treatment, suggesting that the Clostridium difficile might be pathogenic in this age groups as well.

Conclusion: The epidemiology of CDI has changed over the past decade and pediatric CDI seems to be increasing, especially in populations not previously considered at risk (such as those with community-acquired infection). CD might be consider pathogen also in children younger than 2 year-old.

Disclosure of Interest: None Declared
THE EFFECT OF A LACTOBACILLUS REUTERII ON THE DURATION OF DIARRHEA AND LENGTH OF HOSPITAL STAY IN CHILDREN WITH ACUTE DIARRHEA IN TURKEY: PROSPECTIVE, SINGLE BLIND, RANDOMIZED CONTROLLED TRIAL


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Objectives and Study: The ESPGHAN-guidelines on the treatment of acute gastroenteritis (GE) state that probiotics can be considered in its treatment. Data with Lactobacillus (L.) reuteri in acute GE are very limited.

Methods: A multicenter, randomized, single blind, hospital based clinical trial was performed in children (3 to 60 months) with acute watery diarrhea lasting > 12 hours but < 72 hours, requiring hospitalization. We enrolled children with clinical signs of mild to moderate dehydration. Children received conventional therapy (oral or intravenous rehydration) with or without a 1x10^⁸ CFU of L. reuteri DSM 17938. The primary endpoint was the duration of diarrhea (in hours). Secondary outcome measures were duration of hospitalization (days), diarrhea at the 3rd day of intervention , mean frequency of the daily stool, and diarrhea at the end of therapy (5th day). Adverse events were also recorded.

Results: In total, data from 127 children could be evaluated: 64 in the probiotic and 63 in the control group. The clinical characteristics and severity of gastroenteritis did not differ; stool frequency during the 24 hours prior to admission was 9.53 ± 2.2 per day in the L. reuteri group and was 9.1 ± 2.7 per day in control group (p>0.05). The duration of diarrhea was significantly reduced in the L. reuteri group when compared to the control group. The number of stools per day was significantly lower in the L. reuteri group after 24, 48 and 72 hours. The % of children that was diarrhea-free was significantly larger after 24, 48 (greatest effect, 50 vs 5 %, p<0.001) and 72 hours. Mean length of hospital stay was shorter in the L. reuteri group than the control group (4.31 ± 1.3 days vs. 5.46 ± 1.77 days, p<0.001). No adverse effects related to the probiotic use were noted.

Conclusion: L. reuteri is a very effective probiotic in acute GE, reducing both the duration of acute diarrhea and hospital stay.

DELAYED INITIATION OF ENTERAL FORMULA FEEDING REDUCES THE INCIDENCE OF NECROTIZING ENTEROCOLITIS (NEC) IN PRETERM PIGLETS

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Objectives and Study: Necrotizing enterocolitis (NEC) is a major complication of enteral feeding in premature infants with a high morbidity and mortality. Early enteral feeding of fortified human milk is considered optimal nutrition for the preterm infant. However, human milk is not always available and commercial formulas are needed that mimic human milk as closely as possible. Our aim was to test the effects of early vs. late enteral feeding of an intact vs. partially hydrolyzed protein formula on NEC incidence in a preterm piglet model being developed to closely simulate clinical practice.

Methods: Moderately preterm pigs (at 90% of gestation) were randomized to either an early (EA) or late (LA) feeding protocol. The EA and LA groups received 2 d and 5 d of total parenteral nutrition (TPN), and orogastric formula feeds (50% full intake) began on d of life 3 and 6, respectively and PN continued. Pigs in the EA and LA groups also were randomized to one of two formulas containing either intact or hydrolyzed protein. All four groups were euthanized due to NEC onset or after 5 d formula feeding. NEC severity and incidence was assessed based on macroscopic and histological scoring in the stomach, proximal jejunum, distal ileum, and colon.

Results: Nineteen of 25 pigs in the EA group developed NEC (76%) as compared to 9 of 22 pigs in the LA group (41%) (p = 0.02). The mean total clinical NEC severity score was significantly greater in the early vs late group (11.08 vs 6.55; p = 0.004). There was no significant difference in the incidence of NEC in pigs that received hydrolyzed protein formula (75% in EA, 45% in LA) and those that received intact protein formula (77% in EA, 34% in LA).

Conclusion: Although TPN has been associated with impaired gut development, this study provides evidence that delayed initiation of enteral feeding at 5 d vs 2 d is protective and reduced both the incidence and severity of NEC in preterm pigs. The formula containing intact or hydrolyzed protein had no effect on NEC development. Future studies will explore whether more gradual rather than an abrupt introduction of feeds impacts NEC incidence.

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GUM ARABIC IN MANAGING DIARRHEA IN CHILDREN IN SUDAN

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Objectives and Study: To evaluate effect of GA as an additive to WHO-ORS in managing acute diarrhoea in children.

Methods: Interventional randomized controlled clinical trial was performed in GIO, Khartoum, between March to August, 2011. 180 children with acute diarrhoea were enrolled. They were randomly divided into 2 groups, their ages range 6-60 months. The control received conventional treatment of diarrhoea, the other group received in addition, GA, 5-10 gm until recovery. Data analyzed using SPSS.

Results: Children received GA, diarrhoea stopped within 24 hours in 90%, 80% were discharged after 24 H. 3 developed complications. weight increased in 47.8%.61 followed for 6 weeks only, (3.3%) had recurrence of diarrhoea. In control group diarrhoea stopped within 24H in 38.9%, 30% were discharged after 24 H. Complications developed in 23.3%, 2 developed severe dehydration with shock. weight decreased in 35.6%.67 followed, (19.4%) of them developed diarrhoea.

Conclusion: GA as additive to WHO-ORS reduces duration & complications of diarrhoea, hospital stay & facilitates regaining weight. It has a Prebiotics effect in prevention of diarrhoea. These, indicate its potential as antidiarrheal therapy for acute diarrhoea in children.


Disclosure of Interest: None Declared
CLINICAL SPECTRUM OF ABDOMINAL TUBERCULOSIS IN CHILDREN: AN EXPERIENCE AT A TERTIARY CARE CENTRE.
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Objectives and Study: Tuberculosis poses a serious and increasing problem in developing countries like Pakistan affecting thousands of people. Abdominal Tuberculosis(TB) may be difficult to diagnose and requires a high index of suspicion. The disease has varied presentations including fever, abdominal pain, loose motions, weight loss, intestinal obstruction, peritonitis and perforation. Early detection would decrease the mortality and morbidity associated with this fatal condition. The objective was to determine the frequency of different clinical presentations of abdominal tuberculosis in children.

Methods: A prospective observational study was conducted at The Gastroenterology Department of the Children's Hospital Lahore, Pakistan from Jan 2012 to Oct 2012. Forty children between 1 to 15 years of age, diagnosed to have abdominal TB were included in the study. Data was collected regarding mode of presentation, results of investigations like ESR, ultrasound abdomen, Barium studies, Chest Xray, CT scan, Mantoux test, GI endoscopy and diagnostic laparoscopy findings. Response to treatment and outcome was recorded.

Results: 45% patients presented between 5-10 year of life, 45% after 10 years while only 10% presented before 5 years. 65% were females and 35% were males with male to female ratio of 1:1.8. 90% cases presented with abdominal pain, out of which 70% had chronic abdominal pain and 30% came with acute abdomen. 10% of these presented with sub-acute intestinal obstruction and 5% with abdominal mass. 80% patients presented with fever, 70% with loose motions, 40% with vomiting, 30% with constipation and 10% with PR bleed. Weight loss and pallor was found in 70%, and ascites in 50%. Generalized lymphadenopathy was found in 30% while pulmonary TB was present in 20%. Contact was positive in 70%. T Spot test was done in 20% and was positive in all. USG pointed towards the diagnosis in 70% while CT and Barium meal was diagnostic in 90% of cases. Thick walled bowel loops were found in 95% while thick walled caecum and ascending colon was present in 90%. Mesenteric lymphadenopathy was present in 85% of cases. 12 patients had colitis on colonoscopy. All the patients with tuberculous colitis were younger than 7 years. 6 patients were surgically explored for perforation and peritonitis. One patient died while all other responded well to ATT.

Conclusion: Abdominal tuberculosis is very common in developing countries and has variable presentations. Majority of the patients presented with ileocecal TB and signs of severe inflammation. Differentiation from inflammatory bowel disease is important especially in cases of tuberculosis colitis. Early diagnosis and prompt treatment can make a difference in outcome of these patients.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GERD, PEPTIC DISEASE AND HELICOBACTER PYLORI
PD-G-0095

COMPARATIVE STUDY OF HELICOBACTER PYLORI ERADICATION RATES WITH 10-DAY QUADRUPLE "CONCOMITANT" THERAPY AND SEQUENTIAL THERAPY IN CHILDREN
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Objectives and Study: The currently recommended first-line eradication treatment of Helicobacter pylori (HP) in children is usually successful in about 75%. Recently, a novel 10-day sequential treatment (omeprazole plus amoxicillin for 5 days, followed by omeprazole plus clarithromycin plus tinidazole for another 5 days) has achieved an eradication rate of 90% in children although it has been criticized for the difficult scheme and a simpler strategy has been proposed (concomitant: omeprazole plus amoxicillin plus clarithromycin plus tinidazole for 10 days) with high success rate in adults. The aim of the study was to assess the HP eradication rate of the concomitant compared to sequential treatment in children.

Methods: Eighty-five consecutive children with HP infection were randomized to receive either concomitant [n:44; median age: 10,8 years (4,5-16 years)] or sequential therapy [n:41; median age: 9,8 years (4,8-16 years)]. HP infection was based on 2 out of 3 positive tests results: 13C-urea breath test, rapid urease test, and histology. Side effects and compliance were assessed during treatment. Eradication was assessed by 13C-urea breath test 8 weeks after therapy. All children completed the Gastrointestinal Symptom Rating Scale (GSRS) at entry, during and after treatment.

Results: H pylori eradication was achieved in 40 children receiving sequential treatment (91%; 95% confidence interval: 87,1-98,5) and 35 children receiving concomitant treatment (85%; 95% confidence interval: 81,5-93,1) (P=NS). Compliance with therapy was good (>95%) in all. Overall, GSRS score were similar in both groups during and at the end of treatment (P=NS); however, children treated with concomitant treatment complained more often abdominal pain (18% vs. 42%; difference: −24%; P<0,03). Concomitant treatment increase the costs of 45 euros as compared to sequential regimen.

Conclusion: Our study shows, for the first time in children, that 10-day sequential treatment achieves a higher eradication rate than standard triple therapy, which is consistent with the results of adult studies.

Disclosure of Interest: None Declared
SMALL BOWEL BACTERIAL OVERGROWTH IN CHILDREN TREATED WITH OMEPRAZOLE

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Objectives and Study: A decreased gastric acid secretion is known to favor small bowel bacterial overgrowth (SBBO). However, the impact of proton pump inhibitors on the development of SBBO in children has not been thoroughly studied. Moreover, the role of probiotics in the prevention of SBBO has not been evaluated in children. The objective was to evaluate the incidence of SBBO in children treated with omeprazole and test if probiotics influence the incidence.

Methods: A double-blind, placebo-controlled trial was performed in 70 children treated orally during 4 weeks with 20 mg omeprazole per day. Lactobacillus rhamnosus R0011 (1.9 x 10⁹ cfu) and Lactobacillus acidophillus R0052 (0.1 x 10⁹ cfu) was given daily simultaneously to 36 subjects (probiotic group), while 34 subjects received placebo (placebo group). The diagnosis of SBBO was based on the development of suggestive symptoms in combination with a positive glucose breath test.

Results: After one month of PPI treatment, 30% (21/70) had a positive breath test suggesting SBBO, but only 13 of these were symptomatic. Five children developed SBBO-like symptoms but had a negative breath test; 44 (63%) were symptom free and had a negative breath test. There was no difference in the incidence of positive breath tests in the probiotic versus the placebo group (33% vs 26.5%; p: 0.13).

Conclusion: Since symptoms suggesting SBBO develop in 26% of PPI-treated children, and since a glucose breath test confirms this diagnosis in 72% of them, this side-effect should be considered more frequently.

Disclosure of Interest: B. Hegar: None Declared, E. Hutapea: None Declared, Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals
PREVALENCE OF GASTROESOPHAGEAL REFLUX IN A POPULATION STUDY OF 12-MONTH-OLD INFANTS.
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Objectives and Study: Gastroesophageal reflux (GER) is a common presenting complaint in the pediatric population. Data on the prevalence of GER at the population level in the first year of life are limited. Our objective was to report the prevalence and approach to care of GER from a population-based study of infants in Melbourne, Australia.

Methods: The HealthNuts study is a longitudinal, population-based food allergy study of 5276 12-month-old infants in Melbourne, Australia. Infants were recruited from 120 council-run immunization sessions for allergy testing. Parents completed a detailed questionnaire at recruitment, which captured information on GER in infancy, because of the possible association between GER and cow’s milk allergy.

Results: Of those approached 5276 infants (73%) participated in the study and 4674 completed questions on GER. The parent-reported prevalence of GER was 22.6% (95% CI 21.4 – 23.8; n=1054/4674). GER symptoms commenced in the first month of life in the majority of infants (55%). 38% of infants developed symptoms between 1 and 3 months of age, and only 7% of parents reported the onset after 4 months of age. Parents consulted a doctor in 64% of reported cases (n=662/1033), and 55% were prescribed antireflux medications (n=353/646). Ranitidine was most commonly prescribed (60%), followed by omeprazole (29%). For doctor-consulted GER that was not treated with medications, 37% of parents changed their infant’s formula in response to GER. GER symptoms resolved within 6 months of onset in 77% (95% CI 73.8-79.3) of infants.

Conclusion: GER affects a significant proportion of infants and is a common reason for medical consultation, use of medication and change of formula in the first months of life.

Disclosure of Interest: None Declared
ESOPHAGEAL PRESSURE TOPOGRAPHY INCORPORATING PRESSURE FLOW ANALYSIS DISCRIMINATES DYSPHAGIA DUE TO WEAK PERISTALSIS FROM DYSPHAGIA DUE TO ABNORMAL BOLUS FLOW RESISTANCE IN CHILDREN.

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Objectives and Study: Background: Automated impedance-manometry pressure-flow analysis (AIM analysis) allows the dynamics of bolus transport to be assessed in relation to the pressures within the bolus. We hypothesize that AIM analysis may have clinical utility in diagnosis and treatment in patients with esophageal dysphagia.

Objectives and study: To characterize esophageal pressure topography metrics and AIM analysis pressure flow metrics in relation to dysphagia symptoms in a population of pediatric patients.

Methods: Methods: Esophageal pressure impedance recordings of 5ml liquid and viscous swallows from 46 children (mean age 14.5 years, 22 male) were analyzed. The primary reasons for referral included 21 GERD, 6 Post-fundoplication dysphagia, 12 swallowing disorders, 4 TEF and 3 other. Peristaltic integrity was assessed using the 20mmHg iso-contour defect (ICD) and the relationship between intrabolus pressure and bolus flow timing in the esophagus was assessed using the pressure flow index (PFI), which is a predictive measure elevated in relation to dysphagia (Myers et al., Neurogastroenterol. Mot. 2012). Patients were stratified in relation to reporting of symptoms of dysphagia during swallowing of solids and also in relation to peristaltic defect size (weak peristalsis = ICD >2 cm).

Results: Results: Dysphagia was characterized by a larger ICD overall for liquids (no dysphagia vs. dysphagia ; 2cm [1, 3] vs. 4cm [2, 8] p<0.05) and higher PFI overall for viscous (no dysphagia vs. dysphagia; PFI 32 [13, 67] vs. 61 [25, 139] p<0.05). When patients were stratified based on weak or normal peristalsis, dysphagia in relation to weak peristalsis was associated with a larger ICD size and dysphagia in relation to normal peristalsis was associated with higher PFI (see Table).

<table>
<thead>
<tr>
<th>Dysphagia Symptoms</th>
<th>Peristalsis Type(EPT)</th>
<th>PFI(AIM)</th>
<th>ICD size</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>Weak</td>
<td>15[5,30]</td>
<td>3 [2,9]</td>
</tr>
<tr>
<td>YES</td>
<td>Weak</td>
<td>49 [24,83]</td>
<td>8 [4,10]</td>
</tr>
<tr>
<td>NO</td>
<td>Normal</td>
<td>53 [23,92]</td>
<td>0[0,1]</td>
</tr>
<tr>
<td>YES</td>
<td>Normal</td>
<td>118 [33,350]</td>
<td>1 [1,2]</td>
</tr>
<tr>
<td>ANOVA</td>
<td></td>
<td>p&lt;0.001</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>
Conclusion: The combination of EPT and pressure-flow analysis enables better differentiation of patients with dysphagia symptoms in relation to either weak peristalsis (poor bolus clearance) or abnormal bolus flow resistance (high intra-bolus pressure relative to flow). This new dichotomous categorization of esophageal function may help guide the selection of optimal therapy.


Disclosure of Interest: None Declared
Objectives and Study: Pediatric short bowel syndrome (SBS) following gut resection results from a variety of etiologies. Reports from pediatric SBS patients indicate that the endogenous level of the intestinotrophic factor glucagon-like peptide 2 (GLP-2) is decreased. The long-acting synthetic human GLP-2 analogue, teduglutide (ALX-0600, Nycomed GmbH) is effective in adult SBS patients whereas less is known from pediatric SBS patients. We tested the efficacy of teduglutide in a neonatal piglet jejunostomy model of SBS that exhibits a deficient endogenous GLP-2 secretion.

Methods: Two-day old, term pigs were subjected to resection of 50% of the small intestine starting from the ileo-cecal junction, and the remnant proximal intestine was exteriorized on the abdominal wall as a jejunostomy. All pigs were subsequently given total parenteral nutrition for 7 days and a single daily injection of the following doses of teduglutide: 0.01 (n=6); 0.02 (n=6); 0.1 (n=5) or 0.2 mg/kg/day (n=6) and compared with placebo (n=9). Digestive capacity was studied during a 24 h enteral nutrition balance study where stoma output was collected quantitatively.

Results: A regression analysis showed dose-dependent increase in weight per length of the remnant intestine (P<0.01). Body weight increment was similar for all four teduglutide groups but higher than for placebo pigs (P<0.05). Activity of disacharidases and aminopeptidases in the intestinal mucosa was similar for all groups and digestive capacity was not affected by the end of the experiment. Villus heights and crypt depths were numerically higher in teduglutide groups but not significantly different from placebo. Immunohistochemistry showed no apparent differences in the staining intensities for Ki67 (cell proliferation), villin, fatty acid binding protein, chromogranin A and GLP-2 receptor in the remnant intestine. Pharmacokinetic measurements after teduglutide injection showed a plasma half-life of ≈ 30 min during the elimination phase.

Conclusion: A single daily injection of teduglutide dose-dependently increases the weight per length of the neonatal remnant intestine after distal gut resection, but has limited effect on intestinal function. Significant effects of teduglutide on nutrient digestion and gut function may require a longer adaptation period and/or a more frequent administration of the peptide. In perspective GLP-2 or its analogues may be relevant to improve intestinal adaptation in pediatric SBS patients.

A REGIONAL STUDY IN ENTERIC NEURAL STEM CELLS
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Objectives and Study: Enteric neuropathies have so far been a challenging group of clinical entities with their current management being mainly palliative, thus driving research towards enteric nervous system (ENS) cell replenishment therapies using enteric neural stem cells (ENSCs). Human ENSCs have been isolated only from colonic full thickness and mucosal biopsies, while mouse ENSCs have usually been derived from either colonic or small intestine. In order to determine which region of the gut would be a good source of cells for transplantation, this study attempted to establish which region contained a higher percentage or proportion of ENSCs. The accessibility of tissue from each region was also considered.

Methods: The studied regions were the colon, caecum, small intestine, stomach and oesophagus from wild type and the transgenic mouse line (Rosa26rFPstop: TgWnt1Cre), where all neural crest cells (NCCs), inclusive of ENSCs, express yellow fluorescent protein (YFP). By using fluorescence-activated cell sorting (FACS) the percentage of YFP positive cells was calculated for each region and clonal cultures were established to see how many single cells gave rise to colonies indicating percentage of ENSCs. Several methods of investigations were conducted to characterise the cells such as immunochemistry and FACS. Either the entire gut or muscle peels from the transgenic and wild type mouse gut were used for wholemount or sections of gut immunohistochemistry, using various markers.

Results: The study revealed qualitative and quantitative differences in ENS across the regions. Wholemount on entire gut or muscle peel and section immunochemistry revealed more GFP, p75NTR, Tuj1, Sox10 and S100 stained cells in the colon and caecum followed by small intestine with much less percentages in stomach and oesophagus. A uniform difference in favor of myenteric plexus instead of submucosal was noted in all these markers. FACS sorting demonstrated highest percentage of YFP positive cells in colon with a peak in the caecum followed by a reducing pattern in the rest of the gut regions. Cell counting of Sox10 only stained cell in wild type mouse Sox10/S100 co-labeling revealed the same pattern with a peak at caecum and its appendix.

Conclusion: In conclusion, by using FACS and immunohistochemistry, we have demonstrated a predominance ENSC-related ENS components in the colon and caecum. We have also shown a gradual reduction in the percentage across the gut from colon to the ileum to the stomach and oesophagus. Considering these findings and the balance between which region would contain more progenitors as well as be easily accessible to take tissue, we suggest that future ENSCs studies should continue to focus on the colonic region. In particularly, our study indicated that the appendix, as part of the caecum, may contain a more advanced niche of ENSCs, not yet elucidated.

Disclosure of Interest: None Declared
MESENCHYMAL STROMAL CELL THERAPY FOR GASTROINTESTINAL ACUTE GRAFT VERSUS HOST DISEASE: THE IMPORTANCE OF GUT BIOPSIEST
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Objectives and Study: Acute gastrointestinal graft-versus-host disease (GI aGvHD) is an immune mediated complication after hematopoietic stem cell transplantation. Histological examination of gut biopsies ranging from crypt apoptosis to diffuse mucosal necrosis with denudation confirm the diagnosis. Mesenchymal stromal cells (MSC) have been successfully infused as a salvage therapy in steroid refractory disease. Assessing response to treatment may be hampered by persistent diarrhea resulting from damage to the gut in the absence of ongoing GvHD. We aimed to determine the importance of biopsies to evaluate the response to treatment with MSC and compared the results to serial plasma biomarkers.

Methods: From 2004 to 2012, all 25 children with severe GI aGvHD (>stage 2) were included. Histological evaluation of the GI tract was performed in 22 children (colon and rectum n=6; duodenum, colon and rectum n=3; rectum n=13), 3 patients being too ill to undergo endoscopy/biopsies. Serum concentrations of sIL2Ra, sCK18F (soluble cytokeratin 18 fragments) and sTNFR1 were measured weekly in samples taken before conditioning until 6 weeks after MSC infusions.

Results: 18 patients proved refractory to steroids and received MSC infusion as salvage therapy. One child died within 7 days of MSC infusion and another responded completely (CR =no aGvHD). Profuse diarrhea persisted in 16 children and a second (and in 3 cases a third) MSC infusion was given. Nine patients underwent further GI endoscopy before subsequent MSC infusion and multiple biopsies were taken from the upper (n=6) and lower (n=9) GI tract. In 6 patients the biopsies showed no histological signs of aGvHD and 3 patients showed a clinical response after a subsequent MSC infusion. All together, 9 out of the 18 patients showed a CR, 4 a partial resolution (PR = improvement of at least 1 grade) and 5 no resolution (NR) at 28 days after MSC therapy.

At onset of aGvHD, serum concentrations of sIL-2Ra, sTNFR1 and sCK18F were significantly elevated compared with previous samples. Patients with CR/PR (n=13) have lower sIL-2Ra concentrations compared to NR (n=5) (p=0.015). Significant decrease of sIL-2Ra concentrations at day 7 after MSC infusion predicts resolution at day 28.

Conclusion: Without histological examination of multiple GI biopsies after MSC infusion, the response to treatment may be underestimated and overtreatment occurs. In contrast patients with persistent histological alterations may benefit from additional MSC treatment. Sequential biopsies should be included in randomized controlled trials to validate the use of biomarkers like sIL-2Ra in monitoring response to experimental therapy.

Disclosure of Interest: None Declared
NONALCOHOLIC FATTY LIVER DISEASE PREVALENCE IN URBAN SCHOOL-AGED CHILDREN AND ADOLESCENTS FROM THE YANGTZE RIVER DELTA REGION: A CROSS-SECTIONAL STUDY

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Objectives and Study: To determine the prevalence of nonalcoholic fatty liver disease (NAFLD) and explore the relationship of NAFLD with anthropometric parameters among schoolchildren from the Yangtze River delta region.

Methods: An epidemiological survey on childhood NAFLD was conducted using the stratified cluster sampling method in four regions of the Yangtze River delta in September and October 2009–2011. In all, 7,229 students, aged 7–18 years, from 12 primary, middle and high schools participated in the study. The inclusion criteria were (a) no history of liver disorders (e.g., autoimmune disease, hepatitis B and C, drug-related disorders), (b) age 7–18 years and (c) residence in the survey region for ≥3 years. Height, weight, and waist circumference were measured; body mass index (BMI) and waist to height ratio (WHtR) were calculated, and liver ultrasonography was performed. NAFLD was diagnosed according to the Fatty Liver and Alcoholic Liver Disease Study Group of the Chinese Liver Disease Association, guidelines for diagnosis and treatment of nonalcoholic fatty liver diseases (2006).

Results: The overall NAFLD prevalence was 5.0%; it was 7.5% in boys, 2.5% in girls, 5.6% in subjects with peripheral obesity, 12.9% in those with abdominal obesity, and 44.8% in those with mixed obesity. Binary regression analyses showed that WHtR was the major independent risk factor for childhood NAFLD, causing a 12.955-fold increase in NAFLD risk.

Conclusion: Mixed obesity had the strongest association with NAFLD. Male gender and regional urbanization also influenced NAFLD prevalence among schoolchildren. WHtR may be an effective indicator of NAFLD.

Disclosure of Interest: X. Zhang Grant / Research Support from: Shanghai Key Laboratory of Pediatric Gastroenterology and Nutrition (No.11DZ2260500); the Project of Health Opportunity for People Everywhere (No.AFINS-HOPE-2011-03); Shanghai Education Committee (No.HJTY-2010-A09), Y. Wan Grant / Research Support from: Shanghai Key Laboratory of Pediatric Gastroenterology and Nutrition (No.11DZ2260500); the Project of Health Opportunity for People Everywhere (No.AFINS-HOPE-2011-03); Shanghai Education Committee (No.HJTY-2010-A09), S. Zhang: None Declared, L. Lu: None Declared, Z. Chen: None Declared, H. Liu: None Declared, X. Jiang: None Declared, K. Luo: None Declared, D. Cao: None Declared, W. Cai Grant / Research Support from: Shanghai Key Laboratory of Pediatric Gastroenterology and Nutrition (No.11DZ2260500)
**Objectives and Study:** Recently non-alcoholic fatty liver (NAFLD) has become a more common condition in children and adults what reflects higher prevalence of overweight and obesity. At present NAFLD is considered as a liver presentation of metabolic syndrome and it carries increased, independent risk of cardiovascular diseases. There is an urgent need to find effective and safe therapy for children with NAFLD.

**Methods:** 76 overweight/obese children with NAFLD aged 13.2±3.1 yrs [mean±SD] with established NAFLD were included in the study. Diagnosis of NAFLD was based on elevated ALT ≥ 1.3 of upper limit of normal (ULN) and hyperechogenic liver on ultrasound. We conducted a double-blind, randomized controlled trial of omega-3 fish oil supplementation (containing docosahexaenoic acid (DHA) + eicosapentaenoic acid (EPA), DHA/EPA= 3:2, 800-1200mg per day, dose weight-dependent) versus omega-6 sunflower oil (as comparator). Weight reduction by low calorie diet and increased physical activity were also advised.

The primary outcome was the number of patients who decreased ALT activity by ≥ 0.3 ULN. The secondary outcomes were alterations in the biochemical liver function tests, liver fat content on ultrasound, insulin resistance and other metabolic markers after 6 months of intervention.

**Results:** Out of 76 enrolled patients, 64 completed the trial and were analyzed statistically. We have not found any significant difference in the number of patients who lowered ALT activity by ≥ 0.3 ULN between the groups of fish oil and placebo (23 vs. 23). Fish oil was not superior to placebo in decreasing ALT activity (48.5;31-62 vs. 39;27-55 U/I) [median, lower-upper quartile], ultrasound liver fat content (1.0;0-1.5 vs. 1.0;0.5-1.5 by Saverymuttu scoring system[1]), fasting glucose, insulin, HOMA-IR or serum lipids.

However patients supplemented with fish oil had markedly lower AST (28;25-36 vs. 39;27-55 U/I, p=0.04) and GGTP activity (26;17.5-36.5 vs.35;22-52, p=0.03) after 6 months when compared to placebo. We also observed significantly higher adiponectin level (6.1;0.6-20 vs. 3.94;0.6-13.7 ug/ml), p=0.02) in children treated with fish oil.

**Conclusion:** Fish oil supplementation does not have a significant effect on liver steatosis expressed by decrease in ALT activity and liver steatosis on ultrasound, but it markedly improves AST and GGTP in children with NAFLD when compared to placebo. Omega-3 fatty acids do not improve most of the metabolic biomarkers but they significantly increase adiponectin level in patients with NAFLD.


**Disclosure of Interest:** None Declared
HEPATITIS B VACCINATION FAILURE IN CHILDREN BORN TO HEPATITIS B POSITIVE MOTHERS
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Objectives and Study: To evaluate the reasons for HBV vaccination failure in children born to HBV positive mothers in the UK.

Methods: We retrospectively evaluated patients referred between 1997 and 2012, who were infected following HBV vaccination at birth. We collected data on demographics, child and maternal HBV serology, viral load, genotype, vaccine escape mutations and vaccine schedule. Statistical analysis was performed using SPSS version 15.0.

Results: 40 patients (16 girls) born to 33 HBV positive mothers in the UK were reviewed. Median age at diagnosis was 14 months (range 6 to 109 months). The majority of mothers originated from the Indian subcontinent and the Far East and none received antiviral treatment during pregnancy. All children were HBsAg positive. We divided the children in two groups: 21 children did not receive a correct vaccination schedule and 17 children had been fully and correctly vaccinated (true vaccination failure). Vaccination schedule was unknown in 2 children. The reason for incorrect vaccination was: unknown in the majority, failure to attend appointments in 3, no appointment given in 2, unknown HBV infection in 1, incorrect vaccination schedule in 3 and change of address in 1. The majority of incorrectly vaccinated children missed more than one dose of vaccine. Four children in the true vaccination failure had vaccine escape mutants. The majority of mothers were HBeAg positive. The following table shows the characteristics of the children with true vaccination failure and with incorrect vaccination schedule and the p values obtained using chi².

<table>
<thead>
<tr>
<th></th>
<th>True Vaccination Failure (n=17)</th>
<th>Incorrect Vaccination Schedule (n=21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal HBeAg+ (n=29)</td>
<td>14 (82%)</td>
<td>15 (71%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Maternal HBVDNA &gt;10 copies/ml (n=21)</td>
<td>13 (76.5%)</td>
<td>8 (38%)</td>
<td>0.01</td>
</tr>
<tr>
<td>HBV Genotype (n=17)</td>
<td>1A, 2B, 7C, 3D</td>
<td>3B, 2D</td>
<td>0.001</td>
</tr>
<tr>
<td>Vaccine Escape Mutant (n=5)</td>
<td>4 (23.5%)</td>
<td>1 (5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HBIG (n=29)</td>
<td>17 (100%)</td>
<td>12 (57%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Summary: The majority of children who failed HBV vaccination had not received the correct vaccination schedule either from failure of primary care services or non attendance by parents. True vaccination failure was associated with high maternal viral load and genotype C, presence of HBV vaccine escape mutant and HBIG administration. The majority of mothers were HBeAg positive in both the true vaccination failure and incorrect vaccination schedule groups. 

Conclusion: It is essential that children born to HBV mothers receive adequate HBV vaccination, with appropriate communication, follow up and involvement of primary care. Mothers with high viraemia should receive antiviral treatment in pregnancy to reduce infectivity. True vaccination failures must be investigated to ensure that the use of Hepatitis B immune globulin is not selecting for vaccine escape mutants.

Disclosure of Interest: None Declared
**HEPATOLOGY**

PD-H-0129

**AUTOIMMUNE HEPATITIS AND PRIMARY SCLEROSING CHOLANGITIS: A SERIES OF SPANISH CHILDREN**  
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**Objectives and Study:** Description of a series of autoimmune hepatitis (AIH) and primary sclerosing cholangitis (PSC) observed in a tertiary-care Spanish centre.

**Methods:** Review of 92 cases with clinical diagnosis and treatment as AIH or PSC registered from 1985 to 2011. Autoantibodies (ANA/SMA/LKM) were tested by indirect immunofluoresce. Pre-treatment biopsy was obtained in 81 cases. Biliary changes were explored by MRI since 2005. AIH score was calculated according to IAIHG (J Hepatol 1999) in a retrospective fashion. Wilson disease, HBV and HCV were ruled out. Patients with immunodeficiencies or previous transplantation were excluded.

Characteristics of type I AIH (AIH1), type II AIH (AIH2), seronegative AIH (AIHneg), and PSC are described.

**Results:**
1. Diagnosis was AIH in 78 cases (85%) and PSC in 14 (15%). Among AIH, there were 31 AIH1, 30 AIH2 and 17 AIHneg. Age ranged 0.55-16 years. All AIH but 1 case (female, LKM+, minimal lesions, receiving anticonvulsants) fulfilled a score of probable or definite AIH (≥10). "Definite AIH" scores (>15) were achieved in 81% AIH1, 67% AIH2, and 18% AIHneg. Among 14 PSC (age 1-16 years), 10 patients showed scores of AIH (probable 8, definite 2).
2. Presentation: Table depicts the main features in each group. ALF was more frequent in AIH2 and AIHneg, ALF in AIHneg was more sensible to treatment than ALF in AIH2. IBD was rare in AIH and universal in PSC. Celiac disease was especially prevalent in AIHneg.

<table>
<thead>
<tr>
<th></th>
<th>AIH1 (n=31)</th>
<th>AIH2 (n=30)</th>
<th>PSC (n=14)</th>
<th>AIHneg (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group &lt;2/2-11/&gt;11 yrs (%)</td>
<td>13/52/35</td>
<td>37/43/20</td>
<td>7/50/43</td>
<td>18/59/23</td>
</tr>
<tr>
<td>Female</td>
<td>71%</td>
<td>87%</td>
<td>43%</td>
<td>53%</td>
</tr>
<tr>
<td>Presentation</td>
<td>Jaundiced</td>
<td>42%</td>
<td>48%</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td>Failure acute (ALF)</td>
<td>3%</td>
<td>23%</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Failure chronic liver disease (CLD)</td>
<td>19%</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>Signs of CLD, not failure</td>
<td>48%</td>
<td>33%</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>Asymptomatic LD</td>
<td>29%</td>
<td>33%</td>
<td>86%</td>
</tr>
<tr>
<td>IgG mg/dl ,mean / IgG&gt;2xULN ,%</td>
<td>2959 /60%</td>
<td>1731/ 27%</td>
<td>1906 /31%</td>
<td>1603/ 18%</td>
</tr>
<tr>
<td>Inflammatory Bowel D/ Celiac</td>
<td>3% /16%</td>
<td>3% /3%</td>
<td>100% / 0</td>
<td>0/ 41%</td>
</tr>
</tbody>
</table>
4. Outcome:
   a) AIH: Treatment achieved remission in 83% AIH1, 70% AIH2 and 94% AIHneg. Transplantation (LT) for end-stage CLD or ALF was required in 13%, 27% and 6%, respectively. One CLD died in waiting list (aspergillus).
   b) PSC: Most (13/14) received steroids for IBD or LD, biochemical remission was not achieved in 57%, 14% underwent LT.

**Conclusion:** Diagnosis of 92 Spanish children was AIH1: 33.6%, AIH2: 32.6%, AIH-seronegative: 18.4% and PSC: 15%. IAIHG 1999 criteria fitted AIH-1 especially but were also met in children with a clinical diagnosis of AIH2 and AIHneg. Seronegative AIH showed distinct features, with high incidence of ALF and celiac disease (mostly previous, on gluten-free diet). Although PSC usually shared features with AIH, underlying IBD and unremitting liver disease made this group different from AIH.

**Disclosure of Interest:** None Declared
RITUXIMAB THERAPY IN CHILDREN WITH GIANT CELL HEPATITIS AND AUTOIMMUNE HEMOLYTIC ANAEMIA- A SINGLE CENTER EXPERIENCE
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Objectives and Study: Giant cell hepatitis with autoimmune hemolytic anemia (GCH with AIHA) is a severe progressive disorder of young children. Routine immunosuppressive treatment (steroids, azathioprine) is often ineffective. Anti-CD20 monoclonal antibody- rituximab was reported to be used successfully in a few cases including 2 cases from the largest cohort of 16 patients described recently. The aim of the study was to analyze the efficacy of rituximab in children with a severe course of GCH with AIHA based on a single center experience.

Methods: We reviewed retrospectively 4 children with GCH with AIHA treated with rituximab, admitted to our Department between 2006-2012.

Results: 2 girls and 2 boys with median age at onset 7 months (range 2-12) were followed-up for 57.5 months (range 12-76), median (min-max). The main observed symptoms were jaundice and hepatosplenomegaly. Anemia in 3 children preceded GCH. Liver failure was observed in 3 children. All children had positive direct Coombs’ test and diffuse giant-cell transformation in liver biopsy. As conventional therapy (prednisone, azathioprine) was ineffective in all children the second line therapy was started. Methylprednisolone was effective in 1 girl only for controlling severe haemolysis, still Methylprednisolone, Cyclosporine and MMF did not result in aminotransferases normalization. Finally, after 6 years from the onset of the disease, Rituximab was adminstered once a week for 4 weeks which resulted in the decrease of aminotransferases activity. The second girl achieved normalization of hemoglobin concentration after the 4th dose of Rituximab, but aminotransferase activity returned to normal 20 months after the first dose. She is off treatment and well now, with no relapses during 54 months after Rituximab. One boy after unsuccessful therapy with cyclosporine and immunoglobulins received 2 doses of Rituximab with good initial response, but subsequently anaemia recurred and next 4 doses were administered after 5 (2 doses), 12 (1 dose) and 24 months (1 dose). He is off treatment and well now, 17 months after the last dose. Another boy after the 2nd dose of Rituximab still suffered from haemolysis, ascites and liver failure, required plasmapheresis and peritoneal drainage. Finally, after the 5th dose of Rituximab full clinical remission was obtained, with no relapse after 10 months from the last dose of Rituximab, but low dose prednisone is still used.

Conclusion: Rituximab therapy should be considered as the second line treatment for severe GCH with AIHA if steroid and azathioprine therapy is ineffective. Minimum 4 doses of initial rituximab therapy seem to be required to obtain full clinical remission, still liver function tests may improve gradually over a longer time period.


Disclosure of Interest: None Declared
IMMUNE DYSREGULATION IN ALAGILLE SYNDROME: A NEW FEATURE OF THE EVOLVING PHENOTYPE
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2Division of Transplantation Immunology&Mucosal Biology, MRC Centre for Transplantation, King's College London,
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Objectives and Study: Alagille Syndrome (ALGS) is an autosomal dominant disease caused by mutations in one of two NOTCH Signalling Pathway genes (JAG1 95% & NOTCH2<1%). Alagille Syndrome causes significant morbidity associated with liver, cardiac, renal and vascular malformations. Susceptibility to infection in ALGS is a cause of morbidity presenting over a wide ‘severity range’ representing 25% of our ALGS Cohort of 105 patients. The mechanisms of this immune dysfunction and its link to mutations in the NOTCH pathway have been entirely unexplored. Recently it was shown that CD46 (complement regulator) regulates NOTCH expression during T cell activation after binding to C3b/C4b and that the Jagged1 and the C3b/C4b binding sites on CD46 overlap1. These findings suggested the possibility of an impaired T-cell response among a population exhibiting JAG1 mutations. We hypothesised that the abnormal CD46-Jagged1 interactions would disturb CD46-NOTCH crosstalk providing an explanation for recurrent infections among our ALGS population.

Methods: 4 ALGS patients with JAG1 mutations and persistent but quiescent infections were enrolled along with 2 healthy donors. None of the subjects were taking immunosuppressants. T cells from the 6 consented subjects were isolated, activated and cultured. Cytokines from cell cultures were measured using the human T H Cytometric Bead Arrays or the human IFN-γ, and IL-10 Cytokine Secretion Assay Kits. Resting and activated T cells’ cytokine productions were studied in both low and high IL-2 concentration media to assess the T H ability to shift from INFγ to IL-10 production.

Results: In vitro, initial ALGS PBMC population and subpopulation assessments were normal but further assessment of the lymphocytes revealed that while NOTCH1 expression and regulation was normal on resting T H, Jagged1 expression was increased. Resting T H cells from all patients exhibited high CD132 levels. Upon activation, T H cells managed to produce TNF but failed to produce sufficient IFNγ levels. On the other hand, T H2 cells exhibited an exaggerated response. T H were unable to down regulate CD127, resulting in prolonged immune activation and failed to shift from IFNγ to IL-10 production. These findings are significantly different from normal responses.

Conclusion: JAG1 mutations result in deregulated surface markers on T cells from ALGS patients. This is compatible with immune dysregulation in favour of a prolonged defective pro-inflammatory state, in turn suggesting a mechanism for the previously unexplained recurrent or prolonged inflammatory symptoms in ALGS patients. The ALGS description should be extended to include immune dysregulation whose significance requires further study.

References: 1. Le Friec G.; The CD46-Jagged1 interaction is critical for human T H1 immunity; Nat Imn.2012 Oct 21

Disclosure of Interest: None Declared
LIVER NATURAL ACELLULAR SCAFFOLDS PRODUCED WITH THE DETERGENT-ENZYMATIC METHOD MIMIC ORIGINAL TISSUE ARCHITECTURE AND PROMOTE CELL GROWTH
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Objectives and Study: Hepatic tissue engineering may provide an alternative therapeutic solution to patients with liver failure. A tissue-engineered organ approach requires the combination of a scaffold that mimics original organ architecture with appropriate cells. The aim of this study was to produce a natural acellular matrix for the regeneration of the liver.

Methods: Mouse livers were decellularized with detergent-enzymatic treatment (DET) and assessed using DNA quantification, collagen quantification, haematoxylin and eosin (H&E), masson’s trichrone (MT), verhoeffs van gieson (EVG), alcian blue (AB) staining and trypan blue (TB) injection in the vasculature. HepG2 cells were injected into the lobes of the scaffold and incubated in suspension in an incubator. Following 24 hours, the lobes were fixed, embedded in paraffin and staining with H&E, albumin and Cleaved Caspase-3 (CC-3).

Results: Macroscopic appearance of the scaffolds demonstrated complete decellularization following 1 cycle of DET (Fig.1a,b), which was confirmed by DNA quantification and H&E staining. MT, AB and EVG staining demonstrated preservation of the components of the ECM. Collagen quantification demonstrated a significant increase in the scaffold when compared to fresh tissue (p<0.001), as expected due to the lack of cells in the tissue. The resulting liver-derived scaffolds maintained the complex vascular network of the organ as evident by TB infusion. Following seeding, the cells were viable at 24 hrs, occupying the spaces that remained in the extracellular matrix. Cell survival at 24 hrs, assessed by CC-3 staining, appeared greater in more densely seeded areas than in areas where cell density was low (Fig.1c,d).

Conclusion: The production of a scaffold that preserves hepatic architecture has significant potential for regenerative medicine applications in liver diseases. The viability of seeded cells suggests dependence to a combination of signals from the ECM and the surrounding cells to ensure survival.

Disclosure of Interest: None Declared
HEPATOLOGY

PD-H-0133

CLINICAL AND MOLECULAR CHARACTERISTICS OF MITOCHONDRIAL DNA DEPLETION SYNDROME: A CAUSE OF NEONATAL CHOLESTASIS AND INFANTILE LIVER FAILURE

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Objectives and Study: Mitochondrial DNA (mtDNA) depletion syndromes (MDS) are a genetically heterogeneous group of Mendelian disorders of infancy and childhood, leading to a quantitative loss of mtDNA copy number in clinically-affected tissues. The clinical phenotypes of MDS are therefore highly variable, leading to three main clinical presentations: myopathic, encephalomyopathic, and hepatocerebral. The aim of this study is to report the clinical, biochemical, histopathological, and molecular characteristics of 8 infants with hepatocerebral MDS presenting with neonatal cholestasis and infantile liver failure of hepatocerebral form, including 4 patients with novel mtDNA maintenance gene mutations.

Methods: We studied 14 infants with suspected hepatocerebral MDS referred to the Children’s Hospital at King Fahad Medical City, Riyadh, Saudi Arabia between 2007 and 2012. Total genomic DNA was isolated from blood leukocytes, liver or skeletal muscle samples by standard methods. MtDNA copy number relative to nuclear DNA levels was determined in muscle and/or liver DNA using real-time quantitative PCR, comparing these data to age-matched controls. Nuclear candidate genes including POLG, MPV17 and DGUOK were undertaken using standard analyses.

Results: We identified pathogenic MPV17 and DGUOK mutations in 8 (5 females) out of 14 infants with suspected hepatocerebral MDS, representing 2% of the 400 cases of infantile cholestasis referred to our center during the study period. MtDNA depletion was demonstrated in liver or muscle for 6 out of the 8 cases where tissue was available. Five patients (from 3 families) had a homozygous MPV17 gene mutation (3 are novel mutations): c.62T>G (p.Leu21Arg), 278A>C (p.Gln93Pro), c.279+1G>T. The remaining 3 patients (from 2 families) had a homozygous DGUOK gene mutation (1 is a novel mutation): c.223T>A (p.W75R) and c.766_767insGATT (p.Phe256X). Age at presentation ranged from one to 7 months. All patients manifested with cholestasis, hypotonia, and failure to thrive. Age at onset of liver failure ranged from 3 to 7 months. Three of 5 patients with MPV17 mutation died at before 1 year of age whilst 2 are still alive at 13 and 15 months. Two of the 3 patients with DGUOK mutation died before 1 year of age, one is still alive at 5 months.

Conclusion: We describe novel mutations in the MPV17 and DGUOK genes which confirm previous data that hepatocerebral MDS presents in infancy with cholestasis, progressing to liver failure.

Disclosure of Interest: None Declared
NEUTRALIZATION OF INTERLEUKIN-17 DISRUPTS DISEASE PROGRESSION IN EXPERIMENTAL BILIARY ATRESIA: A NEW THERAPEUTIC APPROACH?
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Objectives and Study: Biliary atresia (BA) is characterized by an inflammatory, progressive destruction of the biliary system and subsequent obstructive cholestasis, liver cirrhosis, and failure. Interleukin-17 (IL-17) has been identified as a cytokine driving inflammatory and autoimmune processes. Researching early initiators of BA, we investigated the role of IL-17 producing lymphocytes in the pathogenesis of experimental BA.

Methods: For induction of experimental BA, neonatal Balb/c mice were infected with rhesus rotavirus (RRV) postpartum. Animals were sacrificed at various time points and livers harvested for further analysis. Viral load was assessed by quantitative PCR (qPCR). Liver infiltrating leukocytes and their cytokine production were phenotyped by flow cytometry. Additionally, liver infiltrating T cells were isolated from animals with or without BA by magnetic activated cell sorting. Freshly isolated cells were analyzed by qPCR for cytokines and transcription factors of the IL-17-axis. Additionally, isolated T cells were restimulated in vitro and cytokine production assessed by ELISA. In vivo, IL-17 was neutralized by treatment with a monoclonal antibody following RRV infection and disease progression was monitored. In addition, human liver samples of patients were analyzed by qPCR for the expression of proinflammatory cytokines including IL-17.

Results: IL-17 producing T cells were significantly (p < 0.001) increased in livers of animals with symptomatic disease whilst absent in non-symptomatic animals. The percentage of IL-17 producing T cells proved to greatly increase as the diseases progressed and showed no correlation with viral load. Liver infiltrating T cells from mice with BA are characterized by upregulation of typical markers of the IL-17-axis, such as IL17a, RORyt, CCR6 and the IL-23-receptor. In vivo blockage of IL-17 by administration of monoclonal antibodies considerably ameliorated disease progression. Concerning the situation in humans, IL-17 transcripts were significantly upregulated in patients suffering from BA compared to individuals with other neonatal cholestatic diseases.

Conclusion: We demonstrate that IL-17 producing T cells are a causative factor in the inflammatory destruction of the biliary system in experimental BA. Our data also suggests an important role in human BA. We hypothesize, that these dysregulated T cells are an early initiator of BA and that their inhibition could prove beneficial for patients. However, further studies are needed to clearly identify the role of IL-17 in human BA and to investigate the therapeutic potential of treatments targeting the IL-17 axis.

Disclosure of Interest: None Declared
COMMON ESPGHAN TOPICS
TRANSPLANTATION
PD-H-0135

BENEFITS OF RAPAMYCINE AS IMMUNOSUPPRESSIVE TREATMENT IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS WITH POLYMORPHIC, POLYCLONAL, EBV-RELATED POST-TRANSPLANT LIMPHOPROLIFERATIVE DISEASE (PTLD)

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Objectives and Study: PTLD is a severe complication of transplantation, linked in most cases to EBV infection. Little is known about prevalence and natural history of early, polyclonal variants. Since they are considered to be at risk of progression in more aggressive variants, treatment is mandatory and withdrawing/modulation of immunosuppressive treatment is usually the first line therapy. There is emerging evidence that mTOR inhibitors can have cytostatic effects that may be particularly relevant in the setting of EBV-associated PTLD. The aim of this study is to report on our experience with Rapamycin as first line therapy for polyclonal PTLDs in pediatric liver transplant recipients.

Methods: 28 PTLD were diagnosed in our Institution after a median time from OLTx of 4 years and 2 months (range 9 m – 12 y and 2 m). 16 of them were classified as “Early Lesions” and 12 as polymorphic polyclonal. 9 children with polymorphic PTLD in adenotonsillar and/or gastrointestinal lymphoid tissue, were treated with the shift of from Tacrolimus to Rapamycin. 7 of them received Rapamycin in monotherapy while in 2 was associated with micofenolate mofetil. Target blood trough level was between 3 and 6 ng/ml. After a median time of 6 months (range 4 – 30) all patients underwent histological revaluation of affected tissues and liver biopsy.

Results: Results of histological examination of adenotonsillar tissue and gastrointestinal-associated lymphoid tissue at diagnosis and after treatment with Rapamycin are summarized in table. Liver biopsy, performed after a median of 13 months (range 6 – 30 months) of Rapamycin therapy did not show signs of rejection. After a median follow up of 20 months (range 13 – 35) all patients are alive and without signs of rejection or progression of PTLD.

Image:

<table>
<thead>
<tr>
<th>Before treatment</th>
<th>Adenoids/Tonsils</th>
<th>Gut</th>
<th>Before treatment</th>
<th>Adenoids/Tonsils</th>
<th>Gut</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>PM</td>
<td>PM</td>
<td>-</td>
<td>PM</td>
<td>4 months</td>
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</tr>
<tr>
<td>P2</td>
<td>PM</td>
<td>-</td>
<td>EL</td>
<td>EL</td>
<td>6 months</td>
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<tr>
<td>P3</td>
<td>PM</td>
<td>EL</td>
<td>EL</td>
<td>EL</td>
<td>6 months</td>
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<td>P4</td>
<td>PM</td>
<td>EL</td>
<td>EL</td>
<td>EL</td>
<td>5 months</td>
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<tr>
<td>P5</td>
<td>PM</td>
<td>EL</td>
<td>NEG</td>
<td>NEG</td>
<td>12 months</td>
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<tr>
<td>P6</td>
<td>PM</td>
<td>PM</td>
<td>NEG</td>
<td>EL</td>
<td>6 months</td>
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</tr>
<tr>
<td>P7</td>
<td>PM</td>
<td>PM</td>
<td>PM</td>
<td>EL</td>
<td>4 months</td>
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</tr>
<tr>
<td>P8</td>
<td>PM</td>
<td>EL</td>
<td>EL</td>
<td>EL</td>
<td>12 months</td>
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</tr>
<tr>
<td>P9</td>
<td>PM</td>
<td>EL</td>
<td>EL</td>
<td>EL</td>
<td>30 months</td>
<td></td>
</tr>
</tbody>
</table>

P: patient, PM: polymorphic PTLD, EL: “Early Lesions” PTLD, NEG: negative
**Conclusion:** Current first-line treatment of EBV related polyclonal variants of PTLD in liver transplanted children is reduction or even temporary withdrawal of immunosuppressive therapy. Although usually effective, this approach carries a high risk of rejection. Treatment with Rapamycin allowed a good control of PTLD with downgrade to “Early Lesions” in 6 of 9 patients and complete remission in one, without exposing patients to risk of rejection.

**Disclosure of Interest:** None Declared
COMMON ESPGHAN TOPICS
TRANSPLANTATION

PD-H-0136

VANISHING BILE DUCT SYNDROME IN PAEDIATRIC LIVER TRANSPLANTATION: IMPACT OF IMMUNOSUPPRESSIVE TREATMENT ON BIOCHEMICAL AND HISTOLOGICAL PROGRESSION
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Objectives and Study: Vanishing bile duct syndrome (VBDS) is still a significant complication in the long term follow-up of paediatric liver transplantation (OLT). The aim of this study was to retrospectively analyse the impact of medical treatment to stop the progression of VBDS.

Methods: We analysed the files of children who received a OLT from 1997 to 2012 at our institution. The diagnosis of VBDS was based on liver biopsies performed because of liver tests abnormalities. The Banff Criteria were considered to standardise the evaluation of the VBDS as “early chronic rejection” (ECR), and “late chronic rejection” (LCR). For this group of patients we analysed immunosuppression modification, liver function tests and follow up biopsies.

Results: VBDS was diagnosed in 76/500 grafts (12%), after a mean follow up of 3,1 (±3) years from OLT; 53 biopsies (70%) showed ECR, 14 (18%) LCR, 9 (12%) were not defined according to the standard criteria. Patients with VBDS had had a significantly higher number of episodes of acute rejection (60,5%) compared to patients who did not develop VBDS (25,8%, p<0,0001). At the first diagnosis 80% of patients were on tacrolimus-based therapy, 12% on cyclosporine, 8% on other regimens. After the diagnosis of VBDS the immunosuppressive strategy was modified in 72% of patients, either by switching from cyclosporine to tacrolimus or adding mycophenolate mofetil to tacrolimus. Histological progression from ECR to LCR was observed in 25/53 patients (47%) over a mean follow-up time of 5 years (±3,6); this evolution was independent from the modification of immunosuppressive treatment (p=0.2, Fisher exact test). On the contrary, we observed a significant decrease in biochemical parameters; AST/ALT levels at the first biopsy were respectively 157 (±176) and 211 (±254) IU/l; at the second biopsy the levels were respectively 78 (±79) and 98 (±114) IU/l (p <0,001 and p< 0,002 at paired sample t-test). No significant changes were observed in GGT and bilirubin levels. Overall 8/76 (10.5%) patients with VBDS lost their graft and required re-transplantation.

Conclusion: Increased immunosuppression is the standard of care following a diagnosis of VBDS. This strategy seems to have a favourable effect in improving liver function tests, but does not influence the histological progression of the disease in a large proportion of cases. A better approach to prevent and treat VBDS in this setting is warranted to avoid irreversible modifications and graft loss in children who received a liver transplant.

Disclosure of Interest: None Declared
LOW URIC ACID IS AN IMPORTANT BIOCHEMICAL CLUE FOR THE DIAGNOSIS OF WILSON DISEASE IN CHILDREN.
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Objectives and Study: Various biochemical indices (Aspartate to alanine transaminase ratio > 4, Alkaline phosphatase to bilirubin ratio < 2) point towards diagnosis of Wilson disease (WD). Hypouricemia occurs in WD primarily due to renal tubular involvement. This finding although mentioned in the literature but has not been studied well. So, the present study was conducted with the following objectives - 1. To study the uric acid (UA) levels in children with chronic liver disease (CLD) and acute hepatitis (AcH) with or without WD and compare with controls. 2. To establish the diagnostic value of UA for WD.

Methods: Serum UA levels on presentation were determined in 169 children on presentation - 23 with WD (Group A), 109 with liver disease other than WD (Group B) and 37 controls without any liver disease (Group C). Diagnosis of WD was established as per AASLD guidelines.

Results: UA levels were significantly low in children with WD (1.93±0.78mg/dL) as compared to Group B (3.81±1.13mg/dL) and Group C (4.03±1.07mg/dL) (p< 0.001). In the WD group, UA levels were not different with regard to gender or mode of presentation (CLD or AcH) (p=NS). Overall, presentation as CLD or AcH, a UA level less than or equal to 2.65mg/dL predicted WD with a sensitivity, specificity, positive likelihood ratio, positive and negative predictive values of 87%, 89.9%, 8.61, 65.6% and 98%, respectively, with area under receiver operating characteristic curve of 0.926.

Conclusion: Low uric acid level in a child with either CLD or AcH as presentation predicts diagnosis of WD with fair good accuracy.

Disclosure of Interest: None Declared
IMMUNOMODULATORY PROPERTIES OF SPECIFIC BOVINE MILK PROTEIN PREPARATIONS IN DC-T CELL CO-CULTURES
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Objectives and Study: Protein preparations with immunomodulatory function in cow milk based infant formula may be beneficial for supporting immune reactivity by specific interactions with dendritic cells (DCs). As a model for the potential immunomodulatory property of bovine milk whey proteins we investigated the polarizing effect of monocyte-derived DCs (MoDCs) treated with milk-derived protein preparations. Specific whey protein preparations processed differently such that there was differential retention of bioactive proteins were compared in these immune cell assays on T-cell responses by MoDC-CD14- cells co-cultures.

Methods: Immature DCs were generated from peripheral blood monocytes of healthy donors, and subsequently stimulated with bovine whey protein preparations (WPC1, WPC2) or skimmed milk protein control preparation (PC) in combination with the maturation factor LPS. WPC1 was previously analyzed to have higher levels of relevant bioactive proteins, e.g. TGF-β. After stimulation, mature MoDCs (mMoDCs) were co-cultured with autologous CD14- cells for seven days, and subsequently, T cell differentiation, proliferation and cytokine profiles were determined.

Results: mMoDCs stimulated by WPC1 produced significantly lower levels of inflammatory cytokines TNF-α, IL-6 and borderline significance for IL-8. In mMoDC-CD14- cell co-cultures, WPC1 stimulated MoDCs increased the percentage of CD4+CD25+ T cells and decreased proliferation of effector T cells. mMoDCs simulated by WPC1 and WPC2 at concentrations of 100 and 250 μg/ml inhibited the Th2 response of CD14- cells by decreasing IL-5 and IL-13 as compared with LPS stimulation alone. Moreover, mMoDCs particularly exposed to WPC1, showed a more potent capacity to induce TGF-β production by CD14- cells as compared with LPS stimulated controls.

Conclusion: Both whey protein preparations, but most prominently, the WPC1 with higher TGF-β1 content, can direct the immune response in DC-CD14- cell co-cultures by skewing the Th1/Th2 balance away from a putative Th2 profile. This is accompanied by increased production of DC-derived TGF-β1, which may be indicative for expansion of a more tolerogenic CD4+CD25+ Treg population. Thus, this study underlines the qualitative differences of whey protein preparations with respect to their immunomodulatory capacities.

OBJECTIVES AND STUDY: Eosinophilic esophagitis (EoE) is usually associated with a history of atopic diseases, indeed, the pathogenesis of EoE is frequently compared to other allergic diseases. Using microarray analysis, we have identified new Th2-induced genes in EoE disease such as the TNF-alpha induced protein-6 (TSG6) previously shown to inhibit neutrophil accumulation in inflammatory site. We aimed at identifying Th2-induced epithelial genes in vitro and in vivo and at investigating the molecular differences between EoE, and other Th2 diseases such as atopic dermatitis (AD) and acute asthma (AA).

METHODS: Transcriptomic analyses were performed in human disease of EoE, AD and AA, as well as in Th2-related murine models and in vitro, in IL-13-stimulated epithelial cells, using publically available and newly generated data. Confirmation of gene expression in vitro and in vivo was performed by qPCR.

RESULTS: TSG6 mRNA and protein was induced in epithelial cells of the esophagus in EoE disease. Interestingly, TSG6 mRNA was also increased in AD and AA disease and induced by IL-13 stimulation in primary epithelial cell from the skin and the esophagus but not in nasal epithelial cells. Using knockout animals, we demonstrated that the transcription factor STAT6 was involved in TSG6 mRNA upregulation in these murine models. In order understand the global and specific involvement of IL-13 and epithelial cell in EoE, AD and AA, the global transcriptomic analysis of Th2 diseases was analyzed. A 2%, 6% and 13% of the total probed genes were dysregulated by at least 2-fold in EoE, AD and AA, respectively. The involvement of IL-13-stimulated epithelial cell transcriptome in the diseases was evaluated to 22%, 9% and 5%, in EoE, AD and AA respectively. We identified new sets of Th2/IL-13-related genes, many known genes were found dysregulated in the three diseases such as filaggrin, histamine receptor H1, claudin 1, cathepsin C, Plasminogen activator and SOCS3. Finally, despite numerous transcripts found dysregulated independently in a specific disease or animal or in vitro models, a strong and sticking overlap between EoE and AD (but not AA) transcriptomic profiles was observed.

CONCLUSION: All together, these data emphasize the involvement of IL-13 in the EoE and AD disease and suggest a stronger overlap of the human eosinophilic esophagitis and atopic dermatitis rather than with other Th2 related diseases or models. These data allow a direct comparison of three diseases and may enlighten the similarities and difference of treatment efficacy.

THE DOUBLE-BLIND PLACEBO-CONTROLLED FOOD CHALLENGE IN THE SUSPICION OF NON-IGE MEDIATED COW’S MILK ALLERGY

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Objectives and Study: Unspecific gastrointestinal symptoms in infants often raise suspicion of cow’s milk allergy. We used the double-blind, placebo-controlled food challenge to ascertain this diagnosis.

Methods: We recruited infants and young children with predominantly gastrointestinally manifested symptoms, suspected of cow’s milk allergy, in a prospective study. All patients underwent a five-day double-blind, placebo-controlled food challenge for cow’s milk. Fecal calprotectin levels were analyzed before the challenge and 3-6 days after the start of the active provocation.

Results: Fifty-seven children (median age 8.7 months) underwent the double-blind, placebo-controlled food challenge and it was positive in 18 (32%) patients. Among the challenge negative, placebo reactions occurred in 13 (33%). The challenge positive (compared to provocation negative) reported significantly more often loose stools (78% vs. 46%, p=0.0436) than other gastrointestinal symptoms. None of the children had detectable cow’s milk specific IgE. No serious adverse effects appeared during challenges. On elimination diet the fecal calprotectin levels were higher in the challenge positive (mean 119.4 µg/g vs. 38.49 µg/g, p=0.0037), and this difference remained after cow’s milk challenge (mean 129.8 µg/g vs. 57.97 µg/g, p=0.0336). In 10 out of 18 challenge positive patients the calprotectin levels were within the reference range (<100 µg/g).

Conclusion: The diagnosis of cow’s milk allergy in infants with gastrointestinal symptoms is seldom confirmed. Other reasons for the perceived gastrointestinal symptoms should also be explored. The elevated fecal calprotectin levels on elimination diet in some infants may indicate a persistent proinflammatory state in the intestinal mucosa and this finding should be further studied.

Disclosure of Interest: None Declared
USE OF EARLY PREBIOTIC AND PROBIOTIC SUPPLEMENTATION PREVENTS VIRAL RESPIRATORY TRACT INFECTIONS IN PRETERM INFANTS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Objectives and Study: Our aim was to study whether early prebiotic and/or probiotic supplementation during the two first months of age impacts the incidence or the clinical picture of viral respiratory tract infections (RTIs) during the first year of life in a preterm cohort.

Methods: In this randomized, double-blind trial 94 preterm infants (gestational age ≥ 32+0 and ≤ 36+6 weeks, birth weight > 1500g) were allocated to receive enterally prebiotics (galacto-oligosaccharide and polydextrose 1:1), probiotics (Lactobacillus rhamnosus GG), or placebo (microcrystalline cellulose) between days 3 and 60 of life. Incidence of viral RTI episodes and intensity and duration of viral excretion of viruses was assessed by nasal swab tests samples analyzed by quantitative reverse transcription-polymerase chain reaction. Clinical picture of infections was analyzed by diaries fulfilled by parents. This study is registered with ClinicalTrials.gov, number NCT00167700.

Results: A statistically significant difference was detected in the incidence of symptomatic RTIs among the study groups, the mean (SD) incidence of episodes being 0.6 (0.8) in the prebiotic, 1.2 (1.6) in the probiotic, and 2.5 (2.0) in the placebo group; \( P = 0.001 \) (Table 1). In most of the cases (96 %) a viral aetiology was detected, the single most common virus being human rhino virus, found in 82 (80 %) episodes. No differences were found in the viral load during infections, time of viral shedding, the duration or severity of infections, nor in the occurrence of subclinical viral infections among the study groups.

Table 1. Grouping of patients in the three study groups according to the number of symptomatic viral respiratory tract infection episodes during the 12 months’ follow-up period.

<table>
<thead>
<tr>
<th>Group</th>
<th>Prebiotic (n = 23)</th>
<th>Probiotic (n = 21)</th>
<th>Placebo (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of episodes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>14 (61 %)</td>
<td>10 (48 %)</td>
<td>4 (17 %)</td>
</tr>
<tr>
<td>1 – 3</td>
<td>9 (39 %)</td>
<td>9 (43 %)</td>
<td>12 (50 %)</td>
</tr>
<tr>
<td>&gt; 3</td>
<td>0 (0 %)</td>
<td>2 (9 %)</td>
<td>8 (33 %)</td>
</tr>
</tbody>
</table>

Conclusion: Early gut microbiota modification with prebiotics and probiotics may offer a novel and cost-effective means for the prevention of RTIs. Further studies are needed to reveal the repeatability of our results also in fullterm infant population.

Disclosure of Interest: None Declared
PLASMA NONESTERIFIED FATTY ACIDS AS NON-INVASIVE BIOMARKER FOR ADIPOSE TISSUE FATTY ACID COMPOSITION
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Leipzig, Germany

Objectives and Study: Adipose tissue (AT) is an accepted long-term biomarker for fatty acid status. During fasting, AT lipolysis leads to the release of nonesterified fatty acids into plasma (pNEFA). The objective of this study was to investigate the association of pNEFA composition with AT fatty acid composition, as a close correlation would enable virtual AT biopsies for patients, like children, in whom it is difficult to perform an AT biopsy.

Methods: Fatty acid (FA) composition of subcutaneous AT (sAT), visceral AT (vAT) and pNEFA of 30 non-diabetic women, with BMI ranging from normal to extremely obese, were analysed. FA of AT triacylglycerols were liberated by base catalysed hydrolysis and quantified, like pNEFA, by liquid chromatography/tandem mass spectrometry. Spearman's rho statistics were used to estimate rank-based correlation coefficients for individual FA percentages between the studied compartments.

Results: Correlations were studied for 42 FA. For all FA, strong correlations (>0.7) between sAT and vAT were found, except for 18:1 (r=0.554), 20:1 (0.648) and 24:3 (0.608). While all FA correlate significantly between sAT and vAT, the correlations of pNEFA and AT fatty acid percentages varied widely between FA, with correlation coefficients from -0.034 for 24:3 (pNEFA~sAT) to 0.862 for 15:0 (pNEFA~vAT). Strong correlations between pNEFA and sAT/vAT were found for odd-chain FA 15:0 (r=0.838/0.862), 17:0 (0.839/0.833), 17:1 (0.667/0.735), 19:0 (0.658/0.739), 19:1 (0.779/0.744) and 19:2 (0.803/0.560) as well as for omega-3 FA 22:6 (0.719/0.535) and 24:6 (0.694/0.693). Furthermore, 16:0 showed a strong correlation (0.681/0.775), while saturated and mono-unsaturated very long chain FA (C≥20) and 20:4 (0.386/ns) have low or no significant correlation. Medium correlations were found for essential FA 18:2 (0.541/0.610) and 18:3 (0.577/0.513).

Conclusion: The determination of odd-chain FA and long-chain omega-3 FA in the pNEFA fraction provides information about the content of these FA in adipose tissue. Thus, NEFA analysis in fasted plasma/serum can serve as a virtual adipose tissue biopsy for these FA and as biomarker for long-term dietary intake of dairy products and sea fish or fish oil. The lower correlation for some pNEFA species with adipose tissue FA indicates that adipose tissue is not the only quantitatively important source for these FA in the fasted state.


Disclosure of Interest: None Declared
‘NEONATAL PERIPHERAL ADIPOSITY MEASUREMENTS USING 2D ULTRASOUND IN PREMATURE INFANTS AND COMPARISON WITH FETAL ADIPOSITY MEASURES’ - A NOVEL MARKER FOR NUTRITIONAL STATUS.
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Objectives and Study: A feasibility study to develop ultrasound image based bedside nutritional measurement, which is independent of body weight and which can be used to compare fetal versus neonatal growth, in premature and growth-restricted infants. We postulate that, this peripheral fat measure in fetal and neonatal period could potentially be a biomarker for nutritional status.

Methods: 2D ultrasound-derived cross-sectional images at the level of mid arm were acquired from 28 preterm infants. A specially adapted gel pad was used to acquire these images. Subcutaneous tissue was delineated from muscle and bone compartment using specially developed software and this cross sectional area measure was used as a proxy for amount of fat.
Similar measures were collected from fetuses of women of various gestations having normal course of pregnancy to construct fetal trajectories.

Results: Cross sectional adiposity measurements were plotted against corrected gestational age for (n=28) and a good correlation was observed ($R^2 = 0.65$). When growth restricted (n=4) and infants of mothers with impaired glucose tolerance tests (n=2) were excluded, a strong correlation was noted ($R^2 = 0.91$). This data was compared to previously presented ultrasound-derived fetal fat cross sectional adiposity measures. (178 fetal measures from healthy women with normal pregnancies at various gestations.) All premature infants had lower peripheral fat measures as compared to their fetal counterparts at any given gestation.

Conclusion: Preliminary results suggest that ultrasound derived neonatal peripheral adiposity measures have the potential to be a novel nutritional measure, with emphasis on fat accretion. Premature babies seem to accrete lower amounts of fat than their fetal peers. A larger data collection exercise is underway to elucidate the relationship of growth, gestation, peripheral fat accretion and body compositional changes. With fetal data available, we hope to demonstrate if post natal peripheral fat accretion tracks normative fetal trajectories, and thus be a proxy to track body compositional changes across in utero and post natal life.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: In our previous study we found significant increase in n-6 and n-3 long chain polyunsaturated fatty acid (LCPUFA) values of German human milk samples from the 6th week to the 6th month of lactation (Szabó et al, JPGN 2010). The aim of the present study was to corroborate these findings in an independent study investigating milk fatty acid composition in Hungarian mothers.

METHODS: Forty-six mothers of healthy, full-term and appropriate for gestational age newborns were included into the study at the Department of Obstetrics and Gynecology, University of Pécs, Hungary. Milk samples were obtained at the first day, sixth week and sixth month of lactation. High resolution, capillary gas-liquid chromatography was used for the analysis. The statistical analysis was performed by SPSS 15.0 programme using ANOVA and Wilcoxon signed-rank tests.

RESULTS: Values of n-6 and n-3 essential fatty acids, linoleic acid and alpha-linolenic acid were significantly lower in colostrum than in breast milk sampled, at both the 6th week and the 6th month of lactation. In contrast, their principal metabolites, the arachidonic acid (AA) and the docosahexaenoic acid (DHA) decreased significantly by the 6th week of lactation. Values of AA decreased significantly further, whereas no change of DHA values was seen between the 6th week and the 6th month of lactation. Sum of trans fatty acids was significantly higher in colostrum than in breast milk sampled at both the 6th week and 6th month of lactation (Table).

TABLE: Changes of fatty acid composition of human milk in Hungarian mothers (n = 46)

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Colostrum</th>
<th>6th week milk</th>
<th>6th month milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic acid</td>
<td>13.54 (2.84)^A,B</td>
<td>15.37 (4.84)^A</td>
<td>16.15 (7.22)^B</td>
</tr>
<tr>
<td>a-linolenic acid</td>
<td>0.42 (0.09)^A,B</td>
<td>0.60 (0.44)^A</td>
<td>0.66 (0.40)^B</td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>0.91 (0.38)^A,B</td>
<td>0.53 (0.17)^A,C</td>
<td>0.46 (0.13)^C,B</td>
</tr>
<tr>
<td>Docosahexaenoic acid</td>
<td>0.29 (0.12)^A,B</td>
<td>0.14 (0.04)^A</td>
<td>0.12 (0.10)^B</td>
</tr>
<tr>
<td>Trans isomeric</td>
<td>1.18 (0.51)^A,B</td>
<td>1.04 (0.47)^A</td>
<td>0.96 (0.40)^B</td>
</tr>
</tbody>
</table>

Data are median (IQR), A, B, C: significant difference (p < 0.001); Trans isomeric: sum of trans fatty acids (t16:1n+ t18:1n-9/7+ tt18:2n-6)

CONCLUSION: 1. In this study we failed to corroborate the previous finding of increasing docosahexaenoic acid values in German human milk between the 6th week and the 6th month of lactation. 2. Hungarian mothers, both arachidonic acid and docosahexaenoic acid content of the breastmilk decreased during lactation. 3. Contribution of trans fatty acid was the highest at the beginning of lactation.
References: Fatty acid profile comparisons in human milk sampled from the same mothers at the sixth week and the sixth month of lactation.
PMID:20118808

Disclosure of Interest: None Declared
RESIDUAL SMALL BOWEL LENGTH PREDICTS RAISED D-LACTATE WHEN SCREENING FOR BACTERIAL OVERGROWTH IN CHILDREN WITH INTESTINAL FAILURE

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Objectives and Study: Small bowel bacterial overgrowth (SBBO) may cause non specific symptoms in children with intestinal failure (parenteral nutrition (PN) >28days). Delayed diagnosis may result in significant morbidity. Rapid detection of raised serum D-lactate (DL) produced by excess luminal bacteria, such as lactobacilli, may be a clinically useful non invasive marker of SBBO. We identified all patients with current or recent Intestinal Failure (IF) who had developed new symptoms suggestive of SBBO. Risk factors for DL and response to treatment were recorded to present the first large cohort of DL in a tertiary referral centre.

Methods: Retrospective case note review over a 3 year period (01/01/2009 to 31/12/2011). Patients aged 0-18 years with IF and suspected SBBO due to new symptom onset were included. Demographics, aetiology of IF, symptoms, recent radiology and treatment were recorded. In those with short bowel syndrome, length of remaining small bowel was expressed as percentage of expected small bowel length appropriate for age (SBL) using a published formula. Raised DL was identified as DL>20µmol/L and recurrence as DL>20µmol/L at least 4 weeks after the last measurement and with standard treatment (rehydration, withholding or alteration of feeds and/or bicarbonate and antibiotics). Chi-square test, Fisher's exact test and Mann-Whitney U test were used for statistical analysis.

Results: A total cohort of 209 patients with IF over the 3 years period was identified. 49 patients (28 males; age range 0.16-13.07 and mean 4.76 years) were screened for DL. Seventeen had bowel resection due to congenital malformation, 15 had necrotising enterocolitis, 3 had dysmotility and 10 had an enteropathy as a cause of IF. 25/49 had raised DL and 24/49 did not have raised DL. There was no statistically significant difference in risk factors for raised DL when comparing age, symptoms (diarrhoea, vomiting, abdominal pain/bloating and neurological symptoms), bowel resection, absence of ileo-caecal valve, abnormalities on barium study and use of proton pump inhibitors. SBL was significantly shorter (p=0.001) in raised DL group (median 29.6%; range 11.4-100) than in group without (median 100%; range 19.10-100). Patients with <35% SBL, had 77% sensitivity for developing raised DL. Relationship to feed could not be analysed due to lack of accurate information on patients’ carbohydrate intake. Response to treatment was available in 12/25 and all had improvement in symptoms with fall in DL. Recurrence following treatment occurred in 48%.

Conclusion: Children with IF due to <35% expected SBL, when screened, have a 77% likelihood of having SBBO shown by raised DL. Screening in at risk patients allows prompt detection and treatment of SBBO. Recurrence is common necessitating prolonged antibiotic regimens.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: For the third consecutive year, we conducted a systematic nutritional assessment survey using a one-week cross-sectional methodology. France (38 centers), Belgium, Canada, Colombia, Democratic Republic of the Congo (DRC) and Tunisia participated in this survey for which we developed a web-based tool for this purpose “Epinut Web site”.

METHODS: All participating centers followed the same standardized procedure. All children admitted the same week were measured and weighted. Diagnostic procedure (clinical examination) was conducted only for children under 3rd centile of BMI for age and sex (French reference).

RESULTS: Forty-seven centers and 6 countries participated in this survey. On 3097 data collected, 2882 were analyzed (54% boys), 2413 of whom were French. Median age was 3.7y (Q1: 0.9y, Q3: 10.1y). Weight for height (WFH) <-2SD (acute malnutrition) was found in 10.6% of the whole population: 39.2% in DRC, 18.9% in Colombia, 16.3% in Belgium, 9.0% in France, 8.3% in Tunisia and 5.9% in Canada. Chronic malnutrition (WFH<-2SD and Height for age <-2SD) was found in 1.7% of cases. Within 2179 patients with documented diagnosis, 57.3% were children with chronic diseases. Malnutrition was not different in that population (13.1% vs. 11.7%, NS). We found that wasting was overdiagnosed before 6 months of age and underdiagnosed between 6 month-old and 4 year-old children with French compared to WHO BMI reference curves. BMI >2SD was found in 9.0% children.

CONCLUSION: Present initiative contributed to increase the awareness of malnutrition in hospitalized children in a growing number of pediatric wards in France and other countries. Results are consistent with previous studies performed in France. Specific input of the present survey is to compare different countries with a same methodology. Our objective for 2013 is to increase the number of participating countries and centers to strengthen the promotion of systemic nutritional assessment in pediatric wards.

DISCLOSURE OF INTEREST: A. De Luca Grant / Research Support from: Nutricia, Advanced Medical Nutrition, H. Piloquet: None Declared, V. Colomb: None Declared, M. Fischbach: None Declared, D. Guimber: None Declared, N. Peretti: None Declared, R. Hankard: None Declared
VAGINAL DELIVERY AND EARLY GUT COLONIZATION WITH STAPHYLOCOCCUS AUREUS IN BREASTFED INFANTS AND IN INFANTS FED INFANT FORMULA WITH OR WITHOUT PREBIOTICS

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Objectives and Study: S. aureus was found in high amounts in breast milk of mothers after vaginal delivery and was shown to be an early gut colonizer of breastfed (BF) infants, declining after a few weeks probably due to poor intestinal adaptation. We aimed to compare S. aureus gut colonization in vaginally delivered BF infants and vaginally delivered infants fed an infant formula with or without polydextrose (PDX) and galacto-oligosaccharides (GOS).

Methods: In this double-blind, randomized study, 21- to 30-day old infants received a control cow’s milk-based formula (C) or the same formula with PDX/GOS (4 g/L, 1:1 ratio; PG) for 60 days; a reference breastfed (BF) group was included. All participants were vaginally delivered. Stool samples were obtained at baseline and at 30 and 60 days of feeding. Fecal bacteria levels measured by quantitative real-time polymerase chain reaction (qPCR) were ranked and analyzed by Kruskal-Wallis (KW) test. KW mean rank scores are presented.

Results: Stools from participants were analyzed at baseline (n: C=79, PG=74, BF=69) and at 30 (C=81, PG=78, BF=67) and 60 days (C=76, PG=69, BF=56). The detection limit for S. aureus was $1.49 \times 10^5$ colony forming units/g stool. The percent of infants in whom S. aureus was detected was 14%, 24%, and 29% at baseline, 11%, 13%, and 25% at 30 days, and 12%, 16%, and 32% at 60 days for C, PG, and BF, respectively. No differences between groups were detected in counts of S. aureus at baseline ($p=0.094$). Counts were significantly higher in BF vs. C (KW score 124 vs. 108, $p=0.030$) and tended to be higher than PG (110, $p=0.058$) at 30 days. At 60 days, counts were higher in BF vs. C (115 vs. 94, $p=0.005$) and PG (97, $p=0.023$).

Conclusion: Vaginally delivered BF infants showed higher rate of colonization with S. aureus than vaginally delivered formula-fed infants. This finding is consistent with previous data showing abundant S. aureus in breast milk following vaginal delivery. We suggest that the increased amounts of S. aureus in the gut of BF infants originate from the breast milk. S. aureus has not been previously recognized as a commensal intestinal species, so the implication of this finding warrants further research.


METAGENOMIC ANALYSIS OF FECAL SAMPLES FROM HEALTHY AND COLICKY INFANTS

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Objectives and Study: The bacterial composition of fecal microflora is different in colicky infants compared to healthy subjects, although studies have so far been limited to the cultivatable part of the human gut microflora. For evaluating the differences in the infant gut microbiome we adapted the new techniques of Metagenomics, which lets us look at a much wider set of microorganisms inside the human intestinal tracts.

Methods: We collected feces samples from 33 healthy and 30 colicky infants and extracted all microbial DNA. Using a custom designed human gut microbiome microarray, specifically targeting 840,000 microbial genes out of the 4 million microbial gene catalogue made by the MetaHIT consortium (Metagenomics of the human intestinal tracts), we can profile the individual infant feces samples and determine which microbial genes are different between colicky and healthy subjects. In order to side-step the problem of unknown bacteria, these genes were mapped to a set of 741 Metagenomic Species previously identified in the adult human gut. In brief Metagenomic Species (MGS) are gene sets corresponding to species detected directly from metagenomics data using a co-abundance based method, which allows for detection for both known and previously unknown species.

Results: The raw gene abundance data was preprocessed using the robust multiarray average (RMA) for normalization and gene abundance calculation and a summary abundance measure was calculated as the 0.75 quantile of all gene abundance values in the gene set. Subsequently, each MGS was defined as present in a sample when the MGS summary abundance was above a cut-off of 7.3. Using this approach we were able to detect presence of 77 out of the 387 MGS in the infant gut samples. To test whether any of the 77 MGS was associated to colicky, a chi-squared test of association was performed for each MGS. The resulting p-values for the MGS detected in more than one species were randomly distributed, with a minimum p-value of 0.023.

Conclusion: The top five species are Clostridium bolteae, Eggerthella lenta, Clostridium bartlettii, Clostridium clostridioforme, and Ruminococcus gnavus. The ranking of the 77 MGS based on the association p-values is in itself interesting, since indication of association to other diseases have been observed for three out of top five significant species. These results might indicate an association to colic for the top ranking species. However, in order to validate the results, an independent test on a larger cohort needs to be performed.

The observed differences between a healthy infants gut microflora and a colicky ones confirms that the infant gut microflora could play a role in infantile colicky.

Disclosure of Interest: None Declared
MECHANISM OF LACTOGENIC EFFECT OF MEDULLA TETRAPANACIS IN LACTATION

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Objectives and Study: Medulla Tetrapanacis is traditionally consumed by Chinese breastfeeding women and is believed to increase breast milk production during lactation. Our study is to explore the mechanism of lactogenic effect of Medulla Tetrapanacis in lactation, and investigate the effect of Medulla Tetrapanacis on the composition of expressed milk.

Methods: Sixteen ICR dams were divided into negative control group (n=8) and Medulla Tetrapanacis treatment group (n=8) after delivery. Intragastric administration of 0.25 mL Medulla Tetrapanacis extract to dams was conducted daily in Medulla Tetrapanacis treatment group, and the same amount of normal saline was given in negative control group. The amount of expressed milk and the contents of protein and lactose in milk were compared between two groups, and serum prolactin level of mice was measured by ELISA. Mouse HC11 mammary epithelial cells were treated by different doses of Medulla Tetrapanacis extract, RT-PCR was employed to detect the expression of β-casein and lactalbumin mRNA in mammary epithelial cells. STAT5 protein and phosphorylated STAT5 protein was determined by Western blotting.

Results: The amount of expressed milk in Medulla Tetrapanacis treatment group was higher than that in control group. The milk protein in Medulla Tetrapanacis treatment group (119.567 μg/mL) was significantly higher than that in negative control group (100.562 μg/mL)(P<0.05), while the milk lactose in Medulla Tetrapanacis treatment group (53.072 mmol/L)was significantly lower than that in negative control group (63.290 mmol/L)(P<0.05). There was no significant difference in the prolactin level between Medulla Tetrapanacis treatment group and negative control group (P>0.05). The expression of β-casein and lactalbumin mRNA in mammary epithelial cells treated by Medulla Tetrapanacis was higher than that in control group. The expression of phosphorylated STAT5 protein was increased by Medulla Tetrapanacis treatment.

Conclusion: Medulla Tetrapanacis can increase the phosphorylation of STAT5 protein and promote the prolactin signaling transduction in mammary epithelial cells, which results in the increase of milk amount and protein content.

Disclosure of Interest: None Declared
PROBIOTICS MAY INCREASE THE SENSITIVITY TO PATHOGEN-INDUCED DIARRHEA IN NEWBORN PIGS
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Objectives and Study: Pathogen induced diarrhea in neonates is a problem worldwide. Probiotics may improve gut colonization and intestinal health in neonates and thereby prevent diarrhea, but the effects are highly strain-dependent. We hypothesized that early administration of two probiotic bacteria, *Pediococcus pentosaceus* (PEP) and *Lactobacillus paracasei* (LAP) would reduce infectious diarrhea in neonates. To test this, we used an infection model in newborn piglets inoculated daily with a porcine pathogen, *E. coli* F18.

Methods: Fifty-nine caesarean-delivered newborn pigs were fitted with umbilical catheters and orogastric feeding tubes. Parenteral nutrition was given for 24 h followed by full enteral formula feeding (15 mL/kg/3h) until euthanasia on day 5. To standardize initial gut colonization, maternal fecal slurry (1 mL, 2×10^7 cfu) was inoculated immediately after birth. From day one, pigs received *E. coli* F18 (10^10 cfu/d) or water combined with PEP (10^10 cfu/d) or LAP (10^8 cfu/d) or placebo. This resulted in five bacteria inoculated groups: F18, F18-PEP, F18-LAP, PEP, LAP (all n=10) and controls (n=9). Pigs were weighed daily and feces was scored twice daily (normal feces = 1, pasty feces = 2, droplets of diarrhea = 3, moderate diarrhea = 4, intense diarrhea = 5).

Results: Diarrhea was noted in 34, 30, 11, 4, 0 and 2% of the total observations in the F18-PEP, F18-LAP, F18, PEP, LAP and control group, respectively (P<0.01 for group effect), and their corresponding fecal scores were 0.8±0.3, 1.6±0.4, 1.4±0.5, 0.5±0.2, 0.3±0.1 and 0.4±0.1. Pigs given *E. coli* F18 had significantly more diarrhea than pigs not given the pathogen and both probiotic bacteria potentiated the *E. coli* F18-induced diarrhea (P<0.05). Compared with healthy pigs (n=47), pigs with diarrhea (with ≥2 observations of fecal score 4) showed a significant increases in mean fecal score (2.9±0.2 vs. 0.4±0.0), reduced weight gain (-3.5±18.5 vs. 108.0±9.3 g) and higher intestinal permeability measured as the urinary lactulose/mannitol ratio (0.11±0.05 vs. 0.02±0.00) (all p<0.05). Pigs with diarrhea also had more blood lymphocytes and monocytes (49.4±2.9 and 4.5±0.6 vs. 43.1±1.5 and 2.8±0.3%, P=0.06 and P<0.01, respectively) and less neutrophils (43.1±3.3 vs. 52.6±1.7, P<0.05).

Conclusion: Both probiotic bacteria increased the sensitivity to diarrhea induced by the porcine pathogen, *E. coli* F18. The results suggest that probiotics may cause unexpected detrimental effects in the un-colonized intestine of sensitive newborns and should be given with caution to vulnerable groups of newborn infants.

Disclosure of Interest: None Declared
BIFIDOBACTERIUM SPP. LEVELS IN BREAST MILK REGARDING GESTATIONAL AGE, TYPE OF DELIVERY AND STAGE OF MILK SECRETION.

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Objectives and Study: Currently, there is an increasing interest regarding the agents that elicit the protective properties of breast milk (BM), in particular probiotic factors. Bifidobacterium spp. predominates in the intestinal microbiota of breastfed children. These bacteria exert multiple beneficial effects such as prevention and mitigation of intestinal infections. It has been described that certain conditions such as mastitis, Raynaud syndrome, overweight and obesity may decrease Bifidobacterium spp. levels in BM. However the influence of perinatal factors in its concentration remains unknown.

The aim of this study was to analyze the impact of gestational age, type of delivery and stage of milk secretion on Bifidobacterium spp. levels in BM.

Methods: Longitudinal milk samples from 15 term (5 vaginal deliveries, 5 elective and 5 non-elective caesarean sections) and 15 preterm gestations (5 from each stage of prematurity: extreme, moderate and mild) were collected.

Results: Bifidobacterium spp. levels in BM were clearly higher in term gestations than preterm ones (p-value=0.033 in colostrum, 0.002 in transitional and 0.027 in mature milk samples). Regarding the analysis of different stages of prematurity we observed a progressive increase of Bifidobacterium spp concentration with the gestational age, but these differences did not reach statistical significance. Bifidobacterium spp. levels were also affected by lactation time, although significant differences were only found between transitional and mature milk (p-value=0.039 and 0.008 for term and preterm gestations, respectively) finding higher levels in the latter. The mode of delivery seemed to have an impact on bifidobacteria content of term deliveries BM, showing higher levels in vaginal deliveries vs. caesarian sections samples, but no significant differences were found.

Conclusion: Bifidobacterium spp. levels in BM differ from term to preterm samples. This would support a hypothetical mechanism of bacterial translocation in mother’s bowel in the third trimester of gestation. The differences observed regarding the type of delivery might suggest an influence of triggering hormones in the Bifidobacterium spp. content in BM. These probiotic factors might confer their beneficial properties through out all stages of milk secretion.

Disclosure of Interest: None Declared
Objectives and Study: Breast milk plays a major role in protecting infants from infections. Recently, human milk oligosaccharides have been implicated in this protective role, due to their chemical structure which resemble those of receptors on pathogenic bacteria and host cells. In this respect, they can function as decoys by blocking the adhesion of pathogens to epithelia at the early stage of colonisation and, consequently, protect the newborns against infections. 

Pseudomonas aeruginosa is a ubiquitous, opportunistic pathogen, which is often associated with community- and hospital-acquired respiratory and urinary infections. The associated antibiotic resistance of this pathogen makes it difficult to treat and cure. Moreover, its pathogenicity is due to both adhesion and invasion of epithelia. Consequently food components, which are capable of reducing the adhesion and/or the invasion of P. aeruginosa, have excellent potential as novel therapeutics. 6′-sialyllactose (6SL) and 3′-sialyllactose (3SL), which are predominant oligosaccharides in both human and bovine milk, have previously been shown to inhibit the adhesion of a non-mucoid strain of P. aeruginosa to human pneumocytes (Thomas & Brooks, 2004). In this study, we investigate the ability of 6SL and 3SL to reduce invasion of human pneumocytes by both non-mucoid and mucoid strains of P. aeruginosa.

Methods: The non-mucoid and mucoid strains of P. aeruginosa were incubated in presence of 6SL and 3SL in a concentration range of 1 mg/mL to 0.0125 mg/mL. After 1 h incubation at room temperature, the bacteria were introduced to human pneumocytes (A549) and incubated at 37°C for 90 min. Gentamycin was used to kill the bacteria which had not invaded the human pneumocytes. The internalised bacteria were recovered by treating the human pneumocytes with 0.1% triton X-100 and plating on tryptic soy agar.

Results: When 6SL was tested at the highest estimated systemic concentration (0.125 mg/mL) i.e. what infants are likely to ingest during breastfeeding, it resulted in a 56 and 62% reduction in invasion by non-mucoid and mucoid bacteria, respectively. At the lowest estimated systemic concentration (0.0125 mg/mL), 6SL reduced invasion of non-mucoid and mucoid bacteria by 38 and 59%, respectively.

Conclusion: The data presented here demonstrates the ability of the milk oligosaccharide 6SL to reduce invasion of human pneumocytes by P. aeruginosa in a concentration-dependent manner. This study shows the potential of milk oligosaccharides as ingredients in functional foods aimed at lowering the incidence of infectious diseases.


Disclosure of Interest: None Declared
EARLY INFANT FEEDING PRACTICES DICTATE INFANT IMMUNITY, GUT MICROBIOME, AND METABOLOME

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Objectives and Study: Many health benefits are attributed to breast-feeding but the mechanisms that impart these protective measures are poorly understood. We have performed comprehensive metabolite, cytokine, and microbial profiling on infant rhesus macaques either fed standard infant formula (FF) or breast-fed (BF).

Methods: Infant monkeys (n=6/group) were randomly assigned from birth to either exclusive BF or FF from birth until 3 months of age. Urine and serum samples were collected at birth and every 2 weeks, up to 12 weeks and metabolite profiles were measured by 1H NMR spectroscopy identifying 69 serum and 96 urine metabolites. Gut microbial colonization was determined by culture-independent analysis of amplicons generated by primers directed against the V4 region of bacterial 16S rRNA genes found in fecal samples collected at birth, 4, 8, and 12 weeks.

Results: The FF infants weighed significantly more and were taller than their BF counterparts at all time points from 4 to 12 weeks of age. Bacterial community structures at each time point showed distinct separation between samples derived from different feeding strategies, suggesting significantly different microbial communities. Twenty-eight serum metabolites differentiated BF from FF, including amino acids, ketones. Differentiating urinary metabolites included those associated with the gut microbiome, amino acid, galactose, and fatty acid metabolism. Total circulating essential amino acids (p<0.0001) and non-essential amino-acid levels (p=0.0354) were higher in the FF group. Branched chain amino acids (Ile, Leu, Val) were significantly higher in FF infants. The higher concentrations of BCAAs are particularly interesting given the evidence for their contribution to insulin secretion as well as reports linking BCAA-related metabolic profiles with an insulin resistant phenotype. Substantially different gut microbial patterns, cytokine profiles, and metabolism were observed between FF and BF rhesus monkeys. The larger body size and higher blood insulin level in formula fed infants support the idea that postnatal nutritional manipulation can induce specific metabolic responses in pathways involved in galactose and amino acid metabolism and may explain the increased growth rate and adiposity reported in FF infants.

Conclusion: Our results support that the choice of infant feeding practice holds consequences for developing infants. We clearly establish distinct metabolic phenotypes for BF and FF infants. With the current focus on early life influences and the prevention of chronic disease the potential for nutritional intervention during critical developmental periods must be explored.
LACTOFERRIN-ENRICHED FORMULA MODULATES NECROTISING ENTEROCOLITIS AND INTESTINAL INFLAMMATION IN PRETERM PIGS
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Objectives and Study: Preterm infants are sensitive to develop gut inflammatory disorders, such as necrotising enterocolitis (NEC), especially when fed with formula. In this study, we investigated whether the inclusion of bovine lactoferrin (bLF) into formula for preterm pigs would affect NEC and gut inflammatory parameters.

Methods: Preterm pigs were delivered by caesarean section at 92% gestation. The pigs received parenteral nutrition (PN) with minimal enteral nutrition (MEN) consisting of either a control formula (CON, n=15) or a 10 g/L bLF-enriched formula (LFn, n=13) for the first two days after birth followed by another two days of full enteral feeding (15 mL/kg/3h). In addition, the dose-dependent effects of bLF on gut inflammatory pathways were also studied in porcine intestinal cells (Pslc1) in-vitro at 0.1, 1 and 10 g/L bLF.

Results: There were no differences in NEC incidence, villus heights and intestinal enzymatic activities between the two groups. In the pigs that developed NEC, bLF administration led to higher intestinal permeability and NEC severity in the colon (P < 0.05) and a tendency to lighter small intestine than in CON pigs (P = 0.10). In addition, crypt depth in the healthy proximal intestine was greater in the LFn group. In intestinal cells in-vitro, dose-dependent effects of LF were observed. Low doses (0.1-1 g/L) increased cell proliferation through ERK activation and limited both IL-8 secretion and NF-kB activation. In contrast, a high dose of LF (10 g/L) reduced cell proliferation, stimulated IL-8 release, restricted ERK phosphorylation, and activated NF-kB, compared with the control.

Conclusion: A relatively high dose of bLF (10 g/L) provided no protection against NEC in preterm pigs, but actually tended to increase the severity of NEC. Combined, these in-vivo and in-vitro studies may suggest a dose-dependent effect of LF in preterm infants, and the dose in infant formulas should be carefully considered. Studies on lower LF doses are important to confirm the beneficial effects of LF documented in-vitro.

Disclosure of Interest: N. Nguyen: None Declared, Y. Li: None Declared, P. Sangild: None Declared, S. Bering: Grant / Research Support from: Danish Dairy Research Foundation, D. Chatterton: None Declared
GROWTH AND TOLERANCE OF INFANTS FED FORMULA SUPPLEMENTED WITH LACTOFERRIN AND PREBIOTICS
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Objectives and Study: Recent research has further elucidated the composition of human breast milk, allowing for the potential to continuously improve the nutritional content and functionality of routine infant formula. Lactoferrin (LF) is a prominent functional protein in human milk that may play an important role in infant gastrointestinal and immune development. The objective of this study was to evaluate growth and tolerance in healthy infants who received routine cow’s milk-based formula supplemented with bovine LF, as well as with a prebiotic blend of polydextrose (PDX) and galactooligosaccharides (GOS).

Methods: In this multi-center, double blind, controlled, parallel-group, prospective study, 480 infants (269 males and 211 females) were randomly assigned to receive one of three infant formulas: marketed, routine infant formula (Control, n=155), a similar formula supplemented with PDX (2.0 g/L), GOS (2.0 g/L), and 0.6 g/L LF (LF 0.6, n=165), or a similar formula supplemented with PDX (2.0 g/L), GOS (2.0 g/L), and 1.0 g/L LF (LF 1.0, n=160). 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 and achieved anthropometrics on days 14, 30, 60, 90, 120, 180, 275, and 365 were analyzed by gender using analysis of variance. Tolerance was assessed at each time point by parent’s 24-hour recall of stool characteristics, fussiness, and gas.

Results: There was no difference in growth rate by gender from 14 to 120 days. While the mean growth weight was higher for female infants in the Control versus the LF 1.0 group from day 14 to day 60 (2.7g/day; p=0.024), this difference was not clinically relevant. No significant differences were observed in growth rate by gender in any other age range. No significant differences were observed among the groups for mean achieved weight, length, or head circumference at any time point assessed. Discontinuation rates were not significantly different among study groups. Significant differences in stool consistency were detected between control and investigational formulas. Infants fed either of the investigational formulas, which contained, along with LF, the prebiotic blend of PDX and GOS, reported softer, looser stool from day 30 to day 180 compared to controls (p<0.005). No differences in stool frequency, gas, or fussiness were observed.

Conclusion: In healthy infants, routine infant formulas that provided bovine LF at either 0.6 or 1.0 g/L and along with a prebiotic blend of PDX and GOS were well-tolerated and associated with normal growth throughout the first year of life.

CHEMOTHERAPY-INDUCED GASTROINTESTINAL TOXICITY IN MILK-FED PIGLETS
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Objectives and Study: Gastrointestinal toxicity remains a clinical problem for patients subjected to chemotherapy. Little is known about gut structure and function in such patients, and the relations to clinical outcomes. The objective of this study was to develop a piglet model for chemotherapy-induced gut toxicity and the responses to different diets.

Methods: Experiment 1. Nine-day-old piglets were given doxorubicin (single dose, i.v., 75 mg/m², DOX1, n=9) or saline (Control, n=8). The piglets were fed a milk-replacer for 9 days before being euthanized for tissue collection. Experiment 2. Seven-day-old piglets were given doxorubicin (single dose, i.v., 100 mg/m², DOX2, n=18) or saline (Control, n=14) and euthanized 6 days later for tissue collection. The piglets were distributed into groups fed bovine colostrum (DOX2-COL and Control-COL, both n=9) or a bovine milk formula (DOX2-FORM and Control-FORM, both n=7). For all pigs, diarrhea scores and body weight were recorded before and after treatment. Intestinal dimensions and digestive enzyme activities were measured by the end of the experiments as markers of intestinal damage.

Results: Experiment 1. During the study, diarrhea was more frequent in DOX1 pigs vs. controls (100 vs. 33%, p<0.05). Relative to Controls, the DOX1 pigs showed reduced growth rate (7 vs. 37 g/kg/d), reduced weight of the intestine (40.4 vs. 48.4 g/kg) and colon (9.6 vs. 13.4 g/kg) (all p<0.05). DOX1 reduced activity of dipeptidyl peptidase IV (DPPIV) and lactase, and increased sucrase activity in the distal intestine (all p<0.05). Villus heights and amount of mucosa were not affected. Experiment 2. Diarrhea was more frequent in DOX2 pigs vs. controls (67 vs. 22%, p<0.05), and DOX2 pigs had lower growth rate (20 vs. 35 g/kg/d, p<0.05), weight of the intestine (31.7 vs. 40.6 g/kg p<0.05) and colon (11.5 vs. 13.5 g/kg, p=0.09), with no consistent effects of diet. However, DOX2-COL pigs showed increased villus heights, increased activity of sucrase, maltase, and lactase in the proximal intestine, and increased DPPIV activity in the distal intestine (all p<0.05), compared with the three other groups.

Conclusion: Milk-fed piglets show clinical and tissue response to doxorubicin that are similar to chemotherapy-induced toxicity symptoms in patients. Gut structural damage may be most pronounced within 6 days of treatment while clinical symptoms continue after this time. Increased structural and functional parameters in the DOX2-COL pigs indicate that gut restitution after chemotherapy may be enhanced by colostrum feeding.

Disclosure of Interest: None Declared
THE ANTI-INFLAMMATORY AFFECT OF β-CAROTENE AND VITAMIN A REVERSE IRON DEPENDENT INTRA CELLULAR ABNORMALITIES IN INFAMED CACO-2 CELL-LINE

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Objectives and Study: Introduction: The inflammatory process can lead to the development of anemia due to iron sequestration in intestinal epithelial cells resulting in a decrease in body iron availability. However, treatment with iron supplementation can further aggravate inflammation followed by a subsequent escalation in iron sequestration which enhances the anemic state. The anti-inflammatory compounds β-carotene or vitamin A may both improve the inflammatory associated anemia by releasing iron from storage proteins and reduce inflammation thus effectively ameliorating the negative effects of iron supplementation.

The aims of this study are to confirm that under inflammatory process iron is “locked” inside the intestinal epithelial cells and to investigate the role of iron related proteins (transferrin receptor, L- and H-ferritin, ferroportin) in “unlocking” the iron during alleviation of the inflammatory state, induced by pro vitamin A or vitamin A.

Methods: Methods: An in vitro model of IL1 β stimulation of Caco-2 cells was used to study the inflammatory state confirmed by measurement of IL8 release. The effect of iron application on the cells was studied in a time and dose dependent manner. β-carotene and vitamin A were used as anti-inflammatory agents, verified by suppression of IL8 release. The effects on iron related proteins (H-, L-ferritin, ferroportin, transferrin receptor) was compared in inflamed Caco-2 cells with or without β-carotene and vitamin A treatment.

Results: Increasing concentration of iron (0, 10, 100, 200, 250, 350 µmol/L) and incubation period (4h, 12h, and 24h) lead to a significant increase in IL8 release. Applying β-carotene resulted in reduction of IL8 (from 1306.2pg/ml to 253.75pg/ml) while L- and H-ferritin levels were increased to 45.7%, 215.7%, 118.2%, and 70% respectively, and Ferroportin were decreased by 20%, 44.4%, 47.7%, 40.8% respectively (P<0.05). Vitamin A alone had no effect on the stabilization of iron metabolism. A strong correlation between pro-inflammatory cytokine IL8 and L-, H-ferritin was found.

Conclusion: β-carotene but not vitamin A stabilized the main iron related proteins (ferroportin, L-, H-ferritin and transferrin receptor) and diminished pro-inflammatory cytokine production (IL8). These results suggest that by applying anti-inflammatory compounds, in chronic inflammatory conditions, less iron is locked in intestinal epithelial cells, leading to increased iron bioavailability. This may be a possible approach to combat iron deficiency anemia associated with inflammation. Further studies are needed to see whether these findings can be applied in vivo.

Disclosure of Interest: None Declared
BREASTFEEDING PATTERNS AMONG DANISH WOMEN – USE OF A NEW SMS-TECHNOLOGY IN A PROSPECTIVE BIRTH COHORT STUDY
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Objectives and Study: Benefits of breastfeeding for both infant and mother are well known, as well as the recommendation of six months of exclusive breastfeeding given by the World Health Organization in 2001. Danish women are known to have had one of the highest rates of breastfeeding[i]. The objective of this study was to use a new SMS-technology to make exact estimates of breastfeeding initiation and duration of exclusive and partial breastfeeding in a Danish birth cohort.

Methods: The Odense Child Cohort is an unselected birth cohort consisting of children born in the municipality of Odense from January 2010 to July 2013. Mothers in the cohort who gave birth from April 8, 2012 were included into the breastfeeding subproject. The mothers received up to five SMS-questions about breastfeeding, use of infant formula, and introduction to solid foods, first time three days after birth and thereafter once a week. The questions were simply answered by replying to the SMS-messages one by one. The incoming answers were stored in a web based database ready for further data processing and analysis. The study was approved by The Regional Scientific Ethical Committee for Southern Denmark.

Results: From April 8 to October 8, 2012, a total of 461 women who gave birth to a single infant were enrolled in the study regardless of gestational age. Response rates as well as breastfeeding rates can be seen in the following table:

<table>
<thead>
<tr>
<th></th>
<th>3 days after birth</th>
<th>10 days after birth</th>
<th>8 weeks after birth</th>
<th>4 months after birth</th>
<th>6 months after birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants (n)</td>
<td>461</td>
<td>460</td>
<td>396</td>
<td>241</td>
<td>65</td>
</tr>
<tr>
<td>Answers obtained</td>
<td>98,0 % (452/461)</td>
<td>97,0 % (446/460)</td>
<td>92,9 % (368/396)</td>
<td>92,1 % (222/241)</td>
<td>93,8 % (61/65)</td>
</tr>
<tr>
<td>Any breastfeeding</td>
<td>96,2 % (435/452)</td>
<td>93,5 % (417/446)</td>
<td>82,9 % (305/368)</td>
<td>74,8 % (166/222)</td>
<td>73,8 % (45/61)</td>
</tr>
<tr>
<td>Exclusive breastfeeding</td>
<td>59,1 % (267/452)</td>
<td>73,5 % (328/446)</td>
<td>61,7 % (227/368)</td>
<td>52,3 % (116/222)</td>
<td>0</td>
</tr>
<tr>
<td>Partial breastfeeding</td>
<td>31,9 % (144/452)</td>
<td>14,8 % (66/446)</td>
<td>17,9 % (66/368)</td>
<td>19,8 % (44/222)</td>
<td>73,8 % (44/61)</td>
</tr>
<tr>
<td>Unknown if formula</td>
<td>24</td>
<td>23</td>
<td>12</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Introduced to solid foods</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2,4 % (2/96)</td>
<td>96,7 %</td>
</tr>
</tbody>
</table>
Conclusion: The breastfeeding initiation rate among the women was high (96.2 %). In total 31.9 % supplemented their breastfeeding with infant formula in the first days after birth, declining to 14.8 % ten days after birth. Four respectively six months after birth 74.8 % and 73.8 % were still breastfeeding either with or without supplementation of infant formula. All infants were introduced to solid foods six months after birth (data missing for one breastfed and one formula-fed infant).

The use of SMS-questions resulted in high response rates at all times (>92%).


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TRYPTOPHAN REQUIREMENT IN THE ENTERALLY FED TERM NEONATE IN THE FIRST MONTH OF LIFE
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Objectives and Study: Tryptophan is not only an essential amino acid, it also serves as a precursor in the serotonin and the kynurenine pathways. It is considered to be the first limiting amino acid in artificial feeding, and several studies suggest that enrichment with α-lactalbumin, a protein source rich in tryptophan, benefits growth in infants. The objective of this study was to determine the tryptophan requirement of term infants using the Indicator Amino Acid Oxidation (IAAO) method with L-[1-¹³C]phenylalanine as the indicator.

Methods: Enterally fed infants were randomly assigned to tryptophan intakes ranging from 0.5-73 mg/kg per day. After 1 day adaptation to the test diet, [¹³C]bicarbonate and L-[¹-¹³C]phenylalanine tracers were given enterally. Breath samples were collected at baseline and during isotopic plateaus. The mean tryptophan requirement was determined by using the biphasic linear regression crossover analysis on the fraction of [¹³CO₂] recovery from L-[¹-¹³C]phenylalanine oxidation (F[¹³CO₂]). Data are presented as mean ± SD.

Results: Thirty term neonates (gestational age 39 ± 1 wk) were studied at 9 ± 4 days. F[¹³CO₂] decreased until a tryptophan intake of 15 mg/kg/d; additional increases in tryptophan intake did not affect F[¹³CO₂]. Mean requirement was determined to be 15 mg/kg/d (r² = 0.17).

Conclusion: The mean tryptophan requirement for elemental formula fed term infants is 15 mg/kg per day. This requirement is lower than the current recommended intake of 29 mg/kg per day, which is based on the average intake of a breastfed infant.

Disclosure of Interest: J. Hogewind-Schoonenboom Grant / Research Support from: The study formulas were manufactured by SHS UK and transportation to Shanghai was facilitated by Dumex China. Financial support was received from Danone. The study sponsors had no influence on the study design, the analysis of the data, or the writing of this...
manuscript., L. Huang Grant / Resarch Support from: The study formulas were manufactured by SHS UK and transportation to Shanghai was facilitated by Dumex China. Financial support was received from Danone. The study sponsors had no influence on the study design, the analysis of the data, or the writing of this manuscript., L. Zhu: None Declared, J. Kraaijenga: None Declared, N. van Haren: None Declared, G. Voortman: None Declared, H. Schierbeek: None Declared, J. Twisk: None Declared, Y. Huang: None Declared, C. Chen: None Declared, J. van Goudoever Grant / Resarch Support from: The study formulas were manufactured by SHS UK and transportation to Shanghai was facilitated by Dumex China. Financial support was received from Danone. The study sponsors had no influence on the study design, the analysis of the data, or the writing of this manuscript.
INFANT FORMULA WITH REDUCED PROTEIN CONTENT AND OPTIMIZED AMINO ACID COMPOSITION DOES NOT COMPROMISE GROWTH OR ORGAN DEVELOPMENT IN PIGLETS

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Objectives and Study: Excess protein intake in early life has been related to later life development of obesity and metabolic syndrome. We tested whether a modified infant formula with 20% less protein and with an optimized amino acid (AA) composition based on recent studies in infants, would display similar growth rate and organ development, relative to a standard formula. We used artificially-reared piglets on restricted dietary intake as a model for infant growth because of their high sensitivity to dietary AA, related to fast growth in early life.

Methods: Seven day-old piglets were fed isoenergetic amounts of an AA-based formula for 14 days (700 kJ/kg/d) with a standard suboptimal protein level (100%, 8 g/kg/d n=22), 20% less protein (80%, n=19), 20% less protein and optimized AA composition (80% opt AA, n=17) or 50% less protein (50%, n=13). Growth rate, body composition, organ weights and intestinal brush border enzyme activities were measured.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Protein intake, g/kg/d</th>
<th>Weight gain, g/kg/d</th>
<th>Protein efficiency, Weight gain/protein intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>7.68</td>
<td>14.85</td>
<td>1.93</td>
</tr>
<tr>
<td>80%</td>
<td>6.08</td>
<td>13.88</td>
<td>2.28</td>
</tr>
<tr>
<td>80% opt AA</td>
<td>6.14</td>
<td>15.38</td>
<td>2.50**</td>
</tr>
<tr>
<td>50%</td>
<td>3.80</td>
<td>7.80*</td>
<td>2.05</td>
</tr>
</tbody>
</table>

Body weight gain was significantly reduced in the 50% group (*P<0.05, -50%, Table), relative to the three other groups which showed comparable growth. The efficiency of utilization of protein was higher in the 80% opt. AA versus the 100% group (**P<0.01, +30%, Table). Organ weights showed no differences among groups, except for kidney weight that was reduced in the 50% group. This group also showed decreased blood platelet count and increased platelet volume at day 7, compared with the 100% group. No other differences were seen in hematology, fat mass and fat-free mass. The 50% group showed lowered bone accretion compared with the other groups. Groups with reduced protein did not show any decreases in activities of six brush border enzymes, compared with the 100% group.
**Conclusion:** No developmental effects were detected when reducing the protein content to 80% of a standard formula. This suggests that 20% reduction of the protein load with an optimal AA composition does not induce any acute growth deficits or disproportional growth effects in young artificially-reared pigs fed a restricted diet.

**Disclosure of Interest:** None Declared
IMPACT OF A MULTIFACETED PROGRAM FOR SCREENING AND CARE OF MALNUTRITION IN HOSPITALIZED CHILDREN: PREDIRE CLUSTER-RANDOMIZED TRIAL
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Objectives and Study: Malnutrition is frequent among hospitalized children. Early screening combined with effective care is essential to avoid related complications. We assessed the impact of an intervention to improve the management of malnourished children.

Methods: A controlled-randomized trial was conducted in medical and surgical units of a pediatric university hospital (219 healthcare workers). Following a 4 months observational period (before period), all units were randomized between 2 clusters groups according to the frequency of malnourished children. Then, a multifaceted program coordinated by a nutritional support team was implemented in the intervention group over a 18 months period (after period), combining access to a computerized clinical decision support system, education of healthcare workers and periodic multidisciplinary meetings. Simultaneously, nutrition management remained unaltered in the control group units. Endpoints comparison between groups was modeled using mixed effect regressions to adjust for patients-risk and consider the clustered nature of the data.

Results: Among the 7010 children hospitalized during the study, 1457 malnourished children were included (313 during period before and 1144 period after intervention). Mean age was 5.1 y and 55.5% were boys. The malnutrition rate was 21% [95\%
CI, 19.3\%–22.7\%], including 26.7\% of severe malnutrition. Compared to the control group, the intervention improved the identification of malnutrition etiology (Odds Ratio, 4.8 [1.4–16.3]), as well as the appropriate management by dietician (OR 3.1 [1.1–8.8]). All measured endpoints were significantly improved in the intervention group, while being unchanged in the control group before and after the program had been implemented (see Table).

Table: Multivariate comparison before-after intervention by group

<table>
<thead>
<tr>
<th>Adjusted endpoints</th>
<th>Group</th>
<th>Before period</th>
<th>After period</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of weighing (mean)</td>
<td>Control</td>
<td>0.84</td>
<td>0.72</td>
<td>0.141</td>
</tr>
<tr>
<td></td>
<td>Intervention</td>
<td>0.62</td>
<td>0.72</td>
<td>0.014</td>
</tr>
<tr>
<td>Identification of malnutrition etiology (%)</td>
<td>Control</td>
<td>12.6</td>
<td>21.6</td>
<td>0.191</td>
</tr>
<tr>
<td></td>
<td>Intervention</td>
<td>12.3</td>
<td>43.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Management by dietician (%)</td>
<td>Control</td>
<td>32.5</td>
<td>34.1</td>
<td>0.852</td>
</tr>
<tr>
<td></td>
<td>Intervention</td>
<td>33.5</td>
<td>46.1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Refeeding protocol (%)</td>
<td>Control</td>
<td>31.0</td>
<td>40.2</td>
<td>0.138</td>
</tr>
</tbody>
</table>
Conclusion: The introduction of a comprehensive program combining computerized screening tools with awareness campaign of healthcare workers was associated with a rapid and significant improvement of clinical practices for better care of malnourished children at hospital.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

PO-AHP-0001

ASSESSMENT OF DIET AND LIFESTYLE FACTORS ASSOCIATED WITH PAEDIATRIC NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD)
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Objectives and Study: An observational case control study to investigate any differences in dietary intakes, physical activity levels and eating behaviours in a UK paediatric NAFLD population compared to a group of BMI-matched controls.

Methods: Children with biopsy-confirmed NAFLD and obese controls were recruited from Kings College Hospital’s paediatric liver and obesity clinics. Consent was obtained and subjects were asked to complete a 7-day Food and Activity Diary (with daily pedometer readings), a 24-hour Dietary Recall, a Physical Activity Questionnaire and the Dutch Eating Behaviour Questionnaire. Anthropometrics and routine biochemical, histological, physiological and non-invasive hepatic biomarkers were measured at recruitment. Nutrient intakes were estimated from diet records using Dietplan 6 and personalised feedback was given to each participant to optimise their diet. Statistical analysis was performed using SPSS (v19). NHS and University ethical approval was granted.

Results: 7 NAFLD and 4 obese children have so far successfully completed Phase 1 of the study. Preliminary analysis suggests few significant differences in biochemical and anthropometric measurements between the groups with the exception of a greater waist circumference (p=0.044) and lower albumin (p=0.030) in NAFLD patients. No significant differences were identified in eating behaviours or physical activity levels; however, the NAFLD participants reported spending greater time undertaking sedentary behaviours and less time in moderate & vigorous intensity activities. Available pedometer readings showed that both groups failed to meet the recommended 10,000 steps per day. The NAFLD participants typically consumed greater quantities of all macronutrients. NAFLD participants consumed significantly more sodium than controls, whether absolute or expressed as a percentage of the age-and-gender specific RNI (p=0.047 and p=0.018 respectively). Calculation of energy intake to estimated basal metabolic rate ratios (Ei:BMR) demonstrated that under-reporting was prevalent (9 out of 10 children) (Ei:BMR <1.14).

Conclusion: Whilst clear differences in dietary intakes, physical activity levels and eating behaviours between cases and controls were not identified, recruitment and analysis are on-going in order to address the issues of small sample size and prevalent under-reporting. In addition, follow up of the subjects aims to identify any associations between dietary composition and activity levels and disease progression. This remains the first study to investigate dietary intake in a UK paediatric NAFLD population, and as such provides novel data that will inform the development of innovative dietary advice for paediatric NAFLD patients.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

PO-AHP-0002

GASTROENTEROLOGY PATIENTS REVIEWED BY VIDEO CONSULTATIONS

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Objectives and Study: Children and young people with gastroenterological conditions are traditionally reviewed in outpatient clinics in a hospital setting. The North of Scotland covers a wide geographical area including remote and rural locations and the Shetland Islands. This means families have to travel long distances to attend a clinic in Royal Aberdeen Children’s Hospital. The multidisciplinary team of Consultant Gastroenterologist, Specialist Nurse and Dietician, have reviewed twenty nine patients by video consultation over a fifteen month period to prevent families having to travel to Aberdeen. The team wished to gain families perceptions of video consultations.

Methods: An audit questionnaire was devised by the specialist nurse and clinical effectiveness department and was distributed to both parents and young people involved in video consultations to ascertain their opinions of the process.

Results: Fourteen parents and eleven young people completed the questionnaires. Over 80 % of both the parents and young people stated that speaking to the team by video consultation fully met their needs. 92% said that attending a video consultation was more convenient for their family and 85% were more relaxed being able to attend a video consultation closer to home rather than having to travel to a specialist centre. Families saved an average of 10.8 hours travelling time which ranged considerably from 2 to 48 hours. Some journeys would have involved taking a car, ferry, plane and bus to reach the clinic. An average of £230 was saved on transportation and other costs for each family.

Conclusion: The audit results clearly demonstrate that both parents and young people really value the use of video consultations and there are also considerable time and cost savings. The multidisciplinary team plan to continue using video consultations for the benefit of our families. This model has been shared with our adult colleagues who plan to develop this for their patients.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

PO-AHP-0003

EXCLUSIVE ENTERAL NUTRITION IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE: EXPERIENCE IN ONE UK CENTRE
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Objectives and Study: Exclusive enteral nutrition (EEN) is now an established treatment for induction of remission of Crohn’s disease in childhood. The optimal treatment regimen is not known and consequently varies between centres. We report our experience with EEN at one centre over an 18-month period.

Methods: A retrospective case note review of all patients treated with EEN for inflammatory bowel disease at the Royal Manchester Children’s Hospital over an 18-month period was carried out. Children receiving more than one course of treatment had only their first treatment included. Data relating to feed regimen and clinical outcome was recorded.

Results: Seventy-one children were included. Their average age at treatment was 13.1 years [range 4.4-17.7]. Most patients used 1.5kcal/ml polymeric feeds. Four patients used a higher calorie feed (2kcal/ml) as all or part of their intake. One patient used a juice-based supplement as part of their intake.

56 children (79%) completed the planned duration of EEN. 46 completed this orally, 9 used a nasogastric tube and one patient used a gastrostomy. Of the 15 children who did not complete the treatment, 14 were taking the feed orally, and one via nasogastric tube.

Of these patients, 33 received a 6-week course of EEN, and 23 received a longer course (8 weeks in 21 cases, 9 weeks for 1 patient and 11 weeks for 1 patient). Of those completing a 6-week course of treatment 94% took the feed orally, compared with only 65% in the group who had a longer course of treatment.

Of the patients who completed the course of EEN, the reported symptoms resolved in 39 patients (80%). A significant increase in BMI z-score from -1.0 to -0.2 [p<0.005] was seen for those patients who completed the full course of EEN.

Average (mean) weight gain for this group was 3.6kg [range -0.5 to 8.3kg]. Patients treated with steroids during EEN were excluded from these analyses. No significant difference was seen in weight gain or symptom resolution between the group of children treated for 6-weeks and those treated for a longer period. The increase in BMI z-score was significant for both groups.

Conclusion: In our patient group, variation in treatment regimen was observed. Most patients took their EEN orally, particularly those treated for 6-weeks rather than for a longer duration. There was no significant difference in weight gain or symptom resolution between those treated for 6-weeks compared with those treated for longer.

Our symptom resolution rate of 80% is similar to reported remission rates. Patients who completed the EEN course showed significant improvement in BMI z-scores after treatment. Due to the confounding factors associated with retrospective work, future prospective work to determine the optimal regimen for EEN treatment will be useful.

Disclosure of Interest: None Declared
Objectives and Study: The ketogenic diet is a high-fat very restricted diet with adequate protein and carbohydrate that may be disrupted by medications containing carbohydrate excipients. We imagined a tool calculating the quantity of carbohydrates of the children medication.

Methods: We collected first the qualitative and quantitative composition in carbohydrate excipients of paediatric medications from official medicines references. The IT program is organised into twelve sheets corresponding to the twelve therapeutic classes, from anti-allergy drugs to vitamins. Each sheet includes one section with oral solutions and another one with units. The original and the generic drugs are listed in alphabetical order. The carbohydrate-free drugs are entered with a green font while the carbohydrate ones are entered with a red font. The user enters either the weight and the dosage (mg/day) or the daily number of units. The quantity of carbohydrates will be automatically calculated with a pre-programmed formula. A thirteenth and last sheet is a balance sheet summing up the total carbohydrate quantity from the drugs. The quantity of carbohydrates that was previously calculated by dieticians is also indicated.

Results: In 2012, this tool was valued by paediatric dieticians to appreciate the ease in use. In this way, the balance sheet has been modified to display the quantity of carbohydrates remaining, when the carbohydrate quantity from the drugs has been subtracted from the quantity of carbohydrates calculated by the dieticians. Depending of these final results, the physician has two possibilities. He may either refine the ketogenic diet, considering the carbohydrate quantity provided by the drugs, or modify the prescription (for instance, by choosing a carbohydrate-free-drug), if the carbohydrates quantity from the prescription is too important for the diet. Moreover, in 2012, we used the spreadsheet to analyse, retrospectively, the quantity of carbohydrates from 25 prescriptions of children who where treated with ketogenic diet from 2006 to 2011. This study revealed that, for seven prescriptions, the quantity of carbohydrates from medication exceeded 3 grams, which represented more than 10% of the total quantity of carbohydrates for a day. This IT tool is also available in a book version matching a drugs index. Given to the parents, this index is a help for the GP and the pharmacist allowing them to choose the right drugs which will not interfere with the ketogenic diet.

Conclusion: This medical prescription help answers the physicians’ expectations about avoiding the ketosis rupture due to the introduction of carbohydrate drugs. It also contributes to increasing the effectiveness of the ketogenic diet.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

PO-AHP-0005

PREDICTORS OF A SUCCESSFUL OUTCOME IN A MULTIDISCIPLINARY FAMILY-BASED LIFESTYLE INTERVENTION FOR OVERWEIGHT AND OBESE CHILDREN
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Objectives and Study: To determine baseline predictors of treatment success in terms of Body Mass Index-Percentiles (BMI-P) in a multidisciplinary family-based behavioral lifestyle intervention for overweight and obese children.

Methods: Overweight and obese children (N= 257; age 6 – 13 years) and their caregivers participated in a prospective study and attended a lifestyle intervention. Baseline data assessment included anthropometrics, demographics, family characteristics and lifestyle. BMI-P with a target reduction of 1% or greater was measured. Logistic regressions were used for analysis.

Results: 79% of children achieved reductions in BMI-P with 50% achieving the target reduction over the course of 6 months. Baseline BMI-P was found to be the most important predictor of treatment success. Children with the lower baseline BMI-P achieved larger reductions in BMI-P over 6 months. Furthermore, Children who exercised regularly before the intervention, older children, firstborn children and children with non-overweight mothers were more likely to achieve greater reductions in BMI-P. No effects on treatment success were found for the number or weight status of siblings, overweight fathers or having divorced parents.

Conclusion: These results suggest that screening for baseline characteristics in childhood obesity treatment could identify who will benefit most from a pediatric lifestyle intervention. Tailored programs should be developed and the treatment team should focus on children who are less successful in achieving weight reductions. Future research should study baseline predictors of long term treatment success.

Disclosure of Interest: None Declared
**ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)**

**PO-AHP-0006**

**SINGLE-CENTRE EXPERIENCE OF AN MULTIDISCIPLINARY PRE-TRANSITION CLINIC FOR YOUNG PEOPLE WITH LIVER DISEASE**

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**Objectives and Study:** Dedicated services for young people with chronic conditions have shown to improve quality of care and outcome for this growing population. As part of the liver transition service at King’s College Hospital, a multidisciplinary (MD) pre-transition clinic was set up for patients aged 12 years onwards to complement the liver transition clinic (> 16 years) held in the adult liver outpatient department. The MD team consists of a liver transition consultant, 2 paediatric liver clinical nurse specialists (CNS) and an adolescent clinical psychologist (PSY). The clinic is held twice a month allocating 1 hour slots and clinics are prepared and reviewed by all members of the MD team.

**Methods:** Retrospective review of pre-transition clinic activity between April and October 2012.

**Results:** Thirty-four patients were seen during 44 clinic appointments with the majority (n=25) being seen once. Twenty-one (62%) were female and underlying diagnosis was as follows: liver transplantation (13), autoimmune liver disease (12), biliary atresia (5) and others (4). Of 5 patients who did not attend an appointment, 3 attended a rescheduled appointment and 2 are scheduled to be seen. Nineteen out of 27 patients were referred by doctors and the remainder by clinical nurse specialists using an electronic referral document. The most common indications for referral were adherence issues (10) and psychological problems (10) followed by social issues (5) and others (2). Seven patients were previously seen by the liver transition consultant in a different clinic setting.

At time of preparing the clinic patients were allocated to the various MD professionals depending on indication for referral however a flexible approach during the clinic meant that patients could be seen by other team members if indicated. The HEADSS score was used by all members of the team as a screening method and the clinic content was tailored to the individual’s needs eg education, adherence issues etc. During the consultation, all patients were seen by the consultant, 23 by CNS and 15 by the PSY. Focusing on the CNS role patients were seen independently (8), jointly with PSY (12) or consultant (3). After MD discussion follow up was arranged in the liver pre-transition in 20, liver transition clinic in 9 and paediatric liver clinic in 2 depending on the individual’s needs.

**Conclusion:** The MD pre-transition liver clinic is well attended with the most common indications for referral being adherence and psychological issues. The clinic has highlighted a need for an individual approach to adolescent care in which the CNS acts as a coordinator and promoter of self management. Focusing on early intervention will hopefully improve long term outcome for our patients as supported by RCN guidelines.

**Disclosure of Interest:** None Declared
THE EFFECT OF FAMILY-BASED MULTIDISCIPLINARY COGNITIVE BEHAVIORAL TREATMENT IN OVERWEIGHT AND OBESE CHILDREN

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Objectives and Study: To determine whether a multidisciplinary family-based behavioral lifestyle intervention effectively improves Body Mass Index Percentiles (BMI-P) in overweight (85%≤BMI-P<95%) and obese children (BMI-P≥95%).

Methods: A Total of 307 overweight and obese children (mean BMI-P 97.05+/−2.54%), aged 6-13 years (mean 9.4 ± 1.6), participated in an intensive 6 months family-based multidisciplinary cognitive behavioral intervention that treats pediatric obesity using medical management, nutrition education, behavioral intervention, and physical activity. Child BMI-P was measured at baseline, after 3 months, and at the end of the intervention.

Results: 257 children (84%) completed the program in full. The intervention was associated with a significant decrease in BMI-P after 3 and 6 months: -1.58±1.10% and -3.67+/−2.71%, respectively (p <0.0001 vs baseline). 34.9% of overweight children achieved normal weight (BMI-P <85%) and 22.9% of obese children achieved BMI-P at the overweight category range. Baseline BMI-P was found to be a significant predictor of treatment success. A decrease in 1 unit resulted in a 1.6 fold (95% confidence interval 1.4-1.9) increase odds of success.

Conclusion: A family-based behavioral lifestyle multidisciplinary pediatric weight management program can improve the weight status of obese and overweight children. Higher pre-intervention BMI percentiles were associated with less favorable responses to the intervention.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (including Nurses and Dieticians)

PO-AHP-0008

ALARMING HIGH INTAKE OF SUGAR-SWEETENED BEVERAGES IN SLOVENIAN ADOLESCENTS
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Objectives and Study: Sugar-sweetened beverages (SSBs), which include fruit nectars, syrups, sweetened teas, iced teas, soft drinks, energy drinks, and vitamin drinks, are widely available to children. Higher consumption of SSBs is associated with development of obesity, metabolic syndrome and type 2 diabetes (1). In Health Behaviour in School-aged Children (HBSC) study on frequency of soft drink consumption, which included 41 countries, Slovenian 15-year-old adolescents took the first place (2).

Methods: Dietary habits were assessed using a food frequency questionnaire (n = 2,224), and present nutrition was assessed using a 3-day weighted dietary protocol (n = 197) for validation purposes. Beverages were classified into the following groups: a) beverages with sugar: a1) added (SSBs); a2) naturally presented (fruit juices); b) sugar-free beverages: b1) water, mineral water; b2) tea; b3) non-caloric beverages with synthetic sweeteners.

Results: SSBs represented 44% of consumed beverages (mean: 683ml/day) in boys and 41% in girls (mean: 715ml/day). Fruit juices have contributed 7% of beverages in boys and 6% in girls. Intake of beverages with sugar (a1 + a2) was 52% in boys, whereas 47% in girls. Water and mineral water contributed (b1) 42% in boys (649 ml/day) and 47% (828 ml/day) in girls. Water and non-caloric beverages together (b1 + b2 + b3) contributed 49% of consumed beverages in boys and 53% in girls. Sugar-sweetened beverages contributed an excess 9% (274 kcal) of daily energy intake in boys and 10% (231 kcal) in girls.

Conclusion: Slovenian adolescents are drinking excessive amounts of SSBs. It is necessary to raise awareness about the adverse health effects of SSBs. We started a pilot school-based intervention programme on encouraging water drinking in the school settings (http://vodazmaga.si/). In several countries, the public health and economic benefits of taxing SSBs have been examined. A SSB tax may effectively reduce the consumption of SSBs, and consequently reduce the risk of chronic diseases.

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Disclosure of Interest: None Declared
HOME PARENTERAL NUTRITION: A 5-YEAR RETROSPECTIVE ANALYSIS IN NEW SOUTH WALES, AUSTRALIA

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Objectives and Study: Parenteral nutrition (PN) was developed in the 1960's and in the later part of the 20th century was adapted for use in the home. There are many associated risks with using PN most significant of all is infection, with which comes an increased risk of mortality, particularly in children. In New South Wales (NSW), Australia, parenteral nutrition for children is managed by the 3 children’s Hospitals.

Recently published data in the United Kingdom (UK) reviewed 19 children on HPN over a 10 year period, however they reported only 7 children currently on HPN and this is a smaller ratio per head of population than what is currently being managed in NSW, we also continued to compare our data to other national and international published data. Another review in 2012 from one paediatric centre in Australia reported 11 children reviewed over a 1 year period, their data identified 8 of the 11 children had confirmed line sepsis during the 12 month period, we wanted to compare our data with published papers and include data extending back 5 years.

Methods: The nursing clinicians from the 3 Hospitals fostered a mutual collaboration to collect data; this was done retrospectively in 2 centres and prospectively in another. The data were collated into one de-identified format for review. Of particular relevance to us was the rate of catheter related blood stream infection and how that may have been reflective of different hospital practices in relation to central venous catheter (CVC) management and parent education.

Results: The total number of children on HPN at the beginning of 2012 was 18, of these 8 had confirmed CVC infection. There was consistency in CVC type and placement, with differing practices in line management and blood collection at each site.

Conclusion: The data revealed a number of noteworthy features, including consistency in the report by Gillanders et al and the type of bacteria isolated in the lines. However the numbers of episodes were less than they had reported in children. Of note was the use of an ethanol protocol had significantly reduced line infections in this group of children.


Disclosure of Interest: None Declared
A RETROSPECTIVE STUDY OF SEROLOGIC TEST FINDINGS FOR CELIAC DISEASE COMPARED WITH HISTOPATHOLOGIC FEATURES IN THE LIGHT OF NEW ESPGHAN GUIDELINES

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Objectives and Study: The new ESPGHAN guidelines allows for symptomatic children with strong positivity for celiac disease-specific antibodies to omit a diagnostic biopsy. The aim of the study was to compare retrospectively results of antibodies with histological findings in children and adolescents and to assess the specificity and sensitivity of serological tests for histologically proven celiac disease.

Methods: A cohort of children and adolescents aged 0-19 years who were examined in years 2003 to 2012 was retrospectively reviewed (n = 392). Antibodies against tissue transglutaminase (anti-TG) and endomysial antibodies (EMA) were tested in all patients and the biopsy of the small intestinal mucosa was simultaneously performed. The average age at which the biopsy was taken was 8.5 years, median 7 years. Results of anti-TG and EMA were compared with histological findings, which were evaluated according to Marsh classification. Retrospective calculation of HLA antigens in the whole cohort was not possible for technical reasons.

Results: Among 392 patients 247 (63%) children had high anti-TG titers with levels >10 times higher than normal values and positivity of EMA and 111 (28%) children had also the same high titers of anti-TG, EMA positivity and symptoms suggestive of CD. In patients who do not have symptoms and have positive EMA and anti-TG 10 times higher than normal values the specificity of tests for Marsh 2-3 was only 68 % and sensitivity 83 %. In patients who had the same values of antibodies and also were symptomatic the sensitivity was 70 % and the specificity was 96 %.

Conclusion: In patients with positive EMA and anti-TG 10 times higher than the normal values the specificity of tests was significantly influenced by the presence of symptoms. The high specificity which was found in symptomatic patients raises the question if the testing of HLA antigens to enhance diagnosis of CD is really necessary. In patients with associated diseases and asymptomatic individuals the specificity of serological tests is low and it is therefore always necessary to perform a biopsy. Supported by VZ FNM 64203/6001.

Disclosure of Interest: None Declared
Objectives and Study: Celiac disease (CD) has been associated with HLA class II heterodimers. This study assessed correlations between HLA Class II high resolution genotyping and clinical, serological and histological characteristics in Greek children with CD

Methods: Clinical and serological data and histopathologic reports from upper gastrointestinal endoscopies were recorded for 109 children with CD. All children were typed for HLA - DRB1, DQA1, and DQB1 genes and divided into 3 groups according to the number of DQB1*02 alleles: group 1, homozygous; group 2, heterozygous; group 3, negative. Statistical analyses included Fisher’s exact test, logistic regression reporting odds ratios (OR), Kruskal-Wallis and Mann-Whitney test.

Results: HLA-DQA1* allelic distribution and haplotypic distribution were significantly related to the age of diagnosis. Children carrying at least once the DQA1*05:01 allele were 3.4 and 3.8 times more likely to be diagnosed after the 2nd year of life compared to those having at least one copy of DQA1*02 (OR=3.4, p=0.027, 95% ci: 1.1-10.6) and DQA1*05:05 (OR=3.8, p=0.022, 95% ci: 1.2-12.7), respectively. Children carrying at least once the DR3-DQ2 haplotype had 3.3 times higher chance of having been diagnosed > 2 years of age compared to those carrying the DR7-DQ2 (OR=3.3, p=0.029, 95% ci: 1.1-10.4) and 3.8 times compared to those having the DR5-DQ3 (OR=3.8, p=0.024, 95% ci: 1.2-12.5). At the genotype level a strong correlation with age was also observed: Individuals homozygous for DR3-DQ2 were 9.2 times more likely to be diagnosed > 2 years of age compared to those carrying the DR5-DQ3/DR7-DQ2 genotype (OR=9.2, p=0.029, 95% ci: 1.2 - ∞). DQ2/DQ8 positivity was related to the number of gastrointestinal symptoms: DQ2 positive patients had 4.1 times higher odds of having more gastrointestinal symptoms compared to DQ8 positive/DQ2 negative individuals (OR=4.1, p=0.018, 95% ci: 1.3-13.3). Finally, a statistically significant correlation was recorded between EMA titer (geometric mean concentration, GMC) and the number of DQB1*02 alleles: group 1 had significantly higher (p=0.008) EMA titers (GMC=5.19, 95% ci: 4.83-5.57) compared to group 3 (GMC=4.29, 95% ci: 3.60-5.12).

Conclusion: This study provides evidence that the HLA-related genetic background of CD might produce diverse clinical and serological phenotypes. Such observations could be applied in the clinical practice by selecting specific HLA class II high resolution genotyping markers according to different clinical and serological characteristics.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Studies in adults have shown an increased prevalence of celiac disease (CD) in patients with irritable bowel syndrome (IBS), while in children this association is still matter of debate. Few data exist on the prevalence of IBS in patients with CD on gluten free diet (GFD). We aimed at assessing the prevalence of CD among the different abdominal pain-related functional gastrointestinal disorders subgroups, and the prevalence of IBS in patients with CD on a strict GFD.

METHODS: We studied two cohorts of consecutive patients. First cohort included 1050 children (range: 4-16 yrs) referred for recurrent abdominal pain in the last 6 years. 210 were excluded because of organic diseases/functional constipation. 840 were classified (Rome III criteria) in: irritable bowel syndrome (IBS), functional dyspepsia (FD), functional abdominal pain (FAP) and abdominal migraine (AM). In all patients a celiac screening [total IgA, anti-transglutaminase-IgA (TTG-IgA) and anti-endomysium] was performed followed by duodenal biopsy in case of its positivity. Second cohort included 272 CD patients [122 adults (range 18-62 yrs), 150 children (range 2-17 yrs)], on strict GFD and persistently negative TTG-IgA. 615 non-celiac patients [484 adults (range 19-65 yrs), 131 children (range 1-17)] enrolled among the first-degree relatives of CD patients were used as controls. All were prospectively evaluated for IBS diagnosis.

RESULTS: In the first cohort, 252 children (30%) were classified as IBS, 201 (24%) as FD, 311 (37%) as FAP; 76 (9%) were unclassifiable. None had AM. Coeliac serology was positive in 15 (1.7%): 12 IBS (4.7%), 2 FD (1%) and 1 FAP (0.32%). IBS Children had a 4 times higher risk of having CD as compared to Italian paediatric population (OR: 4.5; CI 95%: 2.3-8.79). No increased risk in FD or FAP children was found. In the second cohort the overall prevalence of IBS was significantly higher in CD than controls (39.7% vs 15.8%; p <0.001). The prevalence of IBS was higher in both children [(37.33% vs 15.3%; p<0,001); RR 2.4: CI95%: 1.6-3.8] and adults CD patients [(42.6% vs. 15.9%; p<0,001); RR 2.7: CI95%: 2.0-3.6]. No correlation was found between the IBS prevalence and CD presentation, diseases duration and histological damage.

CONCLUSION: In our study, the prevalence of CD in IBS children is about 5%. IBS patients have four times higher risk developing CD than the general population. Patients with CD have an increased risk of developing IBS, which is doubled in children and tripled in adults. Our results suggest that new strategies aiming at the management of irritable bowel syndrome in celiac patients should be planned.

Disclosure of Interest: None Declared
THE ROLE OF HLA DQ2.2 AND DQ7 ALLELES IN CELIAC DISEASE AND GLUTEN SENSIBILITY

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Objectives and Study: Celiac disease (CD) is currently associated with mandatory presence of HLA-DQ2 (DQA1*05/DQB1*02) and DQ8 (DQA1803/DQB1 *302) haplotypes. However, some researchers believe that a few patients may develop CD in the presence of alleles DQA1*0505(501)/DQB1*301(DQ7), or DQA1*201/DQB1*202(DQ2.2). Independent role of DQ7 and DQ2.2 alleles in the development of CD remains controversial. The aim of our study was to determine the frequency of HLA DQ2, DQ8 and DQ7 alleles in children with CD and gluten sensitivity (GS) in Russia.

Methods: HLA-typing (PCR) was performed in 177 children aged 11 months to 17 years with a chronic non-infectious diarrhea and/or malnutrition. The diagnosis of celiac disease was established in 68 children according to ESPGHAN criteria (1999), having villous atrophy (Marsh 3), CD group. The remaining children (n=109) were diagnosed with gluten sensitivity on the grounds of elevated antibodies to gliadin, but negative to tissue transglutaminase, positive effect of a gluten-free diet and lack of villous atrophy (Marsh 0-1), GS group.

Results: All children with CD had associated alleles. The largest proportion (n=58; 85.3%) was DQ2, homozygous in 17 (29.3%), significantly more than in GS group (p=0.001). The most of DQ2 allele (n=43; 74.1%) was presented by DQ2.5 (n=29.5%) and a combination of DQ2.5 with DQ2.2 (n=14; 24.1%). In 15 patients (25.8%) DQ2 was presented only by alleles DQA1*201 DQB1*201 (DQ2.2). 20 patients (29.4%) had combination of DQ2 with DQ7. In 4 patients (5.9 %) only DQ7 was found.

In GS group, the alleles associated with celiac disease were identified only in 66% of children (p<0.001). DQ2 had 33.9% (p<0.001) and DQ8 10.1%, while DQ7 single had 22% (p<0.05). The combination of DQ2 with DQ7 (8.2%) was found significantly less than in the CD group. The DQ2 heterodimer structure was presented equally as DQ2.2 (n=14; 40.5%), and DQ2.5 (n=14; 40.5%). Only one child (2.7%) had combination of DQ2.5 with DQ2.2 (p<0.05). In 6 patients (16.3%) a partial DQ2 was revealed, represented either by DQA1*501, or DQB1*201, which never occurred in the CD group.

Conclusion: Homozygosity for DQ2, the combinations of DQ2.5 with DQ2.2, DQ2 with DQ7 provides a high risk of developing celiac disease. Haplotypes DQ2.2 and DQ7 may probably play an independent role in the development of celiac disease, but provide a lower risk. A high percentage of DQ7 in the GS group is likely to play a role in gluten sensitivity, which requires further study.

Disclosure of Interest: None Declared
PO-G-0014

POTENTIAL CELIAC DISEASE IN CHILDREN: MUCH MORE TO LEARN.
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Objectives and Study: The prevalence of Potential Celiac Disease (CD) (producing anti-TG2 without developing any damage to duodenal mucosa) considerably increased in the last 10 years. Potential CD is a precious natural model to explore the progress of the gluten-induced damage in genetically predisposed subjects. Up to now there is yet no agreement about the treatment of the asymptomatic patients with potential CD.

Aim of this prospective longitudinal study is to explore the natural history during 5 years after the diagnosis of potential CD while investigating genetic and environmental risk factors associated with the development of mucosal damage.

Methods: We followed 210 children (F 141, median age 6.4 years) with potential CD diagnosis (anti-TG2 antibodies positivity + architecturally normal duodenal mucosa) for at least 5 years. Asymptomatic patients were left on a gluten containing diet. Every 6 months health status and antibodies were checked, and every 2 years a small bowel biopsy was taken. HLA and non-HLA candidate genes were analyzed by Real-Time PCR using single nucleotide polymorphisms (SNPs) to identify risk alleles. Duodenal biopsies underwent histological and immuno-histochemical analysis and intestinal deposits of anti-TG2 IgA were looked for.

Results: Thirty five cases were put on a gluten-free diet at entry (GFD-E) and 22 during follow up (GFD-FU) because of clinical symptoms or parent’s choice. One hundred and fifty six children were left on a gluten containing diet for at least 5 years. Twenty three of these developed villous atrophy at a median follow up of 3 years. None developed complications. The cumulative incidence of CD was of 12% at 3 years and 46.8% at 5 years.

Among the risk factors associated to the development of mucosal damage, male sex was the first to be identified, since 56.8% of males became celiac after 5 years compared to 37.6% of females. None of the Potential CD with low risk HLA developed CD, while DQ2 and DQ8 carriers showed similar relapsing rates (36%). The presence of intestinal deposits of anti-TG2 was not significantly associated to the outcome. Discriminant analysis showed that sex, signs of infiltration at time 0 (gd and CD25) and SNPs of 3 CD associated genes (IL12A, IL2-IL21, RGS1) do contribute significantly to predict patients that developed villous atrophy during follow-up.

Conclusion: The management of potential CD children is so far a complex issue. The natural history of this condition showed a progression of the intestinal damage at 5 years from the diagnosis in about half of the cases. It is important to extend the follow up time in order to identify risk factors that can distinguish children that really need a GFD at entry from those who don’t.

Disclosure of Interest: None Declared
COELIAC DISEASE AND HEADACHE: MUCH MORE THAN AN ASSOCIATION.

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Objectives and Study: The clinical picture of coeliac disease (CD) is modifying with the emergence of subclinical forms and the reduction of the coeliac iceberg depth. Among the extra-intestinal manifestations of CD, there are growing evidence reporting several neurological disorders. The aim of our study was to establish the prevalence of CD in children affected by headache.

Methods: In our retrospective study we have revised data from 883 children (481 females; age ranged from 3 to 19 years; median: 9.9 years) attending our Centre for Paediatric Headache over the period 2000-2011. They were screened for CD using IgA anti-transglutaminase autoantibodies, IgA EMA and total IgA. Positive patients were referred to our Operative Unit on Coeliac disease, where they were submitted to a further serological evaluation. Confirmed positive children underwent upper endoscopy with multiple duodenal biopsies. Histological lesions were evaluated according to Marsh classification, as modified by Oberhuber. Coeliac children started the gluten-free diet (GFD).

Results: 11 children (7 females; age ranged from 4.8 to 13.9 years) were diagnosed to be coeliacs. Ten showed total villous atrophy (type 3c lesions) whereas one showed moderate villous atrophy (type 3b). 7 children (5 females, age ranged from 10.3 to 13.9 years) were diagnosed to be coeliacs prior to the neurological evaluation. The prevalence of CD in our sample of children and adolescents affected by headache is 2.04%. After starting the GFD, among the eleven children screening-detected, 6 showed disappearance of headache, whereas 5 referred a reduction of frequency and intensity of the attacks.

Conclusion: Our study demonstrates, on a large series, that CD prevalence is quite doubled in patients with headache. Screening for CD could be advised as part of the diagnostic flow-chart in these paediatric patients. In fact, a timely diagnosis and the prompt GFD, in otherwise asymptomatic patients, could improve symptom as well as drugs’ absorption.

Disclosure of Interest: None Declared
INTESTINAL DEPOSITS OF ANTI-TISSUE TRANGLUTAMINASE ANTIBODIES IN INFANTS FROM A COHORT AT RISK FOR CELIAC DISEASE.

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Objectives and Study: Antibodies against anti-transglutaminase (anti-TG2) are produced in intestine and deposited there before being detected in the serum and they are considered very specific for celiac disease (CD). Infants with a 1st degree relative with CD have been recruited in 8 countries shortly after birth (EU-PreventCD project, www.preventcd.com), to participate in a double-blind intervention study investigating the effect of early gluten introduction on CD development.

Aim of this part of the study was to assess the presence of intestinal deposits of anti-TG2 in infants from the Prevent-CD cohort undergoing a jejunal biopsy.

Methods: 814 children, HLA-DQ2+ and/or DQ8+, have been followed clinically and serologically until the age of 3y. Small bowel biopsies (SBBs) were performed based on symptoms suggestive of CD, and/or anti-tissue transglutaminase antibodies (TG2A) or antigliadin antibodies (AGA) in serum. Seventy-four SBBs were performed in 68 children. Intestinal deposits of anti-TG2 IgA were detected by double immunofluorescence.

Results: CD was confirmed by SBBs in 53 children. In 43 of these biopsies intestinal deposits of anti-TG2 IgA were searched for, 33 biopsies with villous atrophy Marsh 3B or 3C), 10 normal villous architecture (Marsh 0 or 1). 33/33 (100%) of patients with villous atrophy (one seronegative) showed the presence of anti-TG2 intestinal deposits, compared to 5/10 (50%) of those with normal mucosa (four with serum anti-TG2). One child developed villous atrophy in the third biopsy after having deposits already 2.1 and 1.6 years earlier. One other child received two biopsies, the first for persistently high serum AGA aged 18 months and the second at 4 years of age for high titer of anti-TG2 and AGA: the first biopsy showed an inflamed mucosa without intestinal TG2 deposits, while the second one presented villous atrophy and intestinal TG2 deposits.

Conclusion: Also in Prevent-CD cohort detection of intestinal deposits of anti-TG2 has a high grade of concordance with anti-TG2 in the serum and with villous atrophy. There are a few CD cases where the sensitivity of detecting celiac antibodies or the sensitivity of the biopsy evaluation can be increased by this method. The follow-up will tell us if the presence of such deposits is a very early sign of CD independently on histology.

Disclosure of Interest: None Declared
Tissue Transglutaminase Antibody Levels Predict IgA Deficiency

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Objectives and Study: There is increased prevalence of coeliac disease in IgA (Immunoglobulin A) deficiency. IgA tTGA (tissue transglutaminase antibodies) are the most widely used screening test for coeliac disease, however there is a risk of false negative results in patients with IgA deficiency. As a result, patients screened for coeliac disease using IgA tTGA are also frequently tested for total IgA levels in many healthcare settings.

The aim of this study was to determine whether all tTGA assays should be combined with a measure of total IgA. We aimed to assess whether tTGA may be used quantitatively, with total IgA levels only requiring assessment below a specific lower threshold value of tTGA.

Methods: Retrospective analysis of 11532 samples-paired tTGA and total IgA results obtained from 9429 children and young adults between 6 months to 18 years across 5 hospitals and primary care practices in East of England between October 2007 and November 2011. All tests were performed in the same laboratory.

Results: The index tTGA results of 9429 patients were included in this study. We used ROC curve analysis and found the tTGA ≥0.10u/ml to be the value above which total IgA assessment could be avoided. This corresponded to a sensitivity of 0.92 and specificity of 0.84. All patients with a tTGA less than 0.10u/ml should therefore have a total IgA measurement taken. Using this cut-off, only 16.4% (n=1545) of our patient sample would have needed total IgA measurement to rule out a false negative result in IgA deficiency (Table 1).

Table 1

<table>
<thead>
<tr>
<th>tTGA</th>
<th>Absent IgA</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>≥0.10</td>
<td>7877</td>
<td>7</td>
</tr>
<tr>
<td>&lt;0.10</td>
<td>1466</td>
<td>79</td>
</tr>
<tr>
<td>Total</td>
<td>9343</td>
<td>86</td>
</tr>
</tbody>
</table>

Conclusion: We report a simple means of avoiding unnecessary additional measurement of total IgA in the assessment of coeliac disease. By using the tTGA value quantitatively, only values < 0.10u/ml require subsequent measurement of total IgA to rule out true IgA deficiency and hence a potentially false negative screening result. Implementation of such recommendations in the screening for coeliac disease could lead to significant cost savings for the healthcare economy.

Disclosure of Interest: None Declared
CORRELATION BETWEEN ANTITRANGLUTAMINASE LEVELS AND HISTOLOGICAL LESION IN A WIDE POPULATION OF CD CHILDREN FROM THE SPANISH COELIAC DISEASE REGISTRY (REPAC2)


Objectives and Study: The 2012 ESPGHAN celiac disease (CD) diagnosis guidelines offer the option to avoid the small bowel biopsy (SBB) under certain circumstances, this including obligatorily tissue transglutaminase antibody (TTG) being above 10 times the upper limit of normal (ULN). However this recommendation relies only on a few studies including pediatric patients. Our aim is to assess the correlation between TTG levels and duodenal histology in a large series of CD pediatric patients from a multicenter nationwide registry.

Methods: In a prospective observational study nationwide registry in Spain (REPAC2), including new pediatric CD cases <15 years from 01-2011 till 10-2012, patients with serology and SBB (Marsh-Oberhuber classification) were considered. IgA-TTG were referred as multiples of the ULN (different laboratory cut-offs).

Results: In 1269 out of 1470 new diagnosed CD cases have both TTG and SBB. 864 children had TTG >10xULN; 840 (97.3%) out of the had a Marsh 2 or 3 lesion compatible with CD diagnosis, 820 (95%) corresponding to a M3(a/b/c) lesion. Only 24, representing 2.7%, had M 0-1 (Figure). Looking at histology, 1060 had M3(a/b/c) and 820 out of these, i.e. 76.7%, had TTG higher than 10xULN, while, for a cut off of 6x ULN, 92% (N=977) were above this limit. 28 children negative for TTG had M3(a/b/c), 21 (75%), being younger than 3 years of age at sampling (18 younger than 2).

Figure: number of cases within each histology group clustered according to TTG values

Conclusion: Our data confirm, in a large sample of recently diagnosed patients, the relationship between TTG levels and the degree of histological lesion and strengthen the high specificity of TTG and its usefulness both for CD diagnosis and for CD diagnostic approach, as recommended in the new ESPGHAN CD guidelines.

Disclosure of Interest: None Declared
**Objectives and Study:** We reviewed data on worldwide prevalence of celiac disease (CD), wheat consumption, and frequencies of HLA DQ2 and DQ8 haplotypes and we combined the three geographical maps to conclude on their mutual relationship.

**Methods:** Studies published in English assessing prevalence of CD in low risk adults and children were identified through a MEDLINE search (1950–2012). Worldwide level of current wheat consumption and frequencies of HLA-DQ2 and HLA-DQ8 were obtained from the Food and Agriculture Organization of the United Nations (FAO) database (http://www.fao.org) and from the allelefrequencies.net database (http://www.allelefrequencies.net), respectively. To assess the correlations between CD and wheat consumption and HLA frequencies and between wheat consumption and HLA frequencies we performed the linear Pearson’s correlation.

**Results:** Twenty-nine studies on CD prevalence were included. Overall, the worldwide prevalence of CD ranged from 0 to 5.6%, with an overall cumulative rate of 0.9%. We observed a significant correlation between the prevalence of CD and the frequency of DQ2 (r = 0.45, P value = 0.04) and DQ8 haplotypes (r = 0.5, P value = 0.03), and between wheat consumption and the frequency of HLA DQ2 (r = 0.7, P value = 0.0001) and DQ8 (r = 0.5, P value = 0.03). There was a not quite statistically significant correlation between the prevalence of CD and wheat consumption (r = 0.4, P value = 0.06).

**Conclusion:** The worldwide level of wheat consumption and the frequency of HLA DQ2 and DQ8 are highly correlated. These data confirm the evolutionary hypothesis of a selective advantage to the species of genes predisposing to CD or CD itself in areas with high wheat consumption.

**Disclosure of Interest:** None Declared
INFLUENCE OF GENETIC RISK OF DEVELOPING COELIAC DISEASE ON INTESTINAL MICROBIOTA OF INFANTS IN EARLY LIFE.

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Objectives and Study: The objective was to determine the influence of the genetic determinants of coeliac disease (HLA-DQ genes) on intestinal microbiota composition of exclusively breast-fed infants. A subset of cases (n=23) from a cohort of infants with at least one first-degree relative with CD, included in a larger study, were selected. All infants were breast-fed and vaginally delivered to eliminate these variables. The study was approved by the ethics committees of CSIC and the Hospitals involved and conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983. Written informed consent was obtained from the parents of infants included in the study.

Methods: HLA-DQ genotype was determined by PCR-SSP DQB1 and DQA1 typing. The microbiota was analysed in stools collected at 1 month of age by massive sequencing of 16S rRNA gene amplicons using a 454 Life Sciences Genome Sequencer FLX instrument (Roche). The subjects were subdivided in two groups according to the HLA-DQ genotype: the subgroup of high risk (n=11) included those individuals carrying the DQ2 haplotype in both cis (DQA1*0501-DQB1*0201 in homozygosis) and trans conformations (DQA1*0201-DQB1*0202 with DQA1*0505-DQB1*0301 in heterozygosis) and the subgroup of low risk (n=12) included those individuals with other common genotypes not associated with CD. Differences in relative abundance of different taxa were analysed by Mann-Whitney U test.

Results: Infants of the high genetic risk group showed significantly higher percentages of Firmicutes and Proteobacteria than those of the low genetic risk group (P=0.014 and 0.045, respectively). In relation to family, infants with high genetic risk also had significantly higher percentages of Clostridiaceae (P value<0.001), Corynebacteriaceae (P value 0.017), Enterobacteriaceae (P value 0.045), Staphylococcaceae (P value 0.031) and Veillonellaceae (P value 0.030) than those with low genetic risk.

Conclusion: This study confirms that the HLA-DQ2/DQ8 genotype influences the microbiota composition of exclusively breast-fed infants early in life, which could constitute an additional factor contributing to the risk of developing CD.

Disclosure of Interest: None Declared
ROLE OF PARKINSON’S DISEASE 7 IN CHILDHOOD COELIAC DISEASE

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Objectives and Study: Earlier we have demonstrated elevated expression of hypoxia-inducible factor (HIF)-1α in the duodenal mucosa of children with coeliac disease (CD), which has been shown to play an important role in the maintenance of intestinal barrier function. Since Parkinson’s disease 7 (PARK7) molecule was suggested to be an upstream activator of HIF-1α and it has been proposed to participate also in immune system regulation and apoptosis, we aimed to investigate its involvement in the pathomechanism of CD.

Methods: From 11 children with newly diagnosed CD, 5 children with treated CD (maintained on gluten free diet) and 10 control children duodenal biopsy specimens were collected. mRNA expression of PARK7 and its protein levels in the duodenal mucosa were determined by real-time PCR and Western blot, respectively. Localization of PARK7 was detected by immunofluorescent staining.

Results: We found increased PARK7 protein level in the duodenal mucosa of children with untreated CD compared to children maintained on gluten free diet or controls (p <0.03). Interestingly PARK7 was mainly present in the enteroendocrine cells of CD patients.

Conclusion: Elevated PARK7 levels in the duodenal mucosa of children with CD may refer to its potential involvement in the pathomechanism of CD. Localization of PARK7 in the enteroendocrine cells suggests that PARK7 may influence the pathomechanism of CD by acting on enteroendocrine cells. However further studies are needed to better understand the precise role of PARK7 in CD.

Disclosure of Interest: None Declared
INFLUENCE OF BIFIDOBACTERIUM LONGUM CECT 7347 IN LIVER IRON MOBILIZATION AND INFLAMMATORY
BIOMARKERS PRODUCTION IN A GLUTEN-INDUCED ENTEROPATHY ANIMAL MODEL
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Objectives and Study: To evaluate the influence of orally administered Bifidobacterium longum CECT 7347 on nutritional iron status of weanling animals with gliadin-induced enteropathy.

Methods: Weanling rats were sensitized with interferon (IFN)-g and fed gliadins alone or with B. longum CECT 7347. Hemoglobin (Hb) concentration (Drabkin’s reagent), liver transferrin receptor (TfR)-2, IL-6 and TNFα expression (mRNA), active hepcidin peptide production (LC-Ms/Ms) and total liver iron content (Atomic Absorption Spectrometry) were determined.

Results: Gliadin feeding in IFN-g sensitized animals increased hepatic iron deposition and reduced serum Hb concentrations in comparison with controls. These observations were accompanied by decreased TfR2 expression and increased IL-6 and TNFα gene expression. However, B. longum CECT 7347 administration to this animal model increased circulating Hb concentration and reduced iron deposition in the liver. B. longum administration also increased TfR2, IL-6 and TNFα gene expression in comparison with IFN-g sensitized animals fed gliadins. A similar trend was observed in hepcidin peptide production.

Conclusion: Animal with gliadin-induced enteropathy had reduced serum Hb concentrations in comparison with controls, demonstrating the enteropathy-associated anemia; however, administration of B. longum CECT 7347 increased the expression levels of TfR2, thus contributing to restoring normal liver iron mobilization and serum Hb concentrations. Although both TfR2 and IL-6 are involved in hepcidin regulation, their action seems to be dependent on iron serum levels.

Disclosure of Interest: None Declared
MODE OF DELIVERY AND RISK FOR CELIAC DISEASE IN THE OFFSPRING: RESULTS FROM THE TEDDY STUDY

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Objectives and Study: Caesarean section (CS) is considered as risk factor for various immune mediated diseases such as asthma, allergic rhinitis and type1 diabetes (T1D). There are conflicting data regarding CS and risk for celiac disease (CD). We used the TEDDY cohort (The Environmental Determinants of Diabetes in the Young) to study the relation between CS and CD.

Methods: The TEDDY study follows children born 2004-2010 with HLA-risk haplotypes for T1D and CD, DR3-DQ2 or DR4-DQ8, identified at birth from the general population or 1st degree relatives with T1D at 6 centres in Germany, Finland, Sweden, and in the US, Colorado, Georgia/Florida and Washington. TGA are measured annually using radiobinding assays. TGA positive children are re-tested after 3 months and if confirmed positive defined as persistent TGA and referred to a pediatric gastroenterologist for further evaluation. The association between CS and maternal or child characteristics was examined using unadjusted logistic regression, between CS and CD using survival regression models.

Results: After excluding twins, triplets, and deliveries using forceps/vacuum 6003 subjects remained for analysis. CS rate was 26.3% (1576/6003), ranging from 16–37% in the countries; 4427 infants were born by vaginal delivery (VD). Mothers giving birth by CS compared to VD had higher level of education, were older (31.7 vs 30.4 yrs), had higher pre-pregnancy BMI (26.3 vs 24.4 kg/m²) and more often diabetes in pregnancy (17.1 vs 7.5%) (all p<0.0001). Infants born by CS as compared to VD had shorter gestation (39.0 vs 39.7 wks), shorter duration of exclusive (35 vs 55 days) and total breast feeding (235 vs 265 days), and were later introduced to gluten (199 vs. 186 days) (all p<0.0001). No group differences occurred regarding gender, HLA-DR3/DR3 status, or family history for CD. Persistent TGA and confirmed CD were found in 8% and 3% of CS compared with 11% and 4% in VD children. Crude and adjusted hazard ratios (HR) did identify CS neither as risk factor for persistent TGA (HRcrude 0.833 [95%CI 0.687–1.011], HRadj=0.886 [0.713-1.102]) nor for CD (HRcrude 0.850 [0.623-1.160], HRadj 0.989 [0.702-1.394]).

Conclusion: In this large multi-national cohort of children with HLA-risk genotypes, CS was not associated with the risk for persistent TGA positivity or CD.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
COELIAC DISEASE

PO-G-0024

DUODENAL MUCOSAL MICROBIOTA AND EXPRESSION OF MUCOSA-ASSOCIATED GENES IN CHILDREN WITH COEALIC DISEASE


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Objectives and Study: Gastrointestinal mucosal barrier and mucosa-associated commensal microbiota are considered to be important factors in the homeostasis of the gut epithelium and mucosal immunity and thus may play a role in coeliac disease (CD). The aim of the study was to explore duodenal microbiota and expression of mucosa-associated genes in children with CD.

Methods: Duodenal mucosa-associated microbiota was assessed in 10 untreated CD (median (SD) age 6 ± 3.68 y) and 9 healthy (median (SD) age 8 (3.68) y) Finnish children by using the high-throughput bacterial phylogenetic microarray (HITChip) covering over 1000 intestinal phylotypes. The gene expressions of a tight junction protein zonula occludens-1 (ZO-1), a gap junction protein connexin-43 (Cx43), a mucus protein mucin 2 (MUC2), an antimicrobial peptide RegIIIg, a chemokine CXCL16 and its receptor CXCR6 in duodenal biopsies were assessed by relative quantitative reverse transcription-PCR.

Results: Duodenal microbiota was found to be individual specific, Proteobacteria, Bacilli and Bacteroidetes being the dominant phyla. Duodenal microbiota was comparable between CD and healthy children as assessed in phylum-like, genus-like and species-like level by HITChip. However, microbiota differences between CD and healthy children could be found in a profile comprising of 8 genus-like bacterial groups by bagged redundancy analysis (p<0.05). The gene expression of a chemokine receptor CXCR6 was increased (p=0.001, Mann-Whitney U test) and that of an antimicrobial peptide RegIIIg tended to be decreased (p=0.07, Mann-Whitney U test) in CD children as compared with healthy children.

Conclusion: Certain bacterial groups and mucosa-associated factors in duodenum may contribute to the development of CD.

Disclosure of Interest: None Declared
PANCREATIC-SPECIFIC AUTOANTIBODIES TO GLYCOPEPTIDE 2 IN PEDIATRIC COELIAC DISEASE

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Objectives and Study: Glycoprotein 2 (GP2) was recently discovered as the major autoantigenic target of Crohn’s disease-specific pancreatic autoantibodies. These antibodies are regarded highly specific for Crohn’s disease but positive only in about 25% of patients. Prevalence of anti-GP2 in celiac disease (CD) is unknown.

Methods: We investigated anti-GP2 IgA in sera from 155 patients with histologically proven celiac disease (CD) at the time of diagnosis and in 13 patients in the course under gluten-free-diet (GFD). Anti-GP2 and tissue transglutaminase (TG) antibodies were detected by ELISA employing recombinant human GP2 and human TG and endomysial IgA antibodies by indirect immunofluorescence. Values >20 U/ml for anti-GP2-IgA were considered positive.

Results: Anti-GP2-IgA was found to be significantly more often positive in patients with CD compared to controls: positive in 29/155 (18.7%) of patients with CD, but only in 1/65 (1.5%) of healthy controls (Fisher’s exact test, p<0.001). Most patients in the CD-cohort with positivity for GP2-IgA had very high anti-TG-IgA (over 300 U/ml) and very high endomysial antibodies at time of diagnosis.

All controls were negative for anti-TG-IgA. Values for anti-GP2-IgA were significantly higher in the CD patients compared to the controls (Mann-Whitney test, p<0.001). 4/26 (16.8%) patients with diabetes type 1 and CD were positive for anti-GP2-IgA.

In all patients (n=13) with follow-up samples, CD-specific antibodies (anti-TG-IgA and endomysial IgA antibodies) and anti-GP2 levels declined to normal values under GFD. A close correlation was found between anti-GP2 IgA and anti-TG-IgA with a Spearman’s coefficient of rank correlation of 0.574 (95% CI 0.441 to 0.683, p<0.05) and between anti-GP2 IgA and anti-deamidated gliadin IgA with a Spearman’s coefficient of rank correlation of 0.633 (95% CI 0.513 to 0.729, p<0.001).

Conclusion: In a subgroup of patients with CD anti-GP2-IgA seems to be associated with disease activity. Pathogenesis of CD and of inflammatory bowel diseases is only partly understood to date, but an abnormal intestinal barrier function leading to a leaky gut appears to be crucial in both clinical conditions. However, since GP2 is involved also in antigen presentation and immunoregulation, GP2 itself may be involved in pathogenesis of CD. GP2 is expressed on the apical plasma membrane of M cells of Peyer’s patches and serves as a transcytotic receptor for mucosal antigens. Patients with active CD have also an impaired pancreatic function, which may be associated with autoimmunity to GP2. More detailed analysis of patient characteristics and further studies with more patients are warranted to investigate this hypothesis.

PO-G-0026

DOES MODERN SEROLOGY LEAD TO EARLIER DIAGNOSIS OF COELIAC DISEASE (CD) WITH LESS MUCOSAL DAMAGE?

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Objectives and Study: CD is an increasing autoimmune disorder affecting almost 1% of populations worldwide. There is a hypothesis that highly sensitive and specific tests as transglutaminase antibodies (tTGAb) may detect cases earlier with less mucosal damage.

Methods: In a retrospective study we compared 44 CD cases diagnosed at our center between 1988 - 1999 (period 1 before tTgAb) to 111 cases detected later (period 2: 2000-2011). The following parameters were analysed: median age at diagnosis, diarrhea, protuberant abdomen, failure to thrive, anemia, abdominal pain, constipation and mucosal damage. Appropriate statistical methods as x²-test and logistic regression were used.

Results: There are significant differences in median age at diagnosis, 3.9y in period 1 versus 8.0y in period 2 (p<0.01) and in clinical parameters as diarrhea (odds ratio (OR) 7.5 for diarrhea in period 1, p<0.01), protuberant abdomen (OR 3.5 for period 1, p=0.01), failure to thrive (OR 6.3 for period 1, p<0.01), anemia (OR 6.8 for period 1, p<0.01), abdominal pain (OR 3.5 for period 2, p=0.01), constipation (OR 10.0 for period 2, p=0.27). However, there was no significant difference in mucosal damage (p=0.56); all but 5 patients in both periods had severe mucosal damage (Marsh 3A–C).

Conclusion: Our results show the expected difference in age at diagnosis and in clinical presentations, but not concerning severity of mucosal damage in the two time periods.

Disclosure of Interest: None Declared
BIOLOGICAL EFFECT OF GLIADIN PEPTIDES ON DENDRITIC CELLS FROM HEALTHY SUBJECTS
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Objectives and Study: Previous studies showed that gliadin peptide P31-43 can alter actin cytoskeleton (Barone, Gut 2007) and can induce an increase of trans-presented IL-15/IL-15Ralpha complex (Barone, PlosOne 2011) in CaCo2 cells. Studies exploring the effects of gliadin on peripheral immune cells are lacking. In order to reveal any immunological implication of an alimentary antigen like gliadin, we aimed to explore the effects of the gliadin peptide P31-43 on dendritic cells (DCs) from healthy subjects.

Methods: DCs were generated from peripheral blood monocytes from healthy subjects after 6 days stimulation with IL-4 and GM-CSF. Gliadin peptide P31-43 was used to stimulate DCs. Crystal violet and phalloidin staining were used to determine cell shape and actin cytoskeleton. FACS analysis was performed to assess surface CD83 and both surface and intra-cytoplasmatic IL-15 expression. Real time PCR was performed to investigate IL-15 mRNA levels.

Results: Our data show that P31-43 induces DCs to make more dendrites by rearrangement of actin cytoskeleton. Indeed DCs with more than 3 small and/or 1 long dendrite show an increase from 36.8±8.9% without any treatment to 49.3±8% after 3h P31-43 treatment (p=0.049). In addition P31-43 can induce an increased surface expression of the maturation marker CD83 (p<0.05) and of membrane-bound IL-15 (p<0.05) but not of intra-cytoplasmic IL-15 as assessed by FACS. Moreover acid treatment does not change IL-15 surface expression, suggesting that the observed increase is not due to the receptor-bound but to the membrane-bound form. All data are from at least 5 healthy subjects for each experiment. Furthermore preliminary data show that P31-43 treatment can induce higher IL-15 mRNA levels on DCs from healthy subjects, as assessed by qPCR.

Conclusion: Our data show that gliadin peptide P31-43 exert several biological effects on DCs from healthy subjects. This peptide induces actin cytoskeleton rearrangements interfering with cell shape, contributes to DCs maturation and increases IL-15 expression in DCs. Altogether those data suggest that gliadin could influence the immune system of healthy subjects, potentially contributing to the development of gluten related disorders.

Disclosure of Interest: None Declared
LIPOMA-PREFERRED PARTNER PROTEIN (LPP), A GENETIC MARKER FOR COELIAC DISEASE PREDISPOSITION IS INTERACTING WITH TRANSGLUTAMINASE 2

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Objectives and Study: The genetic risk for coeliac disease is determined by the presence of HLA-DQ2 or DQ8 and other non-HLA genes with lower contribution. The Lpp gene encoding a structural protein important for cell motility and smooth muscle cells shows high association with coeliac disease in four consecutive intronic single nucleotide polymorphisms. It is currently unknown how Lpp in involved in the disease pathogenesis. The aim of this study was to investigate whether Lpp can associate with transglutaminase 2 (TG2) or targeted by serum antibodies from coeliac disease patients.

Methods: Biopsy samples from 6 normal and 6 coeliac disease patients as well as human umbilical cord endothelial vein (HUVEC) and arterial muscle cells derived from normal and coeliac subjects were analysed for Lpp expression by real time PCR, Western blot and immunohistochemistry. Human recombinant Lpp, full length TG2 and its domain deletion fragments were expressed in E. coli and used for interaction studies by enzyme-linked immunoassay (ELISA) and surface plasmon resonance real-time binding analysis.

Results: Lpp was similarly expressed in normal and coeliac tissues. Both TG2 and Lpp localised to focal adhesion complexes and associated with the cytoskeleton of muscle cells maintained in culture. The expression in HUVECs was very low. Recombinant Lpp bound dose-dependently to TG2 and the interaction involved multiple domains of TG2. Serum antibodies of coeliac disease patients did not recognize Lpp in ELISA.

Conclusion: Lpp is directly binding to TG2, the main coeliac autoantigen. Further analysis of this binding and cellular handling of Lpp in coeliac cells may reveal disease-specific differences.

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Disclosure of Interest: None Declared
OATS IN THE DIET OF CHILDREN WITH CELIAC DISEASE: PRELIMINARY RESULTS OF A RANDOMIZED, DOUBLE-BLIND, MULTICENTER ITALIAN STUDY

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Objectives and Study: to determine the safety and the acceptance of selected oats varieties in the treatment of Italian children with celiac disease (CD).

Methods: Children with CD were enrolled in a 15 months, randomized, double-blind controlled multicenter trial. Participants were randomized in 2 groups following either A-B treatment (6 months of diet “A”, 3 months of standard GFD, 6 months of diet “B”), or B-A treatment (6 months of diet “B”, 3 months of standard GFD, 6 months of diet “A”) (crossover with washout design). A and B diets included GF products (flour, pasta, biscuits, cakes and crisp toasts) with either purified oats or placebo, given in a double blind fashion. The oat varieties used to manufacture experimental gluten-free products were selected in vitro, in a previous study, for their low amount of gluten-like proteins. Clinical data (GSRS score, growth data) and intestinal permeability test (IPT) by measurement of urinary lactulose/mannitol (L/M) ratio were monitored at 0, 3, 6, 9, 12 and 15 months. Serological (IgA-TTG, IgG-DGP, anti-avenin and anti-zonulin antibodies) and biochemical data were measured at 0, 6, 9, and 15 months.

Results: During the period September 2008-September 2011, 247 children were enrolled. 137 children have received at least 6 months of treatment and 85 completed the protocol. No significant differences were found in GSRS score, BMI and urinary L/M ratio between 0 to 6 months in each group and between the 2 groups after 6 six months of treatment.

Conclusion: These preliminary results show that addition of selected varieties of non-contaminated oats in the treatment of children with CD does not determine changes in intestinal permeability. No gastrointestinal disturbances were associated with either product A or B consumption. The final results will clarify the safety, tolerability and acceptance of oats containing products in the GFD of Italian children with CD.

Disclosure of Interest: None Declared
THE 3RD NATIONAL SURVEY ON CHILDHOOD CELIAC DISEASE IN THE NETHERLANDS: INCIDENCE AND CLINICAL PRESENTATION.

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Objectives and Study: We previously performed 2 surveys on the incidence and clinical presentation of childhood celiac disease in The Netherlands (1,2). We performed this study was to investigate if the incidence and clinical presentation of childhood celiac disease (CD) in The Netherlands are still changing.

Methods: Children (0-14 years) newly diagnosed with CD were identified through the internet-based Dutch Pediatric Surveillance Unit. The DPSU comprises all Dutch paediatric practices, and has a mean response rate of 90%. Data on clinical presentation, diagnosis and treatment of CD were anonymously collected using protocolled questionnaires.

Results: Between January 2010 and December 2012, 445 new cases of childhood CD were reported. We collected and analyzed data on all cases. The male: female ratio was 1:2.0. The median age at presentation was 4.5 yrs. (±4.3SD) (survey 1: 1.5 yr and survey 2: 2.5 yr, p<0.001). The percentage of children diagnosed <2 years of age was 20%, (survey 1: 60% and survey 2: 47%, p<0.0001). The incidence was 1.2/1000 live born infants (survey 1: 0.22/1000 and survey 2: 0.81/1000 live born infants).

Cases were diagnosed on clinical grounds (82%), screening in associated disorders (8%), and in family members (10%). The most common symptoms were abdominal pain (45%), wasting (36%), distended abdomen (28%), chronic diarrhea (25%), and lassitude (24%). The percentage of children presenting with diarrhea or distended abdomen decreased significantly, and the percentage of children with lassitude, abdominal pain and anorexia increased significantly compared to the 1st and 2nd survey on childhood CD (figure 1). However the actual number of children with diarrhea, distended abdomen, stunting lassitude, abdominal pain and anorexia increased compared to the previous surveys.

Serological screening was performed in 99% of the cases, and the use of EmA increased from 42% in 2010 to 50% in 2011 (p=0.03). In the 1% of cases without serological screening, biopsies were performed. A duodenal biopsy was performed in 95% of cases in 201 and 86% in 2011 (p<0.0001), and of the cases without biopsy all had positive serology.

Conclusion: The incidence rate of childhood CD in the Netherlands is still rising. The clinical presentation is still changing with failure to thrive, abdominal pain and anorexia occurring relatively more often, and chronic diarrhea and distended occurring relatively less often. Possible explanations for these changes be increased awareness in pediatricians in addition to active case-finding strategies in CD families and patients with associated disorders.


Disclosure of Interest: None Declared
INTESTINAL ANTI-TISSUE TRANSGLUTAMINASE IGA DEPOSITS IN CHILHOOD CELIAC DISEASE
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Objectives and Study: TG2 IgA are produced and secreted in the intestinal mucosa of celiac disease (CD) patients and deposited on extracellular TG2 of the intestinal mucosa, where they settle even before blood appearance. Celiac patients present mucosal deposits specific for TG2 below the villous and the crypt basement membrane and around mucosal vessel. The aim of this study was to establish the diagnostic value of intestinal deposits of anti-TG2 IgA for celiac disease in a paediatric cohort, to assess the degree of concordance with serum anti-TG2 and finally to provide a pattern and staining intensity classification of anti-TG2 IgA mucosal deposits.

Methods: Fifty-four children who underwent small intestinal biopsy for suspected CD were prospectively recruited and divided into 2 groups: group A, 43 celiac children with villous atrophy (Marsh3) and group B, 11 children with high serum levels of CD markers but normal intestinal mucosa (Marsh0,1). Control group (group C) included 10 children without CD. At the time of biopsy, serum samples from all patients were collected to evaluate serum levels of anti-tissue transglutaminase IgA antibodies. From all patients duodenal sections were evaluated for the presence of intestinal deposits of anti-TG2 IgA antibodies by double immunofluorescence. The evaluation of anti-TG2 IgA mucosal deposits was performed considering the pattern and the intensity of the staining.

Results: Double immunofluorescence showed specific anti-TG2 IgA deposits, appearing as a yellow-orange staining due to the colocalization of IgA with TG2, in all samples from group A and B. In group C only 2 subjects presented IgA deposits. Sensibility and specificity of intestinal TG2 IgA were respectively 100% and 83% in both group A and B. Positive predictive value was 95% and 83% in group A and B respectively, negative predictive value was 100% in both these groups. There where no statistically significant difference between the intensity of anti-TG2 IgA mucosal deposits in celiac patients and in potential CD patients. We detected a difference, even if not statistically significant, in term of distribution: patchy distribution was prevalent in CD patients (67,4%) while homogeneous distribution was prevalent in potential CD (70%).

Conclusion: These preliminary results evidenced the high diagnostic sensibility of anti-TG2 IgA deposits in pediatric CD. In patients with potential celiac disease the presence of anti-TG2 IgA deposits has an important diagnostic value since it validates the presence of an initial mucosal damage. Deposit’s features are independent from Marsh grading and from serum levels of anti-TG2 IgA. In patients with potential celiac disease could be useful a perspective evaluation to identify the predictive capacity of anti-TG2 IgA deposits.

Disclosure of Interest: None Declared
THE CHANGING EPIDEMIOLOGY OF COELIAC DISEASE IN SOUTH WALES – A 28 YEAR PERSPECTIVE
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Objectives and Study: The diagnosis of coeliac disease (CD) has increased in frequency, particularly since the accuracy of serological antibody testing has improved. Previous studies from our region have shown an increasing incidence of CD from 1983 to 2004, with a change in clinical presentation and decrease in specific gastro-intestinal symptoms, as well as an increase in age at diagnosis.

Methods: We reviewed all patients with CD presenting to the Regional Centre between 2005-11 and compared the incidence, age and documented mode at presentation with previous published data from the same area between 1983-2004.

Results: 163 cases (23 per year) of CD were diagnosed between 2005 to 2011, with a median age at diagnosis of 14 years (range 0.8 to 16 years) compared with 50 cases (8 per year) a median age of 8 years between 1999 to 2004. 41% presented with classical symptoms, 23% with non-classical symptoms and 36% asymptomatic and diagnosed after serological screening of high risk group. Compared with the most recent previous study from the same population, the percentage of patients presenting with gastro-intestinal symptoms remained similar (42% vs 41%) but patients diagnosed after targeted screening had increased from 26% to 36%.

Conclusion: Frequency of diagnosis of CD in this stable and well defined population has risen dramatically in the last 7 years, although it is likely that many patients still remain undiagnosed in childhood. The median age at diagnosis has increased and over 50% of patients present with few or no symptoms.

References: None

Disclosure of Interest: None Declared
ASSESSMENT OF MAJOR CARDIOVASCULAR RISK PARAMETERS DURING ONE YEAR GLUTEN-FREE DIET IN CHILDREN WITH NEWLY DIAGNOSED CELIAC DISEASE


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Objectives and Study: The diet in celiac disease (CD) may affect several risk cardiovascular risk factors—e.g. carbohydrates may be replaced by fat. Taking this into consideration, together with the reports concerning increased cardiovascular episodes among patients with CD, we decided to check the impact of gluten-free diet on the lipid profile and other biochemical risk factors of atherosclerosis in newly diagnosed children with CD.

Methods: We performed a multicenter, one-year lasting prospective study. 67 consecutive patients aged 2-20 yrs were included at the time of the diagnosis of CD. Due to negative serological tests we excluded 19 pts from further analysis. Final analysis was performed in 39 pts who followed gluten-free diet with negative serological tests for tTG 1 year after diagnosis and in whom all lab tests were available. We obtained selected clinical data, measurements and serological and histopathological results (IgA EmA, IgA tTG and Marsh scale). At the time of diagnosis and 1 year after gluten-free diet we measured: lipids, apolipoproteins (A1,B,E), lipoprotein(a), homocysteine, as well as antioxidants (folic and uric acid) and hCRP. We compared baseline results with those obtained after 1y therapy in whole group and in subgroups of classical (16 pts) and atypical CD (19 pts).

Results: We found 8 pts to have increased cholesterol concentration (>190 mg/dl), 7 pts had increased serum LDL-C (130 mg/dl) and 9 had decreased HDL-C (< 40 mg/dl). Other abnormal results recorded were low ApoA1 (9 pts), increased lp (a) (n=6), high hCRP (n=6) and high homocysteine (n=7). After 1 year there were no significant changes in all investigated parameters except for a significant decrease of folic acid (from 19,0 µg/l to 10,1µg/l) and hCRP (from 1,7 mg/dl to 0,77 mg/dl). When analyzed in subgroups (classical and atypical CD) hCRP decreased significantly (from 1,2 mg/dl to 0,6 mg/dl) and from 1,7 mg/dl to 0,77 mg/dl, respectively).

Conclusion: One year of gluten-free diet does not affect significantly lipid metabolism. hCRP decreases during therapy which is a good indicator of decreasing inflammation as one the risks of atherosclerosis. Still, folic acid also decreases which may predispose to atherogenesis on long term.

Disclosure of Interest: None Declared
Objectives and Study: Lymphocytic gastritis (LG) is reported to be found in 15-45% of children diagnosed with coeliac disease (CD). Some recommendations therefore state that gastric mucosal biopsies should be obtained from children with suspected CD, as finding of LG could strengthen the diagnostic specificity in borderline cases [1]. Recent studies have reported that eosinophilic esophagitis (EE) was found in 3-4% of children diagnosed with CD. Some authors thus suggest that also esophageal biopsies should be routinely obtained during diagnostic endoscopy in children with suspected CD [2]. The aim of this study was to investigate the prevalence of LG and EE in paediatric patients with suspected CD in northern Stockholm County, Sweden.

Methods: Files of all children with suspected CD who underwent upper endoscopy from January 2007 till May 2010 at our department were reviewed.

Results: A total of 362 patients underwent upper endoscopy during the study period. Out of these, 248 patients had histopathological findings in duodenal biopsies consistent with CD. In the remaining 114 patients CD was excluded. In the CD cohort esophageal biopsies were obtained in 133 patients (53%) and gastric biopsies in 162 patients (65%). In the non-CD patients esophageal biopsies were obtained in 70 patients (61%) and gastric biopsies in 77(67%).

Prevalence of LG and EE in children with CD and in children with non-CD were compared. The prevalence of microscopic gastritis was 27% in CD patients and 10% in non CD patients (p<0.01). LG was diagnosed in 4 CD patients (2.4%). None of the children with non-CD had LG (p<0.05).

The prevalence of microscopic esophagitis was 14% in CD patients and 9% in non CD patients (p=0.21). None of the CD and non-CD patients demonstrated findings in esophageal biopsies consistent with EE.

Conclusion: Our results suggest that the prevalence of LG and EE in children with CD in northern Stockholm County is lower than reported from most other regions. Microscopic gastritis was significantly more common among CD patients, however only 4 (2.4%) of these presented with LG. As all these four patients presented with total/subtotal villous atrophy, routine biopsies from gastric mucosa did not increase the diagnostic specificity in children with suspected CD in our cohort.

Routine biopsies from esophageal mucosa in children with suspected CD in our cohort did not unveil any case of EE.


Disclosure of Interest: None Declared
COELIAC DISEASE IS MORE COMMON IN CHILDREN WITH HIGH SOCIO-ECONOMIC STATUS

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Objectives and Study: There are a number of genetic and environmental factors which are associated with an increased risk of developing coeliac disease (CD). Socio-economic deprivation is one of these but it is not clear how this increases or reduces the development of CD.

Methods: A cross-sectional study identified all children <16 years old diagnosed with CD in the same tertiary paediatric centre between January 1995 and December 2012. Data, including age at diagnosis and post code, were collected and these were linked with the quintile rank of the Welsh Index of Multiple Deprivation score 2008, a robust measure of socio-economic status.

Results: The overall prevalence of CD in the population studied was 0.75 over 1,000, with a median age at diagnosis 8 years (range 0.8-16 years). There was a graded association between the prevalence of CD and the rate of socio-economic deprivation, with the rate higher in children living in more affluent areas (OR 0.48 in 95% CI 0.279-0.597) with the difference between the lowest deprivation quintile and highest deprivation quintile the most significant.

Conclusion: In our population it is clear that CD is more common in children in the higher socio-economic group, despite the higher rates of breast feeding and lower rates of infection in affluent communities. The reasons for this are not clear but perhaps both the ‘hygiene hypothesis’ and the health seeking behaviours of parents with high socio-economic status are possible factors in the more frequent diagnosis of CD in this group.

References: None

Disclosure of Interest: None Declared
MOLECULAR BASIS FOR THE MYOCARDIUM INVOLVEMENT IN COELIAC DISEASE
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Objectives and Study: Coeliac disease (CD) is characterized by autoantibodies against endomysium (EMA), a connective tissue sheet around muscle cells. These antibodies target tissue transglutaminase (TG2). It has earlier been reported that CD prevalence is higher among patients with end-stage heart failure or cardiomyopathy. Aim of this study was to characterise the myocardial lesions and assess if anti-TG2 antibodies play a role in the cardiac manifestations of CD.

Methods: Myocardium and mediastinal lymph node biopsy samples were analysed by immunohistochemistry in two adolescent patients (18 and 20 years old) with known CD who presented with severe myocarditis after stopping the gluten-free diet. Consecutive childhood myocarditis cases treated at the intensive care unit were prospectively followed up and investigated for coeliac disease antibodies (anti-TG2 and EMA) and HLA-DQ. Human umbilical cord cells prepared from high-risk newborn first degree relatives of CD patients or cells prepared from the intestinal biopsy specimens of CD patients were differentiated into striated muscle cells and investigated in vitro in the presence of tissue-eluted or cloned coeliac antibodies.

Results: Both coeliac adolescents were critically ill and required balloon pump-assisted cardiac support, one of them died. Ultrasound and MRI studies revealed low ejection fraction and signs consistent with myocardial oedema and inflammation, but no viral agent could be identified. Frozen samples of the affected myocardium specimens contained high amounts of in vivo EMA deposition bound to TG2, but no cellular infiltrate of inflammatory cells. Severe myocarditis was diagnosed in 8 children of whom 3 died, 2 were diagnosed with CD by anti-TG2 and EMA serum antibody positivity and jejunal biopsy, both DQ2 positive. The other 3 survivors had neither anti-TG2/EMA antibodies nor DQ2 or DQ8 at the screening for CD, one was later diagnosed with cystic fibrosis and one other with Alström syndrome. During prospective follow up of the risk cohort two children developed CD. In vitro experiments with normal, risk and coeliac muscle cells revealed high susceptibility of affected persons to TG2-specific antibody action, especially when the cells were triggered to move.

Conclusion: Severe myocarditis could be a sentinel sign of other chronic childhood diseases and HLA-DQ2 or DQ8 carriers should be screened for CD. Anti-TG2 antibodies deposited around myocardial fibres can play a role in the severe clinical presentation upon an otherwise benign (perhaps viral) precipitating illness.

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Disclosure of Interest: None Declared
DETERMINATION OF 7 ALPHA-HYDROXY-4-CHOLESTEN-3-ONE IN SERUM AS MARKER FOR BILE ACID LOSS IN CHILDREN

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Objectives and Study: The measurement of 7 alpha-hydroxy-4-cholesten-3-one (C4) as semi-quantitative serum marker for bile acid synthesis has been validated in adults against 75-SeHCAT scintigraphy and proven as reliable marker for bile acid loss. So far, no data are available in children. This prospective study aims a) to establish age dependent reference values in a pediatric population and b) to investigate bile acid loss in children with short bowel syndrome (SBS).

Methods: Serum samples taken after overnight fasting were prospectively collected from 100 healthy children (52% males, 9 months to 18 years of age) and 12 pediatric patients with SBS. Following solid-phase extraction and purification, C4 was determined by high-performance liquid chromatography using a UV detector at a wavelength of 241 nm.

Results: The mean concentration of C4 in healthy children was 22.8 ± 15.8 ng/mL (range 4.7-80.3 ng/mL; median 19.0 ng/mL; 95% CI: 20.6-32.0 ng/mL). No relation to age or sex was found. Values were <54 ng/mL in 96 of 100 children. All 12 children with SBS showed C4 concentration levels above 54 ng/mL (mean 299.6± 167.8 ng/mL; range 105.7-562.1 ng/mL; median 221.9 ng/mL; p<0.0001).

Conclusion: For the first time we report normal values for C4 concentration in children, which correspond to previously published levels in healthy adults. Fasting values lower than 54 ng/mL should be considered as normal. Patients with SBS show consistently elevated C4-concentrations. Thereby, we confirm the reliability of this non-invasive, non-isotopic method to assess bile acid loss in children independent of age and sex.

Disclosure of Interest: None Declared
SUCCESSFUL TREATMENT WITH MESENCHYMAL STROMAL CELLS FOR STEROID REFRACTORY SEVERE ACUTE GRAFT VERSUS HOST DISEASE IN CHILDREN; DEVELOPMENT OF SUBSEQUENT COMPLEX GASTROINTESTINAL COMPLICATIONS

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Objectives and Study: Acute gastrointestinal graft-versus-host disease (GI aGvHD) complicating hematopoietic stem cell transplantation (HSCT) is a cause of severe morbidity and mortality. Steroid therapy resistant cases have a poor prognosis. Mesenchymal stromal cells (MSC) have been reported as salvage treatment. We aimed to document long term GI complications in MSC treated children who have survived extensive GI aGVHD.

Methods: From Dec 2004 to Aug 2012, children with severe steroid refractory GI aGvHD (>stage 2), who received MSC as salvage treatment were included. Clinical records were evaluated to determine GI complications occurring after the MSC infusion.

Results: 21 patients were included. The diagnosis was histologically confirmed in 81% (n=17). One child died within 7 days of MSC infusion and was not included in the analyses. Ten children responded completely (CR: no evident GVHD clinical/biopsy proven) and 6 partially (PR: at least one grade) at 28 days following the first MSC infusion, after 1-3 infusions. Twelve patients survived and were evaluated. Two patients developed GI fibrosis and obstruction. One, aged 15 mnths with total bowel involvement required total parenteral nutrition (TPN). She died 3 years later from pulmonary GHVD. In the second aged 15 yrs, fibrosis was localized to the terminal ileum and caecum. He underwent surgical resection, but had chronic diarrhea and atrophy of the pancreas due to chronic GVHD.

Two patients, both younger than 1 year, developed massive ascites, one with evident esophageal varices and portal hypertension. Both required intermittent mechanical drainage and long term diuretics. No hepatic GVHD was proven. Additionally, 7 children all aged < 3 years developed protracted diarrhea and protein losing enteropathy, without histological aGVHD, which persisted up to 4 months. TPN and enteral feeding were necessary and protracted. Growth in these children was delayed most likely due to chronic immunosupression.

One girl, aged 18 years, developed alloimmune hepatitis 12 months after her GVHD, requiring further immunosupression. Only two children aged >10 years had no evident sequalae. Five surviving children developed chronic GVHD, which was in one patient extensive.

Conclusion: Despite 80% response to MSC, most children experienced subsequent complex protracted chronic gastro-intestinal or hepatic diseases, which was worse in young children. Response to MSC for severe GI aGVHD heralds subsequent clinical complications that require close co-operation amongst specialist pediatric transplant physicians and pediatric gastroenterologists.

Disclosure of Interest: None Declared
GENETIC POLYMORPHISMS IN THE NRG3 GENE ARE ASSOCIATED WITH HIRSCHSPRUNG DISEASE IN THE HAN CHINESE POPULATION

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Objectives and Study: Hirschsprung disease (HSCR) is a complex genetic disorder characterized by the absence of the enteric ganglia along a variable length of the lower digestive tract. Recent study reported that genome-wide copy number variants of the Neuregulin3 (NRG3) gene might be involved in HSCR etiology. In the present study, we aimed to search for NRG3 polymorphisms conferring genetic susceptibility to HSCR in the Han Chinese population.

Methods: A total of 255 participants were recruited for the study, including 104 sporadic HSCR cases and 151 normal controls of Han Chinese origin. We conducted a case-control analysis of 8 single nucleotide polymorphisms (SNPs) within the region of NRG3 gene using the iPLEX Gold technology (Sequenom MassArray platform).

Results: We observed that two genetic polymorphisms showed statistically significant differences between HSCR patients and normal controls (rs6584471, genotype p = 0.002; rs7074694, genotype p = 0.005, allele p = 0.004). In addition, the haplotype which combined all eight SNPs was the most significant, giving a global p = 4.79 × 10^-14.

Conclusion: Our findings indicate that NRG3 may be a potential susceptibility gene for HSCR in the Han Chinese population, confirming a possible role of NRG3 in etiopathogenesis of HSCR.

Disclosure of Interest: None Declared
NEONATAL AUTOIMMUNE COLITIS - AN UNRECOGNIZED DISEASE MECHANISM?
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Objectives and Study: Autoimmune enteropathy due to antibodies directed towards the enterocyte represents a rare form of intestinal inflammatory disease, seldomly seen in the neonates. Determination of enterocyte antibodies as a biomarker has been very sparsely used in the differential diagnosis of gastroenterological inflammatory conditions. Our hypothesis is that maternal IgG enterocyte antibodies can pass the placenta and be present in the neonate during the first months of life. The transferred enterocyte antibodies may cause signs of autoimmune enterocolitis, which diminish as the antibodies are cleared from the circulation.

Methods: In a two-year period, a total of 14 neonates presented at the Hans Christian Andersen Children's Hospital with enterocolitis in infancy within the first year of life, where the clinical history suggested an autoimmune background. The infants and in some cases the mothers had a blood sample taken to determine enterocyte antibodies. Enterocyte antibodies were determined semiquantitatively by immunofluorescence based on intestinal tissue from monkey (Euroimmun).

Results: In total 5 cases with a positive enterocyte antibody test were identified. In two of these cases the mother had also a blood sample taken to determine her level of enterocyte antibodies at the time of debut and in both cases displayed enterocyte antibodies. Both mothers complained of gastrointestinal problems but had no known inflammatory bowel disease. In a third case the mother had been diagnosed with inflammatory bowel disease. In the two last cases the mother did not have her level of enterocyte antibodies determined.

Conclusion: These data suggest a link between the level of enterocyte antibodies in the mother, transplacental transmission to the neonate and the disease mechanism in the neonate. As the level of the enterocyte antibodies decreases in the neonate the symptoms resolve. These preliminary results may present a new path in the understanding of neonatal autoimmune colitis.

Disclosure of Interest: None Declared
ENTEROPATHY WITH LOSS OF GASTROINTESTINAL ENDOCRINE CELLS IN A CHILD WITH TYPE I DIABETES AND IMMUNDYSREGULATION.

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Objectives and Study: The secretory granules from gastrointestinal endocrine cells (GIECs) contain peptides that act as systemic or paracrine mediators for the regulation of digestion and motility. The lack of intestinal enteroendocrine cells in enteroendocrine cell dysgenesis causes severe malabsorptive diarrhea and leads to severe, life-threatening watery diarrhea [1]. Recently, we described loss of GIECs in patients with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) as specific gastrointestinal feature [2]. We hypothesized that an autoimmune attack against the cells of the gastrointestinal (GI)-associated diffuse endocrine system may be a specific feature of GI dysfunction in autoimmune polyendocrine disorders and not restricted to APECED.

Methods: We investigated gastrointestinal endocrine cells in patients with GI dysfunction and autoimmune endocrine disorders.

Results: We report a patient who developed severe diarrhea and juvenile-onset diabetes in his second year of life. Endoscopy revealed a massive inflammation in the bowel. Histology showed a chronic inflammation of the GI-tract, with duodenal villous blunting, crypt hyperplasia and focally increased intraepithelial lymphocytes. FOXP3 expression in lymphocytes in the GI-tract was reduced. Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome, an extremely rare X-linked disorder with fulminant widespread autoimmunity, early onset type 1A diabetes and autoimmune enteropathy caused by a mutation in the FOXP3 gene was excluded. Neither mutations in the FOXP3 gene nor in the promoter region for IPEX syndrome were found. Therefore, the patient was classified as IPEX-like syndrome. Interestingly, immunohistochemistry showed a marked reduction of GIECs in the gastric, duodenal and colonic mucosa similar to other APECED patients, however an AIRE mutation was genetically excluded.

Conclusion: In addition to a widespread loss of gastrointestinal endocrine cells in patients with APECED we identified now an IPEX-like phenotype with loss of GIECs in all parts of the bowel. Suggesting an autoimmune attack against the cells of the GI-associated diffuse endocrine system is not restricted to APECED and may be also a common feature in other autoimmune polyendocrine disorders with GI dysfunction.


Disclosure of Interest: None Declared
ECONOMIC BURDEN OF CROHN’S DISEASE IN PÆDIATRIC PATIENTS: RESULTS FROM A RETROSPECTIVE ANALYSIS OF INSURANCE CLAIMS
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Objectives and Study: To compare health care utilisation and direct medical costs in US pædiatric patients (pts) with Crohn’s disease (CD) to matched controls not diagnosed with CD.

Methods: Pædiatric pts <18 years old with ≥2 CD diagnoses (ICD-9: 555.xx) were selected from the Truven Health MarketScan® Commercial Claims and Encounters Database (1/1/2000 to 12/31/2010). Pts with any claim for ulcerative colitis (UC) (ICD-9: 556.xx) were excluded. The CD cohort was matched 1:1 to controls (no UC or CD) by sex, age, and health plan type. All pts had continuous eligibility for ≥6 months before (baseline period) and 1 year after (study period) a randomly chosen diagnosis date (index date). At baseline, demographic and clinical characteristics were compared between groups. During the study period, medical resource utilisation (overnight hospitalisations, emergency room visits, hospital day visits, physician outpatient visits, and prescription drugs) and their associated costs (adjusted to 2010 US $ using the Consumer Price Index) were compared using Wilcoxon rank sum tests. Multivariate analysis compared study period direct costs adjusting for age, sex, and Charlson Comorbidity Index (CCI) scores.

Results: 2,554 pædiatric pts with CD and 2,554 matched controls (mean age, 14 years; 42.5% female) met the inclusion criteria. The CD cohort had higher baseline CCI (0.5 vs. 0.25, P<.0001) vs. controls. Medical resource utilisation was greater in the CD cohort vs. controls (table). The CD pts incurred significantly higher annual medical care, prescription drug, and total annual direct health care costs vs. controls.

<table>
<thead>
<tr>
<th>Health Care Utilisation and Costs of Pædiatric CD</th>
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<tbody>
<tr>
<td>CD Pts</td>
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<tr>
<td>--------</td>
</tr>
<tr>
<td><strong>Average Annual Utilisation Rate</strong></td>
</tr>
<tr>
<td>Emergency visits</td>
</tr>
<tr>
<td>Overnight hospitalisations</td>
</tr>
<tr>
<td>Hospital day visits</td>
</tr>
<tr>
<td>Physician outpatient visits</td>
</tr>
<tr>
<td><strong>Average Number of Days In Hospital</strong></td>
</tr>
<tr>
<td>Length of overnight hospitalisation</td>
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### Average Annual Direct Costs

<table>
<thead>
<tr>
<th>Service</th>
<th>$2013</th>
<th>$2014</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency visits</td>
<td>$318.1</td>
<td>$121.2</td>
<td>&lt;.0001b</td>
</tr>
<tr>
<td>Overnight hospitalisations</td>
<td>$5,117.3</td>
<td>$232.3</td>
<td>&lt;.0001b</td>
</tr>
<tr>
<td>Other services*</td>
<td>$981.7</td>
<td>$115.0</td>
<td>&lt;.0001b</td>
</tr>
<tr>
<td>Hospital day visits</td>
<td>$9,310.2</td>
<td>$531.7</td>
<td>&lt;.0001b</td>
</tr>
<tr>
<td>Physician outpatient visits</td>
<td>$3,122.4</td>
<td>$566.4</td>
<td>&lt;.0001b</td>
</tr>
<tr>
<td>Prescription Drug</td>
<td>$3,790.8</td>
<td>$167.8</td>
<td>&lt;.0001b</td>
</tr>
<tr>
<td><strong>Total Direct</strong></td>
<td><strong>$21,330.9</strong></td>
<td><strong>$1,773.5</strong></td>
<td><strong>&lt;.0001c</strong></td>
</tr>
</tbody>
</table>

*a*Ambulance and durable medical equipment services.

*b*Wilcoxon rank sum test.

*c*Generalised linear regression model.

### Conclusion:

Pædiatric pts with CD had greater use of medical resources and higher medical and pharmacy costs compared with matched controls. More effective treatments for pædiatric CD should be implemented to potentially reduce the overall economic burden in this patient population.

INCREASED TOLL-LIKE RECEPTOR 9 EXPRESSION BY B CELLS FROM INFLAMMATORY BOWEL DISEASE PATIENTS
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Objectives and Study: Objectives: To evaluate TLR9 expression in peripheral B cells, taken from IBD patients before and after anti-inflammatory treatment.

Methods: Twelve patients with IBD (7 - crohn's disease, 5 - ulcerative colitis) and 15 healthy controls were included in the study. Disease severity was assessed using the Pediatric/Adults crohn's disease activity index and the ulcerative colitis activity index as needed. Accordingly, patients were classified as mild, moderate or severe disease. Peripheral B cells isolated from IBD patients, before and after anti-inflammatory treatment, and from the control group, were cultured for 24 hours with and without CpG oligodeoxynucleotides (ODN-CpG) 0.5μM. TLR9 expression by memory B cells (CD19+CD27+) was assessed by flow cytometry.

Results: TLR9 expression by peripheral B cells was significantly higher in IBD patients than that in healthy controls (13.39±10.8 MFI vs. 6.35±2.6 MFI p=0.02). The addition of ODN-CpG to B cells resulted in a significantly increase of TLR9 expression in B cells from healthy controls (7.2±3.3 MFI vs. 9.1 ±4.3 MFI p=0.03). On the contrary, B cells from IBD patients only partly respond to the addition of ODN-CpG after anti-inflammatory treatment (6.0±3.8 vs. 7.2±3.3, p=0.06). TLR9 expression was positively correlated with IBD disease severity (r= 0.694, P =0.0003).

Conclusion: TLR9 expression in memory B from IBD patients is elevated and associated with disease severity.

Disclosure of Interest: None Declared
THE ROLE OF FECAL CALPROTECTIN IN MONITORING MUCOSAL INFLAMMATION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASES

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Objectives and Study: An accurate monitoring of mucosal inflammation is important for an effective management of children with inflammatory bowel disease (IBD). The aim of the study was to evaluate the efficacy of fecal calprotectin (Cal) as indicator of inflammatory activity in children with Crohn’s disease (CD) and ulcerative colitis (UC) by correlating it with biological, clinical and endoscopic indices.

Methods: A total of 22 children presenting IBD were evaluated (16CD/6UC). Fecal Cal, blood tests, Pediatric CD Activity Index (PCDAI), Pediatric UC Activity Index (PUCAI), CD Endoscopic Index of Severity (CDEIS) and Mayo Disease Activity Index (MDAI) were used for evaluation at diagnosis and after one year of treatment.

Results: In CD children, Cal proved a high correlation \((r=0.775)\) with mucosal inflammation, showed by CDEIS and a medium correlation with CRP \((r=0.623)\). It didn’t correlate with PCDAI \((r=0.325)\). In UC children, Cal correlated moderate \((r=0.581)\) with CRP and it was strongly correlated with PUCAI \((r=0.752)\) and MDAI \((r=0.796)\). Cal levels decreased significantly after one year of treatment in all patients \((p=0.038)\).

Conclusion: In CD children fecal Cal was more accurate in detection mucosal inflammation when compared to clinical score and CRP. The poor correlation between Cal and PCDAI may be due to the fact that PCDAI is mostly a clinical score, not sensitive enough to detect subclinical activity of the disease. Fecal Cal correlated well with endoscopic indices both in CD and UC children, being valuable not only for IBD screening, but also for monitoring disease activity and reducing the need for colonoscopy in children.

Disclosure of Interest: None Declared
CONCENTRATION-EFFECT RELATIONSHIP OF INFliximab IN A COHORT OF CHILDREN WITH CHRONIC INFLAMMATORY BOWEL DISEASES

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Objectives and Study: Treatment with infliximab (anti TNF) significantly changed the management of patients with inflammatory bowel disease. Infliximab is increasingly used in children with IBD in maintenance treatment. Although its effectiveness has been demonstrated, there is a significant proportion of patients with a decrease or loss of effectiveness of treatment over time, with a failure rate reported in pediatric up to 50% at 5 years. Dosing infliximab concentrations seems a useful tool in monitoring treatment. The main objective was to study the concentration-effect relationship of infliximab in a cohort of children with IBD and secondarily to determine the influence of associated immunosuppressive therapy.

Methods: A retrospective study was conducted including children with IBD who received maintenance therapy with IFX in our hospital between 2003 and 2011. Scores of disease activity (PCDAI or PUCAI), inflammatory biomarkers (ESR and CRP), infliximab concentrations, infliximab antibodies (ATI) and associated treatments were recorded for each injection. The pharmacological analysis was performed on the first year of maintenance treatment. The relationship between concentration and markers of clinical and biological activity of the disease were studied by linear regression and by nonlinear model Emax.

Results: Twenty-four patients (13 males) aged 13 (± 2.4 years) were included. Twenty two had Crohn's disease. The proportion of patients in complete remission at 3, 6, 12, 24 and 36 months were respectively 33%, 68%, 71%, 67% and 33%. The average residual concentration of infliximab in patients in complete remission (PCDAI or PUCAI ≤ 10 without corticosteroids) was higher than that of patients in partial remission or relapse: 4.6 ± 0.3 mg / l versus 2.3 ± 0.3 mg / l (p < 0.0001). CRP and the score of disease activity were inversely related to the residual serum infliximab (p <0.0001). For 12 patients who received azathioprine and infliximab over 14 weeks, there was no increase of the markers of disease activity or change in concentration of infliximab 24 and 48 weeks after stopping the immunosuppressant.

Conclusion: The serum concentration of residual infliximab is significantly related to markers of clinical and biological disease activity in pediatric patients with IBD. In our model a concentration greater than 2.8 mg/l provides a clinical remission (PCDAI or PUCAI ≤ 10). Immunosuppression associated with infliximab does not alter the clinical, biological and concentration of infliximab in our population. Monitoring of patients undergoing pharmacological maintenance treatment with infliximab may be useful in optimizing treatment but larger prospective studies are needed to establish it.

Disclosure of Interest: None Declared
ANTI-TNF ALPHA THERAPY AND MUCOSAL HEALING: THE KEY TO CHANGE THE STORY OF PEDIATRIC CROHN’S DISEASE?

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Objectives and Study: Efforts have been made to optimize the use of available therapies to improve Crohn’s disease (CD) patients’ outcome, but up to now no therapy changed the natural history of the disease. Mucosal healing (MH) appears as a therapeutic goal able to predict sustained clinical remission. Therapy with anti-TNF α antibodies, Infliximab (IFX) and Adalimumab (ADA), have been proven effective in achieving MH with a more potent and rapid effect compared to immunomodulants (IMM). Few pediatric studies evaluating MH in CD as a therapeutic goal are available. Aim of our study is to assess the efficacy of IFX and ADA in obtaining MH in a pediatric CD cohort. Secondary aim is to evaluate differences in response in children with early (<1 year) or late (>1 year) disease.

Methods: CD patients (pts), between 6 and 18 years of age, starting IFX or ADA from January 2009 were enrolled. All pts were naïve to biological therapies but could have been previously treated with corticosteroids, IMM and aminosalicylates. Pts’ characteristics collected at baseline are: age at diagnosis, indication for therapy, age at enrollment, disease duration and location, and concomitant medications. An endoscopic procedure 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) respectively at time 0(T0) and at the time of endoscopic follow-up(FU). Pts underwent anti-TNF α therapy with appropriate induction and maintenance therapeutic schemes.

Results: Thirty-one pts (21 IFX and 10 ADA) were enrolled, 18 males. At enrollment mean age was 12,7± 2,9 years and mean disease duration was 13 ± 15,3 months. Fifteen pts (6 IFX) were in the early disease group, 16 (15 IFX) in the late disease group. At T0 16 pts (52%) of pts were on IMM, of these 10 were still on IMM at FU. Mean values of PCDAI and SES CD at T0 and FU are in table 1, both values were significantly reduced at FU(p< 0,05). The correlation between the indexes was at T0 r 0,2 and at FU r 0,4. Dividing patients on the basis of disease duration prior to therapy introduction SES CD values decreased significantly at FU both in early and in late disease pts but more significantly in the first group (p<0,0001 vs 0,02).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>T0</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES CD</td>
<td>15,5± 8,6</td>
<td>6,5 ± 7,5</td>
</tr>
<tr>
<td>PCDAI</td>
<td>30±17,6</td>
<td>11,3 ± 11,5</td>
</tr>
</tbody>
</table>

Conclusion: In our cohort biological therapy appears effective in achieving mucosal healing, probably more effectively if introduced early in the course of the disease. Larger studies with longer FU will highlight the effect of MH on disease evolution.
Disclosure of Interest: None Declared
A NEW SYNTHETIC BUTYRATE DERIVATE N-(1-CARBAMOYL-2-PHENYL-ETHYL) BUTYRAMIDE IS EFFECTIVE TO LIMIT INTESTINAL INFLAMMATION IN DEXTRAN SODIUM SULPHATE-INDUCED COLITIS ANIMAL MODEL

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Objectives and Study: The short chain fatty acid butyrate has been proposed as potential therapeutic strategy for inflammatory bowel diseases. The low palatability and stability limit a wide therapeutic use of this substance. We have recently obtained a high palatable and stable synthetic butyrate derivate, N-(1-carbamoyl-2-phenylethyl) butyramide (BuBull). In this study we comparatively evaluated the effects of this new compound and of equimolecular doses of sodium butyrate (BuNa) in dextran sulfate sodium (DSS)-induced colitis animal model.

Methods: Young male ICR mice were used in all experiments. The oral treatment with BuNa (20 mg/kg/d, once daily) or BuBull (42.5 mg/kg/d, once daily), started 10 days before DSS challenge (2.5% for 5 d in drinking water) and continued for all experimental period (7 days). All mice were sacrificed 7 days after DSS challenge. Inflammatory markers in colonic tissue were analyzed.

Results: Both substances were able to significantly limit mucosal inflammation, a similar effect potency was observed even if BuBull showed a stronger effect on reducing COX-2 expression: iNOS 58.4% of inhibition for BuNa; 62.5% for BuBull, p<.05), COX-2 (20.1% of inhibition for BuNa; 50.5% for BuBull, p<.05), and TNFa (30.2% of inhibition for BuNa; 30.8% for BuBull, p<.05).

Conclusion: The new synthetic butyrate derivate, N-(1-carbamoyl-2-phenyl-ethyl)butyramide (BuBull) is effective in inhibiting mucosal inflammation in an animal model of colitis. The effect open new therapeutic perspectives for this compound in the treatment of inflammatory bowel diseases.

Disclosure of Interest: None Declared
GENDER DIFFERENCES IN SWISS PAEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS

D. Herzog, P. Buehr, K. Rebekka, V. Rueger, A. Nydegger, J. Spalinger, S. Schibli, C. Braegger and Swiss IBD Cohort

Objectives and Study: Studies on gender differences in paediatric patients with inflammatory bowel disease (IBD) are scarce and the results heterogeneous. The new Paris classification now facilitates a systematic approach. Paediatric IBD patients registered to the Swiss IBD cohort study database between 2008 and 2012 were evaluated for gender differences at diagnosis, at study inclusion and during follow-up.

Methods: Data of 196 patients, 105 with Crohn’s disease (CD) and 91 with ulcerative or indeterminate colitis (UC/IC), and follow-up data 1 and 2 years after inclusion in 113 and 65 patients were assessed. The median age at diagnosis was 11.0 (1.8-15), at inclusion 14.0 (4.3-15.8) years, and the median disease duration 1.6 (0.5-7.25) years.

Results: At diagnosis of CD boys were younger than girls (median age 11.5 vs 15.5 years, p=0.05). Boys also were more numerous at study entry (67 vs 38 p<0.05). No such gender difference was found in patients with UC/IC. At diagnosis of IBD, 67 (34.2%) patients were ≤10 years of age. No significant difference regarding disease prevalence and age at diagnosis of IBD was found in this patient group (CD: 21 boys (median age 7.7 years), 8 girls (8 years), UC/IC: 16 boys (7.8 years), 22 girls (8.4 years)). Subgroup analysis focusing on age ≤10 years and disease location at diagnosis revealed ileo-colonic disease to be more frequent in boys with CD (19m vs 5f, p< 0.05), and proctitis to be more frequent in girls with UC/IC (8f vs 2m, p<0.05). Girls of any age at diagnosis of UC/IC were taller than boys at follow-up 1 year after study entry (mean z-score for height: 0.12 in girls vs -0.55 in boys p<0.05). At any time after inclusion disease complications occurred more frequently in boys with UC/IC (5/31f vs 10/24m, p=0.06). No other gender difference regarding anthropometric or disease related data was found in CD and UC/IC patients.

Conclusion: The gender difference in age and disease prevalence emerging at the analysis of the whole cohort of CD patients was not present in the subgroup of pre-pubertal patients, and is the result of new diagnoses after the age of 10 years. In contrast, the gender difference in disease location present in both groups of IBD patients at age ≤10 years disappears as soon as pubertal patients are included to the analysis.

Disclosure of Interest: None Declared
FAECAL GAS ANALYSIS OF PAEDIATRIC IBD PATIENTS AND HEALTHY CONTROLS, AS MEASURED BY ELECTRONIC NOSE: A PILOT STUDY

T. G. J. de Meij 1,*, Y. E. Lentferink 1, M. P. C. van der Schee 2, T. Paff 3, C. M. F. Kneepkens 1
1Paediatric gastroenterology, VU University medical centre, 2Respiratory medicine, Academic Medical Centre, 3Paediatric pulmonology, VU University medical centre, Amsterdam, Netherlands

Objectives and Study: The diagnosis of inflammatory bowel disease (IBD) is mainly based on typical macroscopic and histologic findings by endoscopy, an invasive procedure with significant burden on patients. Non invasive diagnostic tools therefore are welcome. Patients with IBD often report that the odour of flatus or faeces is abnormal during a flare. Analysis of faecal volatile organic compounds (VOCs) with gas chromatography and mass spectroscopy (GC-MS) has shown differences in VOC profiles between adult IBD patients and healthy controls. The aim of this pilot study was to compare faecal VOC profiles of children with ulcerative colitis (UC), Crohn’s disease (CD) and of healthy controls (HC), during periods of exacerbation and in remission.

Methods: From 10 UC children (median 12.6; 8.2-15.8 years of age) and 9 CD children (14.2; 9.8-17.4 years) multiple faecal samples were collected during active disease and during remission. In addition, from 10 HC (6.5; 2.2-9.2 years) faecal samples were collected weekly during 4 weeks. Headspace VOCs of all samples were measured with the Cyranose320® electronic nose (Smiths detection, Pasadena, CA, USA). This portable device for measuring VOC profiles is based on changes in electrical resistance of 32 carbon black polymer sensors. Data were analysed by principal component reduction and canonical discriminant analysis, which were used to make an internally cross-validated receiver operator characteristic curve (ROC).

Results: VOC profiles of HC differed significantly from UC children with active disease (p=0.011) (ROC AUC 0.75, sensitivity 75%, specificity 77%) and from CD children with active disease (p<0.001) (ROC AUC 0.98, sensitivity 92%, specificity 100%). HC profiles also differed significantly from UC children in remission (p=0.008) (ROC AUC 0.80, sensitivity 82%, specificity 77%) and CD children in remission (p<0.001) (AUC 1.00, sensitivity 100%, specificity 100%). Headspace prints of the faeces of UC children differed also significantly from CD children during active disease and in remission (p=0.024) (ROC AUC, 0.71, sensitivity 75%, specificity 58%) and (p=0.001) (AUC 0.89, sensitivity 91%, specificity 77%), respectively. Intra individual variability of VOC profiles from HC subjects in time may reflect daily changes in diet. All HC samples, however, differed significantly from UC and CD, regardless of the week the faecal sample was provided.

Conclusion: Analysis of faecal headspace profiles seems to have potential in the recognition of UC and CD during active disease as well as remission. Further research with external validation and with larger sample sizes is warranted.

Disclosure of Interest: None Declared
CLINICAL EFFICACY OF TWO REGIMENS OF MAINTENANCE THERAPY IN PATIENTS WITH CROHN DISEASE AGED 7-17 YEARS - MULTICENTER RANDOMIZED STUDY


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Objectives and Study: Optimal use of biologics in Crohn’s disease (CD) requires balance between benefits and risk, and concern of serious side effects may question the concomitant immunomodulators use in pediatric patients. The study was conducted to compare the efficacy of two infliximab maintenance regimens: (1) infliximab alone and (2) infliximab with immunomodulator in pediatric patients with moderate to severe active CD.

Methods: Patients (n=99; 14.5 mean age, 62% males) with PCDAI>30 were involved to the study and received induction therapy with infliximab 5 mg/kg at weeks 0, 2, and 6. Clinical (PCDAI score) evaluation were performed at week 10 and patients with clinical response (decrease of PCDAI≥15 AND PCDAI<30) and/or remission (PCDAI≤10) were randomized to Group I receiving infliximab 5 mg/kg every 8 weeks with immunomodulator until Week 54 (n=45) or Group II receiving infliximab 5 mg/kg every 8 weeks with immunomodulator stopped at Week 26 (n=39). Clinical assessment (PCDAI score) was performed at week 54 in both groups. Primary endpoint was loss of clinical response defined as increase of PCDAI>15 points or PCDAI>30. Secondary endpoint was: necessity to increase/change maintenance therapy.

Results: 84 out of 99 (85%) pts had response, and 58 (59%) clinical remission after induction therapy at Week 10. 2 out of 45 (4%) pts in Group I and 2 out of 39 pts (5%) in Group II had loss of clinical response at Week 54 (n=45) or Group II receiving infliximab 5 mg/kg every 8 weeks with immunomodulator until Week 54 (n=39). Clinical assessment (PCDAI score) was performed at week 54 in both groups. Primary endpoint was loss of clinical response defined as increase of PCDAI>15 points or PCDAI>30. Secondary endpoint was: necessity to increase/change maintenance therapy.

Conclusion: Both regimens of maintenance therapy (1. Infliximab with immunomodulator and 2. Infliximab alone) are clinically equally efficient in children aged 7-17 years with moderate to severe CD.
Disclosure of Interest: None Declared
**GASTROENTEROLOGY**
**INFLAMMATORY BOWEL DISEASE**

**PO-G-0051**

**THE VALUE OF FOCALLY ENHANCED GASTRITIS IN THE DIAGNOSIS OF PAEDIATRIC INFLAMMATORY BOWEL DISEASES**  
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**Objectives and Study:** Focally enhanced gastritis (FEG) has been suggested as a diagnostic marker for Crohn’s disease (CD). In this study we aimed to evaluate the prevalence of FEG in children with inflammatory bowel diseases (IBD) and to assess the ability of FEG to distinguish IBD from non-IBD patients.  

**Methods:** All children who underwent esophagogastroduodenal endoscopy (EGD) between 2004-2011 were retrospectively included, after excluding individuals with H. pylori infection and celiac disease. Two groups were studied: patients with IBD (IBD group, n=185) and non-IBD patients (non-IBD group, n=684). Relations of FEG to age, gender and disease location according to the Paris classification were assessed. The diagnostic performance of FEG in distinguishing between IBD and non-IBD individuals was evaluated by sensitivity analysis.  

**Results:** FEG was more frequent among children with IBD compared to non-IBD (35.7% vs 3.4%, respectively, p<0.001). All types of IBD had higher frequencies of FEG compared to non-IBD individuals (CD: 54.1%, Ulcerative colitis (UC): 21.6%, IBD unclassified (IBDU): 18.4%, all comparisons with the non-IBD group: p-values<0.001). FEG positivity was more common in females compared to males with CD (63% vs 43.6%, p=0.08) and UC (FEG(+): 30.3% vs 5.6%, respectively, p=0.07) and in children with IBDU younger than 2 years (FEG(+): <2 years = 57.1%, 2-10 years = 8.3%, > 10 years = 16.7%, p=0.027). In the CD group, FEG positivity was not related to the involvement of the lower gastrointestinal tract (FEG(+): L1: 44.4%, L2: 69.3%, L3:54.8%, L0 (normal ileocolonoscopy: 25%), p=0.27), nor to the involvement of the upper gastrointestinal tract (FEG(+): L4a+: 52.4%, L4a−: 54.8%, p=0.99). Children with FEG were 15.4 times more likely to have IBD compared to children without (OR: 15.4, 95% ci: 8.9-26.4), after adjusting for age and gender. FEG achieved a sensitivity of 35.7% and specificity of 96.6% in distinguishing between IBD from non-IBD patients.  

**Conclusion:** FEG has significantly higher prevalence in children with IBD, particularly Crohn’s disease and can be a valuable supporting finding especially in females and children younger than 2 years of age.  

**Disclosure of Interest:** None Declared
C-ANCA/PR-3 POSITIVE COLITIS IN CHILDREN: A DISTINCTIVE FORM OF INFLAMMATORY BOWEL DISEASE OR VASCULITIS WITH COLITIS AS INITIAL PRESENTATION?


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Objectives and Study: Anti-neutrophil cytoplasmic antibodies (ANCA) as detected by indirect immunofluorescence (IIF) have been found in sera from patients affected with ulcerative colitis (CU) and Crohn’s disease (CD). Nevertheless, more specific antibodies against myeloperoxidase (MPO) or proteinase 3 (PR3) have been rarely identified in this context and their clinical significance is still unclear. The aim of this study was to investigate whether the PR3-ANCA positive subset represents a distinct type of inflammatory bowel disease (IBD) in children.

Methods: Sera from 30 consecutive paediatric patients diagnosed with IBD at our centre were retrospectively evaluated for ANCA IIF, PR3-ANCA and MPO-ANCA. Demographical data, clinical history and laboratory results of the PR3-ANCA negative and positive IBD patients were compared. Finally, all PR3-ANCA positive patients were evaluated in more detail to exclude the diagnosis of ANCA associated vasculitis.

Results: Five patients within our consecutive paediatric IBD cohort with positive ANCA on IIF (n=25) showed PR3-ANCA specificity (20%). This PR3-ANCA positive subset had significantly more often concomitant biliary disease and more severe anal blood loss (P<0.05). In contrast, no significant differences between the PR3-ANCA positive and negative subgroup could be found for age at diagnosis, male:female ratio, the presence of fatigue, diarrhoea, weight loss, presence of anal blood loss, extraintestinal disease, familial IBD history and disease activity. None of the PR3-ANCA positive patients had vasculitis features at diagnosis nor during follow-up to date.

Conclusion: This pilot study is the first demonstrating significant differences in clinical features between the PR3-ANCA positive and negative IBD patients, PR3-ANCA positivity being associated with signs of biliary disease. Whether PR3-ANCA measurement in IBD has clinical implications regarding adjusted therapy or regarding prognosis remains to be shown.

Disclosure of Interest: None Declared
THE USE OF METABOLITE MEASUREMENT IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE RECEIVING THIOPURINE TREATMENT

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Objectives and Study: To present our experience of using thioguaninemetabolite measurements in children with inflammatory bowel disease (IBD) and to evaluate their effect on clinical practice.

Methods: A retrospective analysis of 6-thioguanine nucleotide (6-TGN) and 6-methylmercaptopurine (6-MMP) level measurement in children treated with thiopurines for at least 3 months. Data were collected on drug dose, laboratory indices, disease activity (by Harvey-Bradshaw score), additional medications, and management changes following metabolite measurement. Therapeutic 6-TGN levels were defined as 235–400 pmol/8・10^8 RBCs

Results: Fifty six individuals (36 males), age 15.7± 4.3years, with Crohn's disease (CD, n=44) and ulcerative colitis (UC, n=12), treated with azathioprine (47) or 6-mercaptopurine (12) were included. A total of 137 separate measurements were made. On initial measurement, drug dosage was below standard in 46% of patients, and in 34% 6-TGN was below therapeutic levels. Out of the total measurements 44% were below therapeutic. Standard drug dosing correlated with therapeutic drug levels (p=0.04). No toxicity occurred. There was no correlation between 6-TGN level and WBC, leukocyte count, mean corpuscular volume (MCV), or disease activity. Concomitant 5-ASA but not Infliximab was related to therapeutic 6-TGN levels (p=0.04). Variations in metabolite level measurements on the same drug dose were analyzed in 6 patients with ≥ 3 measurements- those ranged from -2% to +225%. After initial measurement, management was changed in 28/56 cases (50%).

Conclusion: Standard thiopurine drug dosing correlates with therapeutic 6-TGN levels. Thiopurine metabolites is useful for dosage adjustment in children, and its measurement has a significant implication on clinical decisions.

Disclosure of Interest: None Declared
INTESTINAL BILE ACID TRANSPORT IN PEDIATRIC INFLAMMATORY BOWEL DISEASE
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Objectives and Study: Bile acids (BA) are resorbed by BA-transporters in the terminal ileum and colon, which are areas of inflammation in inflammatory bowel disease (IBD; Crohn’s disease [CD] and ulcerative colitis [UC]. BA associated diarrhea can be caused by disturbed BA absorption.

Methods: We investigated mRNA expression levels of different BA transporters, detoxifying systems and corresponding nuclear receptors (NR) in intestinal biopsy specimens from children suffering from newly diagnosed IBD (n=24) and healthy controls (n=15).

Results: CD ileitis led to downregulation of the ileal BA transporter ASBT (apical sodium dependent BA transporter; 40%, p<0.01) and of the NR FXR (Farnesoid X receptor; 51%; p<0.01). In UC an upregulation of ASBT (150%, p<0.01) was observed in the non-inflamed terminal ileum and a downregulation of MRP3 in pancolitis (multidrug-resistant protein 3; 51%, p<0.01). A downregulation of the expression of the detoxifying enzyme CYP3A4 was observed in UC colitis (20%) as well as in CD colitis (33%). As positiv control served iNOS (inducible nitric oxide synthase) with 450% increase of expression in CD and 470% in UC (both vs. control group).

Conclusion: In summary we show in our pilot study significant changes of the BA transporter expression levels in intestinal biopsy specimens from children suffering from newly diagnosed IBD. This study could be the basis for subsequent investigations to involve targeted medical correction of alterations in BA transport and metabolism in early IBD with recently available nuclear BA receptor agonists (e.g., FXR agonist GW4086). This could be a new therapeutic approach to BA-associated diarrhea in IBD in Pediatric and Adult Medicine.

Disclosure of Interest: None Declared
Objectives and Study: Crohn's disease (CD) is a relapsing remitting disease with no known cure. It presents in childhood in up to 25% of cases. Right hemicolectomy (RH) is recommended for localised disease refractory to medical therapy, and when performed in childhood can promote growth. The outcomes from separate studies of paediatric-onset CD (P-CD) and adult-onset (A-CD) after RH suggest A-CD has a lower relapse rate. Our IBD database contains longitudinal data of both children and adults, and our aim was to do a direct comparison.

Methods: All CD patients who had RH were identified on the IBD database of a single tertiary referral centre for children and adults. This was cross-referenced with theatre data for the last 10 years. Case notes were reviewed for date of diagnosis, time to RH, time to relapse, or duration of follow up if no relapse had occurred. Relapse was defined as recurrent disease identified at endoscopy or by radiological imaging, and/or clinical relapse defined by an escalation in immunosuppression or further Crohns-related surgery.

Results: Sixty-seven P-CD patients underwent RH from 1982-2011, with a median time from diagnosis to RH of 3 years (mean 3.5, range 0-13). There were 116 A-CD patients with RH from 1969-2011, with a median time from diagnosis of 1 year (mean 4.7, range 0-26). Forty-one (61%) of P-CD patients relapsed, with median time to relapse or (relapse-free) follow-up of 4 years. This compared to 81 (71%) A-CD patients, after median 6 years. The Kaplan-Meier curve shows that P-CD patients relapsed earlier than A-CD (p<0.001).

Conclusion: This is a large retrospective longitudinal study of relapse after RH in CD. Relapse rates were comparable to previous studies, and in this direct comparison P-CD relapse earlier than A-CD. This may reflect a more severe phenotype of paediatric-onset Crohn's Disease.
Disclosure of Interest: None Declared
INTERVENTIONS FOR THE TREATMENT OF IRON DEFICIENCY ANAEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Iron deficiency anaemia (IDA) is common in patients with inflammatory bowel disease (IBD). There are many different medications to treat IDA in IBD, however the optimal preparation and route of administration is not clear. We set out to systematically evaluate the efficacy and safety of interventions for treating IDA in patients with IBD.

Methods: Randomised controlled trials comparing iron therapy to placebo or other interventions in patients with IBD and IDA were included. Data sources were MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane inflammatory bowel disease and functional bowel disorders Specialised Register and reference lists of retrieved articles. Data extraction and assessment of methodological quality were performed independently by two reviewers. Data was analysed according to the intention to treat principle.

Results: 7 studies involving 907 participants met the inclusion criteria. 3 compared Intravenous (IV) iron sucrose with oral iron, 2 compared subcutaneous (S/C) erythropoietin (EPO) with placebo, one paper compared IV ferric carboxymaltose with oral iron and one compared IV ferric carboxymaltose with IV iron sucrose. Risk of bias amongst included studies was variable, with some concerns regarding blinding and selective reporting.

In 3 studies, patients receiving either IV or oral Iron preparations had statistically significant rises in haemoglobin (hb) and Ferritin levels, although meta-analysis showed hb increases were marginally higher in patients receiving IV iron (Weighted mean difference 0.28, 95% confidence intervals (CI) 0.05- 0.50). Adverse events requiring withdrawal of therapy were statistically significantly lower in patients receiving IV iron (Odds Ratio 0.11, 95% CI 0.03- 0.43).

There was individual trial data to suggest erythropoietin may be more effective than placebo at increasing Hb levels and no change in disease activity was reported. Due to heterogeneity of data, no meta-analysis was possible. EPO was generally safe and well tolerated.

Conclusion: Both IV and oral Iron preparations appear effective at improving hb and Ferritin levels, although the increase is marginally higher with IV Iron. The available evidence suggests that IV iron is better tolerated than oral iron, but the data set is small and of variable quality. There is some evidence that EPO is effective and safe, but again samples were small and studies were heterogeneous, limiting the strength of these findings. Conclusions about other forms of treatment or comparisons cannot be made due to limited available data. Further research appears warranted.

Disclosure of Interest: M. Gordon Conflict with: travel grants from warner chilcott, ferring pharamceutical, norgine and casen fleet in the past, S. Tudor Jones: None Declared, A. Akobeng: None Declared
TREATMENT INDUCED CHANGES IN PLASMA CYTOKINE AND CHEMOKINE LEVELS IN PEDIATRIC IBD

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Objectives and Study: Objectives: Various cytokines and chemokines increase during the active phase of pediatric inflammatory bowel disease (PIBD). However, their response to different treatment modalities is not yet fully elucidated and may vary. Thus characterization of this response may be beneficial for monitoring of treatment efficacy in addition to the existing parameters. The objective of this study was to characterize the changes in the plasma levels of various cytokines and chemokines following treatment of active PIBD.

Methods: Methods: Twenty-three PIBD patients, 14 with Crohn’s disease (CD) and 9 with ulcerative colitis (UC) were investigated at defined time points after initiation of either 8 weeks of exclusive enteral nutrition therapy (13 CD) or systemic corticosteroids (1CD, 9 UC). For each patient, at the initial visit (V1, active disease), appropriate clinical and non-clinical parameters were assessed. The patients were followed up after 4 weeks (V2) and 12 weeks (V3) of treatment initiation. Plasma was collected at each of the above mentioned visits and analyzed for levels of IFNγ, IL-10, IL-12p70, IL-2, IL-4, IL-5, IL-8, TNFα, Eotaxin, Eotaxin-3, IP-10, MCP-1, MCP-4, MDC, MIP-1β and TARC. The analyses were performed using commercially available kits (Mesoscale Discovery, Rockville, USA) according to the manufacturer's instructions. Kruskal-Wallis one way analysis of variance test was performed to assess statistical differences.

Results: Results: Two CD patients dropped out after V2. Plasma samples were not available at V2 in 1 CD and for one time point each in 3 UC patients. Therapy reduced disease activity index measures in both disease groups. Considering the data set as a whole, treatment induced reductions in plasma levels of TNF-α (median values for V1, V2 and V3 were 1.67, 1.03 and 1.29 pg/ml, respectively; p =0.0027), macrophage-derived chemokine/CCL22 (MDC) (median values for V1, V2 and V3 were 408.5, 183.1 and 209.8 pg/ml, respectively; p=0.0000293) and thymus and activation regulated chemokine (TARC) (median values for V1, V2 and V3 were 204.2, 185.1 and 160.2 pg/ml, respectively; p=0.0788).

Conclusion: Conclusion: Despite known increases in the plasma levels of various cytokines and chemokines during the active phase of PIBD, therapy induced changes in only few of them, including, TNFα and MDC. Thus, monitoring the efficacy of treatment with selected cytokines and chemokines might provide additional insight into disease progression and long-term outcome.

Disclosure of Interest: V. Brahmbhatt Employee of: Employee at Nestec Ltd, M. Oliveira Employee of: Employee at Nestec Ltd, N. Bosco Employee of: Employee at NEstec Ltd, I. Montoliu Employee of: Employee at Nestec Ltd, F.-P. Martin Employee of: Employee at Nestec Ltd, S. Schatz: None Declared, K. Wekstetter: None Declared, E. Schiffrin Employee of: Employee at Nestec Ltd, J. Benyacoub Employee of: Employee at Nestec Ltd, S. Koletzko Grant / Research Support from: The study was supported by a grant from Nestle Nutrition
PROSPECTIVE MONITORING OF TUBERCULOSIS RISK IN IBD PATIENTS ON INFliximab TREATMENT USING QUANTIFERON TB GOLD TEST

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Objectives and Study: Patients on biological therapy have higher risk of tuberculosis (TBC) infection. Screening of TBC is obligatory before the treatment is started. However, data on regular monitoring during therapy are scarce in children.

Methods: Between the years 2008 - 2012, we evaluated prospectively the risk of TBC using Quantiferon TB gold test (QFT) in 71 children and adolescents (36 boys, 35 girls) receiving infliximab (IFX) treatment. Mean age at the beginning of the follow-up was 15 years (range 6-19 years). All patients (57 CD, 10 UC, 4 IBDU) were tested prospectively in 1-year intervals. Mean follow-up was 3 years (1-5 years). All patients had negative TBC screening at the beginning of the biological therapy (RTG, mantoux II, QFT, personal history) and all were previously BCG vaccinated in infancy.

Results: Among 71 patients followed-up since 2008, we identified 5 patients (2 boys and 3 girls, all CD) with conversion of negative QFT test to positive during the treatment (7 %). All of these patients had discontinued biologicals, they received nidrazide (INH) and were followed-up by pneumologist for approximately 3 months with no signs of TBC on RTG and history/physical examination. One patient experienced relapse during discontinuation of the treatment. In all the patients, IFX was re-started after the discontinuation period. All of them had subsequently negative QFT test during the whole follow-up.

Conclusion: Conversion of QFT test during biological treatment in children is not rare, however it does not usually point to TBC infection. Probably, this phenomenon is related to other yet unidentified factors influencing the specificity of the QFT test. Prospective monitoring by QFT test is questionable in patients on biologicals in low-risk countries, however, the situation may be different in areas with higher risk of TBC (non-vaccinated population, immigrants etc.). Supported by VZ FNIM 64203/6001-02.

Disclosure of Interest: None Declared
Objectives and Study: Multidrug resistance protein 1 (MDR1) encodes p-glycoprotein (P-gp) which is as an efflux pump for xenobiotics. Polymorphisms of MDR1 influence tissue expression of P-gp. Aim of this study was to compare the frequencies of C3435T, C1236T, and G2677T/A polymorphisms in children with inflammatory bowel disease (IBD) and healthy controls. Also, the effect of different polymorphisms on corticosteroid response was investigated.

Methods: Children with IBD who were followed at least 6 months in pediatric gastroenterology clinics and healthy children were included in the study. Polymorphisms of C3435T, C1236T, and G2677T/A were studied by polymerase chain reaction and endonuclease restriction methods. Genotype and allele frequencies were compared between study groups.

Results: A total of 175 children were included in the study; 79 of them were in IBD group (35 UC, 43 CD, 1 indetermined colitis). Distribution of genotype was in accordance with Hardy-Weinberg equation in the control group. There were no differences between genotype and allele frequencies of patients and controls (table 1) and between UC and CD patients. In corticosteroid responsive patients 3435TT genotype was more common with respect to corticosteroid dependant/unresponsive ones (43.8% vs. 19.3% respectively, p=0.03). There was no relationship of other polymorphisms with treatment response.
Conclusion: MDR1 3435 TT polymorphism possibly by decreasing the tissue expression of P-gp might positively influence the corticosteroid response in children with IBD. Determination of pre-treatment C3435T polymorphism might help to tailor IBD treatment.

Disclosure of Interest: None Declared
SERUM ADVANCED GLYCATION END PRODUCTS CONCENTRATION IS INCREASED IN CHILDREN WITH ULCERATIVE COLITIS BUT IS NOT RELIABLE BIOMARKER OF DISEASE ACTIVITY

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Objectives and Study: Recent studies suggest that advanced glycation end products (AGEs) level in the serum can be a marker for systemic inflammation and oxidative stress and can reflect AGEs increased tissue formation.

Aim: The objective of this study was to evaluate whether AGEs level is increased in the serum and colon tissues from children with ulcerative colitis (UC) and if it can serve as a reliable circulating marker of UC activity.

Methods: The study included 68 patients diagnosed with ulcerative colitis in acute stage (n= 37) and in remission (n=31). The median age was 14.6, 51% were girls. Patients treated with glucocorticosteroids were excluded. Control group consisted of 48 children, median age 13, 52% girls. A blood samples were obtained from each patient and hematological parameters and several serum biomarkers were determined: C-reactive protein (CRP), albumin, ferritin, IL-6, NGAL (Plasma Neutrophil Gelatinase Associated Lipocalin). Serum AGES levels were measured using commercially available ELISA kit (Cell Biolabs, Inc, USA). The accuracy of each biomarker with respect to UC activity was assessed by the area under the ROC curve (AUC). AGES in the parafined colon biopsies from 16 UC children and 10 controls were identified on the basis of autofluorescence using a fluorescence microscope with confocal imaging system - Nikon ECLIPSE Ti/C1 Plus (Ex/Em filters: 488/515nm and 543/605nm).

Results: We found that AGES autofluorescence was more intensive in all colon specimens from UC patients (active disease and remission) as compared to healthy controls. This was accompanied by increased levels of AGES in the serum of UC patients, and this increase was statistically significant as compared with healthy controls (p = 0.001 for active and p = 0.001 for remission vs controls). There were no however significant differences between AGES serum levels in patients with active UC as compared with inactive disease (p=0.995). AGES levels did not correlate with age of the patients, other examined inflammatory markers and did not allowed useful prediction of UC activity.

Conclusion: AGES levels is increased in the serum of children with ulcerative colitis but it is not useful biomarker for differentiate between active and non-active UC in children. The results also indicate that circulating AGES may originate from inflamed colon tissues.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PO-G-0061

INFLAMMATORY BOWEL DISEASE IN DEVELOPING COUNTRIES --IS IT ON THE RISE?
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Objectives and Study: Inflammatory bowel disease (IBD) ulcerative colitis and Crohn’s disease are chronic inflammatory disorders of the intestines. It has been considered primarily a disease of the developed world. Data from developing countries is scarce due to under reporting and lack of routine pediatric endoscopies. The objective of this study was to look at the clinical characteristics of the patients diagnosed to have IBD and compare them with the developed world as well as analyse the various modes of presentation, severity and where possible outcome and response to treatment.

Methods: All patients proven to have IBD on endoscopy and barium meal and other tests were included in the study. Data was collected regarding age, sex, height and weight, duration of disease, symptoms as well as lab investigations and endoscopic findings. Response to treatment and outcome was recorded on follow up. This was a prospective observational study done over a 10 year period from Jan 2002 – Jan 2012.

Results: The study population comprised of 340 children, 187 (53%) were males while 160 (47%) were females. 275 (81%) had ulcerative colitis while 65 (19%) were having Crohn’s disease. Mean age of presentation among CD patients was 12 years, while for UC it was 9.5 years. The most common symptoms identified were bleeding per rectum in 261 (77%), abdominal pain in 244 (72%) followed by failure to thrive seen in 224 (66%). Other symptoms were diarrhea in 166 (49%), pallor in 51 (15%), swelling of lower limbs 6 (1.7%). Severe Perianal disease was seen in 6 (1.7%). Extra intestinal manifestation were present in 31 (10%) including joint involvement in 8, sclerosing cholangitis in 13 and 3 patients with erythema nodosum. On colonoscopy, 198 (72%) patients had pancolitis. Among CD patients, 22 (30%) had isolated Crohn’s colitis. On Barium only 2 patients of CD had small bowel stricture.

Conclusion: To our knowledge this is the first study of Pediatric IBD from Pakistan. Commonest mode of presentation with UC was bleeding PR while with CD it is abdominal pain. There was higher prevalence of pancolitis in UC and younger patients showed severe disease which is similar to data from the west. Growth failure was a presenting complaint in 2/3 of patients. This is higher than other reports presumably due to delayed referral and repeated GI infections. Most patients with bleeding PR had multiple courses of antibiotics prescribed before referral. Restricting and fistulating disease was uncommon in CD. Family history of IBD was not found in majority unlike the west. IBD is not uncommon in developing countries but are frequently referred late and treated as infections. The presentation and clinical characteristics of Pediatric IBD were similar to the west except there was a higher prevalence of failure to thrive and anemia and absence of family history of IBD.

Disclosure of Interest: None Declared
DELETERIOUS METABOLIC EFFECTS OF INDOMETHACIN IN THE MID-GESTATION HUMAN INTESTINE

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Objectives and Study: Indomethacin (INDO) is a non-steroidal anti-inflammatory drug used for the treatment of patent ductus arteriosus in preterm infants. The use of INDO in preterm infants is associated with an increased risk of developing necrotizing enterocolitis. The goal of our study was to generate an exhaustive biological pathway analysis of the impact of INDO on the global gene expression profiles of the developing human small and large intestine at mid-gestation using serum-free organ culture.

Methods: We used Illumina microarrays to identify gene expression profiles in both small and large intestinal explants (ileum (n=4), and colon (n=4)) cultured for 48 hours in the presence of 1μM INDO.

Results: Differentially expressed genes were analyzed with Ingenuity Pathway Analysis software and revealed that INDO modulated important biological functions such as “cellular growth and proliferation”, “cell death”, “gastrointestinal diseases”, “inflammatory diseases”, “immune cell trafficking”, and “acute phase response signaling”. More importantly, we also found that critical metabolic pathways, namely “oxidative phosphorylation”, “glycolysis/gluconeogenesis” and “free radical scavenging activity”, were highly repressed by INDO in both intestinal segments.

Conclusion: Our study identified that INDO exerts multiple detrimental metabolic effects on the immature human intestinal mucosa and emphasizes the need for a better understanding of the molecular mechanisms of NSAIDs in premature infants.

Disclosure of Interest: None Declared
LONG-TERM FOLLOW-UP OF CHILDREN EXPOSED INTRAUTERINE TO MATERNAL THIOPURINE THERAPY DURING PREGNANCY IN FEMALES WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Inflammatory bowel disease (IBD) affects significant amounts of female patients in their reproductive years. Therefore, many physicians face the dilemma whether thiopurines can be taken safely during pregnancy in maintaining clinical remission. Data on long-term development outcome of children exposed to maternal thiopurine therapy are very limited. Aim of this study was to assess the long-term effects of intrauterine exposure to thiopurines during pregnancy and lactation on infant health status.

Methods: A prospective multi-centre follow-up study was performed in children exposed intrauterine to maternal thiopurine therapy. Physical, cognitive and social aspects of infant health status was assessed with the 43-item TNO-AZL Preschool Children Quality of Life Questionnaire (TAPQOL). Furthermore, information on visits to general practitioner and medical specialists, and physicians advice regarding lactation was evaluated. Data was compared with normative data from a control group consisting of 340 children.

Results: 30 children were included in this study (median 3.8 years (IQR 2.9-4.7). No significant differences were found between children exposed to intrauterine thiopurines and the reference group on global medical and psychosocial health status. Exposure to intrauterine thiopurines was not associated with increased susceptibility to infection or immunodeficiency in childhood. 21/30 children were exclusively formula-fed following negative advice of medical specialists directed at thiopurine use during lactation.

Conclusion: Thiopurine use during pregnancy and lactation did not affect long-term development or immune function of children up to six years of age. Our results underscore the present notion that mothers using thiopurines should be encouraged to breastfeed their infants.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: The human body contains $10^{14}$ bacteria, the majority of which reside in the gut. Aberrant immune responses to these commensal organisms play a role in the pathogenesis of Inflammatory Bowel Disease (IBD). As antibiotics given in infancy predispose to IBD in later life, the normal microbiota may offer protection against inflammation. However, little is known about possible underlying mechanisms. We hypothesized that bacterial products may cross-tolerize intestinal epithelial cells to stimulation by pro-inflammatory cytokines. The aim of this study was to investigate whether pre-stimulation by TLR2 agonists tolerized the epithelial cell’s expression of IL-8 to IL-1β, an important pro-inflammatory cytokine in IBD. We examined if the TLR2 agonist, Pam3CysK, a synthetic analogue of bacterial lipoprotein, affected the IL-1β response.

METHODS: IL-8 production of intestinal epithelial Caco-2 cells was measured by ELISA after stimulation with the pro-inflammatory cytokine IL-1β and/or the synthetic bacterial lipoprotein Pam3CysK. The IL-8 secretion of a single stimulus of IL-1β was compared to its effect when IL-1β or Pam3CysK had been given 24 hours, previously and cleared from the conditioned medium.

RESULTS: Caco-2 cells stimulated with IL-1B produce a large IL-8 response. Pre-stimulation with IL-1β inhibited IL-8 (Figure). When the Caco-2 cells were stimulated first with Pam3CysK, followed by IL-1β 24 hours later, Pam3CysK also significantly decreased the IL-8 produced (although to a lesser extent than IL-1β pre-stimulation). Thus, Pam3CysK can cross-tolerize the cells to IL-1β as shown by the reduction in IL-8 produced after Pam3CysK followed by IL-1β stimulation. A single stimulation of Caco-2 cells with Pam3CysK induced less IL-8 than a single stimulation with IL-1β. Again, a repeated stimulus caused the cells to be tolerized to the stimulant, as shown by the decreased amount of IL-8 produced.
**Conclusion:** The inflammatory immune response of the intestinal epithelium can be tolerized by repeated stimulations of a pro-inflammatory cytokine, or a bacterial product. Bacterial cell wall components cross-tolerize the epithelium to a much stronger pro-inflammatory stimulus.

**Disclosure of Interest:** None Declared
A MULTI-FIBRE MIX INHIBITS THE INFLAMMATION PROCESS IN DEXTRAN SODIUM SULFATE-INDUCED COLITIS AND LEADS TO A RELATIVE INCREASE OF REGULATORY T-CELLS IN MESENTERIC LYMPH NODES

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Objectives and Study: Inflammatory bowel disease (IBD) is a multi-causal idiopathic disease; as many as a quarter of IBD patients experience the first symptoms during childhood. Weight loss, growth failure and frequent nutrient deficiencies are most commonly associated with paediatric IBD. Nutritional therapy has shown to be an important and effective way in the management of IBD, especially in growing children.

Methods: The present study aimed to analyse the effects of a multi-fibre mix, comprising beta-galacto-oligosaccharide, fructan, non-digestible alpha-glucan, and hemicellulose, on dextran sodium sulfate (DSS)-induced colitis. The DSS-induced colitis mouse model is widely used to study both the acute and chronic IBD-related mechanisms and interventions. Recent studies indicate that an imbalance between T helper cell (Th) subsets contributes to the DSS-induced inflammation process.

Results: Dietary supplementation of the multi-fibre mix (1.5% of the total diet) during 2 weeks prior to the DSS-challenge largely prevented the DSS-induced weight loss and changes in stool consistency. After 7 days of DSS treatment, animals were sacrificed. Serological and histological evaluations showed deterioration of gut integrity, elevated serum amyloid A and raised mesenteric lymph node (MLN) cell number by DSS. Multi-fibre mix supplementation significantly reduced these DSS-induced effects. Further analyses of the MLNs by flow cytometry demonstrated a 2.6-, 3.5- and 3.2-fold increase of the number of T-helper type 1 (Th1) cells, Th2 cells and regulatory T-cells, respectively, by DSS in comparison to the control animals. The number of Th17 cells increased 6.8-fold by DSS, pointing to a strong Th17-driven disease process in the MLN. The multi-fibre mix significantly counteracted the DSS-induced increase of these Th17 cells in the MLN, whereas the regulatory T-cell numbers remained more abundant. This resulted in a relative increase in regulatory T-cell count compared to the other T-cell subsets.

Conclusion: In conclusion, DSS-induced colitis leads to strong Th17-driven responses in the MLNs. Dietary supplementation of a multi-fibre mix effectively reduces systemic and local inflammatory disease symptoms, which might be, at least partially, mediated by a relative increase of the regulatory T-cell number in MLNs. This may lead to new ways to optimise nutritional therapy strategies in IBD management.

CHANGED TIGHT JUNCTION PROTEIN EXPRESSION AND FUNCTION IN DSS-INDUED IBD IN RATS

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Objectives and Study: To study the intestinal mucosa permeability and tight junction complex expression in developed inflammatory bowel disease (IBD) experimental rat model by administration of 3% dextran sulfate sodium (DSS).

Methods: Method: Sprague-Dawley (SD) rats were randomly divided into IBD groups and the control group. IBD rat was induced by six days administration of 3% DSS, followed by 14 days tap water only. The control group were fed with water only. On day 7, day 14, day 21, segment of colon of each animal were adequately prepared for light microscope observations. Myeloperoxidase (MPO) activity was measured; Transepithelial electric resistance (TEER) and potential difference (Pd) and short circuit current (Isc) of colon strips were detected by ussing chamber. Expression of the intestinal epithelial tight junction protein (claudin2, claudin3, occludin and ZO-1 were analyzed by RT-PCR, western blot and immunofluorescence technique.

Results: Compared to controlsIBD rats were dysentery diarrhea, weight loss prominent colitis characterized by dilations of gland crypt, ulcer, and inflammatory cell infiltration histologically. Colonic MPO level in IBD group were significant higher than the control group. The result of Ussing chamber test showed that there were significant decreases in TEER and Pd(\(P<0.01\)), however obviously increased Isc (\(P<0.01\)) on day21. The result of RT-PCR, western blot and immunofluorescence showed no claudin2 expression in control group, while in IBD group claudin2, claudin3, occludin and ZO-1 fluorescence were disconous and frature, and the abundance of claudin3, occludin and ZO-1 expression were significantly decreased compared with the control group.

Conclusion: The intestinal epithelial barrier function compromised and an obviously alteration tight junction complex protein expression in rat intestine in experimental IBD model. The tight junction protein may play an very important role in barrier dysfunction because its transcription and translation were significantly changed.


Disclosure of Interest: None Declared
ATG16L1 AND IRGM1 POLYMORPHISMS IN PEDIATRIC CROHN DISEASE: CORRELATION WITH PHENOTYPE.
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Objectives and Study: Genome wide association studies (GWAS) find a significative correlation between several single nucleotide polymorphisms (SNPs) involved in autophagy and the occurrence of Crohn disease (CD) risk. However, few incomplete and discordant evidences about the correlation of these SNPs and a specific phenotype of CD have been described in children. Our purpose is to investigate the relationship between the autophagy gene variants of ATG16L1 and IRGM1 and clinical features in our cohort of children affected by CD with an extensive phenotype analysis.

Methods: Eighty consecutive children with CD (mean age: 179.7 months, range: 17-300) were enrolled in our study. Genotyping for ATG16L1 (rs2241880) and IRGM1 (rs13361189; rs4958847) was performed in all patients. Phenotypic informations including disease localization and behaviour stratified according to the Paris classification were collected. To complete the assessment of the phenotype, data regarding medical therapy, relapses, surgery recurrences and laboratoristic inflammation parameters were analysed.

Results: CD patients with the homozygous variant for the ATG16L1 (var) allele showed a significant tendency to change the clinical behaviour switching to a stenosing or fistolizing phenotype during the course of disease compared with children carrying the homozygous protective allele of ATG16L1 (wt) and heterozygous patients (het) (p=0.05). In addition, the presence of ATG16L1 var resulted to be associated with a major recurrence of clinical relapses and an earlier introduction of immunosuppressants (p=0.006 and p=0.04 respectively). However, ATG16L1 var seems not to be related to a positive family history and extraintestinal manifestations (p=0.4 and p=0.5) and resulted to be protective for perianal disease, which was more frequent in het and wt patients (p=0.06). Patients carrying ATG16L1 var were more frequently males (p=0.07) and presented a significant higher value of fecal calprotectin at diagnosis (p=0.007). IRGM1 rs4958847 homozygous variant was correlated with a trend toward statistical significance regards to a positive family history (p=0.078) and the presence of extraintestinal manifestations (p=0.08). Differently, IRGM1 rs13361189 seems not to be related to a specific CD phenotype.

Conclusion: CD patients carrying ATG16L1 var seem to be characterized by a more aggressive disease course, including changes in clinical behaviour, a higher number of relapses and an earlier use of immunosuppressants. IRGM1 rs4958847 variant gene is correlated with a positive family history and with extraintestinal manifestations. The presence of ATG16L1 and IRGM1 variant genes could be potentially used as predictor of a worse disease phenotype.

Disclosure of Interest: None Declared
Objectives and Study: Control of T cell reactivity within the intestinal mucosa is poorly understood. Type I IFN has been implicated in affecting regulatory T cells and colitis in mice. T cell plasticity is not fully delineated by traditional cytokine measurement. Analysis of phosphorylated signalling proteins, including Signal Transduction and Activator of Transcriptions (STATs), offers a more dynamic picture. Therefore we used Phosflow analysis of pSTATs to define intestinal T-cell responsiveness in IBD at the single cell level.

Methods: Endoscopic biopsies were obtained from IBD patients and controls. Lamina propria mononuclear cells (LPMCs) were isolated and stimulated or not for 15 minutes with Type I Interferon (IFNα/β). The cells were labelled with phospho-specific antibodies (pSTAT1, 3, 5,) and for transcription factors (T-Bet, RORγt, FoxP3), and analysed by flow cytometry. Alternatively, LPMCs were isolated in the presence or absence of IFN neutralising antibody and stimulated with anti-CD3/CD28 and intracellular cytokines were measured.

Results: Constitutive pSTAT1 was increased in CD4+ve T-cells from non-inflamed mucosa of IBD patients compared with controls (n=30 IBD, 16 control, p=0.03). In paired IBD samples, constitutive pSTAT1 was higher in non-inflamed than inflamed areas (n=18, p=0.02). IFNα treatment increased pSTAT1 expression but IBD-related differences were maintained. pSTAT1 was not associated with expression of the Th1 transcription factor T-Bet. There were no differences in expression of pSTAT3, pSTAT5 or unphosphorylated STAT1 irrespective of IFNα stimulation. Blockade of Type I IFN in LPMCs reduced pSTAT1 levels and reduced IL10 production from healthy lamina propria T cells (n=3).

Conclusion: Increased expression of pSTAT1 in CD4 from non-inflamed areas of IBD mucosa is not simply a measure of Th1 cell phenotype, and may indicate a role for Type 1 Interferon in restraining inflammation. Altered responsiveness to Type I IFNs may contribute to the loss of immune homeostasis.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PO-G-0069

GLYCOPROTEIN 2 ANTIBODIES IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: SIGNIFICANCE AND CORRELATIONS WITH THE PHENOTYPE

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Objectives and Study: The zymogen granule membrane glycoprotein (GP2) has been recently recognized as the major antigenic target of Crohn’s disease (CD) specific anti-pancreatic antibodies (PAB). Reactivity to anti-GP2 has been showed in 29% and 10% of adults patients with CD or ulcerative colitis (UC) respectively. Recent investigations revealed an association with distinct disease phenotypes in adults: anti GP2 are more prevalent in patients with a younger onset of CD, ileo-colonic location, stricturing tendency and perianal disease. The prevalence, the significance and association with clinical parameters has never been investigated in pediatric inflammatory bowel disease. This study aims to assess the prevalence of anti-GP2 and anti-Saccharomyces (ASCA) antibodies and their association with clinical parameters in a group of pediatric IBD patients.

Methods: Anti-GP2 IgG and IgA and ASCA IgG and IgA were determined by enzyme-linked immunosorbent assays (ELISA-GA Diagnostics-Germany) in sera of 28 pediatric IBD patients (10 CD, 17 UC and 1 indeterminate colitis IC patients), prospectively recruited from December 2010 to December 2011 at the Department of Pediatrics, Università Politecnica delle Marche. Data were compared with a control group of 25 healthy patients. Anti-GP2 antibodies were assessed in sera using an ELISA technique based on recombinant human GP2 as solid-phase antigen coating. According to previous studies a value > 20 U/ml for both tests was considered positive.

Results: We found an overall IgG and/or IgA anti-GP2 positive result in 40% CD and in 0% UC patients, respectively. Among the CD cases with autoantibodies to GP2, 2 had IgG and 2 had both IgG and IgA reactivity. As far as ASCA we found positivity in 50% of CD and co-occurrence of IgG and/or IgA anti GP-2 in 33% of CD cases. Patients suffering from CD and anti GP2 positivity had most likely an ileo-colonic localization and a stricturing phenotype. Among the control group no IgG and/or IgA anti-GP2 antibody reactivity by ELISA was found. Diagnostic sensitivity for CD of anti GP-2 was 40% and specificity was 100%, while considering either ASCA and/or anti GP2 reactivity, sensitivity for CD raised to 70%.

Conclusion: Anti-GP2 antibodies are highly specific for CD also in pediatric patients and their testing could be of clinical value as their presence significantly relates to ileo-colonic involvement and stricturing disease. The test could be important also in cases of IC and at the onset of CD, to predict evolution toward a particular phenotype.

Disclosure of Interest: None Declared
DIAGNOSING AND TREATING PEDIATRIC CROHN’S DISEASE PATIENTS: IS THERE A DIFFERENCE BETWEEN ADULT AND PEDIATRIC GASTROENTEROLOGIST’S PRACTICES? RESULTS OF THE BELCRO COHORT


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Objectives and Study: Pediatric gastroenterologists treat Crohn’s disease (CD) patients up to 15-18 y. However, adult colleagues can diagnose and treat pediatric patients without restriction.

Methods: We investigated differences in presentation, diagnostic procedures and initial treatment for pediatric CD patients under pediatric vs adult gastroenterologists’care in the BELCRO cohort.

Results: In this cohort, 71% of patients were diagnosed by a pediatric gastroenterologist of whom 58% in a tertiary care centre compared to 37% of the 29% of patients in adult care. Patients diagnosed by adult physicians are significantly older, but 22% were below the age of 12 y. No difference in presenting symptoms (abdominal pain, diarrhoea, growth failure) or disease severity at diagnosis was found. Disease classification according to Montreal and the Paris classification was similar. Pediatric gastroenterologists performed as many upper endoscopies at diagnosis before and after publication of the Porto criteria (75%), whereas adult physicians performed significantly less upper endoscopies. At diagnosis, adult physicians prescribed more monotherapy with 5-ASA and less combination therapy with steroids, immunomodulators, antibiotics or enteral nutrition compared to pediatric colleagues.

Conclusion: Further follow up will indicate whether differences between pediatric and adult practitioners affect long term disease behaviour and outcome.

Disclosure of Interest: None Declared
BODY COMPOSITION USING BIO-IMPEDANCE ANALYSIS IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. CONCORDANCE WITH DUAL ENERGY X-RAY ABSORPTIOMETRY AND COMPARISON WITH HEALTHY CONTROLS

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Objectives and Study: To assess the accuracy of bio-impedance analysis (BIA) compared to the gold standard dual energy X-ray absorptiometry (DEXA) in estimating percentage body fat (fat mass; FM) and lean body mass (fat free mass; FFM) in children with inflammatory bowel disease (IBD). To compare FM and FFM levels between patients with IBD and healthy controls.

Methods: Twenty-nine healthy controls (12 females; mean age: 12.7±1.9 years) and 21 patients (11 females; 14.3±1.3 years) were recruited from August 2011 to October 2012 at our institution. BIA was performed in all children and DEXA in patients only. Concordance between BIA and DEXA was assessed using Lin’s concordance correlation and the Bland-Altman method. Between-group comparisons were made using analysis of variance adjusting for age.

Results: BIA-derived FM % showed a good concordance with DEXA-derived values, while BIA-derived FFM % tended to be slightly higher than DEXA-derived values (table). No differences were found between patients and controls regarding body mass index (mean±SD: 19.3±3.3 vs. 20.1±2.8 kg/m², respectively; age-adjusted P=0.08) and FM % (boys: 25.3±10.2 vs. 22.6±7.1%, for patients and controls, respectively; P=0.20; girls: 28.2±5.7 vs. 26.4±7.7%; P=0.91). Also, no differences were found regarding FFM % in boys (74.9±10.2 vs. 77.4±7.1%; P=0.22) and girls (71.8±5.6 vs. 73.5±7.7%; P=0.85).

<table>
<thead>
<tr>
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<th>Spearman correlation</th>
<th>Lin’s concordance</th>
<th>Bland-Altman limits of agreement</th>
<th>Bradley-Blackwood</th>
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<td></td>
<td></td>
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<td>Difference</td>
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<td>FM %</td>
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<tr>
<td>FFM %</td>
<td>0.907 ***</td>
<td>0.922</td>
<td>0.857–0.987</td>
<td>1.10</td>
</tr>
</tbody>
</table>

§ between difference and mean. CI, confidence interval; SD, standard deviation of the difference. ***, p<0.001

Conclusion: BIA adequately assesses body composition (FM %) in children with IBD and could advantageously replace DEXA, which is more expensive and less available. No differences in body composition were found between children with IBD and healthy controls.

Disclosure of Interest: None Declared
A NATION-WIDE REGISTRY OF PEDIATRIC INFLAMMATORY BOWEL DISEASE: IMPROVEMENT OF DIAGNOSTIC WORKUP AND PARIS CLASSIFICATION

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Objectives and Study: A nationwide registry may serve as a mirror reflecting the quality of health care. It is a method for detecting failure in diagnostic workup or in management practice. We evaluated whether diagnostic workup of paediatric IBD patients fulfils Porto Criteria. Furthermore, we analyzed whether the diagnostic practice has changed since the Hungarian Paediatric IBD Registry (HUPIR) exists (2007). In addition, there has been no large paediatric IBD cohort analyzed according to Paris classification.

Methods: Newly diagnosed paediatric patients with IBD (ages 0–18 years) are registered in this prospective registry. All the twentyseven paediatric institutes with paediatric gastroenterology serve data ensuring a nationwide approach. Questionnaires are collected via email and double checked by the leader of the coordinators (KEM) and the leader of the HUPIR (GV). The questionnaire includes epidemiological data, disease extension, disease activity (PCDAI, PUCAI) and initial therapy.

Results: Between 2007 and 2011, 712 new IBD cases were identified (449 Crohn’s disease (CD), 217 ulcerative colitis (UC) and 46 IBD-unclassified). Upper endoscopy was performed in 52.6% of the patients in 2007, and this rate has increased to 78.2% (p<0.001) by 2011. Proportion of ileoscopy has changed from 53% to 69% (p=0.011). Imaging of the small bowel did not change during the years (range: 31.2-42%), but the modality of imaging has altered. MRI was performed in 7.5% of patients in 2007 and in 24.8% (p=0.0005) in 2011.

Localization (Paris classification) could be evaluated in 512 patients. 84 of the 173 UC patients had E4 classification, 32 children had E3 localization and 10 cases (5.3%) presented with proctitis (E1). S1 severity was found in 15 patients (11.5%) at diagnosis.

In CD 219 (64%) children had upper gastrointestinal involvement, 159 (72.6%) patients had L4a, 27 (12.3%) had L4b, and 33 (15.1%) had L4ab classification. Six patients (1.4%) belonged to B2B3, 10 children (2.3%) had B3 and 46 (10.4%) CD patients had B2 phenotype. Localization differed significantly in age groups: involvement of the terminal ileum was significantly lower in A1a age group than in A1b (U=6216, p<0.001) or A2 groups (U=768, p=0.022). Perianal disease was significantly higher in patients with L4b than in L4a (25.9% vs. 9.4% p=0.023). PCDAI was significantly higher in patients with L3 than in patients with L1 or L2 disease extension (35.9 vs. 28.2 (p=0.001) and 35.9 vs. 27.2 p<0.001).

Conclusion: The quality of diagnostic workup in paediatric patients with IBD improved in the last 5 years. Paris classification of the IBD patients seems to be a more precise classification, providing distinct subgroups for further analysis.

Disclosure of Interest: K. Müller: None Declared, G. Veres Grant / Research Support from: Hungarian Scientific Research Fund grant (OTKA-K 105530)
TOWARD A STANDARD APPROACH FOR ASSESSING QUALITY OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE SERVICES IN THE UK

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Objectives and Study: The publication of national IBD standards in 2009 set a benchmark for quality of care in IBD services in the UK. Most recently, quality improvement (QI) pilot projects have been developed focusing on metrics addressing quality of care and clinical outcomes. Despite this, currently there is no assurance system to document actual improvement in delivery of care. With this in mind the RCP, through sponsorship of the RCN, funded reciprocal informal visits by paediatric IBD units across the UK to assess each other’s quality of care.

The aim of this abstract is to report on this process and the potential to develop a structured quality assessment framework.

Methods: Southampton & Cambridge tertiary paediatric gastroenterology centres reviewed local data from national IBD audit and QI Pilot studies comparing with national benchmark figures. Following discussion, the teams developed a structured programme for each visit and a report template with clearly defined domains that was amended after the first visit. The visiting teams included clinicians and IBD nursing staff with many years experience in paediatric IBD.

Results: Both centres scored well in the 2010 national paediatric IBD audit, improving on the 2008 audit figures.

The visit template included an initial introduction of the entire IBD MDT (including management and clinical teams), followed by open feedback from parents of children using the service. This was followed by presentation & discussion of the local QIP results, followed by a feedback session led by the visiting team. This was compiled into a structured report based on the Institute of Medicine’s criteria of quality of service; safety, efficacy, patient centredness, efficiency, timeliness and equitability.

Both teams found the visit highly valuable. It provided an important opportunity to focus attention on the local paediatric IBD service. By reviewing pathways and systems for presentation to external review, obvious strengths and weaknesses could already be identified. Further discussion during feedback and then the structured report allowed a clear action plan to be developed with sufficient traction with hospital management to implement change in local services.

Conclusion: This initiative has the potential to form the basis of quality assessments of paediatric IBD centres in the future. As outcome-based commissioning becomes increasingly important and services are awarded best-practice tariffs, it is important to develop tools to accurately and efficiently capture the quality of the care we provide for children and young people with IBD. This should help contribute to the aim of driving up quality of care across paediatric IBD units in the UK.

Disclosure of Interest: None Declared
PO-G-0074

ULTRASONOGRAPHIC ASSESSMENT OF COLONIC WALL IN PEDIATRIC ULCERATIVE COLITIS: COMPARATIVE STUDY WITH ILEO-COLONOSCOPY

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Objectives and Study: Bowel ultrasonography (US) is a well established non-invasive tool in the evaluation of patients (pts) with inflammatory bowel disease, especially Crohn’s disease. There are only few data on its role in Ulcerative Colitis (UC), particularly in children. We aimed to evaluate the usefulness of bowel US in the assessment of pediatric UC pts and compare US findings with clinical and endoscopic data.

Methods: 30 pediatric pts (median age 15 years; range 2-21; 16 males) were prospectively enrolled. Eight pts had a clinical suspicion of UC, 22 pts had an already established diagnosis and showed a flare-up of disease. All pts underwent clinical evaluation, bowel US with Color-Doppler examination (Toshiba equipment, with 3.5 MHz convex and 7.5 MHz linear transducers) and ileo-colonoscopy. US and endoscopy were carried out by different operators, blind to the results of the other technique. For each patient Pediatric Ulcerative Colitis Activity Index (PUCAI) and Mayo endoscopic score were calculated. The US parameters assessed were Bowel Wall Thickness (BWT >3 mm), BW stratification, vascularity and presence of austrae: each parameter was assigned a value of 0 or 1 depending on the presence or absence of alteration.

Results: 27/30 pts were finally diagnosed as UC. Extension of disease according to Montreal Classification was: E2 (left-side colitis) in 12/27 (45%), E3 (extensive UC) in 15/27 (55%) pts. This extent was independently confirmed in 25/27 pts by US, that yielded a 85% concordance with endoscopy concerning disease extension. Disease activity was mild (PUCAI 10-34) in 7 pts (25%), moderate (PUCAI 35-64) in 12 (45%) and severe (PUCAI>65) in 8 (30%). The mean values of PUCAI, Mayo score and US score respectively were: 40.5 ± 24.4, 2 ± 1 and 2.8 ± 1.4. The mean BWT in affected colonic segments was 5 ± 2 mm. The US score strongly correlated with PUCAI (r=0.85, p<0.0001) and Mayo index (r=0.90, p<0.0001). A positive correlation was also found between PUCAI and Mayo score (r=0.87, p<0.05). Multiple regression analysis showed that variables making a significant contribution to the final value of Mayo score were BWT (p<0.007) and vascularity (p<0.038)

Conclusion: Our preliminary data show a strong relationship between US and clinical and endoscopic findings, thus suggesting that colonic US might represent a useful first line, non invasive tool in the evaluation of pediatric UC pts. In our experience it allows to assess in a relatively rapid manner the extension and activity of disease and helps to judge the severity of a flare-up in pts with an already established diagnosis, prior to further invasive tests.

Disclosure of Interest: None Declared
ASSESSMENT OF SKINFOLD THICKNESS EQUATIONS IN ESTIMATING BODY COMPOSITION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: To assess the accuracy of skinfold equations in estimating percentage body fat (%BF) in children with inflammatory bowel disease (IBD), compared with assessment of body fat dual energy X-ray absorptiometry (DEXA).

Methods: Twenty-one patients (11 females, 10 males; mean age: 14.3 years, range 12-16 years) with IBD (Crohn's disease n=15, ulcerative colitis n=6) were assessed. Estimated %BF was computed using 5 established equations based on the triceps and subscapular skinfolds (Deurenberg, Weststrate, Slaughter, Durnin & Rahaman, Johnston, Brook) and compared to DEXA. Concordance analysis was performed using Lin's concordance correlation and the Bland-Altman limits of agreement method.

Results: Durnin & Rahaman's equation shows a higher Lin's concordance coefficient with a small difference amongst raw values for skinfolds and DEXA compared to the other equations. Correlation coefficient between mean and difference is close to zero with a non-significant Bradley-Blackwood test.

<table>
<thead>
<tr>
<th>Equation</th>
<th>Spearman correlation</th>
<th>Lin's concordance Coefficient</th>
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<td>0.898 ***</td>
<td>0.850</td>
<td>0.734 – 0.966</td>
<td>2.5</td>
<td>3.3</td>
<td>0.003</td>
<td>5.62</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Slaughter</td>
<td>0.906 ***</td>
<td>0.848</td>
<td>0.744 – 0.952</td>
<td>0.003</td>
<td>4.9</td>
<td>0.570</td>
<td>4.57</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Durnin &amp; Rahaman</td>
<td>0.915 ***</td>
<td>0.871</td>
<td>0.764 – 0.979</td>
<td>-1.0</td>
<td>3.6</td>
<td>-0.033</td>
<td>0.80</td>
<td>0.46</td>
</tr>
<tr>
<td>Johnson</td>
<td>0.919 ***</td>
<td>0.810</td>
<td>0.676 – 0.945</td>
<td>-3.4</td>
<td>3.3</td>
<td>-0.040</td>
<td>10.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Brook</td>
<td>0.900 ***</td>
<td>0.876</td>
<td>0.779 – 0.972</td>
<td>1.8</td>
<td>3.6</td>
<td>0.355</td>
<td>4.18</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

§ between difference and mean. CI, confidence interval; SD, standard deviation of the difference. ***, p<0.001

Conclusion: Body composition in pediatric IBD patients using the Durnin & Rahaman skinfold-equation adequately reflects values obtained by DEXA.

Disclosure of Interest: None Declared
Objectives and Study: Enteral nutritional therapy (ENT) and anti-TNF-α drugs are effective in pediatric Crohn’s disease (CD). Relative efficacy for symptoms and mucosal healing is unknown. PCDAI lacks specificity for intestinal inflammation, but fecal calprotectin (FCP) correlates with endoscopic assessment. Our study compares changes in PCDAI and FCP in children with CD initiating ENT or an anti-TNF.

Methods: PCDAI and FCP were assessed in patients at the start of ENT (n=30) or an anti-TNF (n=18) then at 8 weeks. Steroid exposure was documented. Remission and response were assessed with PCDAI, and FCP thresholds of ≤50, ≤250, and ≥50% reduction. Paired and unpaired t-tests and chi² tests were used to analyze differences within and between treatment groups.

Results: The ENT and anti-TNF groups had similar demographics and initial disease characteristics except for disease duration ≤6 months (ENT 50% vs. anti-TNF 93%; p=0.001). Steroid exposure was similar in both groups (23% ENT vs. 22% anti-TNF; p=0.93). Clinical remission (PCDAI ≤10) at 8 weeks was achieved by 70% ENT and 67% anti-TNF group (p=0.81). The mean decline in FCP over 8 weeks was significant in both groups (paired t-tests p<0.05): 460 µg/g (95%CI 225-697) for the ENT group and 661 µg/g (95%CI 335-966) for the anti-TNF group (p=0.30 for ENT vs. anti-TNF). FCP ≤250 at 8 weeks was achieved by 63% ENT and 39% anti-TNF (p=0.10), and a ≥50% reduction in FCP was achieved by 67% ENT and 67% anti-TNF (p=1). Analysis restricted to children with disease duration ≤ 6 month produced similar results to the primary analysis.

Conclusion: Treatment with either ENT or anti-TNFα results in high clinical remission rates and significant reductions in FCP. Remission rates and reduction in FCP were not significantly different between groups

Disclosure of Interest: None Declared
THE IMPACT-III (HR) QUESTIONNAIRE: A VALID MEASURE OF HEALTH-RELATED QUALITY OF LIFE IN CROATIAN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: To assess the reliability and validity of IMPACT-III (HR), a disease-specific health-related quality of life (HRQOL) instrument, in Croatian children with inflammatory bowel disease (IBD).

Methods: In a multicenter study, 104 children participated in a validation study of IMPACT-III (HR) cross-culturally adapted for Croatia. Factor analysis was used to determine optimal domain structure for this cohort, analysis of Cronbach’s alpha coefficients to test internal reliability, ANOVA to assess discriminant validity, and correlation with Pediatric Quality of Life Inventory, Version 4.0 (PedsQL™) using Pearson correlation coefficients to assess concurrent validity.

Results: Cronbach’s alpha for the IMPACT-III (HR) total score was 0.92. The most robust factor solution was a 5-domain structure: Symptoms, Concerns, Socializing, Body Image, and Worry about Stool, all of which demonstrated good internal reliability (α = 0.60–0.89), but two items were dropped to achieve this. Discriminant validity was demonstrated by significant differences (P < 0.001) in mean total HRQOL scores between quiescent and mild or moderate-severe disease activity groups for total (148 vs. 139 or 125) and following factor scores: Symptoms (84 vs. 71 or 61), Socializing (91 vs. 83 or 76), and Worry about Stool (significant only between quiescent and moderate-severe groups, 90 vs. 62, respectively). Concurrent validity of IMPACT-III (HR) with PedsQL™ showed significant correlation, which was strongest when similar domains were compared.

Conclusion: IMPACT-III (HR) appears to be useful tool to measure HRQOL in Croatian children with Crohn’s disease and ulcerative colitis.

Disclosure of Interest: None Declared
VITAMIN D LEVELS IN CHILDREN AFFECTED BY IBD IN NORTHEASTERN ITALY.
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Objectives and Study: Vitamin D is best known for its role in bone health. Recently, several studies have identified new roles of vitamin D. The aim of this study was to evaluate vitamin D status in children affected by Inflammatory Bowel Disease (IBD) followed by the Institute for Maternal and Child Health IRCCS Burlo Garofolo and to identify potential correlations between vitamin D levels with laboratory and clinical indexes of disease.

Methods: 50 patients with IBD were enrolled. Patients were compared to a group of healthy controls (152 individuals) matched for age and sex. Vitamin D was measured as 25(OH)D3 levels. 25 (OH)D3 levels, inflammatory indexes (ESR and CRP) and disease activity indexes Pediatric Crohn’s Disease Activity Index (PCDAI) Pediatric Ulcerative Colitis Disease Activity Index (PUCAI) were measured in all patients.

Results: The prevalence of Vitamin D deficiency was high among patients with IBD. Specifically, 83% of the patients had levels below 50 nmol/L, 18% of the patients had levels between 50 and 75 nmol/L and none had levels > 75 nmol/L. No correlation was found between 25(OH)D3 levels and PUCAI/PCDAI indexes (p 0.4), ESR (p 0.8), localization of disease (p 0.9), immunosuppressive therapy (p 0.7) and number of relapses in the past year (p 0.14). A significant correlation was found between the levels of 25(OH)D and CRP in patients with Crohn’s Disease (p 0.006) but not Ulcerative Colitis (p 0.129).

Conclusion: The majority of patients with IBD present Vitamin D deficiency. There is no correlation between Vitamin D levels and inflammatory indexes or indexes of disease activity. Further studies that will evaluate the effects of a corrective therapy on the state of inflammation and clinical activity are required to better understand the significance of Vitamin D deficiency and the potential benefits of a corrective intervention in patients with IBD.

Disclosure of Interest: None Declared
HIGH PREVALENCE OF PRIMARY SCLEROSING CHOLANGITIS AND AUTOIMMUNE HEPATITIS IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: In children with inflammatory bowel disease (IBD) concomitant hepatobiliary disease, particularly primary sclerosing cholangitis (PSC) and autoimmune hepatitis (AIH), has crucial impact on prognosis. The aim of this study was to analyse data from the pediatric IBD registry “CEDATA-GPGE” of Austria and Germany.

Methods: Between 2004 and 2010 3669 patients (age 0–18 years) with IBD, including 2253 with Crohn’s disease (CD), 1201 with ulcerative colitis (UC) and 215 with IBD unclassified (IBD-U) were registered in "CEDATA-GPGE". For all patients with indicators of PSC or AIH (n=122) a questionnaire was filled by the treating pediatrician. Diagnosis was reviewed according to defined diagnostic criteria.

Results: Diagnosis of PSC was confirmed in 55 and very likely in 15 patients, while AIH-PSC overlap was proven in 16 and very likely in 9 patients. Six patients with AIH only and 21 patients without evidence of PSC or AIH were excluded from the final analysis. Of the 70 PSC patients 66% had UC, 19% CD and 9% IBD-U; 66% were male. Of the 25 AIH-PSC patients 72% had UC, 12% CD and 8% IBD-U; 65% were male. Of the UC patients with PSC pancolitis was diagnosed in 86%, left-sided colitis in 7% and proctitis in 7%. The only significant difference in symptoms until diagnosis was a lower frequency of blood in the stool in UC patients with PSC (13/47, 72%) than without (956/1090, 86%).

Most striking laboratory value at time of diagnosis was elevated gamma-glutamyl transferase with a median of 168 U/l (range 10-854) in the PSC group and 226 U/l (range 12-807) in the AIH-PSC group. Immunoglobulin G was elevated not only in AIH-PSC patients with 22g/l (median, range 16.5-46.7) but also in many PSC patients with 16.4 g/l (4.0-39.8). Autoantibody positivity differed between PSC and AIH-PSC patients: smooth muscle antibodies (17% vs 80%), antinuclear antibodies (26% vs 64%), and perinuclear anti-neutrophil cytoplasmic antibodies (40% vs 56%). Hepatic fibrosis or cirrhosis was histologically proven in 23% and 4% of the PSC, and in 48% and 20% of the AIH-PSC patients, respectively.

Conclusion: At least 5% of all in CEDATA-GPGE registered UC patients have PSC. The high number of PSC patients with autoimmune phenomena is striking and may be a distinct feature of pediatric PSC with implications for disease management. All children with newly diagnosed IBD should be investigated for concomitant hepatobiliary disease.

Disclosure of Interest: None Declared
**Objectives and Study:** Crohn’s disease in children and adolescents can be treated with enteral nutrition as induction therapy. Some patients have oral complaints, suspicious of orofacial granulomatosis (OFG). Symptoms are lip swelling, aphthous lesions, cheilitis and granulomatous inflammation in the mouth. OFG might be a part of Crohn’s disease and is believed to be, at least partly, an allergic reaction to benzoates and cinnamon. Diet restrictions and elemental diet (amino-acid formula) are used to treat the condition. Retrospectively, we wanted to investigate the efficacy and tolerability of enteral nutrition in children and adolescents with Crohn’s disease and OFG at our institution.

**Methods:** During the period May 2005 to January 2012 we diagnosed altogether 62 patients, 47 with Crohn’s disease according to the Porto criteria, 15 with OFG and 9 with OFG and Crohn’s disease. 6 patients had only OFG.

**Results:** 38 out of 56 (68%) patients with Crohn’s disease, with or without OFG, were treated with enteral nutrition as induction therapy. In mild disease budesonide combined with azathioprine (n=14) was used instead. Infliximab (n=2) was chosen in patients with perianal disease with fistulas. Of the patients who received exclusively enteral nutrition, 3 did not comply to 6 weeks of treatment. Due to aggressive disease the treatment was changed to infliximab within a few weeks in 6 patients. All but one patient with OFG received elemental diet. In the patients with Crohn’s disease, the mean fecal calprotectin was 1041 mg/kg (normal range <50mg/kg), mean CRP was 30 mg/l (normal range < 5 mg/l), and mean erythrocyte sedimentation rate was 24 (normal range < 10 mm) before treatment. The patients with isolated OFG had a normal fecal calprotectin as well as normal CRP and erythrocyte sedimentation rate at time of diagnosis. In 29 (76%) patients with Crohn’s disease, with or without concomitant OFG, we observed complete normalization of the inflammatory markers fecal calprotectin, erythrocyte sedimentation rate and CRP. All OFG patients, with or without concomitant Crohn’s disease responded well to treatment with exclusive elemental diet, all with a reduction of lip swelling and resolution of aphthous ulcers and cheilitis. The improvement was evident within a few days. Their symptoms were later controlled with a diet free of benzoates and cinnamon.

**Conclusion:** Enteral nutrition is efficacious and well tolerated in children with Crohn’s disease and OFG. In OFG the liquid diet should be an elemental formula. Benzoate free and cinnamon-free diet is of benefit in controlling the symptoms.

**Disclosure of Interest:** None Declared
EPIEMIOLOGY OF VITAMIN D DEFICIENCY IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE PRESENTING TO A TERTIARY CARE CENTER IN THE UK

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Objectives and Study: to determine the epidemiology of vitamin D deficiency in a large cohort of paediatric IBD patients presenting to a tertiary care center in the UK.

Methods: this was a retrospective observational study of patients who presented to the Paediatric IBD service at Addenbrooke’s Hospital (Cambridge, UK) between January 2008 and July 2012. We retrospectively recorded 25-hydroxyvitamin D (25-OHD) serum concentration measured in these patients. The first recorded value of 25-OHD for each patient was used in the analysis. Information on age, sex, ethnicity, diagnosis and date/season of sample collection were also obtained. Serum 25-OH D concentration was classified as optimal (> 75 nmol/l), suboptimal (50-75 nmol/l), insufficient (25-50 nmol/l) and deficient (< 25 nmol/l).

Results: a total of 123 children (85 with Crohn’s disease, CD, 27 with Ulcerative Colitis, UC, and 12 with IBD-indeterminate, IBD-U) underwent at least one 25-OHD level measurement. Overall a total of 503 25-OHD levels were recorded, 20 % of patients had 25-OHD levels measured at diagnosis. Patients’ characteristics and main findings are presented in the table. Overall 55 patients (45%) were found to be vitamin D deficient or insufficient, 33% had suboptimal levels and only 22% of the patients had optimal levels. There was no significant difference in the prevalence of vitamin D deficiency between CD and UC patients (40% vs 41%). Patients with vitamin D deficiency tended to be older (13.4 vs 12.3, p= 0.0217) and had a longer disease duration (20.5 vs 10.6 months, p= 0.0158) than those who were not deficient.

<table>
<thead>
<tr>
<th></th>
<th>All IBD patients (n=123)</th>
<th>UC (n=27)</th>
<th>CD (n=85)</th>
</tr>
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<tr>
<td>Age, y</td>
<td>12.7± 1.66</td>
<td>12 ± 2.79</td>
<td>12.9 ±2.63</td>
</tr>
<tr>
<td>F/M</td>
<td>0.73</td>
<td>2.8</td>
<td>0.44</td>
</tr>
<tr>
<td>Ethnicity:</td>
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<td></td>
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<tr>
<td>White</td>
<td>107 (86)</td>
<td>24 (89)</td>
<td>87 (72)</td>
</tr>
<tr>
<td>Asiatic</td>
<td>4 (3)</td>
<td>0 (0)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Other</td>
<td>12(11)</td>
<td>3 (11)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>15.6</td>
<td>16.7</td>
<td>16</td>
</tr>
<tr>
<td>Serum 25-OHD levels, nmol/l,</td>
<td>57.6</td>
<td>57.3</td>
<td>57.6</td>
</tr>
<tr>
<td>Serum 25-OHD levels &lt; 50 nmol/l</td>
<td>55(45)</td>
<td>39(41)</td>
<td>11(40)</td>
</tr>
<tr>
<td>Serum 25-OHD levels &lt; 25 nmol/l</td>
<td>5(4)</td>
<td>0</td>
<td>5(6)</td>
</tr>
</tbody>
</table>
Conclusion: In our study we observed a higher than previously reported prevalence of Vitamin D deficiency amongst children with IBD (45%). Our report is the first attempt to clarify the epidemiology of vitamin D deficiency in children with IBD in the UK. Interestingly, vitamin D deficiency was found to be more common in autumn and winter as well as strongly associated with disease duration of disease. Taken together our data lends further support for a potential role of Vitamin D in IBD disease pathogenesis and indicates that supplements should be considered particularly in patients with longstanding disease during the autumn and winter months.

Disclosure of Interest: None Declared
PO-G-0082

INFliximab Infusion Reactions in Children with Inflammatory Bowel Disease Are Infrequent and Occur Most Frequently During Induction.


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Objectives and Study: Infliximab is effective at inducing and maintaining remission in inflammatory bowel disease (IBD), however there is a risk of infusion reactions. This study aimed to assess the incidence of and characteristics involved in infliximab infusion reactions in children with IBD.

Methods: A retrospective review of IBD patients treated with infliximab (5mg/kg at 0, 2 and 6 weeks followed by 8 weekly maintenance as needed) at our institution from 2003-2012. Information was collected on patient demographics, disease history, concomitant medication and infliximab infusion details.

Results: 75 patients (68 Crohn’s disease, 6 ulcerative colitis, 1 IBD-U) were treated with infliximab, with a combined total of 586 infusions (260 induction and 326 maintenance). There was a median of 2.7 years (IQR 1.2-3.8) between diagnosis and first infliximab treatment. The number of infusions per patient ranged from 2-24 (median 7). 63 patients had a single induction course, 10 patients had a second induction and 2 patients had 3 induction courses. 71 (95%) of patients were on concomitant immunosuppressives; 34 on azathioprine, 33 on methotrexate and 2 on others. 55 (73%) patients had hydrocortisone prior to infusions.

There were 10 documented infusion reactions (1.7% of all infusions; 7/260 (2.9%) of all induction infusions cf. 3/326 (0.9%) of maintenance, p=0.18) in 8 patients (10.6% of all patients). 2 patients had 2 consecutive infusion reactions. 7 occurred during induction, 2 in the first maintenance infusion and one reaction occurred during the 3rd infusion of 10mg/kg. All infusion reactions were acute, and resolved after stopping the infusion and treatment with antihistamine +/- oxygen. After the infusion reaction, 5 patients stopped infliximab; 3 immediately and 2 after a subsequent infusion reaction. 3 patients continued infusions successfully after an infusion reaction, 2 of whom received infusions at a slower rate. There was no significant difference in gender, age at diagnosis and first infusion, concomitant therapies, and dose in those who had a reaction and those who did not. There was a higher percentage of patients with perianal disease in the group who had an infusion reaction (75%) compared to those who did not (29.8%), (p= 0.046).

Conclusion: The rate of infliximab infusion reactions was low and the majority occurred during an induction period. These results indicate that it may be feasible to give maintenance infliximab infusions at standard dosing at a faster rate or outside the traditional hospital setting.

Disclosure of Interest: C. O’Brien: None Declared, L. Curtis: None Declared, V. Garrick Conflict with: received speakers fees from MSD, S. Malik: None Declared, A. Barclay: None Declared, P. McGrogan Conflict with: received speakers fees from MSD, R. Russell Conflict with: received speakers fees from MSD
PHENOTYPE AND CLINICAL CHARACTERISTICS OF EARLY COMPARED TO LATE-ONSET PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Early-onset (EO) pediatric inflammatory bowel diseases (IBD) seem to be more severe and extensive than those with a later-onset. To test this hypothesis we examined the phenotype and clinical characteristics of patients (pts) with IBD diagnosis at 0-5 years (yrs), compared to the ranges 6-11 and 12-18 yrs.

Methods: Anatomic locations and behaviors were assessed in 505 consecutive IBD pediatric pts (54% males): 224 Crohn’s Disease (CD), 245 Ulcerative Colitis (UC) and 37 IBD-unclassified (IBDU). Data were collected between January 2009 and April 2012 and stored in the Pediatric Gastroenterology, Hepatology and Nutrition Italian Society (SIGENP) IBD web-registry, recently developed.

Results: 11% of pts were in the range 0-5 yrs of age at the diagnosis, 39% in 6-11, and 50% in 12-18 yrs. UC was the most frequent diagnosis in EO-IBD and in 6-12 yrs old group, whereas CD was predominant in older children (p: 0.002). A classification as IBDU was more common in the range 0-5 yrs compared to the other groups (p: 0.005). EO-CD was characterized by a more frequent isolated colonic disease (p:0.01). Seventy-nine % of the 0-5 yrs range pts had extensive UC, compared to 50% of 6-11 (p:0.004) and 45% of 12-18 (p: 0.001) yrs range. A proctitis was diagnosed in 0.5% of 0-5 yrs age group, compared to 17% in 6-11 and 19% in 12-18 yrs ranges (p: 0.19). Most of younger pts received steroids and thiopurines at the diagnosis (58% and 55%, respectively), while use of steroids was reduced in older two age range pts (p:0.001). Thirteen % of pts with EO-IBD underwent biological therapy within 1 year from the diagnosis (vs. 12% of 6-11 and 15% of 12-18 yrs range groups). There was no statistical difference for family history for IBD in the 3 age range groups.

Conclusion: EO-IBD exhibit an extensive disease phenotype and benefit from more aggressive treatment strategies. A family history for IBD is not common in younger children. Long prospective studies are needed to define the natural history of EO disease.

Disclosure of Interest: None Declared
25-HYDROXYVITAMIN D CONCENTRATIONS IN CHILDREN WITH CROHN’S DISEASE AFTER 6 MONTHS OF SUPPLEMENTATION: A RANDOMIZED CONTROLLED TRIAL
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Objectives and Study: Current evidence suggests a plausible link between vitamin D deficiency and inflammatory bowel disease (IBD). Although vitamin D status as determined by measurement of serum 25-hydroxyvitamin D (25OHD) concentrations has been evaluated in children with IBD, the cutoff values representing adequacy are controversial. In the healthy population, cutoffs for adequacy of 50 or 75 nmol/L have been suggested. Furthermore, limited data exists on the vitamin D supplemental dose required to promote adequate vitamin D status in pediatric patients with IBD. The primary aim was to determine baseline mean serum 25OHD concentrations in children with quiescent Crohn’s disease (CD) followed by determination of difference in mean serum 25OHD concentrations after vitamin D₃ supplementation. Serum bone specific alkaline phosphatase (BSAP) concentrations and PCDAI following vitamin D₃ supplementation were determined and adverse events were recorded.

Methods: Children aged 8-18 years with CD in remission (PCDAI ≤ 10), and not taking a vitamin D supplement > 400 IU/day were recruited from 2 Canadian pediatric IBD Centers. Subjects were randomized to either 400 or 2000 IU of vitamin D₃ per day for 6 months. Blood samples (serum 25OHD and BSAP), urine samples (safety monitoring of hypercalcuiuria by calcium/ creatinine concentration ratio) and clinical information were collected at baseline, 3 and 6 months.

Results: Eighty-three children were recruited; McMaster Children’s Hospital (n=30), BC Children’s Hospital (n=53); mean (SD) age at recruitment was 14.3 (2.3), 46% female, 78% Caucasian. Mean (95%CI) baseline 25OHD values in Caucasians (n=63) and others (South East Asian, Asian, black; n=16) were 64 (59-68) and 47 (35-59) nmol/L, (p=0.003) respectively. In a univariate analysis after adjustment for baseline 25OHD values and season of enrollment, age and ethnicity, mean (95% CI) endpoint serum 25OHD was 86 (78-92) vs. 63 (56-70) nmol/L in the 2000 and 400 IU groups respectively; a difference of 23 (14-32) nmol/L. Mean endpoint 25OHD concentrations were not significantly different between Caucasian and other patients (p=0.126), although this may be due to insufficient sample size. No significant differences between groups were found in serum BSAP or PCDAI.

Conclusion: Baseline 25OHD vitamin levels are inadequate in pediatric non-Caucasian vs. Caucasian patients with quiescent CD. Higher 25OHD concentrations were attained with supplementation with 2000 IU/day. Larger multicenter trials of longer duration are required to detect ethnic differences in vitamin D level following supplementation and effect on disease activity and BSAP concentrations.

Disclosure of Interest: None Declared
SURGERY AND POSTOPERATIVE RECURRENCE OF SYMPTOMS IN PAEDIATRIC CROHN’S DISEASE.
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Objectives and Study: In Crohn's disease (CD) operation is often the resort treatment, when medical treatment has failed. Historically, > 50% of patients with Crohn's disease need surgery. In paediatrics surgery is traditionally postponed as long as possible.

To describe surgery rates, use of medication before and after surgery, surgical complications and time to recurrence of disease in paediatric CD patients.

Methods: All children < 18 years of age at diagnosis of CD from the period 1.1.1978 – 31.12.2007 were identified using Danish National Patient Registry (LPR). Files from CD patients who had surgery at Hvidovre (HH) and Odense University Hospital (OUH) were used to extract data.

Results: 1545 children were registered in LPR as having CD. 422(27%) underwent surgery and, 138 (33%) at HH or OUH. 23 of 138 (17%) were misdiagnosed and excluded, resulting in a study population of 115 Children.

Disease behavior could be classified according to the Montreal classification at the time of operation in 106/115 patients: 39/106 (37%) B1, 59/106 (56%) B2 and 8/106 (7%) B3.

90% of the patients received corticosteroids, 26 % azathioprine (AZA) and 15% infliximab before surgery and after surgery 36% were treated with corticosteroids, 62% AZA and 11% infliximab.

55 (48%) underwent ileo-coecal resection, 18 (16%) ileal resection, 19 (16%) colectomy, 11 (10%) hemi colectomy and 5 (4%) both colonic and ileal resection. 42% of the colectomized patients was diagnosed with ulcerative colitis before surgery, but changed diagnosis to CD after postoperative pathological evaluation.

The median time from diagnosis to surgery was 23 months (0-147) and 9% were operated at the time of diagnosis. 40 (35%) of the patients had postoperative complications. No difference in occurrence of complications was seen between children who had or had not been treated with corticosteroids within a month before surgery. The surgical complication rate was significantly smaller in patients who had an ileal (7,1%) or ileo-coecal resection (26%) compared to hemi (42%) and total colectomy colon (62%), p<0.01.

The median follow-up time was 121 months (16-226). The median time to disease recurrence was 12 months (0-160), 21% had no recurrence of symptoms in the follow-up period. 26% had recurrence of symptoms within 6 months after surgery. 39% underwent more than one bowel resection for CD. No difference in time to recurrence was shown between AZA treated patients and patients not receiving AZA.

Conclusion: In our cohort followed >10 years postoperatively we found a high recurrence rate of disease and a frequent need for more than one bowel resection.

Disclosure of Interest: None Declared
Objectives and Study: Infliximab (IFX) is approved for the treatment of pediatric Crohn’s disease (CD). The clinical utility of therapeutic drug monitoring of IFX to assess clinical and biomarker disease activity is unknown in pediatric CD. To investigate whether therapeutic drug monitoring of infliximab (infliximab trough levels (ITL)) could be useful in monitoring and predicting therapeutic response to IFX.

Methods: All consecutive children with CD receiving maintenance treatment with IFX 5 mg/kg every 8 weeks at Nancy Children University Hospital were enrolled in observational study with standardized follow-up between April 2004 and September 2011.

Results: A total of 33 children were included: median age: 13.9 years, IQR 12.3-16.7; 61% males; median disease duration at first infusion: 32.5 months, IQR 17.7-51.4; median follow-up: 4.4 years, IQR 0.6-6.6. They received 409 infliximab infusions (median number of infusions per patient, after induction therapy: 7; IQR 3-13).

Overall results: median ITL was 4.2 µg/mL (IQR 1.1-8.4), median Harvey Bradshaw Index (HBI): 1.0 (IQR 0-5), median CRP: 3.4 mg/L (IQR 1-13.2), median fecal calprotectin: 240 µg/g (IQR 87.5-790.5).

Median ITL were greater in patients in clinical remission (HBI < 5) than in those with active disease (respectively 4.6 versus 2.8 µg/mL; p=0.048).

ROC analysis identified 0 µg/mL as the best cutoff for ITL to predict clinical remission. By logistic regression, independent predictors of clinical remission were CRP < 10 mg/L (OR, 11.9; 95% CI, 3.9-36.4; p<0.0001) and ITL > 0 µg/mL (OR, 3.0; 95% CI, 1.0-9.1; p=0.049).

Detectable ITL predicted biological remission (CRP < 10 mg/L) with high sensitivity (84.9%) and modest specificity (44.44%) (LR, 1.53; AUROC, 0.611; p=0.02).

Detectable ITL predicted mucosal healing (fecal calprotectin < 150 µg/g) with high sensitivity (92.7%) and modest specificity (46.15%) (LR, 1.72; AUROC, 0.746; p<0.0001).

Conclusion: Measurement of IFX trough levels accurately predicts clinical and biological remission as well as mucosal healing in pediatric CD. Combined with HBI evaluation, CRP and calprotectin measurements, it appears useful to monitor disease activity among children receiving infliximab for CD.

Disclosure of Interest: None Declared
PO-G-0087

THIOPURINE PHARMACOGENETICS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE
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Objectives and Study: Over last two decades the treatment of inflammatory bowel disease (IBD) has evolved with more frequent use of the immunomodulators as azathioprine (AZA) and 6-mercaptopurine (6-MP). Thiopurine S-methyltransferase (TPMT) genotyping can aid in minimizing toxicity identifying a priori patients populations that can safely initiate AZA therapy. Human TPMT gene exhibits significant genetic heterogeneity. It has been shown that certain polymorphisms in TMPT gene define different TPMT allozymes with different enzyme activity. At present, the TPMT allele nomenclature comprises at least 27 TPMT alleles. The common TPMT variant alleles in Caucasian include TPMT*2, TPMT*3A, TPMT*3B and TPMT*3C. These variant alleles are detected in over 80-95% of Caucasians characterized to have low or intermediate TPMT activity. The aims of this study were to investigate TPMT genotype status in pediatric IBD from South of Italy and correlation with potential adverse events.

Methods: 31 consecutive Italian patients with IBD (16 Crohn’s Disease, 14 Ulcerative Colitis, aged 2-18 years; average age 14 years) were genotyped for the following allelic variants: TPMT*2 allele, TPMT*3A allele, TPMT*3B allele and TPMT*3C allele using TaqMan® Allelic Discrimination assay. In each patient, initial dosing of AZA was independent TPMT genotype and the median starting dose of AZA was 2 mg/kg/day. Safety was determined by WBC measurements. A WBC < 4000 defined leukopenia. WBC was assessed at weeks (wk) 2,4,8,12, and then either every 4 wk or 8 wk, thereafter, up to 52 wk.

Results: Polymorphism heterozygous TPMT*1/TPMT*3A (displaying an intermediate TPMT activity) was found in 3 (10%) out of 30 patients. Between this group, only 1 patient (3%) had developed leucopenia after one year of therapy without the need for suspending the therapy. None of the patients were reported major side effects as myelotoxicity and hepatotoxicity.

Conclusion: Current recommendations suggest that IBD patients should have TPMT genotype prior to start thiopurine therapy to modulate AZA/6-MPT therapy. Our study demonstrates that the prevalence of polymorphisms in TPMT gene determining intermediate, low or deficient enzymatic activity, was not significative and correlated with minor adverse event (leucopenia). Usual AZA dosage in heterozygous TPMT*1/TPMT*3A patients was shown to be safe and without increased risk of major adverse events (myelotoxicity and hepatotoxicity). Cost-effectiveness studies are required to determine whether TPMT genotyping may have allowed for cost saving via the successful optimization of thiopurine therapy.

Disclosure of Interest: None Declared
EFFECT OF SHORT-TERM SUPPORTIVE PARTIAL ENTERAL NUTRITION ON NUTRITIONAL STATUS DURING TREATING CROHN’S DISEASE IN YOUNGER AGE WITH HIGHER DISEASE ACTIVITY

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Objectives and Study: Nutritional therapy is the one of the primary treatment for active pediatric Crohn’s disease, improving disease activity and anthropometry. The aim of this study is to analyze the effect of short-term supportive, temporary, additional partial enteral nutrition therapy with general diet on the nutritional status during treating Crohn’s disease children in younger age with higher pediatric Crohn’s disease activity.

Methods: From January 2007 to December 2011, a total of 78 pediatric Crohn’s disease patients and a total of 85 non-Crohn’s disease (childhood functional abdominal pain) patients were enrolled as a patients group and a control group in this study, respectively. Body weight, Height, Hb, transferrin saturation, ferritin, prealbumin, albumin, Zinc, Calcium, Magnesium, Phosphorous, Vitamin A, Vitamin B12, Vitamin E, folate and 25-OH-Vitamin D were checked as parameters of nutritional assessment. Pediatric Crohn's disease activity index was used to analyze the differences of nutritional status during different disease activity group. For a supportive short-term partial enteral nutrition (SPEN) in severe activity Crohn’s disease, 1 month partial enteral nutrition therapy (20 Kcal/kg) was added after induction of remission during medical treatment and general diet. Analysis of differences between at the time of onset and after 1 year treatment with SPEN and without SPEN was performed.

Results: Crohn's disease group had significant poor conditions on the nutritional status rather than control group. Nutritional status showed significant improvement from onset to after 1 year treatment in each activity groups (mild, moderate and severe). In the differences (Δ) of nutritional status between SPEN group and non-SPEN group in severe PCDAI (PCDAI>45), SPEN group presents better improvement compared to non-SPEN group. Furthermore, in the differences (Δ) of nutritional status of 2 age (under 13 years and over 13 years) groups in severe PCDAI with SPEN, the better improvement of nutritional recovery was documented in the younger group.

Conclusion: The supportive short-term partial enteral nutrition (SPEN) is more effective on improving the nutrition status and disease activity during treating pediatric Crohn’s disease especially in younger age with severe pediatric Crohn’s disease activity index (PCDAI).

Disclosure of Interest: None Declared
Cyclosporine as rescue therapy for acute ulcerative colitis in children: A single Italian centre experience

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Objectives and Study: In comparison to adult-onset disease, severe ulcerative colitis (UC) is more frequent in childhood and more likely associated to steroid failure. In such cases Cyclosporin A (CyA) is an alternative option to Infliximab. We describe our experience in the management of acute moderate-severe steroid-refractory UC with CyA as second-line rescue therapy.

Methods: We carried out a retrospective review of patients (pts) with acute steroid-refractory UC treated with CyA in our Unit between May 1997 and March 2012. The data collected included patient demographics, colitis severity, dose and route of administration of CyA, therapeutic range, adverse effects, timing and rate of clinical remission and CyA failure with need for early colectomy. PUCAI score was used to define the severity of the disease and the response to CyA. A follow-up of responder patients was assessed to evaluate the rate and time of colectomy in the long term.

Results: A total of 43 episodes treated with CyA in 42 pts were analyzed (median age 9.7 ys, range 2.6-17.4; male 20/42). The median PUCAI at onset of acute colitis was 65 (45-85). In 28 episodes steroids were started as first line therapy and CyA commenced after a median of 6 days (range 3-22), with a median PUCAI of 70. In the others 15 cases CyA was started on admission because history of steroid dependence or severe side effects. Most cases (79%) received CyA orally at a mean starting dose of 3.8 mg/kg daily (range 2-5.5); then doses were adjusted with a serum range of 101-167 ng/ml. The other pts (21%) received iv CyA at 1.5-4 mg/kg and then shifted to oral CyA 3 days after. 6 side effects occurred in 6 pts (14%), including 3 headache, treated with dose reduction; 1 urticaria, 1 hepatotoxicity/hypertriglyceridemia and 1 seizure, all treated with CyA discontinuation. The latter occurred in oral CyA, few days after iv administration, with a serum level of 100 ng/ml. Typical RMi cerebral features were detected, spontaneously resolved without any sequelae. 30/43 (69.8%) cases resolved the acute attack (median PUCAI 5) after a median of 6 days (range 2-11) and all discharged on CyA for 3 months. The others (30.2%) undergone urgent colectomy after a median of 4 days (range 3-22). During the follow-up after discharge, 10/30 pts required colectomy (33.3%) after a mean time of 0.8 ys (range 0.2-2.3) while 19/30 (63.3%) maintain the colon at a mean of 3.5 ys (range 0.2-9.8). One patient was lost to follow-up.

Conclusion: Our experience in the use of CyA shows a rate of colon savage in the short- and long-term of 69.8% and 63.3% respectively. In the era of biologics, CyA remains an effective second-line therapeutic option in steroid-refractory acute UC in children, with a good tolerability and safety.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PO-G-0090

POTENTIAL RISKS OF ANTI-TNFA-INDUCED PSORIASIS IN PAEDIATRIC PATIENTS
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Objectives and Study: Anti-TNFa antibodies are used successfully to treat several autoimmune disease. The paradoxical occurrence of psoriasis (PS) in patients treated with anti-TNFa antibodies is increasingly recognised. The aim of this study is to identify paediatric patients with inflammatory bowel disease (IBD) treated with anti-TNFa antibodies who developed PS, to evaluate potential risks and to provide a practical approach for treatment.

Methods: We identified retrospectively all paediatric IBD patients who developed PS while receiving anti-TNFa antibodies at our Centre. We considered type of IBD, age at diagnosis of IBD and at onset of PS lesions, sex, family history for PS, therapeutic options for IBD and skin lesions, time between initiation of anti-TNFa antibodies and onset of PS, locations of PS lesions, other IBD therapy.

Results: 47 patients (22 males; range of age 6-18 yrs) were treated by anti-TNFa antibodies (36 infliximab (IFX), 11 adalimumab (ADA)). Nine (19%) patients (3 males; median age 11 yrs) developed anti-TNFa-induced PS. Five had Crohn disease (CD), 4 ulcerative colitis (UC). Two CD patients were treated with IFX and 3 with ADA. PS appeared 24 months after begin of IFX in 1 case and at the 5th month during 2nd cycle in the other patient. In patients treated with ADA PS occurred after 4, 5 and 14 months respectively after begin of therapy. All 4 UC patients were treated with IFX: PS occurred after an average time of 24 months after begin of therapy. The median age at onset of PS lesions was 16 years old (range 12-18). Overall, 5 patients had a positive family history for PS (father). PS lesions were present on auricular (20%) and periumbilical region (17%), scalp (13%), trunk (13%), axilla (13%), groin/pubic regions (8%), flexures (8%), palmoplantar (8%). Six patients were treated successfully by topical corticosteroids; in 2 patients IFX was interrupted and PS improved, 1 patient was discontinued from IFX and started ADA, but PS appeared after 12 months. PS was treated with topical corticosteroids and ADA was stopped. All patients who need to interrupte anti-TNFa antibodies had a positive family history for PS. All patients were treated with azathioprine too.

Conclusion: Anti-TNFa-induced PS is a common event in IBD and it seem to predominate in females with a positive paternal history for PS. PS during ADA occured earlier than IFX; unusual areas of the body were often involved (periumbilical region). Most patients were treated successfully with topical corticosteroids, however all patients who interrupted anti-TNFa antibodies had an important skin involvement and paternal inheritance. The debate is open: these features could be potential risks for IBD-patients treated with anti-TNFa antibodies? New biological therapy should be used?

Disclosure of Interest: None Declared
CHILDREN WITH CROHN’S DISEASE ON 100% VS. 80% ENTERAL NUTRITIONAL THERAPY: INTERIM ANALYSIS OF A PROSPECTIVE COHORT STUDY


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Objectives and Study: The protocol for treating pediatric Crohn's disease (CD) with enteral nutritional therapy (ENT), recommendations for the avoidance of regular foods, and concurrent steroid use are widely varied. Therapy efficacy can be assessed both clinically and with fecal calprotectin (FCP) which correlates with mucosal healing.

Methods: Thirty children with active CD were initiated on ENT providing either 100% (15 Italian, 6 Canadian) or 80% (9 US) of estimated caloric needs. PCDAI and FCP were evaluated at initiation and 8 weeks later. The 100% group received a polymeric formula (Modulen, Osmolite) while 80% ENT received a semi-elemental formula (Peptamen Jr) plus ad lib food. Steroid exposure was followed. Paired and unpaired t-tests were used to assess differences within and between treatment groups.

Results: The 100% and 80% groups had similar demographics and initial disease characteristics. The majority of the 80% group was exposed to steroids (7 of 9 children), while the 100% group had no exposure over 8 weeks. The mean decrease in FCP was 533 (p= 0.001) for 100% ENT and 281 (p= 0.23) for 80% ENT. Sub-analysis of the 80% group on no steroids or a stable dose for at least 14 days prior to ENT (n=5) showed a mean decline in FCP of 658 (p=0.01). The 80% group (n=4) started on steroids concurrent to ENT had a mean increase in FCP of 348 (p=0.19). The mean decrease in PCDAI over 8 weeks was 28.5 (p < 0.0001) for the 100% ENT group and 23.9 (p= 0.007) for the 80% ENT group. PCDAI change (p= 0.49) and final PCDAI (p=0.31) were similar between groups.

Conclusion: Children on 100% ENT and 80% ENT had significant decreases in PCDAI over 8 weeks, and the 100% group vs. 80% group on no steroids or a stable dose had similar decreases in FCP.

Disclosure of Interest: None Declared
THE MICROAEROPhilIC MICROBiOTA OF DE-NOVo PAEDIATRIC INFAMMAtORY BOWEL DISEASE: THE BISCUIT STUDY

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Objectives and Study: Children presenting for the first time with inflammatory bowel disease (IBD) offer a unique opportunity to study aetiological agents before the confounders of treatment. Microaerophilic bacteria can exploit the ecological niche of the intestinal epithelium; Helicobacter and Campylobacter are previously implicated in IBD pathogenesis. We set out to study these and other microaerophilic bacteria in de-novo paediatric IBD.

Methods: 100 children undergoing colonoscopy were recruited including 44 treatment naïve de-novo IBD patients and 42 with normal colons. Colonic biopsies were subjected to microaerophilic culture with Gram-negative isolates then identified by sequencing. Biopsies were also PCR screened for the specific microaerophilic bacterial groups: Helicobacteraceae, Campylobacteraceae and Sutterella wadsworthensis.

Results: 129 Gram-negative microaerophilic bacterial isolates were identified from 10 genera. The most frequently cultured was S. wadsworthensis (32 distinct isolates). Unusual Campylobacter were isolated from 8 subjects (including 3 C. concisus, 1 C. curvus, 1 C. lari, 1 C. rectus, 3 C. showae). No Helicobacter were cultured. When comparing IBD vs. normal colon control by PCR the prevalence figures were not significantly different (Helicobacter 11% vs. 12%, p=1.00; Campylobacter 75% vs. 76%, p=1.00; S. wadsworthensis 82% vs. 71%, p=0.31)

Conclusion: This study offers a comprehensive overview of the microaerophilic microbiota of the paediatric colon including at IBD onset. Campylobacter appear to be surprisingly common, can be isolated from around 8% of paediatric colonic biopsies but are not more strongly associated with IBD. S. wadsworthensis appears to be a common commensal. Helicobacter species are relatively rare in the paediatric colon.

Disclosure of Interest: None Declared
AN EVALUATION OF THE ‘YOUNG PEOPLE FRIENDLINESS’ OF THE IBD TRANSITION SERVICE IN A TERTIARY PAEDIATRIC CENTRE

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Objectives and Study: Our IBD transition pathway for young people (YP) was reorganised two years ago and a YP clinic was established alongwith new documentation. Assessment of “YP friendliness” of services was highlighted in the recent Department of Health (DoH) “You’re Welcome” policy, which provides a toolkit for self assessment of services seeing YP. A series of 48 criteria are split within 10 domains. A service can then be evaluated against these criteria and given the following levels – You’re welcome, Getting there, Not yet started and Not applicable. In order to achieve the “You’re Welcome” standard, 95% of the criteria must reach the “Meets You’re Welcome” level. Secondary to this, there are 9 crucial criteria which must also be met in order to achieve “You’re Welcome”.

Aims: 1.To audit the IBD transition service using the DoH You’re Welcome toolkit
2. To audit patient notes from the transition clinic against standards derived from the You’re Welcome toolkit (YW toolkit)

Methods: The YW toolkit published alongside the DoH’s “You’re Welcome” Health policy was used to evaluate the IBD transition service for ‘young people friendliness’. Case notes of patients seen in transition clinics in one month (November 2011) were then audited using standards derived from the YW toolkit.

Results: The IBD transition service was evaluated against 8 applicable domains.

<table>
<thead>
<tr>
<th>Domains</th>
<th>'You’re Welcome’ standard achieved</th>
<th>You're Welcome’ or ‘Getting There’ standard achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access</td>
<td>57%</td>
<td>86%</td>
</tr>
<tr>
<td>Publicity</td>
<td>40%</td>
<td>80%</td>
</tr>
<tr>
<td>Confidentiality and Consent</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Environment</td>
<td>60%</td>
<td>100%</td>
</tr>
<tr>
<td>Staff training, skills, attitudes and values</td>
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<td>100%</td>
</tr>
<tr>
<td>Joined up work</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Monitoring and evaluation</td>
<td>67%</td>
<td>100%</td>
</tr>
<tr>
<td>Health issues for YP</td>
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</tbody>
</table>

9 YP were seen in transition clinics in November 2011 and full set of notes were available for 7, whose notes were audited against the standards derived from the YW toolkit.

Standards such as opportunity to be seen alone offered, documentation assuring confidentiality, information sharing, annual transition plan, transition discussion and professionals present at consultation were documented in 100% of the
notes. A copy of the clinic letter addressed to the patient and information given regarding service was documented in 86% notes and evidence of sexual, mental and emotional health discussion with the YP was documented in 79% patient notes.

**Conclusion:** The IBD transition service achieved the ‘Getting there’ level on the YW toolkit. These results are relatively encouraging and identify areas that need improvement (access, publicity, environment and involvement of YP). The new transition documentation served as an aide-memoire in the YP and transition clinics to ensure adequate discussion with YP and their families.

**Disclosure of Interest:** None Declared
SAFETY OF ANTI-TUMOUR NECROSIS FACTOR ALPHA TREATMENT IN PATIENTS WITH COMBINED INFLAMMATORY BOWEL DISEASE AND CHRONIC LIVER DISEASE.

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Objectives and Study: The use of anti tumour necrosis factors alpha in paediatric population with concomitant inflammatory bowel disease and chronic liver disease is largely unknown. There are several reports of infliximab-induced hepatitis in the literature, when used in the treatment of inflammatory bowel disease. We aimed to review the safety profile of TNF alpha in patients with inflammatory bowel disease and chronic liver disease.

Methods: Case notes review of children with autoimmune liver disease treated with infliximab or adalimumab from 2009-2012.

Results: 6 patients (3 male and 3 female, age 13-18 years) were identified. 5 had Ulcerative Colitis and one had Crohn’s disease. 3 had autoimmune hepatitis (type 1 or 2) and 3 had a diagnosis of autoimmune sclerosing cholangitis (ASC). One of ASC was a post-liver transplant. 5/6 patients had deranged liver functions tests (LFT) prior to the onset of treatment. (see table). 4/6 patients were treated with infliximab (5mg/kg 8 weekly) and 2/6 with adalimumab (40mg s.c fortnightly). Mean age of initiation of treatment was 15 years and the longest duration of follow up was 36 months. LFT normalized in marginally elevated group and improved in significantly deranged group following treatment. There was an improvement in LFT in all the 5/6 patients. One patient whose LFT was normal prior to treatment continued to remain normal post treatment, there was no deterioration in LFT in any of the patients either treated with infliximab or adalimumab.

** treated with adalimumab

$ Autoimmune sclerosing cholangitis

<table>
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<tr>
<th>Case number</th>
<th>Mean bilirubin pre and post treatment (N&lt;20umol/L)</th>
<th>Mean AST pre and post treatment (N&lt;35 IU/L)</th>
<th>Mean GGT pre and post treatment (IU/L)</th>
<th>Mean ALT pre and post treatment (N&lt;55 IU/L)</th>
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</tr>
</tbody>
</table>

Conclusion: Anti-TNF therapy appears to be safe for treating IBD in patients with chronic liver disease and do not impair liver functions.
Disclosure of Interest: None Declared
Efficacy of Infliximab in Paediatric Ulcerative Colitis: Single Tertiary UK Centre Experience

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Objectives and Study: The role of Infliximab in the treatment of paediatric ulcerative colitis (UC) is increasingly recognised. The aim of our study was to evaluate the efficacy of Infliximab in children with ulcerative colitis who failed conventional treatment.

Methods: All children with UC who received Infliximab between April 2006 and October 2012 in our centre were identified. Clinical response and long term outcomes were assessed.

Results: Twenty eight (28) patients with moderate/severe UC were included in the study (17 males). Median age at histological diagnosis was 11.6 years (range 2.6y-15.2y), with median duration of disease prior to first Infliximab infusion 1.6y (5 weeks-5.5y) and median follow up post Infliximab regardless of outcome 1.6y (0.5y-5.4y).
Fifteen patients (15/28, 53.5%) responded initially to the treatment. Nine patients (9/15, 60%) had sustained clinical response at 5mg/kg 8 weekly with histological evidence of mucosal healing, with median duration of treatment 1.6y (0.7y-5.4y). In six patients (6/15) Infliximab had to be discontinued due to either loss of initial response or allergic reaction.
Out of 13 patients with partial or no response to Infliximab (13/28, 46.4%), 6 failed escalation of medical treatment with other immunosuppressive agents, including Adalimumab and Sirolimus, and underwent colectomy 1 month-11 months later (median 0.6y), at median age 13.7y (8.9y-15y).

Conclusion: Infliximab was efficacious in 53.5% of children with ulcerative colitis who failed conventional treatment, with response maintained in 60% of those patients. Therefore, Infliximab should be considered not only as rescue treatment, but also as maintenance treatment in children with refractory disease.

Disclosure of Interest: None Declared
CHANGE OF QUALITY OF LIFE DURING ONE YEAR INFlixIMAB THERAPY COURSE IN CHILDREN WITH CROHN'S DISEASE

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Objectives and Study: Quality of life (QoL) is not well known in children and adolescent patients with Inflammatory Bowel Disease. Most publications in this field have been focused on adults. The primary aim of this study was to determine the effects of one year infliximab treatment period in paediatric patient with Crohn’s disease (CD).

Methods: Our prospective study involved 51 children with conventional therapy resistant, severe CD (Mean age: 15.25 year, range: 11-18 year). IFX was given at week 0, 2 and 6, and maintenance therapy at every 8 weeks. During the infliximab courses the QoL of patients was measured by IMPACT-III questionnaire at week 0, 6, 30 and 54. At the same time, the Paediatric Crohn’s Disease Activity Index (PCDAI) score was determined to assess the disease severity. Moreover, some of the laboratory parameters, like serum C-reactive protein (CRP), numbers of serum thrombocyta and serum albumin were followed up. Statistical analyses were based on Friedman test, and Wilcoxon test as post-hoch analysis. Auto-regressive, cross-lagged models were used as well to assess relation between QoL and clinical parameters.

Results: The initial IMPACT-III scores (percentile-25, -50, -75 at week 0: 104, 116.5, 131) increased significantly (p<0.001) during IFX therapy (percentile-25, -50, -75 at week 54: 123, 141, 154.3). Clinical parameter improved also, notably; PCDAI, serum CRP, serum thrombocyta, serum albumin changed significantly (p<0.001). Autoregressive cross-lagged models of IMPACT-III and PCDAI fitted well (χ²=11.525, CFI=1.0, RMSEA=0.0). Auto-regressive regression coefficients (β value) were significant for each variable over time. Cross-relations between IMPACT-III and PCDAI over time were non-significant. The strongest cross-lagged relations were observed between IMPACT-III and serum albumin, respectively IMPACT-III and thrombocyta. However, the fit indices of these models indicated poor fit.

Conclusion: IFX treatment has beneficial clinical effect which is confirmed by decrease of PCDAI, CRP and thrombocyta levels, and increase of IMPACT-III and albumin levels. Regression analysis showed no cross lagged regression relation between IMPACT-III and PCDAI, however cross lagged relations between quality of life and clinical parameters needs further studies.

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Disclosure of Interest: None Declared
GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PO-G-0097

DIGESTIVE PERIANASTOMOTIC ULCERATIONS AFTER DIGESTIVE RESECTION IN INFANCY
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Objectives and Study: Few reports describe digestive perianastomotic ulcerations that develop after digestive resection in infancy. Some of their features may mimic Crohn’s disease. The aim of this study is to describe a small cohort of digestive perianastomotic ulcerations and to propose a physiopathological hypothesis.

Methods: Our study is a retrospective bi-center study of 12 patients operated during infancy. Clinical, biological, radiological, endoscopic and histological features were collected. Eleven patients were investigated for NOD2 polymorphisms.

Results: We describe 12 cases of perianastomotic ulcerations mostly at the ileocolonic anastomosis (n = 8). The median interval onset of symptoms and surgery was 11 years (range 5 - 26 years). Necrotizing enterocolitis in preterm infants is the most frequent underlying disease (n = 7). Patients mostly presented with diarrhea (n = 8), iron deficiency anemia (n = 10) and gastrointestinal blood loss (n = 5). Among 11 patients, 8 carry a polymorphism in NOD2 gene. Six of 12 patients are treated with immunosuppressive drugs and 4 have resection and revision of anastomosis.

Conclusion: In agreement with literature data, risk factors appear to predispose to postchirurgical perianastomotic ulcerations such as ileoceleal valve loss.
Management of postchirurgical perianastomotic ulcerations is not well established in the literature. The use of immunosuppressive drugs seems interesting.
Our study proposes a Crohn’s-like « model » for patients with a particular microbiota, who underwent surgery in infancy especially with ileoceleal valve loss. NOD2 polymorphism could act as a genetic predisposition.

Disclosure of Interest: None Declared
INFLUENZA VACCINATION UPTAKE IN INFLAMMATORY BOWEL DISEASE- IS THERE ROOM TO IMPROVE?
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Objectives and Study: The aim of our study is to assess the seasonal influenza vaccination uptake in patients with inflammatory bowel disease (IBD)

Methods: We have conducted a telephonic survey of our IBD patients in February 2012 to assess the influenza vaccination uptake for winter 2011-2012.

Results: 140 children had responded to this survey (61.6% of our IBD patients). 84 children had Crohn’s disease, 35 had Ulcerative colitis and 21 had IBD unclassified. Majority of these children (90/140) were on immunosuppressive treatments. 61 children (44%) had received seasonal influenza vaccination in that winter. 21 of them received in October, 20 in November, 13 in December and 3 in January. Out of the 79 children who have not received the influenza vaccine, 42 were not aware of the need for vaccination and did not have the influenza vaccine in the previous winters as well. 10 children were aware of the need for the influenza vaccine; however they opted not to receive the vaccine. 14 children intended to receive the vaccine, however this was deferred due to various reasons like intercurrent illness, family bereavement and difficulties experienced the General Practice surgery. Only one IBD patient needed hospitalisation in 2011 and 2012 with Influenza infection, however this was in July before the vaccination had started.

Discussion: Department of Health advises influenza vaccination for immunosuppressed individuals and also for children with medical conditions, who may need treatment with steroids for more than a month. European Crohn’s and Colitis Organisation (ECCO) recommend influenza vaccination for IBD patients on immunomodulators. Experience from Philadelphia, Boston and Poland show that good, but variable, antibody response occurs after influenza vaccination in children and better protection occurs against type A strains. Side effects, both local and systemic, are generally mild. Experience from Australia and Germany show that the seasonal flu vaccination uptake in IBD patients are generally low, 10% and 16% respectively. We would like to hear from other centres about their experience of influenza vaccination uptake in IBD patients. Further efforts need to be done to increase the awareness of influenza vaccination in patients with IBD.

Conclusion: Influenza vaccination uptake in our IBD patients are better than reported from other centres, however further work needs to be done both locally and nationally to improve the influenza vaccination uptake.

Disclosure of Interest: None Declared
COMPARISON OF MR ENTEROCLYSIS AND MR ENTEROGRAPHY FINDINGS WITH ENDOSCOPIC FINDINGS IN PAEDIATRIC PATIENTS WITH SMALL BOWEL DISEASE

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Objectives and Study: The purpose of this study was to evaluate the efficacy of MR enterography and MR enteroclysis in paediatric patients with suspected small bowel disease compared to ileocolonoscopy and histology. The route of contrast administration, the image quality and bowel distention, the side effects, and performance estimates of MR enterography and MR enteroclysis were also evaluated.

Methods: A retrospective analysis of the pediatric gastroenterology clinic database (2010-2012) was performed. Twenty MR enterography studies and six MR enteroclysis studies in twenty one patients were performed without sedation. The main indications were obscure gastrointestinal bleeding (n = 2), suspected Crohn’s disease (n = 17), suspected eosinophilic gastroenteropathy (n = 1) and familial polyposis (n = 1). A water solution containing mannitol 5% was administered orally or through a nasojejunal tube. Patients were imaged on a 1.5-T MR scanner with T1-weighted and T2-weighted sequences. Retrospectively, image quality, mucosal lesions and inflammation were assessed. Correlation between radiographic findings and endoscopic findings was tested by the Fisher exact test.

Results: Twenty MR enterography studies and six MR enteroclysis studies in twenty one patients were performed without sedation (mean age, 13.6 years; age range, 5-16 years) over 24 months. Patients who failed to cooperate or drink the contrast media were selected for MR enteroclysis. A jejunal feeding tube with a single lumen was inserted into the stomach and subsequently self- advance into the small bowel via peristalsis. The results of the MRE were compared to the colonoscopy and pathology reports to determine the presence or absence of disease in evaluable bowel segments. The amount of oral contrast material ingested correlated with patient age (p = 0.005), with acceptable bowel distention occurring in 88%. The overall sensitivity and specificity of MRE (using endoscopy as a gold standard) were 80% and 75% respectively (kappa=0.65). Sensitivity and specificity of MR enterography and MR enteroclysis for active disease of the terminal ileum, right colon, and left colon were 88% and 83.2%, 69.1% and 67.8%, and 92.3% and 67.6%, respectively.

Conclusion: MR enterography and MR enteroclysis are feasible in patients 5 years old and older without sedation. Oral contrast ingestion regimes can be based on patient age and administration of the contrast agent through a self advancing jejunal tube is an option in selected patients. MRE compares favorably to ileocolonoscopy for evaluation of known or suspected Crohn’s disease noninvasively.

Disclosure of Interest: None Declared
POST-OPERATIVE COMPLICATIONS IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY
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**Objectives and Study:** We sought to describe in a paediatric population-based cohort the incidence of and factors associated with post-operative complications in inflammatory bowel disease (IBD).

**Methods:** Using the population-based EPIMAD Registry (Northern France), we identified all children who underwent at least one major abdominal surgery for IBD among 692 incident cases with Crohn’s disease (CD) (n=532) or ulcerative colitis (UC) (n=160) diagnosed between 1988 and 2004. Median age at first major abdominal surgery was 16 years [Q1=14-Q3=16]. Medical records were reviewed for early (within 30 days of surgery) and late (≥ 30 days) complications which were graded according to Dindo’s criteria (1). Factors associated with complication were assessed using multivariate Cox models and expressed as hazard ratios (HR) with 95% confidence intervals (CI).

**Results:** Among 153 IBD patients (22%) who underwent at least one major abdominal surgery until December 2009, 76 (49.7%) experienced at least one post-operative complication with a total of 113 complications; 51 patients had one complication and 25 more than one. The frequency of severe post-operative complications (grade>2) was similar in CD and UC (28% vs 27%; p=0.95). A total of 64 early complications was observed in 47 patients (31%), with 32 infectious and 32 non-infectious. A total of 49 late complications was observed in 37 patients (24%), with 5 infectious and 44 non-infectious. The cumulative probability of any post-operative complication was 31% (95% CI, 24-39) at 6 months, 45% (38-54) at 1 year and 48% (40-56) at 5 years. No death occurred. Multivariate analysis found that the type of IBD was the only factor associated with any post-operative complication (HR relative to UC vs. CD, 2.2; 95% CI, 1.3-3.9). Age, gender, systemic steroid, immunosuppressive therapy during the 3 months before abdominal surgery were not risk factors.

**Conclusion:** About one half of paediatric patients with IBD experienced at least one post-operative complication that occurred either early (31%) or late (24%). Only UC relative to CD was significantly associated with an increased risk of post-operative complications.


**Disclosure of Interest:** None Declared
FREQUENCY OF CORTICOSTEROID USE FOR FIRST INDUCTION OF REMISSION AND CLINICAL RESPONSE OUTCOMES IN PATIENTS WITH NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Retrospective cohort study of patients diagnosed with inflammatory bowel disease and treated with corticosteroids (C/S) in a paediatric tertiary unit. Objectives: to assess use of combination therapy at 30 days and one year after diagnosis and investigate impact on one year clinical outcomes for steroid responsiveness.

Methods: Snap10 Survey software and Microsoft Excel 2007 were used for data input/analysis. 110 patients were diagnosed over 18 months; 61 with Crohn's (CD) and 49 with ulcerative colitis (UC). Clinical outcomes for steroid responsiveness defined as per Tung et al (1).

Results: CD: 6.5% required C/S; the large majority received enteral feeds for induction of remission. No further analysis of this group was performed due to the very small absolute number of C/S treated patients (four).

UC: 86% received C/S at diagnosis (n=40); 70% and 27.5% of C/S treated showed complete and partial clinical response respectively at 30 days, 2.5% were C/S refractory; 60% relapsed within one year, surgery rate was 0%

Higher than reported (2,3) prolonged response rate (65% vs 45%) and lower C/S dependency rate (35% vs 45%) were noted at one year. This may be partly due to the fact that 22.5% of patients on both azathioprine and 5ASA at one year, had been started on them within one month of diagnosis of acute severe colitis. 38% relative risk reduction in C/S dependency risk at one year was noted in patients on combined treatment at 30 days post diagnosis when compared to patients started only on 5ASA within the first 30 days (RR 1.62, 95% CI 0.77, 3.36). No side effects were reported. The C/S refractory patient received infliximab and was excluded from this subgroup analysis.

Conclusion: Our study supports early combination of thiopurines and 5ASA for acute severe UC in order to achieve prolonged clinical response and reduce C/S dependency rate at one year post diagnosis; larger prospective cohort studies and randomised controlled trials are required to investigate potential benefits and risks.


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GASTROENTEROLOGY
INFLAMMATORY BOWEL DISEASE

PO-G-0102

BENEFICIAL EFFECT OF ANTI-TNF TREATMENT IN NUTRITIONAL STATUS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE.
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Objectives and Study: Tumor necrosis alpha factor (TNF-α) plays an important role in malnutrition and growth retardation in pediatric inflammatory bowel disease (IBD) due to perpetuation of chronic inflammation. One of the objectives in the management of these patients should be to optimize their growth, which may be compromised due to uncontrolled disease and the effect of steroids. Our aim is to study anti-TNF treatment effect on nutritional recovery in pediatric IBD, in relation to their efficacy in clinical response, both in short- and medium-term.

Methods: Retrospective analysis of our pediatric IBD patients treated with anti-TNFα between January 2002 and December 2010. We evaluated clinical response as defined by changes in activity scores (Pediatric Crohn's Disease Activity Index (PCDAI) for Crohn's disease and Pediatric Ulcerative Colitis Activity Index (PUCAI) for Ulcerative Colitis) at 2 and 8 weeks, 6 months and 1 year after its initiation, changes in anthropometric measures (height and weight for age and body mass index –BMI- at 6 months and 1 year) and biochemical modifications (ESR, CRP, hemoglobin, platelets and albumin at 6 months and 1 year).

Results: 54 patients (34 boys) received anti-TNF in this period (44 Crohn's disease, 8 ulcerative colitis and 2 IBD unclassified). Age at diagnosis: 11 years 5 months. Mean time from diagnosis to anti-TNF treatment: 17 months (range 0-121). Mean age at first infusion 13 years (range 1.1 to 17.3). Mean follow-up 35 months and mean number of infusions per patient 17 (1-70). Forty-one patients received infliximab (IFX), 21 adalimumab (ADA) and 1 certolizumab pegol. Thirty-one patients (63%) had not previously received steroids. Mean PCDAI and PUCAI before anti-TNF: 28.6 (2.5 to 62) and 39 (27-55) respectively. Clinical response was achieved in 47 cases (87%). Remission rate was 74.2% at 2 weeks, 87.7% at 8 weeks, 90% at 6 months, and 90.6% at 12 months. Seven patients experienced a relapse at some point of the follow-up. Median steroid-free time from the beginning of anti-TNF was 25.9 months (1-76 months). Mean BMI prior to treatment was 17, z-score -1.04 (-4.2 + 1.64). We observed improvement of the anthropometric measures, with a mean BMI of 19.2 (z-score - 0.27 (-2.3 +1.78)) after 12 months. Biochemical parameters improvement was also observed at 6 and 12 months after treatment, with significant reduction of inflammatory markers and increase in hemoglobin and albumin levels.

Conclusion: Anti-TNFα treatment shows high efficacy in obtaining and maintaining clinical remission in pediatric IBD. Furthermore it has a positive impact on the nutritional status as shown by an improvement in BMI. This effect is parallel to the decrease in disease activity.

Disclosure of Interest: None Declared
EFFICACY OF INFliximAB IN THE TREATMENT OF ULCERATIVE COLITIS IN CHILDREN.
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Objectives and Study: Infliximab is the first biological agents that has proven its efficacy in the management of steroid dependent and steroid resistant ulcerative colitis treatment. The principal purpose of the study was to investigate efficacy of infliximab to achieve a clinical and endoscopic remission of ulcerative colitis in children.

Methods: The study included 13 children diagnosed with steroid dependent or steroid resistant ulcerative colitis aged 3.5 to 18 years (mean age at diagnosis was 11.7±3.6 years). All 13 children received infliximab (5mg/kg) in three repeated infusions at 0, 2, 6 weeks. 9 children were qualified to the maintenance therapy with repeat infliximab every 8 weeks. The disease clinical activity was assessed by Pediatric Ulcerative Colitis Activity Index (PUCAI) and endoscopic activity was scored using the Rachmilewitz endoscopic activity index (1998). To the moment of beginning of infliximab therapy 9 children (69.2%) had activity of severe disease (PUCAI 65-85), 4 children (30.8%) had activity of moderate disease (PUCAI 30-65) disease. The results (decrease from baseline in the PUCAI score > or = 57 points; total score < or =8; and Rachmilewitz endoscopic activity index score > or = 5 points; total score < or =4) were evaluated at weeks 12 (after induction therapy) and 54 (after 1 year therapy).

Results: Efficacy of infliximab induction therapy was 85%, while 62% children clinical remission. After 1 year of therapy efficacy of therapy was observed in 89%, clinical remission was reduced to 67%. Endoscopic remission rate after induction therapy was observed in 15%. After 1 year of treatment 43% of children achieved endoscopic remission.

Conclusion: report the high effectiveness of infliximab for UC. However the ability of maintenance infliximab (IFX) treatment to achieve mucosal healing is poor.

Disclosure of Interest: None Declared
INFLAMMATORY BOWEL DISEASE AND FAMILIAL MEDITERRANEAN FEVER

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Objectives and Study: It is reported that familial mediterranean fever (FMF) is diagnosed frequently with inflammatory bowel disease. Our aim in this present study is to determine the frequency of FMF and mutations of MEFV in patients diagnosed IBD in pediatric gastroenterology unit.

Methods: Thirty four patients diagnosed inflammatory bowel disease according to clinic, endoscopic, radiologic findings were enrolled in the study. DNA samples of the patients were screened for the twelve mutation at FMF gene.

Results: Fifteen patients (44.1%) diagnosed crohn’s disease (CD), 13 patients (38.2 %) diagnosed ulcerative colitis (CU) and 6 patients (17.6 %) diagnosed indeterminate colitis (IC) were in the follow-up of pediatric gastroenterology outpatient clinic. Of all patients 19 (55.9 %) were girls and 15 (44.1 %) were boys. Mean age of the patients was 13.2±3.1 (8-19) years and mean age at diagnosis was 11.7 ±3.2(3-17) years. The mutation of MEFV was found nineteen of sixty eight allele (57.9 %). The most common mutations frequently observed were M694V, R202Q and E148Q. FMF is diagnosed in 21 patients with IBD after clinical and laboratory evaluation. Of these patients 16 had MEFV mutations but five patients were diagnosed FMF clinically and laboratory findings despite lack of mutations. FMF was diagnosed 61.8% of the IBD patients. Ten of these patients (47.6%) were CU, 9 of them (42.8%) were CD and 3 of them (14.3 %) were IC. Demographics, laboratory evaluations, growth parameters, extraintestinal manifestations, and treatment with immunosuppressive agents other than steroids were not different statistically in patients with and without FMF

Conclusion: MEVF mutations and FMF disease rate with IBD were found more frequently than known in Turkish children in this study. FMF must be kept in mind in the patients with IBD especially in the countries FMF prevelance increased.

Disclosure of Interest: None Declared
ANAEMIA AND QUALITY OF LIFE IN PAEDIATRIC IBD PATIENTS
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Objectives and Study: Anaemia is a common complication of inflammatory bowel disease (IBD). Quality of life (QoL) and cognitive function (CF) are impaired in patients with anaemia which is associated with chronic disease and IBD in adults. Iron deficiency and chronic disease are the main contributors to anaemia in IBD. There are no reports addressing the relevance of anaemia as a QoL contributor in Pediatric IBD as well as its predictive role in QoL scores. The primary aim of this study was to examine whether changes in Hb and ferritin levels in a population of IBD patients were associated with significant changes in QoL, independent of changes in disease activity (DA).

Methods: A cohort of 48 patients with IBD took part in a prospective observational study. Measures of Hb, serum iron, ferritin and B12 vitamin levels were performed at outpatient visits and QoL and DA were recorded. Anaemia was classified according to predefined sex and age reference values. Ferritin levels were stratified in centile distribution (25, 50 and 75). Iron levels were below 50 µg/dl were classified as low.

Results: The group of 48 patients was composed of 39 Crohn’s disease (81.3%) and 9 ulcerative colitis (18.8%). QoL was assessed by IMPACT III questionnaire, previously validated to Portuguese. The average of QoL was 140.75 (SD±20.48; 92-171). Clinical remission of disease was observed in 97.9% of patients. The majority of cases were diagnosed for more than 12 months (70.8%). 15 of the 48 patients (31.3%) had anaemia and 59.5% had ferritin levels below the 50th percentile. Low iron level was present in 31.7%. There was no correlation between global QoL and hemoglobin, iron or ferritin levels. Average QoL was lower in female group (p 0.004) than in the male group.

Conclusion: Activity of disease did not affect QoL scores in this group of patients. Ferritin levels may be a clinical predictor of low QoL in paediatric IBD patients. These results suggest that mild anaemia even with low iron and ferritin may not interfere substantially with quality of life in adolescents with IBD. This is the first report concerning QoL and iron metabolism in paediatric IBD. Future studies are needed to address this issue.

Disclosure of Interest: None Declared
MONOUNSATURATED C40 GM3 AND C34 GM3 CONSTITUTE TO MOST ABUNDANT GANGLIOSIDES IN BOWEL FROM CROHN’S DISEASE
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Objectives and Study: Crohn’s disease is an inflammatory disorder of unknown etiology. Management of this chronic inflammatory condition is difficult and consists mainly of drug treatment and surgery. There is no cure for Crohn’s disease. Gangliosides are glycolipids that impact cell growth, signaling, and differentiation and therefore influence health and disease. It has been shown in experimental studies that ganglioside degradation creates a pro-inflammatory environment. Treatment with ganglioside was shown to prevent inflammatory signaling by decreasing production of pro-inflammatory mediators. Previous literature has reported the profile of gangliosides in specimens of healthy human bowel, but little is known about the profile of gangliosides in diseased states. Compositional data regarding the fatty acid tail of gangliosides is also lacking. In the present study, the detailed profile of ganglioside species in bowel specimens from Crohn’s disease patients is presented.

Methods: Surgical specimens of apical terminal ileum or bowel were obtained from subjects with active Crohn’s disease undergoing bowel resection or colectomy. Healthy regions of bowel excised from colon cancer patients served as controls. Bowel tissue was mechanically homogenized and subjected to a Folch extraction to isolate the gangliosides. Extracts were injected onto a C18 column where the gangliosides were separated by reverse-phase chromatography prior to detection by an Agilent 6430 triple-Quad LC/MS operated in multiple reaction monitoring mode. The cells were screened against a database of 120 mono-, di- and trisialylated gangliosides.

Results: As a proportion of total ganglioside, GM3 constituted the most abundant glycolipid followed by GD3 with only minor contributions from GD1 and GT1. There was a trend toward decreased GM3 content as a proportion of total ganglioside in Crohn’s disease specimens compared with normal bowel. The ratio of GM3:GD3 for monounsaturated C34 ganglioside was 4.0, and the ratio of GM3:GD3 for monounsaturated C40 ganglioside was 2.5 (p < 0.05).

Conclusion: Catabolism of monounsaturated C34 GD3 into respective GM3 metabolite may occur more frequently than catabolism of monounsaturated C40 GD3. Fatty acid composition may influence enzymatic degradation of ganglioside species. Ganglioside catabolism contributes to a deleterious pro-inflammatory environment and may represent a viable target for treatment of Crohn’s disease and management of bowel inflammation. Consumption of specific dietary gangliosides may increase ganglioside content of the bowel mucosa to alleviate inflammatory conditions.

Disclosure of Interest: None Declared
ANEMIA EVOLUTION OVER TIME IN CHILDREN WITH CROHN’S DISEASE. RESULTS OF THE BELCRO COHORT.
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Objectives and Study: To describe the therapeutic interventions for and the evolution of anemia over 2 years in the prospective BELCRO cohort (Belgian registry for pediatric Crohn’s disease).

Methods: Clinical and laboratory data at diagnosis (M0), 12m (M12) and 24 (M24) months were analysed using IBM-SPSS20. Anemia was considered mild for hemoglobin (Hb) z-score between -4 and -2 S.D. and severe for z-score < -4 S.D. In case of persistent Crohn’s disease activity, anemia was categorized as anemia of chronic disease (ACD) with or without iron deficiency. In case of remission anemia possible iron deficiency anemia (PIDA) was considered.

Results: At M0 Hb values, available from 88/98 patients, shows a median z-score of -2.67 (-8.4, 1.07). Anemia was present in 54 patients (61%), classified as mild in 32 and severe in 22. Hb z-score was associated with disease severity at M0 (P = 0.013) but not at M12 and 24. There was no association between age at diagnosis, duration of symptoms before diagnosis, BMI z-score or height z-score and Hb z-score. Hb improved significantly (P < 0.0001) over time. However, 38% (28/74) (24 mild, 4 severe) of patients had anemia at M12 of which 16 ACD and 12 PIDA. At M24, 38% (31/81) still suffered from anemia (11 mild, 20 severe) of which 11 ACD and 20 PIDA. Iron treatment was prescribed to 14 of which only 1 patient received it intravenously (50% of anemic patients) and 21 (68%) patients at M12 and 24 respectively.

Conclusion: Anemia remains an important problem in the follow up of children with Crohn’s disease. The prescription of oral iron therapy appears to be insufficiently effective.

Disclosure of Interest: None Declared
DIFFERENCES IN THE INTESTINAL MICROBIOTA COMPOSITION IN CHILDREN WITH PERVERSIVE DEVELOPMENTAL DISORDERS AND HEALTHY CONTROLS

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**Objectives and Study:** Children with autistic spectrum disorders (ASD) suffer of gastrointestinal problems more often than healthy children, suggesting a possible role of intestinal microbiota in symptoms determination and severity. The objectives of this study were: to compare the composition of the intestinal bacteria (gut microbiota) of fecal samples obtained from patients diagnosed with DPS compared to a healthy siblings in order to identify differences in the composition.

**Methods:** 20 subjects with DPS (17 males and 3 females) and 20 non-DPS siblings (8 males and 12 females), control subjects considered, were enrolled. Patients were classified (ADOS and ADI-R scales of assessment) into 2 categories of severity: severe (SA) (50%) and mild autism (MA) (50%). Faecal bacterial populations were assessed through the use of a culture-dependent technique. For this study we used 12 growth media (Reinforced clostridial, Mannitol Salt Agar, Slanetz and Bartley, Rogosa, Glucose-M17,Wilkins-Chalgren agar+GN,GSP, MacConkey agar N.2, Wilkins-Chalgren agar base, PCA, Bifidobacterium agar modified, MRS). The results obtained were processed using PCA (Principal Component Analysis Statistics).

**Results:** The faecal flora of ASD patients contained lower levels of Enterococci than that of healthy siblings (6,9 vs. 7,5 log UFC/g; p<0,04). The difference was present in both MA and SA as compared to the controls (6 vs. 7,2 log UFC/g; p<0,05 and 7,2 vs. 7,8 log UFC/g; p<0,04). Children with severe autism had lower levels of Staphylococci (6 vs. 6,8 log UFC/g; p<0,05) and higher levels of Clostridia (4,1 vs. 3,1 log UFC/g; p<0,04). Total bacteria, Bacteroidetes, Enterobacteria, Lactobacilli, Bifidobacteria, Pseudomonas and Aeromonas did not show significant variation among the different groups, using standard culture growth-based techniques. PCA confirmed that ASD patients have a poor microbiota with Clostridia prevailing and Enterococci being less represented as compared to controls.

**Conclusion:** Our study show that the microbiota of children with ASD has significant differences compared to healthy siblings for the presence of a significantly lower rate of Enterococci, Staphylococci and an higher rates of Clostridia. Our study allowed to identify changes in the microbiota in pairs of siblings healthy/sick and not only in controls in the general population, virtually eliminating the bias secondary to different lifestyles, nutrition and genetics.

**Disclosure of Interest:** None Declared
Objectives and Study: Eosinophilic esophagitis (EoE) is a novel chronic inflammatory immune-mediated esophageal disease. We observe the increase in incidence of newly diagnosed cases of EoE, but data in pediatric population are still limited. The aim of the study was to characterize the clinical symptoms, endoscopic features and histology of EoE in children with newly diagnosed EoE in patients hospitalized in one pediatric centre.

Methods: We retrospectively reviewed the clinical records for all patients diagnosed with EoE in one hospital-Medical University of Warsaw for over 3 years (November 2009-October 2012). The diagnosis was based on clinical, endoscopical and histological features typical for EoE. We analyzed typical symptoms: abdominal pain, vomiting, dysphagia, odynophagia, loss of appetite. The endoscopic features we assessed were: vertical furrowing, white plaques, trachealization, oedema, erythema. The histological criteria we applied to this study were: >15 eosinophils in at least one high power field (HPF).

Results: We recruited 20 children (14 boys, 6 girls); aged 1 ½ - 18 years (median age 10 1/6 years). Clinical symptoms were: abdominal pain in 12 patients (pts), vomiting in 3, dysphagia in 2, odynophagia in 2, loss of appetite in 6 and failure to thrive in 2 pts. 16 (80%) children had positive personal history of any allergic disease (asthma, food allergy, eczema). In 13/20 (65%) IgE was assessed and in more than half of them 7/13 (54%) it was elevated. The most common macroscopic features were: trachealization in 5/20 pts and white plaques in 5/20 pts. Other typical findings like: vertical furrowing in 2/20, oedema in 2/20, erythema in 2/20 were rare. Macroscopically normal oesophagus was observed in 5/20. The vast majority of children 16 (80%) had >30 eosinophils per HPF on histological assessment, among them 4/16 (25%) had very high eosinophil infiltration (>60HPF). Each of those 4 pts(EOS>60HPF) had macroscopically normal mucosa and each of them had only one clinical symptom: 2 of them failure to thrive and 2 others abdominal pain.

Conclusion: The majority of patients with EoE had positive allergic history. Abdominal pain was the most common clinical symptom in patients with EoE. Trachealization, white plaques as well as normal mucosa were the most common findings at endoscopy. There is the inconsistency between clinical symptoms, macroscopic features on endoscopy and microscopic findings in children with newly diagnosed EoE. Our study indicate that in patients with any kind of allergy and clinical symptoms for EoE we should take multiple biopsies from esophagus even with no macroscopic findings on endoscopy.

Disclosure of Interest: None Declared
ANTIBIOTIC ASSOCIATED DIARRHEA IN CHILDREN: WHAT HAPPENS IN REAL LIFE?
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Objectives and Study: Data on the use of probiotics in the prevention of antibiotic associated diarrhea (AAD) in children are limited. Prescription of probiotics during antibiotic treatment is controversial for both scientific and economical reasons. The aims of this study were to assess the incidence of AAD in children and the effect of concomitant probiotic administration.

Methods: All children discharged from Emergency Department (of 4 different hospitals) with an antibiotic prescription were enrolled. A phone recall with a standardised interview was made after 1 month. Age, site of infection, antibiotic treatment, probiotic supplementation, occurrence, duration and severity of diarrhea were recorded. AAD was defined as the presence of diarrhea (at least 3 liquid stools in 24 hours) within 2 weeks of discharge without signs of a new infection.

Results: 322 (mean age±SD 54±42 months, median age 43 months, 177 male) completed the follow-up so far. AAD was reported overall in 42/322 (13%) children (median age 21 months), and in 25/92 (27%) subjects younger than 24 months. No case of hospital admission for AAD occurred. Duration of AAD was 1-15 days with 3-15 stools per day. Amoxicillin-clavulanate was the most frequent prescribed antibiotic (171/322 children, 53%) and AAD occurred in 27 (16%) of these patients. AAD was reported in 31/217 (14%) children with probiotic compared to 11/105 (11%) without probiotic supplementation. In 64/217 (29.5%) of children the probiotic supplementation was not suggested by the doctors. The most frequent probiotic strains used were: Lactobacillus GG (n=114), Lactobacillus reuteri (n=55) and Bacillus clausii (n=27). No significant difference on AAD was present among different probiotic supplementation.

Conclusion: AAD occurred in 1:8 children and in 1:4 children younger than 2 years but with mild severity not requiring hospital admission. In our population probiotic supplementation was commonly used but without a protective effect on AAD.

Disclosure of Interest: None Declared
15 YEAR EXPERIENCE OF CLINICAL PRESENTATION OF INTESTINAL VOLVULUS AT A QUARTERNARY GASTROENTEROLOGY CENTRE
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Objectives and Study: Intestinal volvulus can cause potentially fatal bowel ischaemia and/or obstruction. Diagnosis can be difficult and easily missed. Presenting symptoms are variable and there are no published studies describing the clinical presentation in children. Earlier diagnosis may reduce morbidity and mortality. Malrotation is a common underlying cause of volvulus and can be asymptomatic, or present with varied gastrointestinal symptoms at all ages[i]. The aim of this study is to describe our experience over 15 years of the presenting symptoms, age and past history of children presenting with volvulus.

Methods: This study is based on a retrospective case notes review of: 1. All children known to the gastroenterology department. 2. All children identified by the clinical coding department at our hospital as having a volvulus event. 3. Cases known to the histopathology team.

Results: 30 cases were reviewed. The age at presentation was variable with 24/30 (80%) presenting by 11 years, leaving a significant minority not presenting until adolescence. The majority of children (90%) presented with vomiting but in a third of cases it was non-bilious. Only 6/30 (20%) of children presented with all the classic symptoms and signs of volvulus: bilious vomiting, abdominal pain, abdominal distention, and constipation. The majority of children (18/30) had a past history of recurrent abdominal pain for which medical attention had been sought. 11/30 (37%) had a past history of unexplained vomiting and 8/30 (27%) had previous isolated nausea. The minority of children (6/30) had no gastrointestinal symptoms prior to their acute presentation with volvulus.

Conclusion: Presenting features of acute volvulus are variable and can be confusing. An awareness of the possibility that symptoms and signs may not be classic could be life saving for children and prevent a tragic missed diagnosis. Malrotation is a possible cause of highly non-specific symptoms and should remain part of the differential diagnosis in patients for whom a clear cause of chronic gastrointestinal symptoms cannot be identified.


Disclosure of Interest: None Declared
INFLUENCE OF THE COMCOMITAMNT PATHOLOGY ON MORPHOLOGICAL CHARACTERISTICS IN CHILDREN WITH CHRONIC GASTRITIS

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Objectives and Study: Chronic gastritis in children has high rate co-morbidity (as minimum more than one half children has more than 3 accompanied diseases), but this fact is underestimated in investigation and treatment of a basis disease.

OBJECTIVE: To estimate the spectrum of gastrointestinal and extra intestinal associated pathology in children with chronic gastritis, and to assess the influence of concomitant diseases on morphological characteristics of gastritis.

Methods: 360 children aged 13-15 years old (boys: girls – 148:212, average age – 13.2±1.8 years) with morphologically proved chronic gastritis with a mean duration of the disease 3.6±0.74 years have been investigated. We have calculated the index of co-morbidity (IC) as a sum of accompanied pathologies. 90 patients have been investigated repeatedly 6 months after the successful eradication of Helicobacter pylori infection.

Results: The spectrum of gastrointestinal associated pathology has included functional disorders of gastrointestinal tract (GIT): biliary sludge – 28.8%, dysfunction of sphincter Oddy (pancreatic type) – 34.4%, irritable bowel syndrome – 30%, chronic constipation -22%. Extra intestinal associated pathology has been characterized by presence of nutritional status disorders (obesity-23%, dyslipidemia-23%, deficiency of body weight-28%), neuropsychological problems (anxiety-23%, subdepression-25%, asthenic syndrome-46%), musculoskeletal system disorders – scoliosis (25%), endocrine system pathology (hyperplasia of thyroid gland-35.5%), prolapsis of mitral valve-22%.

Low IC (less than 3 associated diseases) has been found in 55% of patients, moderate (4-5 concomitant diseases) – 30% of children, high index (more than 6 pathological conditions) – in 15% of patients. Index of co-morbidity more than 4 in all the cases has been accompanied with the presence of morphological features of chronic gastritis in the stage of remission. Initially all the patients with index of co-morbidity more than 3 have higher contamination rate of H.pylori, more intensive lymphoplasmocytic infiltration both as in fundic part and antral part of the stomach. Atrophic changes have been found in 33.3% patients with IC >4 as compared with 12.2% children with IC <3 (p=0.038).

Conclusion: Chronic gastritis in children is commonly associated with broad spectrum of concomitant gastrointestinal and extra intestinal co-morbid pathologies. 45% of patients have 3 and more associated pathological conditions. Index of co-morbidity more than 3 is associated with more intensive inflammatory changes (infiltration), contamination by H.pylori and presence of atrophy 6 months after successful eradication of infection.

Disclosure of Interest: None Declared
INSIGHTS INTO NEC AND INFECTION FROM MOLECULAR ANALYSIS OF GUT MICROBIOTA IN PRETERM MULTIPLES

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Objectives and Study: Gut microbiota in preterm infants influences health and disease states. Twin cohorts allow exploration of environmental and demographic affects on gut microbiome. We compared gut microbiota in premature twins focusing on dysbiosis and its role in NEC and late onset infection.

Methods: Stool (n=191) from 29 infants (13 twin pairs, 1 triplet set) was assessed using 16S rRNA, with amplicons visualised using denaturant gradient gel electrophoresis (DGGE). Bands were excised and sequenced to obtain taxonomic classification. Profiles were subject to partial least squares discriminant analysis (PLS-DA).

Results: Profiles from siblings were more similar to each other than to unrelated profiles (Fig 1). Exceptions, (samples outside the ellipse defining the 95%CI), were from infants who developed NEC or sepsis and the triplets. Enterococcus and Actinomyces were significantly (P<0.005) more abundant pre and post NEC, respectively. Enterococcus were found in higher levels in infants delivered by caesarean section (P<0.005), whereas Actinomyces predominated in vaginal births (P=0.001) (Fig 2). Although lower in abundance, Corynebacterium was also significantly associated with pre NEC samples (P<0.005). Where several pre NEC samples were available, both diversity indices and evenness were reduced in the affected twin preceding clinical NEC.

Conclusion: Bacterial communities in related twins are more similar than from non-related twins and differences were identified that may predispose to disease. As seen in other cohorts bacterial diversity reduced before clinical NEC occurred, and evenness fell. Diversity also reduced in healthy patients at similar ages but evenness increased: in diseased infants this reduction in commensal bacteria may allow dominance of a pathogen. We identified Enterococcus and Corynebacterium as potentially implicated candidate organisms.

Disclosure of Interest: None Declared
Objectives and Study: Potentially curative treatment options are becoming available for cystic fibrosis patients. Therapeutic trials are performed in increasingly younger, healthier patients. As a result current established outcome measures for in clinical trials in Cystic Fibrosis like pulmonary function (FEV1) and anthropometry will no longer be suitable to detect significant treatment effects. However, the gastrointestinal phenotype of CF disease presents often early in life. In this study, on behalf of the ESPGHAN CF working group, we reviewed potentially gastrointestinal outcome measures for future clinical trials in cystic fibrosis.

Methods: Based on an expert based evaluation within the ESPGHAN CF working group we performed a retrospective literature analysis of potential gastrointestinal outcome measures. Outcome measures were subdivided in either measuring CFTR function or organ dysfunction. We performed a descriptive analysis based on clinical or disease relevance, reliability, validity, responsiveness to interventions, feasibility in particular in young children and the availability of reference values.

Results: Intestinal electric current measurement (ICM) and CFTR function measurement in intestinal organoids have the potential to function as ex-vivo outcome parameters for CFTR function. In the category of CFTR related organ dysfunction intestinal pH, intestinal motility, intestinal permeability, intestinal inflammation markers in particular fecal calprotectine) and intestinal bile salt malabsorption offer the possibility to develop into new outcome measures.

Conclusion: The gastrointestinal tract offers a variety of potential outcome measures for new therapeutic outcome measures in CF. However in the wake of new therapeutic strategies for Cystic fibrosis additional, stringent, research is need to further develop and validate these outcome measures. For this we need a combined research effort of the combined stakeholders including, clinicians, pharmaceutical companies and regulators.

Disclosure of Interest: None Declared
NO EVIDENCE FOR A PROVOKING ROLE OF NUTRITIONAL FACTORS IN DISTAL INTESTINAL OBSTRUCTION SYNDROME (DIOS)

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Objective and Study: The etiology of DIOS remains unclear. Food and pancreatic enzyme replacement therapy (PERT) intake are often blamed for its occurrence. We evaluated in this study the nutritional and PERT intake of cystic fibrosis (CF) patients at a first DIOS attack.

Methods: All CF patients complete annually a 3-day-intake diary of their caloric, protein, fat, dietary fiber, liquid and PERT intake. Patients diagnosed with a first DIOS attack (n = 12) retrospectively filled in an intake diary of the 3 days preceding the DIOS episode supervised by an expert dietitian. Results were compared to those of one year before and also of 36 CF controls matched for age, sex, genotype and disease severity. All were pancreatic insufficient.

Results: A first DIOS episode was diagnosed in 12 CF patients. The median age was 18 years [4.4 - 33.4 years] and 8 were male. Only the absolute median fat intake and pancreatic enzyme intake at the time of the DIOS attack were significantly higher than a year earlier. This difference disappears when enzyme intake is expressed as units lipase/gram fat. This was however also found in the controls. We suspect this could result from the dietary recommendations to increase fat intake and concomitant enzyme intake. No other significant dietary differences were found. An overview of the results is summarized in table 1.

| Median intake of different macronutrients and enzyme intake in the subgroups. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | DIOS (n = 12)   | Controls (n = 36) | DIOS before (n = 12) | Controls before (n = 36) |
| Caloric intake (kcal)          | 2735 [1736; 3370] | 2759 [1364; 3786] | 2638 [1683; 3264] | 2590 [1156; 3859] |
| Protein (g)                    | 99 [57; 140]    | 106 [34; 186]    | 93 [66; 140]     | 93 [31; 141]     |
| Fat (g)                        | 114 [75; 154]   | 123 [55; 201]    | 96 (*1) [68; 139] | 109 (*3) [41; 176] |
| Fibre (g)                      | 16 [6; 25]      | 16 [5; 27]       | 17 [10; 24]      | 13,9 [4; 1; 39]  |
| Water                          | 1,8             | 1,6             | 1,8             | 1,6             |
Table 1: Median intake of different macronutrients and enzyme intake (range) in the subgroups. DIOS is a group CF patients experiencing a first episode of distal intestinal obstruction syndrome, Controls is an age matched CF control group without DIOS, DIOS\textsuperscript{before} and Controls\textsuperscript{before} represent the nutritional data from one year prior to the study year (n = number of patients). Significant differences: group DIOS compared to DIOS\textsuperscript{before}: (1) P = 0.015; (2) P = 0.035 Controls and Controls\textsuperscript{before}: (3) P = 0.046

**Conclusion:** CF patients who experienced a first DIOS attack showed no significant difference in intake when compared to one year earlier or versus controls. This study does not sustain a potential role of nutritional factors or PERT in the first DIOS episode.

**Disclosure of Interest:** None Declared

<table>
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<td>[825; 15162]</td>
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Objectives and Study: Children with acute pancreatitis (AP) have clinically been treated with fasting and parenteral nutritional support. Up to date, efficacy of drugs for AP remains unclear in children. Gabexate mesilate (GM) is a synthetic serine protease inhibitor, which have been used to prevent or treat AP in adult patients. The purpose of this study was to evaluate clinical efficacy of GM for AP in children.

Methods: This study was done with retrospective review of medical records in hospitalized children with AP between 2004 and 2012. GM was infused in 27 children with AP, while the other 27 AP patients without GM infusion were the control group. The severity of AP was graded according to Balthazar scoring on computed tomography. All subjects had mild AP (score below 4) without pancreas necrosis or organ failure. Data from both groups were compared.

Results: The median age of patients was 11 yrs (range, 18 months - 17 yrs). The duration of hospitalization, the duration of abdominal pain, and the duration on parenteral nutrition of GM-treated group were significantly shorter than those of the control group ($p = 0.05$ & $p = 0.00$ & $p = 0.031$). Serum levels of amylase and lipase were significantly lower in GM-infused children than in the controls 7 days after the initiation of treatment (median amylase 77 vs. 139 IU/L, $p = 0.050$; median lipase 290 vs. 542 IU/L, $p = 0.030$).

Conclusion: The present study indicates that GM infusion has some clinical benefits for AP in children and the clinical application of GM might be recommendable in children to manage AP beyond conventional therapy.

Disclosure of Interest: None Declared
STRUCTURAL ABNORMALITIES OF INTESTINAL MICROECOLOGY IN CYSTIC FIBROSIS AND EFFECTS OF PROBIOTICS AND ANTIBIOTIC ADMINISTRATION

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Objectives and Study: Abnormalities of gut microflora have been described in several human diseases. We previously showed that intestinal inflammation is frequent in CF and is reduced by administration of Lactobacillus GG. In addition, gut microbiota of children with Cystic Fibrosis (CF) is characterized by a reduction of species commonly found in healthy children. In the present study we aimed to evaluate the modification in microbiota composition induced by antibiotic or probiotic treatment in CF and healthy children.

Methods: Intestinal microbiota was studied in 47 CF children (15 male; median age 10 years, range 2-18 years) and 29 age and sex gender matched healthy children, using the Fluorescent in situ hybridization (FISH) technique. The presence and load of Bacteroides, E. rectale and F. praunitzii were assessed in basal conditions, after two weeks of Lactobacillus GG (LGG) (6x10^9 CFU/die) and after a 7 days antibiotic course.

Results: In basal conditions, CF children showed a significant reduction in Bacteroides (14±10 vs 2.5±2.8 x10^10/ml), E. rectale (11± 6vs 6±5 x10^10/ml) and F. praunitzii (13±14 vs 2.2±3.3 x10^10/ml (all p<0.01) counts, compared to healthy children. Compared to untreated CF, a further significant reduction in all bacterial species was observed in antibiotic treated CF patients (Bacteroides 2.5±2.8vs 0.5±1.5 x10^10/ml; p<0.01), (E. rectale 5.8±5.3 vs 0.4±1.2 x10^10/ml; p<0.01) (F.praunitzii 2.2±3.3 vs 0.5±2.1 x10^10/ml; p=0.05). Conversely, probiotic-treated CF children showed a significant increase in Bacteroides counts (2.5±2.8 vs 7.2±4.9 x10^10/ml; p<0.05) compared to untreated CF children, although the Bacteroides loads were still lower than that detected in healthy controls (7.2±4.9 vs 14±10 x10^10/ml; p<0.05). Furthermore, in antibiotic-treated healthy children the number of Bacteroides was significantly reduced (13.8±10.2 vs 1.5±2.4 x10^10/ml; p<0.05), but LGG failed to significantly affect the amount of bacterial species.

Conclusion: Intestinal microflora of CF children is different compared to healthy controls, with a consistent reduction of Bacteroides, E. rectale and F. praunitzii species. These species are further reduced by antibiotics. In both CF and healthy children, antibiotic treatment further reduced the amount of healthy bacterial species. In CF, but not in healthy children, LGG is able to partially restore the microbiota, specifically increasing the Bacteroides spp. These data support the efficacy of probiotic therapy in CF and suggest that this is linked with restoration of intestinal microflora.

Disclosure of Interest: E. Bruzzese: None Declared, S. Viscovo: None Declared, R. Scotto: None Declared, F. Chiatto: None Declared, F. Basile: None Declared, E. Nicastro: None Declared, V. Raia: None Declared, V. Buccigrossi: None Declared, A. Guarino Grant / Resarch Support from: This study was partially supported by a grant of “Cystic Fibrosis Foundation and Therapeuthics” (Account number GUARIN10A0/2009)
**Objectives and Study:** We assessed retrospectively the genotype/phenotype relationship in CFTR-related chronic (CP) or acute recurrent pancreatitis (ARP) at a single Italian pediatric Cystic Fibrosis (CF) Centre during the 2003-2012 period.

**Methods:** We studied all consecutive pediatric patients affected by CP or ARP of undefined etiology. All patients underwent chloride sweat test and were studied for the research of CFTR gene mutations by the sequencing of the entire gene.

**Results:** A total of 102 young patients (52 males, mean age at diagnosis 10.1±7 yrs) were enrolled. Forty of them (39.2%) tested positive for CFTR gene mutations. The genotype/phenotype relationship in these patients showed: a) Six of 40 (15%) patients have classic CF, previously diagnosed, and two of them had pancreatic insufficiency; b) Eighteen of 40 (45%) patients showed 2 CFTR gene mutations. In this group 7/18 patients had pancreatitis as the first manifestation of CF: 4 patients had a positive sweat test, 3 patients had borderline values. Eleven of 40 (27.5%) patients with 2 CFTR mutations had a negative (n=9) or borderline (n=2) sweat test. They did not have more than one CF causing mutation and CF diagnosis was clinically excluded. c) Sixteen of 40 patients (40%), finally, did not have CF but they carried one CFTR mutation and showed negative sweat test, except one patient having borderline values.

**Conclusion:** Our study confirms a high percentage of CFTR gene mutations in pediatric patients affected by CP or ARP. Particularly, in 17.5% of patients we diagnosed CF with pancreatitis as the first manifestation of the disease. Furthermore, in 27.5% of patients we found 2 CFTR gene mutations that were not clearly CF causing and CF was ultimately excluded by clinical follow-up. Further studies are needed to assess the clinical impact of this class of mutations.

**Disclosure of Interest:** None Declared
GASTROSTOMY IN CHILDREN WITH CYSTIC FIBROSIS AND ADVANCED LIVER DISEASE: A PANACEA OR A PANDORA’S BOX?
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Objectives and Study: The aim of this study was to: [1] Investigate the morbidity and mortality related to a gastrostomy in a series of children with significant cystic fibrosis associated liver disease (CFALD) with portal hypertension who underwent this procedure to improve nutrition and [2] To assess the pulmonary and nutritional outcome in this clinical setting.

Methods: The CF database at the Royal Children’s Hospital was reviewed to identify all children aged 0-18 years with CFALD and portal hypertension who underwent gastrostomy insertion between 1991 and 2011. Anthropometric, lung function and clinical data were obtained for each patient at insertion and for a 24 month period after gastrostomy placement. Short and long-term complications from the gastrostomy procedure were documented.

Results: We identified 7 children [4 male] who had CFALD and portal hypertension at the time of gastrostomy placement. The mean age at gastrostomy was 10.6 ± 4.3 years. The BMI percentile at insertion was 20.9 ± 18.7. All patients were pancreatic insufficient and had failed to maintain adequate nutritional status with energy dense foods and pancreatic enzyme replacement. Six of the seven had a percutaneous endoscopic gastrostomy and one had an open surgical placement because of pre-existing oesophageal varices. No patient had ascites or coagulation abnormalities. Apart from one patient developing cellulitis in the post-operative phase there were no other problems. The median length of follow up after gastrostomy was 4.8 years and there were 35.7 patient years of follow up. During this time no patient developed stomal varices but 3 developed oesophageal varices. There was improvement in mean BMI z-score from -1.1 ± 0.9 to -0.6 ± 0.8 (n=6), P=0.05 at 2 years after insertion. Similar changes were seen in the WAZ score and there were no significant changes in HAZ scores. FEV1 % predicted data were available for 6 patients (one less than 5 years old). There was significant improvement from 49.5 ± 12.6 to 62.3 ± 20.3, P=0.04 at 2 years post insertion.

Conclusion: In this series of children and adolescents with CF and significant CFALD with portal hypertension, gastrostomy insertion was a safe procedure which was not associated with any major long term complications such as the development of stomal varices. There appeared to be an improvement in both nutrition and lung function at 2 years in this clinical setting. This would suggest that CF patients with established liver disease and portal hypertension benefit from improved nutrition and that the risks of substantial complications related to stoma formation is low.

Disclosure of Interest: None Declared
CLINICAL AUDIT LEADS TO IMPROVED OUTCOMES IN GASTROSTOMY-FED CHILDREN WITH CYSTIC FIBROSIS

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Objectives and Study: The association between nutritional status, pulmonary function and survival in cystic fibrosis (CF) has been demonstrated in multiple studies. A previous case series from the Royal Children’s Hospital, Melbourne (RCH), demonstrated suboptimal referral practices and highlighted the importance of early nutritional intervention in children with CF [1]. Various changes to the CF service were undertaken, including earlier referrals for insertion of a gastrostomy, as well as respiratory cohorting of patients according to Pseudomonas colonization. The present study aimed to assess the effects of these changed practices on clinical outcome.

Methods: We conducted a clinical audit of all CF patients who had undergone gastrostomy insertion between 2002 and 2010 at RCH. Clinical data, including demographics, weight-for-age and height-for-age Z-scores (WAZ and HAZ), and forced expiratory volume in 1 second (FEV1), were collected for 2 years prior and 2 years post gastrostomy insertion. Pulmonary colonization rates with Pseudomonas aeruginosa and 2-year survival were also recorded. Data were compared to the previous study which was conducted for the period from 1989-1997.

Results: Patients with CF who underwent gastrostomy placement between 2002-2010 (n=22), had a higher WAZ score (-1.5 ± 0.68 vs -2.67 ± 1.06; p=0.0001) and higher FEV1 68% ± 22 vs 52% ± 18.5; p=0.006), compared to the cohort from 1989-1997 (n=37). These differences were maintained at the 2-year follow-up. The Pseudomonas aeruginosa colonization rate was 100% in 1989-97 vs 41% in 2002-2010; p=0.0001. The 2-year survival post-PEG improved from 70% to 100%; p= 0.004.

Conclusion: There were significant improvements in WAZ, FEV1 and overall survival as a result of earlier referral of patients for a gastrostomy and strict cohorting of patients according to colonization status. This study confirms the value of a review and audit of clinical services.


Disclosure of Interest: None Declared
PO-G-0121

SODIUM INTAKE IN THE DIET. SHOULD WE WORRY ONLY ABOUT EXCESS?
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Objectives and Study: To describe the presence of hyponatremia and sodium replacement used after a diagnosis of CF by neonatal screening.

Methods: A retrospective study beginning in February 2010 of all CF patients detected by neonatal screening at a Reference Center for Neonatal Screening of Cystic Fibrosis in Brazil. The study included patients with two IRT > 70 ng/mL confirmed by two altered sweat chloride tests (RV < 60 mEq/L). Variables: sex, age at diagnosis, pancreatic sufficiency (steatocrit < 10 %), serum sodium at diagnosis and feeding at diagnosis.

Results: We studied 15 infants with a median age at diagnosis of 44 days, 81.2% of them with pancreatic insufficiency and 60% of them boys. Median IRT 1 and IRT 2 were 194 (±125.2) and 173 (± 102.6) and medians for the first and second sweat chloride tests were 86 (±19.8) and 87.5 (±16.1) mEq/L, respectively. Median serum sodium (mEq/L) at diagnosis was 134 (±6.5), ranging from 121 to 151. Sodium replacement was started at diagnosis in 73.3% of the patients with CF. Median initial daily sodium concentration for oral replacement was 2.4 mEq/L (± 3.5), divided into 4 applications per day. The food consumed at CF diagnosis was exclusive maternal milk in 66.6%, with 60% of these infants having sodium levels below 135 mEq/L at diagnosis.

Conclusion: As expected for CF, most infants had pancreatic insufficiency and were males. Due to neonatal screening, the diagnosis was early; however, even so, the frequency of hyponatremia was high, with oral sodium replacement being necessary, using recommended concentrations (2 to 10 mEq/kg/day). Exclusive breast-feeding predominated at that time and, due to the fact that at times the sodium content of maternal milk is insufficient for CF patients, there was vigilance that showed that this may have been one of the factors that contributed to the initial hyponatremia.

Disclosure of Interest: None Declared
IS GASTRIC EMPTYING DELAYED IN CHILDREN WITH CYSTIC FIBROSIS?

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Objectives and Study: Gastric emptying can be normal, decreased or increased in children with cystic fibrosis according to the literature. We showed in a previous study that 47.4% of children with cystic fibrosis with gastrointestinal and/or respiratory symptoms suggestive for gastro-oesophageal reflux had delayed gastric emptying. We studied now gastric emptying in children with cystic fibrosis without chronic gastrointestinal symptoms.

Methods: Nineteen children with cystic fibrosis (12 boys and 7 girls, mean age of 9 years and range of 5-13 years) without chronic gastrointestinal symptoms were studied. A 13C-octanoic acid breath test was performed to measure gastric emptying of solids. We used a standardized pancake containing 50 microliters of 13 C-octanoic acid. Breath samples were analyzed using Non Dispersive Infrared Spectrometry (Wagner Analysen Technik, Bremen, Germany). Gastric half emptying time was calculated and compared with gastric half emptying time obtained in healthy subjects (Hauser, unpublished data). Gastric emptying was considered as delayed if gastric half emptying time was above the 95th percentile.

Results: Two of the nineteen children (10.5%, 1 boy and 1 girl) had delayed gastric emptying.

Conclusion: Delayed gastric emptying is present in only a minority of children with cystic fibrosis without chronic gastrointestinal symptoms.

Disclosure of Interest: None Declared
NON-INVASIVE EVALUATION OF PORTAL HYPERTENSION IN CYSTIC FIBROSIS RELATED LIVER DISEASE PEDIATRIC PATIENTS USING TRANSIENT ELASTOGRAPHY AND WIRELESS CAPSULE ENDOSCOPY

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Objectives and Study: Cystic fibrosis-related liver disease (CFLD) is present in up to 30% of cystic fibrosis (CF) patients and is the third most common cause of death following cardiopulmonary and post-transplantation complications. In this context, early and non-invasive diagnosis of portal hypertension in these patients is a challenging goal. The main objective of this study was to investigate the relations between transient elastography (TE) and wireless capsule endoscopy in the prediction/detection of esophageal varices (EV) in pediatric patients with CFLD.

Methods: We retrospectively reviewed the charts of 148 patients with CF who underwent a transient elastography during a 14 months period. A wireless endoscopy was prescribed for all the patients presenting a FS > 7.8 kPa and having a medical history of liver disease. The patients who were able to swallow the video capsule performed an ECE carried out using a PillCam ESO2® video capsule (Given Imaging, Yoqneam, Israel). Only 9 patients who underwent both exams (TE and ECE) in a maximum 3 month period interval have been considered for this study. The statistical analysis was done using SPSS 17.0 and the results were expressed as a mean (m) +/- mean standard error (MSE) or median (M) and [Min, Max]. For group comparisons a p value of ≤0.05 was considered as statistically significant.

Results: The charts of 148 pediatric patients (83 M) presenting CF (mean age : 12.25 +/- 0.27 yo at the moment of the TE) were retrospectively reviewed. The median value of the FS in the whole study population was 4.35 [2.3; 58.4] kPa. Only 16 patients presented a FS value > 7.8 kPa((M)FS: 14.45 [9.2; 58.4] kPa). Nine of them were able to swallow the video capsule and 5 presented EV. A significantly (p=0.05) higher fibrosis measured by TE was found for the group of patients presenting EV ((M) [Min, Max] FV: 23.7 [17.5; 58.4] kPa vs 10.65 [10.1; 21.0] kPa for the group without EV).

Conclusion: TE reliably predicts EV. We suggest, for the CFLD pediatric patients, an elastography threshold value of 20 kPa to consider patients with a high risk of EV. We suggest that TE should be recommended for all CF patients with liver disease, both to follow its progression and to select those patients who need a ligation procedure as a primary prevention. Compared to the current gold standard esophago-gastro-duodenoscopy, ECE is a less expensive, non-invasive procedure and an accurate method which can be used for the early detection and the control of the EV in CFLD patients with asymptomatic portal hypertension.

Disclosure of Interest: None Declared
THE DIAGNOSTIC VALUE IN PAEDIATRIC SMALL BOWEL ASSESSMENT BY WIRELESS CAPSULE ENDOSCOPY: A TERTIARY CENTRE EXPERIENCE

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Objectives and Study: Wireless capsule endoscopy (WCE) provides a method to assess small bowel pathology by filling the endoscopic gap between push-enteroscopy and ileocolonoscopy. The aim of this study was to assess the diagnostic value, tolerance and safety of WCE in paediatric patients referred to our unit.

Methods: This is a retrospective review of the WCE studies (PillCam SB, Given Imaging) that were performed during a 5.5-year period (May 2007-October 2012). Indications were confirmed/suspected IBD (n=114, 39%), obscure/occult GI bleeding (n=36, 12%), GI polyps syndromes/tumors (Peutz-Jegher’s S., angiodysplasias, blue rubber bleb syndrome) (n=16, 5%), protein losing enteropathy (PLE) (n=15, 5%), recurrent abdominal pain (n=26, 9%), eosinophilic gastrointestinal disease (n=19, 7%), non-GI conditions with significant gut manifestations (autoimmune diseases, bone marrow transplantation, immunodeficiencies) (n=15, 5%) and other (coeliac disease, diarrhoea, failure to thrive etc.) (n=47, 16%).

Results: 291 children (140 male, median age 10.8 years (range: 6.5 months to 19.0 years) swallowed 102 capsules (35%), 188 were placed endoscopically into the duodenum under General anaesthesia using an acorn-like device (n= 179) “Roth net”. 72 patients (25%) were under the age of 8 years. In 220 cases (76%) the WCE was seen in the coecum at end of recording (8 hours). The swallowed capsule did not leave the stomach in 6 patients.2 patients retained the capsule, only one needing surgical removal of TI stricture with a normal contrast study pre WCE. Positive findings were observed in 184 (63%) of the studies of which 101 (34%) were diagnostic in terms of either establishing the diagnosis or altering the therapeutic approach of the patient. The diagnostic yield is highest in PLE (80%), polyposis syndromes/tumors (68%), Crohn’s disease (39%) and bleeding (27%).

Conclusion: Our experience - which is based on the largest cohort of paediatric patients and the youngest child undergoing WCE - demonstrates that with careful selection of patients, WCE is a useful and safe diagnostic modality in children with suspected small-bowel diseases.

Disclosure of Interest: None Declared
CLINICAL AND INSTRUMENTAL FOLLOW UP OF THE FIRST 2 EUROPEAN PEDIATRIC PATIENTS WITH ACHALASIA TREATED WITH PERORAL ESOPHAGEAL MYOTOMY (POEM)

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Objectives and Study: Achalasia is a disease of the esophageal motility. The surgical treatment is Heller’s myotomy - open or laparoscopic-. Peroral-Esophageal-Myotomy (POEM) has been recently introduced, and has shown to be effective with good clinical outcomes at long term follow-up in adults patients. POEM hasn’t been performed in children, except for a single case reported in the literature. We aimed to perform POEM in 2 children with esophageal achalasia – classic type- and to evaluate their long term outcomes –clinical, manometric and pHmetric -.

Methods: Two girls, aged 10 and 12 years, diagnosed with achalasia classic type (diagnosis made after performing barium esophagogram, esophageal endoscopy and esophageal 8-channel-manometry) underwent POEM under general anesthesia. Children were evaluated at 3, 6 and 9 months. The Eckardt Score was used to score the clinical outcome at 3 and 9 months, 8-channel-manometry and MII-pHmetry were performed at 6 months to study LES resting pressure (LESRP) and to verify the possible presence of gastroesophageal reflux -as a post-myotomy complication.

Results: We obtained a significant reduction of the Eckardt score, from 7 and 4 points to 0 points in both girls, at 3 and 9 months follow-up (values ≤ 3 are of clinical success). At 6 months, esophageal manometry showed a reduction of the LESRP -from 35 mmHg to 26,2 mmHg in one patients, and from 37,9 mmHg to 15 mmHg in the second one-. The MII-pHmetry showed an absence of gastroesophageal reflux in both children (Reflux Index < 5%).

Conclusion: Among the available surgical techniques for the treatment of pediatric esophageal achalasia, to achieve good long-term clinical outcomes is a priority. Being less invasive as possible, having a short post-operative recovery and a rapid restart of eating are also fundamental goals of achalasia treatment in the pediatric age. POEM seems to fulfill all the previously described characteristics. In fact, our clinical and instrumental results suggest that POEM is a suitable treatment in terms of feasibility, safety and clinical efficacy even in children. This study reports our initial experience that seems very encouraging. Further studies with long term follow-up will be necessary to validate our results.

Disclosure of Interest: None Declared
CAN GASTROINTESTINAL SYMPTOMS PREDICT HISTOLOGICAL OUTCOMES IN FOOD ALLERGIC CHILDREN UNDER THE AGE OF ONE?

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Objectives and Study: Up to 60% of children between age 0-3 years diagnosed with food allergy initially display gastrointestinal (GI) symptoms with young infants being affected more often. Endoscopy is difficult at this age and requires general anaesthesia. There are currently no studies that have looked at GI symptoms as a marker of histological outcome after endoscopy. Our aim was to see if there was correlation between the type of GI symptoms in children with food allergy and histological outcome from endoscopy.

Methods: All patients under the age of 1-year-old referred to our tertiary paediatric gastroenterology centre during June 1987 to August 2007 who had an endoscopic procedure (OGD, colonoscopy or both) were included. The symptom presentation and histological outcomes were reviewed.

Results: A total of 736 endoscopic procedures were performed in food allergic children over this 10-year period. We analysed the data for the 4 most common symptoms (diarrhoea, faltering growth (FG), peri-rectal (PR) bleeding, reflux/vomiting) and their combinations with one another. Histology was classified as either “Normal” (normal biopsy) or “Abnormal” (presence of any positive histology including eosinophils, inflammation or other histological findings). The 10 most common symptom combinations were reviewed. The combinations of the four main common symptoms were responsible for 575 of 736 cases (78.1%). Ten of the most common combinations were: Diarrhoea 150 (17%), Reflux 123 (17%), FG 82 (11%), Diarrhoea + FG 77 (10%), Reflux + FG 47 (6%), PR Bleeding 33 (4%), Diarrhoea + PR Bleeding 21 (3%), Diarrhoea + Reflux + FG 18 (2%), Diarrhoea + Reflux 12 (2%), Diarrhoea + Reflux + PR bleeding 6 (1%). In patients who presented with diarrhoea or PR bleeding alone, 28% and 27% of the patients had normal histological findings, respectively. In patients who presented with reflux/vomiting or FG in isolation, 54% and 49% of the patients had a normal biopsy. We also found evidence that the greater number of symptoms a child presented with the more likely they were to have an abnormal histological result.

Conclusion: This data suggests that for children who present with diarrhoea or PR bleeding, having an endoscopic procedure has a higher chance of identifying abnormal pathology which may be beneficial in food allergy diagnosis. The evidence is not as convincing for isolated reflux/vomiting or FG where there is a 50% chance of the child having a normal biopsy. Our data also shows that children who present with a combination of symptoms are more likely to benefit from having an endoscopy than children who present with a single symptom.

Disclosure of Interest: None Declared
OESOPHAGEAL FOOD BOLUS IMPACTION IN CHILDREN
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Objectives and Study: Background: Although foreign body (FB) ingestion is a common occurrence in children, oesophageal food bolus impaction (EFI) is considered uncommon. There is paucity of literature on paediatric food bolus obstruction. With increase in prevalence of eosinophilic oesophagitis (EoE) food bolus obstruction may be becoming more common.

Aim: To describe the clinico-pathological characteristics of children presenting with EFI in a tertiary paediatric centre

Methods: A retrospective chart review of children who presented with food bolus obstruction between January 2007 and April 2012 was undertaken. The patients were identified from the clinical coding database which uses standard ICD coding. Demographic details, endoscopic findings and histological finding of oesophageal biopsies were reviewed.

Results: Sixtyfive children presented with foreign body / food bolus impaction in oesophagus during the study period. Of these, 30 were non food bolus obstruction including coins, metal etc. Of 35 children (53%) who presented with EFI, 26 were boys comprising 74% of the group. Mean age at presentation was 8.44 years (+/- 4.5). Twelve of 35 children with EFI were managed by the ENT specialists with rigid scope and hence these children did not have oesophageal biopsies. The remaining 23 children underwent upper GI endoscopy for EFI and 21 children had oesophageal biopsies for histological assessment. Fifteen out of 21 children (71%) had evidence EoE on histology, with median eosinophil count of 37 (range 20 -100). These children also had endoscopic appearance consistent with EoE, with longitudinal tracks and white exudates in their oesophagus. Four children (11%) had history of repaired Tracheo-oesophageal fistula as the cause, 2 children (9%) had normal biopsy and 2 had spontaneous resolution during the time of endoscopy. One child with EoE presented twice with EFI

Conclusion: This study showed that food bolus accounts for more than 50% of impaction in oesophagus. Majority of the children who had food bolus impaction were boys and had EoE as the underlying cause. Those with EFI managed with rigid scope by ENT team did not have oesophageal biopsies and hence missed the opportunity for correct diagnosis. We recommend all children with food bolus impaction/obstruction should have oesophageal biopsies at the time of endoscopic intervention to ascertain the aetiology which will help in the optimal management of these children.

Disclosure of Interest: None Declared
PROSPECTIVE STUDY OF USE OF MITOMYCIN C FOR ESOPHAGEAL STRICTURES - A BREAKTHROUGH
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Objectives and Study: In developing countries like Pakistan accidental ingestion of caustic agents, is the major cause of esophageal strictures in children. With the advent of Pneumatic endoscopic dilatations more of these children are being referred to the Gastroenterologist. Repeated dilatations are required due to scar formation and restrestructuring. Use of Mitomycin-C has been reported in various laryngeal and ophthalmologic procedures for inhibiting fibroblast proliferation and reducing scar formation. This study documents the use of Mitomycin-C in caustic esophageal strictures

Methods: A prospective study was carried out from Jan 2010 to Nov 2011, in all patients of caustic strictures who came to The Children’s Hospital, Lahore. After taking informed consent patients were subjected to pneumatic esophageal balloon dilatation under general anesthesia and Mitomycin-C was applied. The procedure was repeated at each visit and need for further dilatation was assessed compared to the historical control group. This was done by viewing the retrospective data of patients who underwent balloon dilatation in the preceding year when Mitomycin C use was not practiced. Outcomes in terms of symptomatic relief were assessed after therapy and results were analyzed for effectiveness of Mitomycin-C in comparison with the control group. Patients with very tight stricture in which balloon couldn’t be negotiated through were excluded from the study and referred to surgery.

Results: The present study constituted eighty one children with established esophageal strictures. Out of these 38 (47%) were treated with Mitomycin c, while forty three (53%) were in retrospective group in whom Mitomycin C was not used. Total number of Dilatations done in Mitomycin C group was 61 while control group had 115. Average dilatations were 2.7 per patient in retrospective group versus 1.6 per patient in Mitomycin group. Maximum no of dilatations required for one patient was 14 in control group versus 4 in Mitomycin group. Response was defined as major if both Endoscopic and clinical response was there, Partial if patient had either of two criteria & failure in which there was no response to intervention. Symptomatic improvement was present in all the patients in Mitomycin C group compared with retrospective group and total number of dilatations required was dramatically reduced. With Mitomycin major improvement was observed in thirty two (84%) .Partial response was seen in six patients (16%).

Conclusion: Use of Mitomycin C in caustic esophageal strictures was found to be very promising .The need for repeated dilatations was significantly reduced due to the antifibroblastic properties of the drug.

Disclosure of Interest: None Declared
DIAGNOSTIC AND THERAPEUTIC VALUE OF ERCP IN CHILDREN WITH CHOLANGIOPANCREATIC DISEASES
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Objectives and Study: To explore the diagnosis and treatment value of ERCP in children with pancreaticobiliary diseases, and analysis the spectrum of pancreaticobiliary diseases in children.

Methods: The data of consecutive patients ≤18 years who underwent ERCP procedures between the years of January 2008 and December 2011 were retrospectively identified through a computer database search. The database respectively recorded the clinical manifestations, laboratory examinations, ERCP findings, therapies and complications.

Results: 1. During the study, a total of 137 ERCPs were done in 91 children with a median age of 8.6 years (range 2-18 years). There were 51 males and 40 females. There were 18 patients with 2 ERCPs, 8 ones with 8 ERCPs and 4 with 4 ERCPs.

2. Findings of ERCP

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<tr>
<th>Findings of ERCP</th>
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<th>Findings of ERCP</th>
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<tr>
<td>Bile duct microlithiasis</td>
<td>7</td>
<td>Pancreas divisum</td>
<td>11</td>
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<tr>
<td>Anomalous pancreaticobiliary ductal junction</td>
<td>14</td>
<td>Confluence of low bile duct</td>
<td>2</td>
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<td>Cystic dilatation of bile duct</td>
<td>10</td>
<td>Bile duct Ascaris</td>
<td>1</td>
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<td>Biliary stricture or anastomotic stricture</td>
<td>9</td>
<td>Gallstone</td>
<td>1</td>
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<tr>
<td>Cholangitis</td>
<td>2</td>
<td>Sphincter of Oddi dysfunction</td>
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<tr>
<td>Chronic pancreatitis</td>
<td>48</td>
<td>Injured pancreatitis</td>
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<td>Pancreatic duct microlithiasis</td>
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<tr>
<td>Pancreatic duct stricture</td>
<td>13</td>
<td>Duodenal membrane</td>
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<td>Carcinoma of head of pancreas</td>
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Conclusion: ERCP in the pediatric population has a high success rate; both as a diagnostic tool and for therapeutic interventions and its therapeutic potential make it absolutely superior to other less invasive tools. The complications of ERCP in children were more than in adults. The experienced endoscopists and adequate preparations were necessary

Disclosure of Interest: None Declared
HIATAL HERNIA IS NOT ASSOCIATED WITH DYSPEPTIC SYMPTOMS IN CHILDREN
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Objectives and Study: Esophageal hiatal hernia (HH) has been reported to affect from 10 to 50% of adult population. HH is characterized by a protrusion of the stomach into the thoracic cavity through a widening of the right crus of the diaphragm. Type I or sliding HH represents the most common subtype. HH has been associated with different symptoms and complications. To best of our knowledge, no data are available in pediatric age. The aims of our study were to estimate prevalence of HH in children undergoing upper GI endoscopy (UGE) and to evaluate a possible correlation between HH and dyspeptic symptoms.

Methods: We prospectively enrolled 107 consecutive children (M/F= 49/58; median age= 93 mths; range= 1-216 mths) who underwent UGE with multiple biopsies, from April 2012 to September 2012 at the Department of Pediatrics, University of Naples “Federico II”. The diagnosis of esophagitis was based on histologic features, according to the Yierian-Fiocca classification. A symptomatic score assessment, based on the Rome III Criteria, was administered to the patients over 10 years of age or to the parents of children younger than 10 years.

Results: In our population, the prevalence of HH was 31.8%. HH was significantly associated with histologically defined esophagitis (p=0.032; OR: 0.163; 95%CI: 0.03-0.89). Presence of HH was not correlated with dyspeptic symptoms (p=0.535; OR: 0.948; 95%CI: 0.415-2.166). In addition, no association between dyspeptic symptoms (p=0.696; OR: 1.886; 95%CI: 0.349-10.190), including vomiting (p=0.262; 95%CI: 0.563-4.742), and histological findings was found.

Conclusion: This is the first pediatric perspective study evaluating the prevalence of HH in children. As reported in adults, HH is more likely associated with esophagitis.

In addition, our data suggest that, in pediatric age, HH does not play a role in the pathogenesis of dyspeptic symptoms, including vomiting.

Disclosure of Interest: None Declared
USE OF LARYNGEAL MASK AIRWAY DURING ANAESTHESIA FOR ENDOSCOPIC PROCEDURES IN CHILDREN IS SAFE AND EFFICIENT

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Objectives and Study: To retrospective evaluate the safety and efficacy of general anaesthesia with Sevoflurane and Propofol using Laryngeal mask airway (LMA) in endoscopic procedures over an 18 month period in a children's unit.

Methods: Inclusion criteria: children under 16 years of age who underwent upper GI endoscopy (OGD) +/- insertion of pH/impedance probe +/- colonoscopy in a day surgery theatre in a children's unit. The procedure was conducted by a paediatric anaesthetist, with spontaneous respiration, sevoflurane/isoflurane and Propofol.

Time required for induction of anaesthesia, anaesthesia, endoscopy, recovery, and complications during the procedure were recorded and compared with the same procedure performed under general anaesthesia using endotracheal intubation.

Vital signs including heart rate, respiratory rate blood pressure and pulse oximetry were measured at baseline and every 5 minutes until patient recovery.

Results: 150 patients were included over an 18 month period from 2010-2012. The age range was from 3 years to 16 years with a median age of 8 years.

The average dose of Propofol used was 2-4mg/kg at induction. The average concentration of sevoflurane was 2-3% (MAC 1-1.5)

No patient required to be intubated for complications of the procedures in inability to maintain airway.

There were no haemodynamic complications. Aside from one patient there was no delay in discharge home.

Three patients complained of sore throat required medical review and one patient required an inpatient admission for aspiration pneumonia which resolved spontaneously.

In the cases where a pH/impedance probe was inserted this was inserted successfully by deflating the LMA to allow easy passage.

Conclusion: In our study, we were able to demonstrate that the use of an LMA does not restrict or complicate the procedure of endoscopy. In addition it is shown to be a safe way of administering inhalational agents in children with a short recovery time.

Disclosure of Interest: None Declared
PAEDIATRIC GASTRO-OESOPHAGEAL REFUX DISEASE (GORD): GP KNOWLEDGE, ATTITUDES AND MANAGEMENT
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Objectives and Study: Gastro-oesophageal reflux (GOR) is extremely common occurring in approximately 50% of infants. Gastro-oesophageal reflux disease (GORD) which occurs when reflux-associated symptoms occur is less common but poses a significant burden to both parents and clinicians. GPs (general practitioners) are one of the most important sources of health care and support for parents when their infants have GOR or GORD. The aim of this study was to examine knowledge, attitudes and practices of GPs regarding diagnosis and management of GORD in infants.

Methods: GPs knowledge, attitudes and management of paediatric GOR/GORD were surveyed utilising a structured questionnaire. To try and increase response rates documentation was sent sequentially using a modified Dillman protocol with an initial primer postcard, then information pack/paper copy of quiz and lastly a final reminder post card. Furthermore GPs were given the choice of either paper or online completion of the questionnaire.

The survey was pilot tested by a sample of academic and community GPs prior to distribution. It included 41 questions and could be completed in less than 15 minutes. Response options varied depending on the question content. The survey was distributed to 2319 GPs (10% of national workforce) randomly selected.

Results: The total number of GPs who responded was 480/2319 (21% response rate). There were no significant demographic differences between the responders and the national workforce. 80 responses were excluded (9 incomplete, 71 never see GORD). Of the 400 GPs included in the final analysis, more than 50% saw infants with GOR at least monthly, more than 95% at least annually. GPs rated non-pharmacological interventions to be only slightly or moderately effective, but most GPs usually recommended them in infants with GOR. 86% of GPs surveyed usually prescribe acid suppressive agents for GORD. Whilst more than 50% of GPs surveyed think acid suppression is best achieved by proton pump inhibition, less than 50% use this category of drugs initially. Less than 30% of GPs surveyed had used international or national GOR/GORD guidelines to inform their practice.

Conclusion: Our study is a highly representative sample of Australian GPs which matched the national workforce well. Our study confirms the significant burden of work which GOR/GORD creates in the community. It is also clear that whilst GPs hold concerns regarding insufficient guidelines and education regarding infant GORD, they are not accessing those that do currently exist and furthermore there is significant variability in prescribing practice. Clearly, promotion of best practice in infantile GOR/GORD and education of GPs in general with regards to appropriate treatment in this area needs to be accelerated.

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PEDIATRIC OBESITY AND GERD: CORRELATION BETWEEN IMPEDANCE BASELINES AND ESOPHAGITIS
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Objectives and Study: Introduction: In adults, the obesity epidemic affects the rising incidence of gastroesophageal
reflux (GER) disease and reflux esophagitis (RE). It has been shown that impedance baselines (IB) are significantly
lowered in patients with RE. Inconsistent data are reported in children regarding the association between BMI, RE and IB.
Aim: To assess if impedance baselines and presence of RE correlate with body mass index (BMI) in children (0-18 years)
with GER symptoms.

Methods: Patients suspected of GERD who underwent endoscopy between 2007 and 2012, and had pH impedance
performed, with a maximum time interval of three months between the two tests, were studied retrospectively.
Endoscopies were graded for reflux esophagitis (RE) according to the Los Angeles classification. BMI-for-age z-scores
(BMI-z), using WHO guidelines for infants and children (0-18 yrs), and BMI percentiles (BMI-p) using growth charts for
Centers for Disease Control and Prevention (CDC) (2-18 yrs) were calculated. Overweight was defined as a BMI from the
85th-95th percentile and obesity as a BMI>95th percentile. Statistical analysis, using SPSS Statistics 19, was performed.

Results: 123 children and 54 infants (0-24 months) were included with a mean age of 77.0 months (SD:4.3). Forty-seven
(26.6%) patients had RE. The mean BMI-z was -0.1 (SD:1.3), for BMI-p this was 43.5±31.2. Nine children fulfilled criteria
for overweight (7.3%) and 5 for obesity (4.1%). BMI-z did not differ significantly in patients with esophagitis (p=0.68), nor
did it correlate with the mean of the most distal MII baseline (p=0.86). The same accounted for the BMI-p, esophagitis and
MII baselines (p=0.91 and p=0.76 respectively), neither was a significant correlation found between overweight and obese
children and presence of RE. MII baselines were not significantly lowered in patients with esophagitis (p=0.54).

Conclusion: In children with GER symptoms, impedance baselines do not correlate with BMI. In contrast to adults, RE is
not more common in children suspected of GER disease and overweight or obesity. There is a need for well-designed
case-control studies with valid statistical power, to further investigate these findings.

Disclosure of Interest: None Declared
DO PREMALIGNANT GASTRIC LESIONS EXIST IN CHILDREN REACTIVE GASTRITIS?

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Objectives and Study: Duodenogastric biliary reflux can cause gastric mucosa inflammation, ulceration and/or intestinal metaplasia in the stomach. According to Correa’s theory, intestinal-type of gastric cancer is the final result of the progressive modifications starting with chronic gastritis and followed by multifocal atrophic gastritis and intestinal metaplasia, but this theory refers mostly to H. pylori infection. On the other hand, according to Sobala’s theory, intestinal metaplasia arises from divergent differentiation in regenerating epithelium following erosion or ulceration due to biliary reflux.

The aim of our study was to evaluate the prevalence of atrophic gastritis and intestinal metaplasia in children, considering the causes leading to these premalignant lesions, other than H. pylori. Also, we wanted to identify the age of the onset of gastric atrophy and intestinal metaplasia due to duodenogastric biliary reflux.

Methods: This was a retrospective study over a 13-year period in children presenting gastrointestinal symptoms or being suspected of malabsorption. Reactive gastropathy was defined according to Dixon description as a constellation of nonspecific elementary lesions such as foveolar hyperplasia, interfoveolar smooth muscle fibers, erosions, edema, and hyperemia, in the absence of significant inflammation.

Results: A total of 3257 patients were included, with a mean age of 11.80 ± 5.17 years (CI95% 11.62-11.98). A number of 1494 children had reactive gastritis (45.9%), 868 (26.7%) acute reactive gastritis and 626 (19.2%) chronic reactive gastritis. The mean age of the group with reactive gastritis was 10.65 ± 5.58 years (CI95% 10.37 to 10.93), significantly lower than the rest of the group, which was 12.77 ± 4.48 years (CI95% 12.56 to 12.99) (p <0.001). Two hundred and fifty three children (16.93%), 157 girls, with a mean age of 9.95 ± 5.39 years (CI95% 9.29 to 10.61) had gastric atrophy. Eleven of them had coinfection with H. pylori and H. heilmannii (9, respectively 2) and only 6 were known with previous H. pylori infection. Most of the patients (188) showed atrophy of grade 2, 56 of grade 3 and the rest of them (i.e., 9) had grade 1 atrophy. There were 14 cases (0.93%) of intestinal metaplasia (7 incomplete/7 complete), 10 girls, mean age 13.24 ± 4.15 (CI95% 10.84-15.64). Only 7 were associated with gastric atrophy.

Conclusion: Premalignant gastric lesions such as gastric atrophy and intestinal metaplasia do occur in reactive gastritis of children in the preadolescence period.

Disclosure of Interest: None Declared
DOES H. PYLORI GASTRITIS EFFECT TISSUE MMP IN CHILDREN
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Objectives and Study: Helicobacter pylori (H. pylori) is an extracellular bacteria which causes chronic gastritis, peptic ulcer disease, and even gastric cancer. Matrix metalloproteinases (MMPs) are believed to play an important role in inflammation and carcinogenesis. MMP-9(gelatinase) takes place in malignancy and chronicity and MMP-1(Collageanse) are those mostly evaluated in studies. MMP-9 levels in the antrum of H.pylori infected adult patients are showed to be elevated in recent reports.

Methods: The gastric biopsy materials were reevaluated by the pathologist (FA) for modified Sydney scoring. For the detection of matrix metalloproteinases immunohistochemistry was used. The number of immunopositive cells were counted in 5 different X40 objective areas Image J Image Analysis Software. For statistical analysis SPSS for Windows 16.0 were used.

Results: On histopathological evaluation there was an increase in MMP-1 expression paralel to H.pylori density but that increase was not statistically significant (p<0.05). On the other hand there was statistically significant increase in MMP-9 expression paralel to H.pylori density. There was sinficant increase in MMP-9 expression between H.pylori + and H.pylori+++ (p=0.007poz), and H.pylori++ and H.pylori+++ (p=0.043). The increase between H.pylori + and H.pylori++ was not significant

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
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<tr>
<td>MMP1</td>
<td></td>
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<td></td>
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<td>HP+</td>
<td>16</td>
<td>20,1094</td>
<td>17,09799</td>
<td>4,27450</td>
</tr>
<tr>
<td>HP++</td>
<td>9</td>
<td>28,4167</td>
<td>14,46548</td>
<td>4,82183</td>
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<tr>
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<td>2</td>
<td>60,3750</td>
<td>6,18718</td>
<td>4,37500</td>
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<tr>
<td>Total</td>
<td>27</td>
<td>25,8611</td>
<td>18,67528</td>
<td>3,59406</td>
</tr>
<tr>
<td>MMP9</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>HP+</td>
<td>16</td>
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<td>20,34178</td>
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</tr>
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<td>2</td>
<td>90,3750</td>
<td>17,85445</td>
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<tr>
<td>Total</td>
<td>27</td>
<td>62,1204</td>
<td>21,40041</td>
<td>4,11851</td>
</tr>
</tbody>
</table>

Conclusion: The elevation of the expression of MMP-9 paralet to H.pylori density might be a factor for the chronicity of the infection and even the malignancyc process. On the other hand the increase in expression of MMP-1 paralel to H.pylori density (although not statistically significant) shows the destruction that the microorganism causes on the
collagen tissue of the stomach. The intensity of the destruction can vary from case to case so the changes seen on gastric tissue should be well evaluated histopathologically.

**Disclosure of Interest:** None Declared
IS THERE A BASELINE THRESHOLD FOR OESOPHAGITIS IN CHILDREN?

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Objectives and Study: It is recognised that symptoms to diagnose oesophagitis are not specific in young children. Not all children with symptoms of gastro-oesophageal reflux (GOR) can undergo endoscopy because of technical and/or economical reasons. Recent studies suggested that impedance baseline (IB) may correlate with mucosal integrity. The aim of the study was to analyze the value of IB in a large population of children submitted to endoscopy to test in an association between IB and presence/absence of oesophagitis can be demonstrated.

Methods: Subjects referred from 2007 to 2012 for symptoms of GOR and submitted to both esophageal impedance (MII-pH) and endoscopy were enrolled. MII-pH tracings were reanalyzed retrospectively using the automatic calculation of the IB according to the specific software (Bioview Sandhill or Ohmega MMS) without removing any episode of increased/decreased IB. Tracings with artifacts were discarded. The mean of the IB were calculated and compared for the distal oesophagus (Z6) among different patient subgroups. Los Angeles classification was used to classify oesophagitis; the time frame between endoscopy and MII-pH recording was less than 1 month.

Results: 257 children (median age 46 months, range 0.5-206.5 months) were included (Table 1).

<table>
<thead>
<tr>
<th>Z6 IB (Ohm)</th>
<th>Total No.</th>
<th>Esophagitis</th>
<th>Normal Endoscopy</th>
<th>On PPI treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1000</td>
<td>10</td>
<td>9</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>&gt;1000 but &lt;1500</td>
<td>15</td>
<td>7</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>&gt;1500 but &lt;3000</td>
<td>136</td>
<td>39</td>
<td>97</td>
<td>39</td>
</tr>
<tr>
<td>&gt;3000</td>
<td>96</td>
<td>28</td>
<td>68</td>
<td>26</td>
</tr>
<tr>
<td>All values</td>
<td>257</td>
<td>83</td>
<td>174</td>
<td>71</td>
</tr>
</tbody>
</table>

All except one patient (5.5 month of age on proton pump inhibitor (PPI) treatment) with IB <1000 Ohm had oesophagitis. In our population IB of 1000 Ohm at Z6 showed a sensitivity of 11%, specificity of 99%, positive predictive value (PPV) of 90%, negative predictive value (NPV) of 70% for oesophagitis with accuracy of 71%.

Conclusion: IB value is an additional impedance parameter with possible clinical significance

An IB below 1000 Ohm is nearly always associated with oesophagitis at endoscopy regardless age or previous treatment.

References: (*) SS and RvdP contributed equally to this abstract.
Disclosure of Interest: S. Salvatore°: None Declared, R. van der Pol°: None Declared, B. Hauser: None Declared, T. Devreker: None Declared, E. De Greeef: None Declared, G. Veereman-Wauters: None Declared, M. Benninga: None Declared, Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals
CHARACTERISTICS OF REFLUX DETECTED BY MULTICHANNEL INTRALUMINAL IMPEDANCE-PH MONITORING IN INFANTS WITH CHRONIC LUNG DISEASE AND GASTROESOPHAGEAL REFLUX

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Objectives and Study: Chronic lung disease (CLD) is a heterogeneous lung disease defined as persistent need for ≥30% oxygen beyond 36 weeks postmenstrual age. A relationship between Gastroesophageal reflux (GER) and CLD has been implicated in the worsening of lung disease(1). In neonates, there are no definite standards to aid in the diagnosis of GER, symptom recognition is often difficult and effect of acid suppressive therapy (AST) in CLD is not well studied. German pediatric impedance group published the largest pediatric data and defined abnormal results as >100 refluxes or symptom index >50% in infants <1 year(2).

Aims
1. Study the characteristics of reflux detected by MII-pH monitoring in infants with CLD and GER.
2. Effect of AST on the characteristics of refluxes detected by MII-pH study.

Methods: We retrospectively collected data from infants with CLD who underwent MII-pH study. Exclusion criteria: Congenital heart, airway, lungs, or diaphragmatic abnormalities, chromosomal and genetic syndromes. Background data included birth weight, postmenstrual age, feed regimen and AST. The characteristics of refluxes were analyzed with the software used in the calculation of the Boix-Ochoa score. All refluxes were additionally verified manually. Data was also sub-analysed to compare MII-pH detected reflux characteristics in infants on and off AST.

Results: 20 infants were identified of which AST used in 14. Mean birth weight was 846.8 grams (range-585 to 1198). 18/20 were on full enteral feeds and all had nasogastric tube. 14/20 used omeprazole and 2 had Ranitidine. 19/20 had clinical reflux- Regurgitation- 10/20, suspected aspiration-7/20, arching/distress-5/20, feed related desaturation in 16/20.

<table>
<thead>
<tr>
<th></th>
<th>All infants</th>
<th>No AST</th>
<th>AST</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean postmenstrual</td>
<td>27±1</td>
<td>25±4</td>
<td>27±5</td>
<td>23±5 - 32±2</td>
</tr>
<tr>
<td>age (week)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean corrected</td>
<td>12±1</td>
<td>8±6</td>
<td>13±3</td>
<td></td>
</tr>
<tr>
<td>gestational age at</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>study (Term+week)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acid exposure time</td>
<td>3.99</td>
<td>6.7</td>
<td>2.81*</td>
<td>0-19.5</td>
</tr>
<tr>
<td>( %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All reflux</td>
<td>40.75</td>
<td>34</td>
<td>43</td>
<td>1-111</td>
</tr>
<tr>
<td>Acid refluxes</td>
<td>9.5</td>
<td>16.6</td>
<td>6.42*</td>
<td>0-39</td>
</tr>
<tr>
<td>Non acid refluxes</td>
<td>31.25</td>
<td>17.3</td>
<td>37.2*</td>
<td>1-110</td>
</tr>
<tr>
<td>Proximal refluxes</td>
<td>13.6</td>
<td>6.6</td>
<td>16.5*</td>
<td>0-58</td>
</tr>
<tr>
<td></td>
<td>Proximal Acid</td>
<td>Proximal Non acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------</td>
<td>-------------------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>2.9</td>
<td>3.5</td>
<td>2.6</td>
<td>0-12</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>2.6</td>
<td>0-12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1</td>
<td>13.9*</td>
<td>0-57</td>
<td></td>
</tr>
</tbody>
</table>

* P <0.05 = significance

**Conclusion:** Our small study demonstrates that in infants with CLD and GER,
- Total number of refluxes detected by MII-pH is within normal range.
- AST significantly decreases acid refluxes and acid exposure time.
- AST had no influence on total number of refluxes and seems to be associated with increased frequency of non acid proximal refluxes.

**References:**

**Disclosure of Interest:** None Declared
Objectives and Study: The objective of this study was to assess the prevalence of atrophic gastritis and intestinal metaplasia at children. We also wanted to compare the clinical manifestation, endoscopic appearance and the degree of the gastric atrophy and intestinal metaplasia at children and to identify the possible causes which determine gastric atrophy.

Methods: We evaluated 3257 children with chronic gastritis (2043 female, mean age 11.80 ± 5.17 years). Atrophy was defined as loss of normal glandular components, including replacement with fibrosis and/or intestinal metaplasia.

Results: The prevalence of the atrophic gastritis was 9.2% (299 cases), mean age 10.01±5.49 years (CI95% 9.39-10.64), F/M ratio 1.62/1. The clinical manifestation are correlated with the patient age (infants and toddlers were evaluated mostly for weight loss and older children for epigastric pain). The endoscopic appearance was not characteristic for gastric atrophy, only 8.7% of the patients had endoscopic aspect of atrophic gastritis. The majority of the patients presented grade 2 atrophy (219 cases; 141 female), other 65 (35 female) had grade 3 atrophy. 21 patients (0.64%) had intestinal metaplasia (9 incomplete), 6 were boys. 85 cases were associated with duodeno-gastric biliary reflux, 24 with *H. pylori* infection and 8 had mixed etiology.

Conclusion: Atrophic gastritis is present in childhood, even at very young age (infants, toddlers). The endoscopic appearance is not characteristic for the presence of atrophy. The degree of atrophy and intestinal metaplasia are not correlated with the age of the children. *H. pylori* is not the only etiological factor of atrophic gastritis, biliary reflux induced chemical injury can also lead to gastric mucosal atrophy.

Disclosure of Interest: None Declared
INFLUENCE OF GAS IN THE ANALYSIS OF BASELINE IMPEDANCE IN CHILDREN
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Objectives and Study: Several studies evaluate the baseline esophageal impedance as a marker of esophageal mucosa integrity. In our previous work we evaluated the esophagus baseline impedance (BImp) comparing different methods. The comparison among the analysis methods of the complete 24h tracing (full-screen) with and without exclusion of impedance events (IE), showed a reduction of BImp in the upper channel (channel 1) and an increase of it in the lower one (channel 6). The Aim of our study is to evaluate the influence of gas episodes in relation to the BImp variation.

Methods: We analyzed 20 impedance tracings in children with gastroesophageal reflux suggestive symptoms. All children underwent upper endoscopy and multichannel intraluminal impedance/pH metry. We evaluated in all tracings the BImp with and without exclusion of IE and comparing the results (expressing the differences in percentage), the excess and defect were represented through positive and negative values respectively. Moreover, we evaluated the number of gas episodes in the upper and lower channel.

Results: Mean age ± SD of the study population was 88 ± 53.14 months (range 17-192 months). No patient had endoscopic or histological evidence of esophagitis. The comparison between the two full screen methods showed a BImp of -5.87% (range -48.60% - 5.71%) in the upper channel, and of 6.99% (range -7.56% - 20.83%) in the lower one. We found in all tracings 19,600 IE, of which 7,219 were gas episodes in the upper channel and 2,162 were gas episodes in the lower one (p<0.001).

Conclusion: In the upper channel we found a reduction of BImp after the exclusion of impedance episodes. Our results show that the number of gas episodes influences the BImp in the upper channel more that in the lower one. This result underlines the marginal role of gas episodes in BImp in the lower channels. The increase of BImp in the lower channels comparing both methods, 24h with IE and 24h without IE, suggests that reflux and swallows influence the BImp more than gas episodes.


Disclosure of Interest: None Declared
ASSESSMENT OF METHODS OF PLACEMENT ESOPHAGEAL PH PROBE IN PRETERM INFANTS
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¹Pediatrics, ²Federal University of Uberlandia, Uberlândia, Brazil, ³Mathematics, Federal University of Uberlandia, Uberlândia, Brazil

Objectives and Study: The accurate placement of esophageal pH probe determines the validity of the results of pH monitoring. Equations to calculate this placement, based on clinical and anthropometric patient data propose to replace the imaging exams in preterm infants avoiding their exposure to ionizing radiation. The aim of this study was to assess the methods of placement esophageal pH probe in pH monitoring in preterm infants by comparing Strobel¹ and Gupta & Jadcherla² equations with fluoroscopy.

Methods: In a cross sectional study, a total of 33 esophageal pH monitoring in hospitalized preterm infants (<37 weeks gestation and birth weight <2000g) with clinical suspicion of gastroesophageal reflux disease were enrolled. Probe placement was assessed using Strobel’s equation and specific formulas for preterm infants (Gupta & Jadcherla). These measurements were compared with fluoroscopy.

Results: The pH monitoring was assessed in preterm infants who had median weight and length of 2100 g and 43.5 cm, respectively, and post-conceptual age average of 38.2 weeks. The Pearson correlation analysis showed a significant positive correlation between measurements by Strobel’s equation, Gupta & Jadcherla’s formula based on length and weight, and fluoroscopy (r = 0.789, r = 0.875 and r = 0.740, p <0.001, respectively). There was no significant relationship between probe position using Gupta & Jadcherla’s formula based on post-conceptual age and fluoroscopy (r = 0.360, p = 0.039).

Conclusion: The data suggests that it is appropriate to use Strobel’s equation and Gupta & Jadcherla’s formula based on length and weight as methods of accurate placement of pH probes in preterm infants, thus avoiding their exposure to ionizing radiation by imaging exams.


Disclosure of Interest: None Declared
ABSTRACT TITLE*: EVALUATION OF ENZYME IMMUNOASSAY AND PCR FOR DETECTION OF HELICOBACTER PYLORI IN STOOLS AND GASTRIC BIOPSIES

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1 microbiology & immunology, 2 internal medicine, Faculty of medicine, Alexandria University, Alexandria, Egypt

Objectives and Study: Various tests have been developed to diagnose Helicobacter pylori infection, but all have limitations. H. pylori can be detected by non-invasive and invasive methods, the latter requiring endoscopy. Noninvasive testing is widely available and has been considered as an initial management strategy for uninvestigated dyspepsia. The aim of the present study was the evaluation of the noninvasive techniques used for diagnosis of the organism and to compare these techniques to the traditional invasive ones.

Methods: The present study was carried out on 52 patients suffering from dyspepsia. From these patients gastric biopsy specimens were taken for detection of H. pylori infection by the conventional methods (H & E staining, rapid urease test "RUT", and culture) and the PCR assay. In addition, stool samples were taken for the detection of H. pylori antigen and DNA by ELISA and PCR techniques respectively.

Results: Helicobacter pylori infection was detected in 35 cases (67.3%) . Helicobacter pylori stool assay (HpSA) gave the highest rate of detection (71.2%). The lowest rate of detection of H. pylori infection was by PCR in stool which detected only 44.2% of cases.

Conclusion: Helicobacter pylori stool assay (HpSA) could be used as a routine diagnostic tool for H. pylori infection. It seems to overcome some limitations of the conventional invasive techniques. It has the potential advantages of being simple to perform, relatively cheap, and samples can be submitted directly from primary care.

Disclosure of Interest: None Declared
Positioning of Impedance Probe at Endoscopy: Confirmation at Fluoroscopy vs Blind Insertion

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1 Paediatric Gastroenterology, 2 Royal London Hospital, London, United Kingdom

Objectives and Study: 24Hr IMP/pH study is becoming the gold standard diagnostic modality for the detection of GERD. In children under the age of 2 yrs or children with neurodevelopmental impairment the impedance catheter is increasingly being placed at the time of endoscopy for those children requiring mucosal assessment. It is imperative that the catheter is accurately placed to ensure adequate study analysis. In our unit, whilst the catheter placement site could be estimated at endoscopy the post anaesthetic confirmation Xray in the awake state often found this to be inaccurate therefore requiring replacement under screening. The aim of this study was to review our practice of IMP/pH catheter placement and find out the difference between the impedance probe placement under fluoroscopy and blind insertion during endoscopy.

Methods: We included children who had impedance study between January and October 2012. A total of 46 children had impedance study done, out of 46 children 23 had impedance probe inserted during endoscopy under fluoroscopy guidance and therefore position of the probe was determined at the same time by screening. The remaining 23 children had impedance probe inserted during endoscopy without any fluoroscopy guidance, therefore position was determined by a chest Xray in radiology department. Position was considered acceptable if the impedance probe marker was between T9 and T10.

Results: Out of 23 children who had impedance probe inserted during endoscopy under fluoroscopy guidance in 20 children (86.9%) the probe was in the right position, 2 children (8.6%) could not tolerate the probe post procedure, 1 child (4.3%) the probe was displaced and therefore a repeat Xray was done.

Out of 23 children who had impedance probe inserted during endoscopy without fluoroscopy guidance and children had an Xray in radiology department 13 children (56.5%) had probe in the right position, 10 children (43.4%) had it in the wrong position and therefore adjustments were done followed by a repeat XRay in the radiology department. Position was considered acceptable if the impedance probe marker was between T9 and T10.

Conclusion: This study shows that insertion of impedance probe is more accurate when done under fluoroscopy guidance as compared to when done without fluoroscopy. Although the radiation dose (1.5msv) of fluoroscopy is much higher than as of a routine chest Xray (0.02msv). If there is screening facility available at endoscopy this study suggests that probe positioning at endoscopy is more accurate and cost effective as children usually do not require repeat chest Xrays.

Disclosure of Interest: None Declared
Objectives and Study: Objectives and study: Frequently infants present symptoms of gastroesophageal reflux including regurgitations, some vomiting episodes and excessive crying. The latest NASPGHAN/ESPGHAN GERD guideline recommends for infants as the first step, non-pharmacological intervention including body positioning and thickened formula. The aims of this study are 1- To evaluate a clinical GER score in infants that were fed with an AR formula containing a mixed potato/corn starch 1,8 grams/100ml, ARplus formula containing 2,2 grams/100ml and a standard formula at baseline and after four weeks. 2- To evaluate the body weight variation during this period of time.

Methods: Methods: 66 infants younger than 6 months old were selected to participate for this prospective randomized blind study. A clinical GER score described by Orenstein and modified by Kleinman et al, 2006 and body weight variation were performed at baseline and after 4 weeks in three groups (AR formula, ARplus formula and standard formula). All of them containing 67 Kcal/100 ml of energy and were provided by Nestlé-Brazil.

Results: Results: Median age: 103 ± 42 days. Dropout was 5/66 cases. Median weight at baseline: 5.900±1387 grams. GER score was registered at baseline and after 28 days: AR group N=19 (initial score 18,6 – final score:9,0 delta= -9,6); ARplus group N=21 (initial score :17,6- final score:8,0 delta=-9,6) and standard group N=21 (initial score =20,1- final score=13,8 delta= -6,24) p=0,026. Success Index was defined by the clinical score decreasing more than 6 points and it was 94,7% in AR group, 85,7% ARplus group and 57% in standard formula group (p<0,05 comparing AR groups with standard). Weight variation was 857 grams AR group, 830 grams ARplus group and 543 grams standard group. Delta weight between AR groups and standard was significant (Bonferroni alpha coefficient =0,02 and 0,023 respectively). For the different symptoms ARplus had better performance on refusal to eat (p=0,007), stop feeding (p= 0,007) and arching back (p=0,015).

Conclusion: Conclusions: 1- clinical symptoms of GER decreased in all groups but less consistently under standard formula. AR formulas determined higher weight gain as compared to standard formula. ARplus formula decreased better symptoms concerning refusal to eat, stop feeding and arching back.

Disclosure of Interest: None Declared
NON ACID GASTROESOPHAGEAL REFLUX CAN TRIGGER APNEAS IN NEONATES

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Objectives and Study: The aim of the study was to examine the temporal and causal association between obstructive apneas (OA) and gastroesophageal reflux (GER) in infants under 12 months, with a diagnosis of gastroesophageal reflux disease (GERD) and obstructive apneas.

Methods: Prospective study of 22 infants with a diagnosis of OA underwent a 24 hours simultaneous registration with polysomnography and esophageal multichannel pH-impedance (MII-pH). The symptom index (SI) and symptom association probability (SAP) were calculated both in function of different time windows and depending on the type of reflux (weakly alkaline pH>7; weakly acid 4<pH<7; acid pH<4), to verify a preferential association. We checked intervals of time before and after the apneas (30' - 1'-2').

Results: We have enrolled 22 patients (12 female). Approximately 2/3 of the population was born preterm, but all reached the term at the time of clinical and instrumental evaluation. Mean age was 2.7 months (SD ±1.78 months), median age was 2 months (range 1-7 months).

1358 episodes of reflux have been detected, 347 acid (25.5%), 958 weakly acidic (70.5%) and 53 weakly alkaline (4%). Median SAP for the symptom apnea was 96%. Recorded episodes of apnea were 196.

The group of acid reflux occurring within 2' before apnea, was significantly different (p <0.01) from the group of acid reflux occurring within 2' after apnea. We obtained the same result considering the interval of time of 1' before and after the apnoic event. Regarding acid refluxes occurring within 30" from the apnea, the difference was not significant. Weakly acidic refluxes were significantly causative of OA since they were prevalent in all three windows time(2', 1', 30") before OA (p< 0.01).

Conclusion: Our data confirm that a high rate of apneas can be triggered by non-acid GER in infants. Further studies are needed to recognize the clinical features that identify patients who are more susceptible to GER-induced apnea and confirm the pH-MII characteristics of reflux (weakly acidic in our study) most associated with sleep apnea event.

Disclosure of Interest: None Declared
THE PREVALENCE OF EROSION GASTROESOPHAGEAL REFLUX DISEASE AND HELICOBACTER PYLORI INFECTION IN CHILDREN.
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Objectives and Study: The relationship between Helicobacter pylori infection and erosive reflux esophagitis remains controversial, particularly in childhood. In the recent years the incidence of gastroesophageal reflux disease (GERD) and H pylori infection have opposing trends. The aim of this study was to assess the relationship between H pylori infection and erosive reflux esophagitis among gastroscopied symptomatic children, in our unit, during the last decade.

Methods: We conducted a retrospective study of all 1142 symptomatic children (710 girls, age range to 6 month – 18 years) who underwent esophagogastroduodenoscopy (EGD) between 2001 and 2010, in our unit.

Results: The reflux esophagitis (RE) was graded according to Hetzel-Dent classification, where the grade 2 was considered as erosive esophagitis. H pylori infection was evaluated in the case of all children by rapid urease test and histopathology and sometimes by culture and polymerase chain reaction (PCR) for virulence markers. The demographics, clinical and endoscopic findings were analyzed in relationship with the prevalence of erosive esophagitis and H pylori infection.

Among the 1142 studied children, 606 (53,06%) were positive for H pylori infection and 635 (55,60%) were diagnosed with reflux esophagitis (RE), which had the following repartition: erosive reflux esophagitis was founded in 412 cases (36,07%) and nonerosive reflux esophagitis in 223 cases (19,52%) respectively, p< 0,0001 . The prevalence of erosive reflux esophagitis in the H pylori positive patients was 51,82% (314 cases) compared with 18,28% (98 cases) in uninfected ones (p< 0,05).

Similarly, the nonerosive reflux esophagitis was more prevalent in infected H pylori children compared with uninfected ones (153 cases versus 70 cases; 25,24% versus 13,05%), p< 0,05. The yearly prevalence rate of H pylori infection varied from 46,93% in 2001 to 49,54% in 2010, with an unexpected increase between 2006 and 2009 (69,87% versus 59,64%). Mostly of H pylori infected children had macroscopic aspect of predominantly antral gastritis, with nodular gastrophaty (479 cases versus 88 cases in uninfected ones, respectively 79,04% versus 16,41%).

Conclusion: The recent decline of H pylori infection observed in developed countries is not evident in our study. This study shows that the prevalence of erosive reflux esophagitis was significantly higher in infected H pylori children (p< 0,05), probably because predominantly antral gastritis is more common in H pylori infected children compared with infected adults.
Disclosure of Interest: None Declared
GASTROENTEROLOGY
GERD, PEPTIC DISEASE AND HELICOBACTER PYLORI

PO-G-0146

ACCURACY OF DIAGNOSTIC TESTS FOR PEDIATRIC HELICOBACTER PYLORI INFECTION
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Objectives and Study: Because Helicobacter pylori infection is acquired mostly in childhood, accurate diagnosis of the pediatric infection remains a very important problem.
To investigate the accuracy of invasive and noninvasive diagnostic tests.

Methods:
We conducted a prospective study of 145 children with active H pylori infection (age range 1-18 years old), who were diagnosed by invasive and non-invasive tests, during 2009-2011.
Gastric antral biopsies were obtained for rapid urease test, histopathology, culture and polymerase chain reaction (PCR) for H pylori virulence markers. Non-invasive tests, such serological antibodies and H pylori antigen in stool were analyzed.
Sensitivity, specificity and predictive positive value (VPP) of non-invasive tests were compared with the invasive ones.
Statistical analyses were performed using the GraphPad Prism program

Results: Of 145 children with H pylori infection, the rapid urease test was positive in 115 children (sensitivity 79,31 %; specificity 93,94%; VPP 92%) and histology in 129 cases (sensitivity 89,58%; specificity 99,36%; VPP 99,23%). Culture was performed in 108 cases (sensitivity 74,48%; specificity 100%). The sensitivity of rapid urease test was lower, respectively significantly lower in case of culture, compared with histology. There was no difference in specificity and VPP between histology and culture, but not in the case of rapid urease test, which were lower. The H pylori virulence genotype was analyzed by conventional PCR, which was positive in the cases of 140 children (sensitivity 96,55%; specificity 100%), significantly higher compared with the other invasive tests. The cag A gene was positive in 96 cases, compared with vac A, which was identified in all 140 cases isolated by PCR. The predominant combination for gene vac A allelic types was s1m1 type (86 cases; 61,42%). H pylori fecal antigen was identified in the 132 children with a significantly higher sensitivity (92,96%), specificity (98,10%) and VPP (97,78%) compared with the rapid urease test, histology, culture, respectively lower in comparison with PCR. The serological antibodies against H pylori were positive in 78 cases (IgG), respectively 80 cases (IgA), with a lower sensitivity, specificity than invasive tests and fecal antigen.

Conclusion: Our data suggest that among invasive test PCR, had a significantly higher sensitivity, specificity (p< 0,0001) compared with non-invasive tests. H pylori fecal antigen has shown high sensitivity, specificity (p< 0,0001) and has demonstrated his utility in the diagnosis and follow-up of H pylori infection

Disclosure of Interest: None Declared
TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION FOR OVERACTIVE BLADDER increases rectal motor activity in children: A randomized controlled study
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Objectives and Study: Objectives and study
Neuromodulation is used to treat overactive bladder (OAB) and can alleviate symptoms of constipation in children, but its effect on rectal motility is obscure.

Our aim was to evaluate the acute effect of transcutaneous electrical nerve stimulation (TENS) on rectal motility in children with OAB.

Methods: Methods In this double-blinded, placebo controlled study among 20 children with OAB (mean age 8.6+/−1.8yrs; 7 female) 48- hour natural fill urodynamics including rectal manometry was performed. After 24- hours of baseline investigation without stimulation the children were randomized to either active TENS (n=10) or placebo (n=10). Surface electrodes were placed at the level of S2-S3. The exterior of active and placebo stimulators was identical. Starting in the morning the children received continuous stimulation or placebo until bedtime. Rectal contractions were defined as pressure runs exceeding 5 cm H2O and lasting longer than 5 seconds.

Results: Results: See table 1 for values. At baseline there was no significant difference in time with rectal activity in the two groups on day one (p=0.75) or night one (p= 0.24). However, on the day two during stimulation there was more time with rectal activity in the group receiving TENS compared to the placebo, (p<0.05). Also, there was an increase in time with rectal activity in the group receiving TENS (p< 0.01) but not in the placebo group (p= 0.39). On night two, just after the TENS was disabled, rectal motor activity in both groups returned to the same level as observed during baseline at night one. (p=0.38).

<table>
<thead>
<tr>
<th>Rectal activity</th>
<th>Day one (No stimulation)</th>
<th>Day two (During stimulation)</th>
<th>Night one (No stimulation)</th>
<th>Night two (After stimulation)</th>
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Conclusion: TENS acutely enhances rectal contractions in children with OAB. The effect disappears when the stimulator is turned off.

Disclosure of Interest: None Declared
ESOPHAGEAL SMOOTH MUSCLE CONTRACTION SEGMENTS ON HIGH RESOLUTION MANOMETRY IN PEDIATRIC PATIENTS
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Objectives and Study: Esophageal-high-resolution manometry (EHRM) identifies a sequential chain of pressure segments, one in the striated-muscle region and two in the smooth-muscle region, forming the normal esophageal peristalsis. We compared the smooth muscle contraction segments in neurologically impaired children (NIC) and in children treated for esophageal atresia (EA) to healthy controls in order to characterize esophageal smooth muscle contraction segments in these subgroups of children.

Methods: Thirty-eight pediatric patients (mean age ± SD: 92.3 ± 40.2 months, range 8-215 months; M/F: 25/13) underwent unsedated EHRM. They were divided in three groups: group A included 10 patients with EA; group B included 14 NIC affected by severe psychomotor retardation (Intelligent Quotient ≤ 35); and group C included 14 children without esophageal or bowel disorders, matched for age and sex. Pressure data were acquired and displayed using software especially designed for EHRM. Segments were designated failed when both smooth muscle contraction segments were absent and fragmented when only one of the smooth muscle segments failed.

Results: A total of 410 swallows were analyzed (group A: 125; group B 147; group C 138). The same segmental architecture of esophageal peristalsis was observed in our patients as it had been reported previously. There was no significant difference in pressure troughs among the groups of patients (p>0.05). The first segment was observed in all the subjects of each group (100%). The second and third segments were present in ≥50 % of swallows in all groups of subjects; however, there was a significant difference between group B and group C (p< 0.08) and between group A and group C (p <0.08) in the presence of the third segment. No statistically significant differences were observed for the mean pressures of the three esophageal segments between group A and group C (p=0.95, p=0.89 and p=0.58, respectively). In group B the the mean pressures of the third segment were significantly lower (p<0.02) compared to the control group; whereas no statistically significant differences were observed for the mean pressures of the first and second segments (p=0.6 and p=0.8, respectively). Fragmented esophageal contraction segments were observed in 21.6% of Group A patients whereas synchronous esophageal activity with a low amplitude of the esophageal contractions were observed in 21.4% of Group B patients.

Conclusion: Evaluation of smooth muscle contraction segments adds value to EHRM analysis also in children. Specifically, the characteristic of the third segment may be a useful marker of esophageal hypomotility. The presence of fragmented segments suggests poor coordination of the esophageal motility.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GI MOTILITY AND FUNCTIONAL GI DISORDERS

PO-G-0149

EFFECTS OF EARLY PREBIOTIC AND PROBIOTIC INTERVENTION ON DEVELOPMENT OF GUT MICROBIOTA
AND CRYING IN PRETERM INFANTS - A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL
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Objectives and Study: The aim of this study was to evaluate the impact of early pre- and probiotic intervention on preterm infants’ crying and microbiological programming.

Methods: 94 preterm infants (gestational age 32-36 weeks and birth weight >1500g) who were randomized to receive prebiotics (a mixture of galacto-oligosaccharide and polydextrose 1:1 ), probiotics (Lactobacillus rhamnosus GG) or placebo during the first 2 months of life were followed up for 1 year. Infants were categorized into two groups based on their crying amount during the first two months of life. Their gut microbiota were investigated by FISH (n=66) and qPCR (n=63).

Results: During the first two months of life 27/94 (29%) infants were classified as excessive crying infants. The infants receiving pre- or probiotics manifested significantly less frequently excessive crying (19% in the both groups) than the infants receiving placebo (47%, p=0.02, p=0.02, p=0.72). The placebo group manifested higher proportion of Clostridium Histolyticum counts to total bacterial counts than the probiotic group (13.9% vs 8.9%; p= 0.05 respectively). No adverse events related to the supplementations were reported.

Conclusion: Both prebiotic and probiotic supplementation decreased early crying in preterm infants. This novel observation calls for further studies to reveal the exact mechanism behind this interconnection.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Recently, there has been an increasing interest in the technique of decellularization, which creates natural scaffolds by removing cells from animal or cadaveric organs. Decellularized scaffolds have already been successfully used in a variety of clinical applications. The aim of this study was to compare the three-dimensional structure of acellular human small intestine matrices obtained using three different decellularization methods.

METHODS: Following ethical committee approval, human small intestines were decellularized by use of either a detergent-enzymatic treatment (deionized water, 4% sodium deoxycholate, DNase-I), 1% Triton X-100 or 5% sodium dodecyl sulfate (SDS). Scanning electron microscopy (SEM) analysis was performed to examine the surface structure and three-dimensional organisation of the acellular matrices. Briefly, specimens of approximately 2 cm in length were fixed in glutaraldehyde, dehydrated through an ethanol gradient, critical point dried and coated with gold. Analysis was performed using a Jeol scanning electron microscope.

RESULTS: Decellularization of human small intestine (confirmed by histological absence of cells and loss of DNA) was achieved after 31 hours of detergent-enzymatic treatment (DET), 48 hours of Triton X-100 and 48 hours of SDS. SEM of the intestinal acellular matrices showed preservation of the ultrastructural characteristics of the native tissue after the DET and confirmed the absence of cells. The analysis of the luminal surface after 1 cycle of DET clearly revealed the presence of leaf-shaped villi and preservation of their internal structure, whilst the Triton treated scaffold showed a fragmentation and deformation of the villi structure, with shrinking of the collagen fibers also present with the SDS method.

CONCLUSION: The comparison of different techniques of intestinal decellularization has suggested that a gentle detergent-enzymatic treatment using a combination of deionised water, sodium deoxycholate and DNase is superior to the use of Triton X-100 or SDS in preserving ultrastructural characteristics of the native tissue whilst removing cellular material. This natural acellular matrix provides a valid support for future preclinical studies and eventual clinical application.

DISCLOSURE OF INTEREST: None Declared
PO-G-0151

PSYCHOLOGICAL CHARACTERISTICS OF CHILDREN WITH IRRITABLE BOWEL SYNDROME
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Objectives and Study: Psychological factors play an important role in the development and clinical course of many functional disorders, including irritable bowel syndrome (IBS). The main objectives of our study were to reveal the features of the psychological status of patients with IBS and to determine the effect of psychotherapeutic treatment on this disease.

Methods: Consecutive patients (n = 87) admitted to our Department of Gastroenterology, matching the Rome III Criteria for IBS, were recruited. They were asked to complete Leonhard’s test (to identify accentuated features), Phillip’s questionnaire (to determine anxiety level), Balashov’s questionnaire (to find out depressive disorders) and Pediatric Quality of Life Inventory (PedsQL). The first group of patients (n =57) received only symptomatic drug treatment, the second group (n =30) visited also sessions of cognitive therapy. The control group comprised of 40 healthy subjects.

Results: The control group demonstrated hyperthymic type of personality, associated with optimistic outlook on life (25,0% versus 15,0% in IBS group). At the same time, IBS patients were characterized by a great incidence of anxiety (p<0,05), stuck (p<0,01) and excitable (p<0,05) personality traits. Comparative analyses of patient groups revealed that children with diarrhea had accentuated affective-exalted and anxiety features (p<0,05), while patients with constipation expressed pedantic and stuck traits (p<0,01). Average scores for all anxiety factors were higher by 50% among patients compared with healthy children (p<0,01 for all parameters). The main causes of anxiety among children with IBS were associated with school activity, self-esteem and communication (p<0,001). Also patients with IBS showed a slight tendency to have depressive features being increased (29,7%). At the beginning of the treatment both groups of patients were comparable in all parameters. Three month later, children from the first group showed significantly higher levels of emotional and social functioning (p<0,001). Indicators of physical functioning and school activity were almost identical. Complaints of abdominal pain persisted in 2 patients (6,7%) from the first and in 14 patients (24,6%) from the second group. Up to 60% of patients in both groups suffered from bloating before the treatment. After course of psychotherapy this patients’ complaint disappeared, while 21 (36,8%) of patients in the second group continued to experience this feeling (p<0,05).

Conclusion: Children with IBS have a special psychological status with prevalence of anxiety and neurotic traits and tendency to over-emotional experiences. Addition of psychotherapy in the treatment of IBS has a positive effect on the course of the disease and can significantly improve the quality of life of these patients.

Disclosure of Interest: None Declared
MIGRAINE BASED THERAPY IN CYCLIC VOMITING SYNDROME
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Objectives and Study: CVS is characterized by repetitive bouts of intense nausea and vomiting interspersed with interval return to normal state. Our CVS center initiates treatment based on evidence-based migraine therapy. Between attacks, nutritional strategies are recommended to avoid food triggers as well as hypoglycemia at night and during exertion. Parents and children are taught to recognize a prodrome and to use NSAIDs and a prokinetic drug (domperidone) early to abort incipient attacks. We studied the results of treating CVS as migraine in our patient population.

Methods: A single centre chart review includes 73 children with CVS diagnosed according to standard criteria seen between 2006 to present. Follow-up was available in 55. Mean age was 12.2 yrs. There were 27 males and 28 females. On average children were diagnosed at age 8.7 with a history 5.3 yrs of vomiting at assessment. Twenty-three (23/55) had a first degree relative with migraine. The duration of attacks averaged 33.4 hours (range 2.5 - 72 hours per episode). Improvement was defined as complete resolution of symptoms or 50 % improvement in number or duration of attacks.

Results: Upon analysis, 55 out of 73 total patients had a measurable outcome. Of these, 10 patients received the standard intervention, and 33 received migraine based intervention. Among these, 25 out of 33 patients (76%) treated with the McMaster migraine protocol showed improvement, whereas 4 of 10 patients (40%) receiving the standard intervention improved (p<0.05). Fifteen of 23 (15/23) had a family history of migraine. Twelve of the fifteen (80%) patients with a family history of migraine improved with migraine based therapy (NS).

Conclusion: CVS comprises a heterogeneous group of conditions whose pathogenesis is not fully understood. However, in this population symptoms resolved or improved in a majority of children treated with a protocol adapted from migraine therapy. Further studies are required to predict those children most amenable to this approach.

Disclosure of Interest: None Declared
HIGH PREVALENCE OF VESTIBULAR DYSFUNCTION IN CHILDHOOD CYCLIC VOMITING SYNDROME.
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Objectives and Study: Cyclic vomiting syndrome (CVS) in childhood is usually a benign condition which improves with age. Triggers of the emetic episode include intercurrent infections, travel, tiredness, excitement and in older girls menstrual periods. Once an emetic episode is triggered there follows a commonly stereotypical sequence of events during the emetic phase followed by a rapid return to normality. The vestibular apparatus provides important sensory input to the brainstem vomiting centre and modulates the emetic threshold. We hypothesised that vestibular dysfunction might lower the threshold for emesis in CVS.

Methods: Retrospective review of medical records of consecutive referrals with CVS to a single tertiary centre who had undergone formal vestibular function testing.

Results: Records of 55 patients with CVS, 31 female and 24 male, average age of onset 66 months were reviewed. In 7 children CVS episodes were triggered by travel, in 11 stress/excitement, in 5 infections, in 3 menstruation and in 30 no trigger was identified. 23 suffered from motion/travel sickness, 4 from tinnitus and 9 had hearing problems. 16 reported poor balance and 23 reported headaches. 5 had conductive hearing loss on pure tone audiometry. 11/33 had an abnormal Unterberger’s test consistent with vestibular abnormalities, and 9/16 had abnormal bithermal caloric testing. All 55 had undergone either electronystagmography (ENG) or videonystagmography (VNG), a form of video-oculography (VOG). 6 had abnormal smooth pursuits, 2 optokinetic nystagmus, 12 had directional preponderance on rotational impulse testing, and 14 abnormalities on sinusoidal chair rotation. Overall 19/55 had evidence of vestibular dysfunction and 12 of these underwent vestibular therapies. 44/55 had cranial MRI scans of which 5 were abnormal.

Conclusion: Vestibular abnormalities are prevalent in childhood CVS appropriate treatment of which could potentially modulate emetic threshold favourably and lead to a reduction in frequency of emetic episodes.

Disclosure of Interest: None Declared
VARIATION IN RECTAL DIAMETER MEASURED BY TRANSABDOMINAL ULTRASOUND DEPENDS ON TIME TO DEFECTION
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Objectives and Study: Rectal diameter (RD), which has been shown to be an indicator of rectal impaction, can be measured by transabdominal ultrasound. Rectal impaction is one of the 6 Rome III criteria in childhood functional constipation. Studies describe variation in RD between 2.1-3.29 cm in not constipated children and 3.4–4.9 cm in constipated children. Cut off value for detection of rectal impaction varies between 2.40-3 cm. Studies may be biased by methodological differences in inclusion criteria, standardization of scanning method and registration of defecation. However, it is not known whether there is a diurnal variation in RD or how RD varies with defecation.

In order to describe variation in RD, we measured RD in not constipated and constipated children during 24 hours admission.

Methods: 28 children (14 constipated and 14 not constipated children, age 4-12 years) were included. All constipated children fulfilled the Rome III criteria at time of diagnose and received laxatives for at least 1 month. Not constipated children had no history of constipation or gastrointestinal diseases.

All children were admitted 24 hours and RD was measured every 3 hour. Whenever a child defecated, RD was measured and additional scans were made after one and two hours.

The ultrasound was performed using a 6 MHz convex probe placed 2 cm above the symphysis at a 10 degree downward angel from the transverse plane. RD was measured three times from inner wall to inner wall and mean RD was calculated.

Results: A significant decrease was found in post defecation median RD values. The not constipated group decreased from 1.82 cm (range 1.30-2.98) to 1.46 cm (range 1.05-1.85) (P=0.0001), and the constipated group decreased from 2.19 cm (range 1.61-3.68) to 1.62 cm (range 1.19-2.63) (P=0.0002).

No difference in RD was found between the groups more than two hours before defecation (P=0.073) or less than two hours before defecation (P=0.76). A significant difference in RD was found between the two groups after defecation (P=.0004).

The difference in RD among the two groups remained significant one hour (P=0.021) and two hours after defecation (P=0.0116). After three hours, the difference was no longer significant (P=0.2224).

There were no significant differences in age, weight, height or median RD at admission.

At 2 pm median RD in both groups was elevated to 2.02 cm (range 1.78-3.19) compared to the primary scan at 08 pm 1.74 cm (range 1.30-2.98) (P=0.044).

Conclusion: We found a diurnal variation in RD in both groups, which was related to defecation. RD in constipated children was significantly larger up to two hours after defecation.
These data has to be taken into consideration when using RD as part of the diagnostic algorithm of childhood functional constipation.

**Disclosure of Interest:** None Declared
ALLERGIC DISEASE AND RECURRENT ABDOMINAL PAIN DURING CHILDHOOD – A SWEDISH BIRTH COHORT STUDY
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Objectives and Study: Lately, mast cell activity and different allergic diseases have been linked to recurrent abdominal pain (RAP). Earlier studies have shown conflicting results, and no study has been able to differentiate between allergic disease preceding RAP and allergic disease coexisting with RAP, or to explore the interaction between allergic diseases and RAP.

Methods: In a Swedish birth cohort study parents answered questionnaires regarding asthma, rhinitis, food hypersensitivity and eczema (here called allergic diseases) at birth and at ages 1, 2, 4, 8 and 12 yrs (N=2746). Blood was sampled (n=2396) at 4 and/or 8 years. At 12 yrs the children answered questions regarding RAP (“every month or more often”). Children with celiac disease or inflammatory bowel disease were excluded from the definition of RAP. We used multivariable logistic regression to examine the association between allergic diseases at age 1-12 yrs and RAP at age 12.

Results: At 12 yrs, 9% (n=237) of children reported RAP. Allergic disease at 1, 2, 4 and 8 yrs respectively was not associated with RAP at 12yrs. However, at 12 years all allergic diseases were associated with concurrent RAP (adjusted odds ratio (aOR) (95% Confidence Interval (CI)): food hypersensitivity 2.35 (1.74-3.17), eczema 2.12 (1.52-2.97), asthma 2.15 (1.35-3.43) and rhinitis 1.53 (1.10-2.11). Sensitization to food allergens at 4 or 8 years was associated with RAP at 12yrs (aOR=1.53, 95% CI=1.12-2.09), even when restricting analyses to children without food hypersensitivity, whereas sensitization to airway allergens was not (aOR=1.18, 95% CI=0.85-1.65). We found an increased risk of RAP with increasing number of allergic diseases (aOR (95% CI) for 1, 2 and 3-4 allergic diseases at 12 years respectively: 1.46(1.06-1.99); 2.14(1.42-3.23); 3.24(1.74-6.05)). Children with asthma (aOR=1.27, 95% CI=0.50-3.24) or rhinitis (aOR=1.17, 95% CI=0.71-1.94) but without coexisting other allergic diseases at 12yrs, were not at increased risk of concurrent RAP. In contrast, both eczema (aOR=1.77, 95% CI=1.05-3.00) and food hypersensitivity (aOR=1.86, 95% CI=1.26-2.75) were associated with RAP, even if other allergic diseases were absent.

Conclusion: Allergic diseases were associated with an elevated risk of concurrent RAP and the risk increased with the number of allergic diseases. Eczema, sensitization to food allergens and food hypersensitivity seemed to be independent risk factors for concurrent RAP, whereas asthma, rhinitis and sensitization to airway allergens did not. These results add interesting data to the literature on the pathophysiology of RAP and emphasize the likely role of immune dysregulation in general and mast cell activity in particular.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GI MOTILITY AND FUNCTIONAL GI DISORDERS

PO-G-0156

DEVELOPMENT OF A PSYCHOSOCIAL TAXONOMY OF PAEDIATRIC PATIENTS WITH FUNCTIONAL ABDOMINAL PAIN
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Objectives and Study: While different psychological treatment options exist for the variety of children and adolescents with functional abdominal pain syndrome, criteria for the selection of the appropriate therapy in an individual case are lacking. The delay in effective treatment may cause doubt about the benign nature of the disease and result in unnecessary investigations. To develop a psychosocial taxonomy of paediatric patients with functional abdominal pain and facilitate treatment allocation, we extended the medical evaluation by psychosocial assessment.

Methods: From all patients presenting to our paediatric clinic fulfilling Rome III criteria for the diagnosis of functional abdominal pain, 87 patients (53 male) 4.5-22.5 years old (median 11.7) without somatic findings severe enough to explain their complaints were investigated. Psychosocial assessment included a psychodynamic in-depth family interview and a psychometric test battery (Gießen Physical Complaint List for Children and Adolescents=GBB-KJ and German versions of Children's Depression Inventory=DIKJ, Toronto Alexithymia Scale=TAS-KJ and Family Assessment Measure=FB). Q factor analysis was performed to identify characteristic psychosocial patient profiles in the study population. Typic cases were identified and information from interviews drawn to build a psychosocial taxonomy of abdominal pain cases.

Results: The principal component analysis identified 3 factors with an eigenvalue>1 explaining 91% of the variance. High total scores in TAS-KJ and GBB-KJ were loading on the first factor, high scores on the subscales communication, affective expression and affective involvement of the FB with high total scores in FB and GBB-KJ and high scores on the control scales defence and social desirability of the FB on the third factor. Three psychosocial patient profiles (somatisation with alexithymia and moderate denial of psychosocial conflicts, massive somatisation with openly communicated psychosocial conflicts, and isolated abdominal somatisation associated with denial or repression of conflicts in combination with normative attitudes) were thus empirically identified and substantiated with interview narratives.

Conclusion: The use of methodological triangulation combining qualitative and quantitative methods allows the identification of three different psychosocial profiles of paediatric patients with functional abdominal pain. We suggest adapting the therapeutic approach to the individual patient profile according to the level of defence, degree of alexithymia, and psychological strain. Prompt assignment to an appropriate psychological treatment modality may decrease the use of unnecessary somatic investigations and pharmaceutic therapies.

Disclosure of Interest: None Declared
Objectives and Study: The aims of this twin family case-control study were to test the hypothesis that life prevalence of non-specific paediatric recurrent abdominal pain (RAP) is genetically influenced and to examine potential co-morbidities.

Methods: In Phase I of the study, twins, parents and siblings were asked if they had a history of recurrent abdominal pain, if it was diagnosed by a doctor, the onset and duration. From these responses, a judgement was made about non-specific RAP. In Phase 2, twin and family members who reported RAP were sent Rome III questionnaires for further diagnostic classification (results pending). Standard questionnaires, validated for zygosity, growing pains (GP), migraine, headache and restless legs syndrome (RLS) and screening questions for ADHD, iron deficiency, low back pain (LBP) and chronic pain were randomly distributed by the Australian Twin Registry to twins aged 3-18 years, their biological siblings and parents. To assess heritability, \( \chi^2 \) analyses determined the significance of the difference in the casewise concordance rate between monozygous (MZ) and dizygous (DZ) twin pairs. The case-control design, analysed by \( \chi^2 \), odds ratio (OR; 95% CI) for dichotomous data and t-tests for continuous data, was applied to test the associations between case and control twin individuals and families.

Results: The questionnaires were distributed to 3,909 twin families yielding 1,017 (26%) evaluable responses by time of analysis. 211 twin families had at least one twin identifying as having RAP. 33 out of 107 (31%) MZ twin pairs were concordant for RAP compared with 17 out of 104 (16%) DZ twin pairs. The casewise concordance was 0.47 for MZ pairs and 0.28 for DZ (\( \chi^2 = 6.13, P = 0.021 \)). The prevalence of RAP in parents and siblings in case families was significantly higher than in control families (mothers: \( \chi^2 = 33.21, OR = 2.6 (1.86-3.60), P < 0.001 \); fathers: \( \chi^2 = 16.30, OR = 2.5 (1.57-3.86), P < 0.001 \); siblings: \( \chi^2 = 18.53, OR = 2.5 (1.63-3.84), P < 0.001 \)). Twin individuals with RAP had significant associations with GP (\( \chi^2 = 15.25, OR = 1.8 (1.34-2.43), P < 0.001 \)), RLS (\( \chi^2 = 23.92, OR = 2.4 (1.66-3.34), P < 0.001 \)), migraine (\( \chi^2 = 44.35, OR = 3.5 (2.37-5.13), P < 0.001 \)), headache (\( \chi^2 = 38.08, OR = 2.6 (1.91-3.57), P < 0.001 \)), chronic pain (\( \chi^2 = 84.41, OR = 5.2 (3.53-7.60), P < 0.001 \)), LBP (\( \chi^2 = 8.62, OR = 2.0 (1.25-3.13), P = 0.005 \)), iron deficiency (\( \chi^2 = 19.98, OR = 2.5 (1.66-3.85), P < 0.001 \)), and high anxious depression scores (\( P = 0.037 \)).

Conclusion: Paediatric non-specific RAP might be heritable. RAP has characteristics of a functional pain syndrome, as currently defined, with genetic susceptibility, associations with other common paediatric pain syndromes, and with anxious depression.

Disclosure of Interest: None Declared
EFFECTS OF LACTOBACILLUS REUTERI AND LACTULOSE ON CHILDHOOD CONSTIPATION AND QUALITY OF LIFE.

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Objectives and Study: We aimed to compare the effectiveness of Lactobacillus reuteri and lactulose treatments on children with functional constipation and assess their quality of life scores before and after constipation treatment.

Methods: Turkish version of age specific generic KINDL quality of life (QoL) questionnaires were applied to 103 children aged 8.1 ±0.5 years (53 patients, 50 controls). Proxy version was applied to their parents. This consist of parallel child and parent self-report scales encompassing physical, emotional, social, and school functioning and disease perception. Higher scores indicate better QOL. Functional constipation was defined according to Roma III H3a criteria. Children with functional constipation (n:53), randomly received 5 drops of Lactobacillus reuteri (1x10⁸ cfu, n: 25) or lactulose (1 ml/kg, n: 28) treatments daily for 4 weeks. MgOH was allowed when no stool passage for 3 days was noted. Frequency of defecation, stool consistency with Bristol stool chart, pain during defecation, fecal soiling, flatulence, abdominal pain, and rectal bleeding were noted weekly and compared between the 2 groups. After treatment, QoL questionnaires were re-applied to the children in both treatment groups and to their parents.

Results: The patients who received Lactobacillus reuteri or lactulose improved in terms of defecation frequency per week (before 1.96 ± 0.1 after 5.04 ± 0.3 and before 1.71 ± 0.1 after 4.61 ± 0.4), Bristol scores (before 1.68 ± 0.1 after 3.48 ± 0.2 and before 1.75 ± 0.1 after 3.46± 0.2 respectively) abdominal pain, painful defecation, and stool withholding behavior without significant difference (p<0.05). Abdominal pain and flatulence complaints in the probiotic group decreased significantly when compared to lactulose group (p<0.05). Mean QoL scores of children with functional constipation were significantly lower compared to healthy children (64.7 versus 72.7, p=0.01). After treatment, child reported total QoL scores improved in both treatment groups without significant difference (from 65 to 77, and from 64 to 78).Parent reported QOL scores were significantly lower in constipation group and improved after treatment (p<0.05) Parent disease perception scores related with the QoL of their children was better after lactulose treatment (p<0.05). There was no difference between probiotic and lactulose treatments in terms of MgOH usage.

Conclusion: Lactobacillus reuteri showed comparable efficacy with lactulose on treatment of functional constipation. QoL of patients with constipation is poor when compared to healthy children, and can be improved by both Lactobacillus reuteri or lactulose. Lactulose is more effective for family satisfaction, which may be attributed to the rapid effects of lactulose on constipation.

Disclosure of Interest: None Declared
EB-VIRUS INFECTION-A COMMON CAUSE OF FUNCTIONAL ABDOMINAL PAIN (FAP) IN CHILDREN WITH AND WITHOUT AUTISM
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Objectives and Study: Epstein Barr-virus (EBV) has previously been shown to be a cause of Recurrent Abdominal Pain (RAP) in children. Children with Autism have a high prevalence of RAP. An association between high TNFα-levels and RAP has been reported in Autistic children (1). We analyzed 2 groups of children with FAP (ROME III-criteria) with or without Autism with regards to 1. EBV- serology and 2. Cytokine levels in peripheral blood mononuclear cells (PBMC).

Methods: We performed a prospective study of initially 50 children with RAP, 20 with and 30 without Autism. Extensive (W/U) including blood and stool analysis, EGD and Colonoscopy with biopsies and in some children radiology examination were performed 14 children (mean age 8 years, 100% boys) with Autism and 20 (mean age 14.5 years, 40% boys) without Autism fitted the criteria of FAP (ROME-III) and were further evaluated. EBV-serology panel (Viral Capsid AG(VCA)-IgM and IgG, Early AG(EA)-IgG and Nuclear AG(EBNA)-IgG and extensive Cytokine analysis of 23 different Cytokines were analyzed.

Results: All blood and stool W/U in the remaining 34 patients were normal. A positive EBV-serology was found in 5/11 (46%) of the Autistic and 15/20 (75%) of the non-Autistic children with FAP. The biopsies from the stomach and colon did not show any gastritis or colitis in any of the patients. Of the 23 cytokines analyzed only TNFα was significantly elevated in the Autistic- compared with the non-Autistic group with FAP (7.1 +/- 1.0SE vs 4.3 +/- 0.4 SE, p=0.025). A larger number than expected (65%) of children (mean age 11.5y) with FAP had positive EBV-serology. 2. Neither gastritis nor colitis were found in any of the children in the 2 groups with FAP. 3. A tremendous gender discrepancy between children with Autism (100% boys) and without Autism (60% girls) with FAP.

Conclusion: Children with FAP and Autism had significantly elevated TGFα levels compared with non-Autistic group. It is possible that this reflects increased TNFα production from non allergic hypersensitivity (NFH) in the Autistic children.


Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Thickening of the internal anal sphincter has been observed in children with constipation(1). Whilst it is known that contents of the rectum can be measured using trans abdominal ultrasound, little is understood about structural properties of the rectal wall in constipated children. The aim of this study was to compare rectal wall measurements and causative parameters in a mixed cohort of normative and constipated children.

METHODS: Children between 4 and 12 years attending Centre for Children’s Incontinence were routinely screened for bowel dysfunction and those who fulfilled the Rome III criteria for constipation were included in the study. Normative children of the same age were recruited from the families of staff working at the Centre and were eligible for inclusion if they were free of any symptoms of bowel dysfunction. The bladder was partially full and used as a window to visualize the transverse plane of the rectum. Wall thickness measures were taken from the outer to the inner rectal wall in the anterior muscle, left and right sidewalls and expressed in millimetres. The rectal diameter was computed from a measure of outer wall to outer wall and recorded alongside observation of full or empty rectum. Data was normally distributed and the difference between mean values compared between normal and constipated children.

RESULTS: There was no significant difference in age or rectal wall thickness between the groups. There was no significant overall correlation between rectal diameter and rectal wall thickness (anterior wall r= 0.04; left wall r=0.044; right wall r= -0.122); a significant inverse correlation between rectal diameter and anterior wall was noted in normal children (r=-0.36).

<table>
<thead>
<tr>
<th></th>
<th>Rectal diameter (SD)</th>
<th>Anterior wall</th>
<th>Left wall</th>
<th>Right wall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>27.10 (9.2)</td>
<td>1.48</td>
<td>2.00</td>
<td>1.84</td>
</tr>
<tr>
<td>n=43</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Constipated</td>
<td>37.74 (9.2)</td>
<td>1.60</td>
<td>1.97</td>
<td>1.94</td>
</tr>
<tr>
<td>n=30</td>
<td></td>
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<tr>
<td>p&lt;0.001</td>
<td>n/s</td>
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</tr>
</tbody>
</table>

CONCLUSION: With a full bladder rectal wall parameters do not differ between constipated and healthy children.

REFERENCES: Keshtgar AS, Ward HC, Clayden GS, Sanei A.

DISCLOSURE OF INTEREST: None Declared
CHILDREN WITH IBS AND THEIR PARENTS HAVE HIGHER ANXIETY AND DEPRESSIVE SCORES THAN PATIENT WITH OTHER FUNCTIONAL GASTROINTESTINAL DISORDERS AND THEIR PARENTS

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Objectives and Study: Functional gastrointestinal disorder (FGID) is one of the commonest digestive diseases worldwide and leads to significant morbidity. Concomitant psychological disorders, notably anxiety and depressive disorders are strongly associated with FGID and these psychological co-morbidities correlate with severity of FGID symptoms in adults. The aim of this study is to examine both the differences in depressive mood and anxiety among children with functional dyspepsia (FD), functional abdominal pain (FAP) and irritable bowel syndrome (IBS) and effects of parents’ psychological status on symptoms of children.

Methods: 58 children (20 M/28FM) with FGID (FD n=19, FAP n=12, IBS n=27) and their caregivers and 36 age-matched healthy children (15 M/21FM) were participated in this study. Diagnosis of functional gastrointestinal disorders were based on Rome III criteria. Children Depression Inventory (CDI) was conducted to measure children’s changing depressive mood. Severity of depressive and anxiety symptoms were also assessed by the Beck Depression Inventory, State-Trait Anxiety Inventory, and respectively.

Results: There was a higher prevalence of anxiety and depression in FD, FAP and IBS groups than that in the control group (33.5%, 35.2% and 67.7% vs 14.5%, P<0.001; and 22.6%, 33.9% and 38.7% vs 4.5%, P<0.001). Using the cut-off score (>8) for anxiety or depression, IBS patients had a higher rate of anxiety than FD (P=0.01) and FAP (P=0.02), while no significant differences in depression rates were observed between IBS and FAP groups. In terms of parents, depression rate was no significantly different among the groups whereas parents of patients with IBS was more anxious than the others (P<.001).

Conclusion: Anxiety is more common both in patients with IBS and their parents than in those with FD and FAP. Depression is high in patients with FGID, but its role in symptom reporting is uncertain in children.

Disclosure of Interest: None Declared
OESOPHAGEAL ACHALASIA IN CHILDREN: A TERTIARY CENTRE EXPERIENCE
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Objectives and Study: Achalasia is a rare esophageal motility disorder of unknown origin characterized by esophageal aperistalsis and lower esophageal sphincter (LES) dysfunction. Its optimal initial treatment is still controversial. The aim of this study was to assess the efficacy and outcome of different therapeutic modalities (dilatation, myotomy) in children with achalasia.

Methods: A retrospective analysis of all children treated for achalasia at a tertiary center from 1995 to 2012 was performed. Demographics, presenting symptoms, diagnostic modalities, type of therapeutic intervention [Heller’s myotomy (HM), balloon dilatation (BD)], perioperative events and outcomes (asymptomatic/symptomatic at follow-up, need for further intervention) were analyzed using chi-square and Kaplan-Meier survival analysis appropriately.

Results: Thirty-eight children (17 male, range: 1 to 17) were included in the analysis. Dysphagia was the main symptom prior to treatment [median duration: 11 months (range 1-65 months)]. All underwent barium swallow study and manometry to confirm the diagnosis. Twenty-one patients (55.3%) were initially treated with HM, whereas 17 with BD. Subsequent procedures (HM or BD) were required in 23 children. Eleven had HM and 12 BD as second intervention. Seventeen children underwent more than two procedures. All children had uneventful peri-and post-operative period. At the last follow-up (range 2-6 years), 47.4% were asymptomatic with a significant difference for those who had HM as first procedure (HM: 16/21, 76%, BD: 2/17, 11%, p<0.001). Survival analysis revealed that patients undergoing BD as a first procedure had a higher rate of second intervention (BD: 14/17, 82%; HM: 9/21: 42%, p<0.001) with shorter time to it compared to HM (estimated mean time: BD 19 months, 95%CI: 6-31; HM: 37 months, 95%CI: 25-48; p<0.001).

Conclusion: Throughout the study population, less than half of patients with achalasia achieve freedom from symptoms after primary therapies aimed at relaxing the LES. However, Heller’s myotomy when performed as first procedure was the most reliable first-line therapy providing a longer symptom-free period with a lower incidence of second intervention.

Disclosure of Interest: None Declared
ETIOLOGY OF DYSPEPTIC SYMPTOMS IN A TERTIARY PEDIATRIC CENTRE
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Objectives and Study: Dyspeptic symptoms are a frequent problem in children in adolescents, mostly functional by nature. Although presence of "red flags" may indicate an underlying organic disorder, children sometimes undergo endoscopic evaluation even without the warning signs and symptoms, due to recurrency of symptoms and parental anxiety. The aim of the study was to analyze the etiology and frequency of dyspeptic symptoms in children hospitalized in a tertiary pediatric centre.

Methods: We analyzed retrospectively data of children hospitalized for dyspeptic symptoms in the Referral Centre for Pediatric Gastroenterology and Nutrition, Children's Hospital Zagreb during the year 2010.

Results: 84 children (age 8-18 years, 9.84% of the total number of hospitalized children) were hospitalized for acute or chronic dyspeptic symptoms. Dyspeptic symptoms were more frequent in girls (female to male ratio 2:1) and after the age of 10 (60/84 patients, 71.4%). "Red flags" were found in 45/84 children (52.5%), most frequently persistent vomiting, weight loss and nocturnal pain. Positive family history for H. pylori infection, peptic ulcer disease or inflammatory bowel disease was found in 23 (27.38%) children. Upper GI endoscopy was performed in 73 (86.69%) children and 24-hour esophageal pHmetry in 22 (26.19%) children. Functional dyspepsia was a final diagnosis in 25 (29.7%) children (in 6 of them postinfectious). Reflux esophagitis was diagnosed in 21 children (25.0%) and non-erosive gastroesophageal reflux disease and chronic gastritis associated with H. pylori both in 12 (14.29%) children. Coeliac disease was diagnosed in 4 children, pancreatitis in 3, gallstone disease in 2, and duodenal ulcer disease in 1 child. Portal vein thrombosis, acute appendicitis, food allergy and emotional disorder were found in 4 other children. Proton pump inhibitors were prescribed in 11/19 (57.9%) patients with functional dyspepsia. After 6 months complete or partial regression of symptoms were found in 11 (57.9%) children, 1 child had similar symptoms and 7 patients were lost from follow-up.

Conclusion: Functional dyspepsia was a main reason for referral to a pediatric tertiary centre for dyspeptic symptoms. Almost one third of children hospitalized for dyspeptic symptoms had functional dyspepsia, having a good prognosis after 6 months of follow-up. H. pylori infection was found only in 14% of symptomatic children.

Disclosure of Interest: None Declared
ROLE OF ALLERGY IN CHILDREN WITH CONSTIPATION-PREDOMINANT IRRITABLE BOWEL SYNDROME (C-IBS)
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Objectives and Study: The traditional classification of irritable bowel syndrome (IBS) as a functional disorder has been challenged in recent years by evidence of ongoing low-grade gastrointestinal tract inflammation. Foods and food additives may elicit allergic reaction and thereby alter gastrointestinal motility. Data on adults confirm immunologic reaction to foods in IBS. Dietary elimination and food challenge studies support the role of diet in the pathogenesis of IBS. In this study the role of food and aeroallergen sensitization in children with C-IBS is investigated.

Methods: Thirty seven children with constipation-predominant IBS (F/M: 25/12; mean age ±SDS= 13.6±3.7 years) and 88 children with functional chronic constipation (F/M:41/47; mean age±SDS= 10±4.4 years) defined by ROME III criteria were enrolled. Serum IgE level, total eosinophil count, and food and inhalant allergens were studied in all subjects by skin prick test (SPT). Categorical data were analyzed using the $X^2$ test or Fisher's exact test. $P < 0.05$ was considered significant.

Results: Eighteen IBS patients had at least one skin positive tests (48.6%). SPT for food allergens was positive in 15 (40.5%) IBS patients. The most frequent SPT positive food allergens were cacao (n=12), peanut (n=10), chicken (n=7) and wheat (n=5). 8 patients with IBS had positive SPT for inhalant allergens (21.6%) whereas 3 of them positive for both food and inhalant allergen extracts. Rhinitis was the most common sign (n=15), and 3 patients had a history of asthma. Fifteen of the IBS patients reported symptomatic improvement, upon avoidance of the foods to which they reacted. In constipated group, 6 (6.8%) patients had one or more skin positive tests (compare to IBS; $p < 0.01$). SPT for inhalants and food allergens was positive in 4 and 2 patients, respectively in constipated group. Serum IgE level was not significantly different between two groups, whereas eosinophil count was higher in patients with IBS (median 468; range 168-700 vs median 154 range; 102-586, $p=0<0.01$).

Conclusion: Allergic reaction which may trigger intestinal inflammation appears to play role in children with constipation predominant IBS more than functional constipation. Aeroallergen sensitization is another factor to be considered in these patients.

Disclosure of Interest: None Declared
Objectives and Study: Spina Bifida (SB) patients frequently present constipation and incontinence. The aim of the study is to analyze colon transit time (CTT) in children and young adults with SB in relation to neuronal lesion, mobility, bowel habits and continence in comparison to age-matched healthy controls.

Methods: Study performed at the Spina Bifida Reference Center of the Ghent University Hospital. All patients age 6-18 yr, not using antegrade continence enemas are asked to participate. Care as usual (including laxatives and retrograde enemas) is continued during the study but retrograde enemas (RCE) are stopped 48h prior to the X-Ray. 49 SB patients meet inclusion criteria, 35 participated. Data from the medical file and prospective questionnaires regarding constipation and incontinence were collected. The SB patients are constipated if ≥2 of the Rome III criteria for paediatric functional constipation are fulfilled. The SB patients are incontinent if involuntary faecal loss is > once a month. The control group are 21 healthy age-matched children, not suffering from constipation or incontinence according to the Rome III criteria. Total and segmental CTT is measured using the 6-day method. Non parametric tests are used and multivariate analysis is performed. There is ethical approval (EC UZG 2010/348).

Results: The questionnaires confirm persisting constipation despite treatment in 13/35 SB patients. Seven patients are spontaneously continent and 10 are pseudo-continent. SB patients have a significant (P= 0.006) longer total CTT compared to controls (median CTT 100,8h vs. 43,2h). Of the SB population 13 patients have a normal total CTT. No clinical parameter (lesion level, mobility or mental ability) is associated with the CTT as evaluated by multivariate analysis. Constipated SB patients have a significantly longer total CTT than non-constipated patients (P=0.001) (CTT 122,4h vs. 61,2h). There is a significant difference of CTT in continence status (P = 0.014), spontaneous continent patients have a normal CTT (CTT 33,6h) and other patients have an elongated CTT. An abnormal CTT predicts the necessity of treatment to achieve continence (p<0.05).

RCE influences not CTT as there is no significant difference between the RCE users and the other SB patients. The total CTT (P=0.027), right (P=0.001) and left CTT (P=0.003) is significantly different from the control population. No difference in rectosigmoidal CTT is found between patients and controls.

Conclusion: CTT in patients with SB is significantly prolonged indicating a neurogenic bowel. SB patients with a normal CTT are more likely to achieve spontaneous continence. Better knowledge of the CTT will tailor the future treatment of SB patients to achieve faecal pseudo-continence.

Disclosure of Interest: None Declared
Objective and Study: Aim: To describe the clinical presentation of gastrointestinal symptoms associated with EDS type III (hypermobility type) in a paediatric cohort.

Methods: Methods: Retrospective review of notes and electronic patient records of all children less than 18 years old diagnosed with EDS type III referred to the paediatric neurogastromotility clinic. Patient symptom questionnaire was also used.

Results: A total of 56 children were recruited with a median age 13yrs (range 2yrs-18yrs). Female (66%) vs male (34%). 89% presented with symptoms of abdominal pain associated with either GOR (n=27), bloatedness (n=35) or constipation (n=46). 6 had dysphagia, 33 patients had nausea and 23 patients had associated vomiting. Of the 82% who had constipation, 4 patients had faecal incontinence and soiling, 2 patients had painful rectal spasms suggestive of rectal evacuatory disorder. All the children had joint hypermobility and 52% had persistent chronic joint pain. 14 had balance problems and 9 patients used wheelchair for mobility. 15 reported recurrent joint dislocation and 6 had fractures. 20 children reported chronic fatigue. 28 had autonomic dysfunction, 17 had POTS and 20 had orthostatic hypotension. 8/20 had pathological reflux on impedance study. 13/16 children had delayed gastric emptying. Manometry studies showed oesophageal dysmotility in 6/11, small bowel manometry dysmotility in 3/5 and anorectal dysmotility in 2/3, delayed colonic transit with megarectum noted in 7/15 children. Medical management was required for GI symptoms, orthostatic hypotension and joint pains. 15 children received enteral feeds and 5 children parenteral nutrition. Surgical treatment was required in 6 patients. All of them required multidisciplinary input.

Conclusion: Children with a diagnosis of EDS type III present with a wide spectrum of foregut, midgut and hindgut motility disorders. There is preponderance in females and 41% had a strong family history. Nutritional rehabilitation is very essential to maintain growth and development. Multidisciplinary input with a holistic approach is required.

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Disclosure of Interest: None Declared
24-HOUR INTRAESOPHAGEAL PH MONITORING IN CHILDREN WITH COW’S MILK PROTEIN ALLERGY IN A THIRD LEVEL PEDIATRIC HOSPITAL

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Objectives and Study: Cow’s milk protein allergy (CMPA) is a disease with an increasing prevalence worldwide in children. It shares symptoms with gastroesophageal reflux disease (GERD) as regurgitation, vomiting, refusal to food, irritability, making difficult differential diagnosis between these two diseases. Different studies have shown an association between CMPA and GERD. The prevalence of GER in this children goes from 40-66%. In our hospital we see many children in whom it is difficult clinically rule out CMPA or GER only on the basis of clinical symptoms. The aim of this study was to prove the presence of acid gastroesophageal reflux in children with CMPA, as well to see if there is a characteristic pattern in the 24-hour gastroesophageal pH monitoring test in these patients.

Methods: Retrospective review of medical records of children with CMPA and 24-hour intraesophageal pH monitoring. We analyzed age, sex, reflux index, total number of reflux episodes, number of preprandial reflux episodes, and finally if the pH monitoring has a positive or negative result according to Boyle and Vandenplas criteria as well as the presence or absence of the phasic pattern described by Vandenplas. We analyzed the data using descriptive statistics, quantitative variables with measures of central tendency and dispersion, and qualitative variables as frequencies.

Results: 47 patients (32.4% male, mean age 5±3.7 years) met inclusion criteria. 14/47 (29%) presented gastroesophageal reflux according to the results of the 24-hour intraesophageal pH monitoring by Boyle criteria and 21/47 (44%) according with Vandenplas criteria. The mean time with intraesophageal pH < 4 was 140.79 seconds, mean reflux index was 33±37.6. The phasic pattern was found in 2/47 patients.

Conclusion: GER is associated in 29% of CMA patients according to Boyle criteria and in 44% of patients according to Vandenplas criteria. We did not establish a direct relationship between every clinical manifestation. The relationship between GER and CMPA is clear, we found less frequency of GER in children with CMPA using Boyle criteria compare with the results of Iacono and Farahmand. We need further studies with more patients performing 24 hours pH-impedance monitoring to establish the relationship between acid, weakly acid and non acidi reflux in children with CMPA.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GI MOTILITY AND FUNCTIONAL GI DISORDERS

PO-G-0168

EFFECT OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY ON MYOELECTRIC ACTIVITY OF THE STOMACH DETECTED BY ELECTROGASTROGRAPHY

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Objectives and Study: The aim of the study is to investigate the effect of percutaneous endoscopic gastrostomy (PEG) placement on gastric electrical activity.

Methods: The children who required PEG placement were included in the study. After obtaining informed consent, an electrogastrography (EGG) was performed on children before and after PEG insertion. All children had the same meal through nasogastric tube before PEG placement and through gastrostomy tube after the placement. EGG analysis was made using software (Polygram for Windows, version 6.40, Synetics Medical Inc, Stockholm, Sweden). Spectral analysis was conducted and dominant frequency (gastric slow wave frequency which appears with peak power value of spectra, defined in cycles per minute - cpm) < 2.0 cpm was defined as bradygastria, whereas frequencies between 2.0 and 4.0 were defined as 3 cpm (normal) and >4.0 as tachygastria. The percentage of time spent in each of the frequency rates was calculated.

Results: 14 children (8 females, 57.1%) were enrolled into the study. The mean age of patients at the time of PEG placement was 3.8±2.3 years (0.33-7.0). The indications for PEG insertion were inability to swallow in 12 children with neurologic impairment (85.7%); inadequate calorie intake in one child with cystic fibrosis (7.1%) and special feeding requirement in one child with methylmalonic acidemia (7.1%). An EGG study was performed before and mean 1.7±0.63 months (0.43-2.5) after PEG placement.

Table shows the above mentioned parameters before and after PEG placement. There was no statistically significant difference regarding gastric electrical activity measured by means of EGG, neither in pre-prandial or post-prandial states, between before and after PEG placement.

Image:
### Table. EGG parameters of patients before and after PEG placement, in pre-prandial and post-prandial states.

<table>
<thead>
<tr>
<th></th>
<th>Pre-prandial</th>
<th>Post-prandial</th>
<th>Post-prandial/ post-prandial</th>
</tr>
</thead>
<tbody>
<tr>
<td>% time in normogastric range (3 cpm)</td>
<td>20.9±16.8</td>
<td>20.3±22.3</td>
<td>58.9±25.5</td>
</tr>
<tr>
<td>% time in tachygastric range</td>
<td>58.9±25.5</td>
<td>29.3±20.8</td>
<td>34.7±15.7</td>
</tr>
<tr>
<td>%DFIC</td>
<td>0.076</td>
<td>0.0245</td>
<td>0.510</td>
</tr>
<tr>
<td>% time in normogastric range (3 cpm)</td>
<td>54.0±28.4</td>
<td>16.7±17.7</td>
<td>60.4±19.9</td>
</tr>
<tr>
<td>% time in tachygastric range</td>
<td>60.4±19.9</td>
<td>2.4±3.4</td>
<td></td>
</tr>
<tr>
<td>%DFIC</td>
<td>0.610</td>
<td>0.273</td>
<td></td>
</tr>
</tbody>
</table>

Pre-PEG: before PEG placement; post-PEG: after PEG placement, DFIC: dominant frequency instability coefficient

**Conclusion:** The placement of PEG does not improve or worsen gastric electrical activity.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Infantile colic is a very common problem in otherwise healthy infants, causing a high degree of parental anxiety and an increasing demand for medical consultations. The aims of the study were observation and measurement of: a) daily mean crying time, b) fecal calprotectin levels and c) number of bowel movements and stool consistency in colicky infants before and after the introduction of a probiotics enriched formula.

**Methods:** A total number of 59 colicky infants (Rome III Diagnostic Criteria for FGIDs) aged 21 to 63 days were enrolled (group A). Exclusion criteria were: breast milk feeding, weekly weight gain <200gr, positive fecal occult blood test. Further, the infants were randomly divided in two subgroups: 29 of the infants started bifidobacteria enriched formula (group B) and the rest 30 infants started the same type of formula without probiotics enrichment (group C). Also, fecal calprotectin levels were measured in samples of 20 healthy non-colicky infants (aged 19 to 61 days) (group D). The count of calprotectin levels was done in fecal samples using Elisa method. Statistical analysis was performed using SPSS/19 statistical program and $x^2$-test.

**Results:** Statistical significant differences ($p<0.05$) were found in fecal calprotectin levels between groups A and D. Also, after 3 weeks of intervention, statistical significant differences ($p<0.05$) were found in mean crying time and fecal calprotectin levels between groups B and C, but not between groups B and D. No significant differences were found in the number of bowel movements and stool consistency between groups B and C.

**Conclusion:** Infants suffering from colic have increased levels of fecal calprotectin, but these levels and also mean crying time are significantly reduced by the introduction of bifidobacteria enriched formula.

**Disclosure of Interest:** None Declared
A DOUBLE-BLIND CLINICAL TRIAL ON PREBIOTIC GALACTOLIGOSACCHARIDE IN CHILDREN WITH CONSTIPATION

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Objectives and Study: Functional food, such as prebiotics, has been considered useful for the regulation of bowel habit. This study objective was to evaluate the Galacto-oligosaccharides prebiotic (GOS) in therapy of functional constipation in children. A double-blind, placebo-controlled cross-over clinical trial has included 20 children with functional constipation, defined according ROMA III criteria.

Methods: Children received maltodextrin (placebo) or prebiotic GOS. Each patient was administered 6 ml of GOS or placebo diluted in water daily for 30 days, followed by a 15-day washout period and so, 30 days using GOS or placebo, in a cross-over sequence. Clinical effect was evaluated by a clinical score accounted at baseline, day 15 and day 30, in each phase of cross-over study; greatest score means most severe constipation (range from 48 to zero). Patients were seen at enrollment and once every 15-day interval.

Results: Eleven children were administered to sequence GOS/placebo and 10 placebo/GOS. Differences between GOS and placebo scores were significant, placebo > GOS, at baseline: (p=0.0022), 15th day: (p.0001) and 30th day (p<0.0001).

Intestinal constipation score using GOS presented following least squares: baseline: 38.48; 15th day: 19.35 and 30th day: 12.97 (p<0.0001), and using placebo, baseline: 32.00; 15th day: 33.08 and 30th day: 32.96 (p=0.0646). Stool frequency analysis showed improvement from 1st day (p=0.1964) to 15th day (p=0.0009) when GOS was administered.

Stool frequency using GOS showed following least squares baseline: 1.60 and 15th day: 1.10 (p=0.0014), and using placebo, baseline: 1.51 and 15th day: 1.61 (p=0.1721).

Stool consistency analysis was performed in three stages proposed. In comparing the use of products found 1st day (p=0.0070), 15th day (p<0.0001) and 30th day (p<0.0001) demonstrating significant difference between GOS and placebo. The least squares for stool consistency using the GOS were baseline: 27.4, on 15th day: 15.95 and on 30th day: 8.53 (p<0.0001), and using placebo, baseline: 25.55, on 15th day: 26.51 and on 30th day: 26.46 (p=0.0863) showing no significant difference in stools consistency.

Conclusion: The prebiotic GOS showed no significant side effects and proved to be effective for improvement of constipation symptoms in this group of children with functional constipation.

Disclosure of Interest: None Declared
METABOLIC ACTIVITY OF INTESTINAL MICROFLORA WHILE ANTIBACTERIAL THERAPY
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Objectives and Study: To evaluate the effect the antibiotic therapy on the metabolic activity of intestinal microflora depending on the use of probiotics.

Methods: 74 children receiving antibiotic therapy (ABT) were included into the study. Children were divided into 2 groups. The 1st group of 25 children received probiotics (B. bifidum, B. longum, L. casei 10⁹) from the first day of ABT. Patients from the 2nd group (21 children) received ABT without probiotics. Metabolic activity of intestinal microflora was evaluated based on the level of short chain fatty acids (SCFA) with gas-liquid chromatography analysis on the first and 21st days.

Results: At baseline, children from the 1st and 2nd groups showed increasing level of propionic acid (0,222±0,009 U and 0,219±0,009 U respectively) and butyrate, produced by strict anaerobes (0,103±0,006 U and 0,108±0,007 U respectively), as well as decrease in acetic acid, produced by saccharolytic bacteria (0,675±0,011 U and 0,673±0,010 U respectively). Anaerobic index (AI) was changed to negative values (-0,481 ±0,014 U in the 1st group and -0,486 ±0,015 U in the 2nd group). Such values of oxidation-reduction potential suppress the activity of obligate anaerobic flora and lead for further activation of residual strains of aerobic bacteria. Three weeks later, a group of children who received probiotic from the first day of ABT showed a normal level of C2-C4 fatty acids due to the stabilization of microflora content and removing the negative impact of antibiotic therapy. In the 2nd group changes in SCFA worsened due to microflora disorders while antibiotic therapy.

Conclusion: SCFA levels in stool can be an objective marker of the state of intestinal microflora. Antibiotic therapy can course severe damage to the normal gut flora content and makes necessary preventive use of probiotics to protect against activation of proteolytic microorganisms.

Disclosure of Interest: None Declared
Objectives and Study: OBJECTIVE: In refractory constipation two sites of fecal hold-up can be identified: pancolonic and anorectal. The identification of these sites may allow for a better therapeutic approach, improving patient’s quality of life. If adequately standardized, with a simplified method for image interpretation, intestinal transit could be easily adopted by clinicians as part of the routine investigation of these patients. Our aim was to propose a simplified method for image evaluation of intestinal transit scintigraphy in children with refractory constipation.

Methods: METHODS: We prospectively studied 23 consecutive patients, 14 males, 2 to 15 years old. Fasted for at least 4 hours, they ingested milk (20 ml) added to 99 mTc-colloid, using doses based on an adult dose of 370MBq. Static imaging in the anterior projection of abdomen was undertaken immediately after radiopharmaceutical administration and at 2, 6, 24, 30 and 48 hours. The images were then visually analyzed considering the radiopharmaceutical progression through the colon.

Results: RESULTS: In 22/23 patients (95%), the imaging could be divided in pancolonic hold-up, including ascending, transverse and descending colon, n=12, and sigmoid/anorectal hold-up, n=10.

Conclusion: CONCLUSION: This imaging study permitted to classify patients in only two distinctive patterns of involvement: diffuse retention, compatible with slow transit constipation and anorectal retention. Once the site of hold-up is identified, an optimum treatment can be planned.

Disclosure of Interest: None Declared
ALKYLGLYCEROLS MODULATE THE PROLIFERATION AND DIFFERENTIATION OF UNSPECIFIC AGONIST AND SPECIFIC ANTIGEN – STIMULATED SPLENIC LYMPHOCYTES

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Objectives and Study: Alkylglycerols (AKGs) are ether-linked glycerols derived from shark liver oil and found in small amounts in human milk. These AKGs include such substances as selachyl alcohol (AKG18:1), batyl alcohol (AKG18:0) and chiml alcohol (AKG16:0). Previous studies showed that oral AKGs administration significantly increased the immune response in mice. The aim of the present study was to investigate the in vitro immunomodulatory effect of AKGs on stimulating splenic lymphocyte responses.

Methods: C57BL/6 mice were immunized with Hepatitis B surface antigen (HBsAg). Splenic B cells were purified and stimulated with anti-BCR and anti-CD38 in the presence or absence of 100ng/ml AKG 18:1, AKG 18:0 or AKG 16:0. Meanwhile, splenic CD4+ T cells were purified and stimulated with anti-CD3/anti-CD28 in the presence or absence of 100ng/ml AKGs. For antigen specific stimulation, the purified CD4+ T cells were cocultured with HBsAg-pulsed dendritic cells in the presence or absence of 100ng/ml AKGs. The effect of AKGs on cell proliferation was assessed by [3H]-thymidine and CFSE incorporation assay. The maturation of B cells was assessed by examining the germline (GL) transcription of IgG (γ1) and the percentage of CD80+/CD86+ cells by flow cytometry analyses. Th1/Th2 polarity was assessed by T-BET(Th1)/GATA-3(Th2) flow cytometry assay and by characteristic cytokines ELISA assay (IFN-γ for Th1; IL-4, IL-5 and IL-10 for Th2).

Results: It was found that AKGs (18:1, 18:0 and 16:0) significantly increased BCR/CD38 -stimulated B cell proliferation and division. The transcriptional level of IgG (γ1) was markedly increased by AKGs at 100 nM concentration. The population of CD80+/CD86+ B cells was significantly increased by AKGs upon BCR/CD38 stimulation. The [3H]-thymidine incorporation assay showed that AKGs significantly increased T cell proliferation upon CD3/CD28 or HBsAg specific stimulation. Meanwhile, the results showed that AKGs increased the population of T-BET-positive T cells and IFN-γ production upon CD3/CD28 or HBsAg specific stimulation; whereas, the levels of the Th2 cytokines IL-4, IL-5 and the regulatory cytokine IL-10 were decreased by AKGs stimulation.

Conclusion: AKGs are quite novel immunomodulatory substances present in nutritional products that can modulate immune responses in vitro by boosting the proliferation and maturation of mouse B lymphocytes, and promoting the proliferation and Th1 differentiation of mouse T lymphocytes upon specific antigenic stimulation.

Disclosure of Interest: None Declared

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FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME IS AN ENTEROPATHY DISORDER: THE ROLE OF ENTEROCYTE APOPTOSIS WITH DISRUPTED BARRIER FUNCTION

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Objectives and Study: Expression levels of tumor necrosis factor (TNF)-α on the mucosa of the small intestine is increased in the patients with villous atrophy in food protein-induced enterocolitis syndrome (FPIES). TNF-α has been reported to induce apoptotic cell death in the epithelial cells by disruption of barrier function. The aim of this study was to analyze enteropathy quantitatively in FPIES and to determine the role of apoptosis and disrupted tight junction in its pathogenesis.

Methods: Fifteen infants diagnosed with FPIES using standard oral challenge test and 5 controls were included. Quantitative morphometric analyses of duodenal mucosa were performed. Immunohistochemical stains of CD3 for intraepithelial lymphocyte; TUNEL for overall apoptosis; M30 for epithelial apoptosis; TNF-α expression and claudin-1, claudin-4, and occludin for tight junction were also performed for barrier function. Apoptotic cells of TUNEL and M30 were counted as cells/high power field (HPF). The expression of other immunohistochemical stainings was graded as 0~3 score according to the extent and intensity of staining.

Results: Villous atrophy was observed in all FPIES patients (50~210 μm vs 305~380 μm in controls, p=0.0001). CD3 (p=0.038), TUNEL (p=0.043), and M30 (p=0.042) were significantly higher expressed in the duodenal mucosa of FPIES patients than the controls. TNF-α was significantly higher expressed in FPIES patients than the controls (p=0.0001). Claudin-1 (p=0.01), claudin-4 (p=0.001), and occludin (p=0.003) were considerably lower expressed than the controls.

Conclusion: FPIES is an enteropathy disorder. Villous atrophy is induced by enterocyte apoptosis which may be induced by up-regulation of TNF-α with disrupted tight junction.

Disclosure of Interest: None Declared
THE RELEVANCE OF BASOPHIL ALLERGEN SENSITIVITY TESTING FOR THE DISTINGUISHING OF SEVERE VERSUS MILD PEANUT-ALLERGIC CHILDREN

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Objectives and Study: Peanut sensitization is common in children visiting the pediatric gastroenterologist. However, it is difficult to assess which children will react mildly and which severely. This study evaluated the relevance of basophil allergen sensitivity testing for the distinguishing of severity of peanut allergy in children.

Methods: Twenty-seven peanut-sensitized children with symptoms varying from mild symptoms to severe anaphylaxis underwent peanut CD63 dose-response curve analysis with the inclusion of basophil allergen sensitivity calculation (CD-sens) and peanut components IgE testing.

Results: Eleven children (41%) which experienced anaphylaxis to peanut showed a markedly higher peanut CD63 response at submaximal allergen concentrations and CD-sens (median 1,667 vs. 0.5, p < 0.0001) than 16 children which experienced milder reaction. Furthermore, a negative or low CD-sens to peanut unambiguously excluded anaphylactic peanut allergy. Children with anaphylaxis have higher levels of IgE to Ara h 1, 2, 3 and 9, but comparable levels of IgE to Ara h 8 and whole peanut extract. The diagnostic specificity calculated with ROC analysis reached 100 % for CD-sens and 73 % for Ara h 2.

Conclusion: We demonstrated that severe peanut allergy is significantly associated with higher basophil allergen sensitivity. This cellular test should facilitate more accurate diagnosis of peanut allergy.
Disclosure of Interest: None Declared
Objectives and Study: Food allergy is often the first manifestation of the allergic march. Epidemiology studies suggested that the rural environment is protective against the development of asthma or allergies. The aims of this study are to determine if a rural environment is protective against the development of food allergies. We also tested if past history of common fecal-oral infections may be protective against food allergies.

Methods: Random groups of primary school children aged 6-11 years from Hong Kong, Guangzhou city and rural Shaoguan were recruited for study. Guangzhou is a city in Southern China about 200 miles north-west of Hong Kong. Shaoguan is a rural area 140 miles north of Guangzhou. Parents or guardians were asked to complete the Europrevall Food Allergy Screening questionnaire and the validated ISAAC core questionnaire. Random subsample of children was recruited for skin prick testing and serum samples were obtained for determination of specific IgE (24 food and aero-allergens). Probable food allergy is defined as reported symptoms to a specific food along with evidence of sensitization (SPT ≥3 mm, or serum specific IgE ≥0.35 kU/l). Relationship between probable food allergies and fecal-oral infections (Salmonella, Hepatitis A, and Toxoplasmosis) was determined by multiple logistic regression analyses adjusted for age, gender and maternal level of education.

Results: A total of 16875 children were screened and 1152 children were studied in details in the second phase. The symptom of wheeze ever was most frequent in children from Hong Kong (27%) when compared with children from Guangzhou city (12%, P < 0.001), and Shaoguan (2.5%, P <0.001). Shrimp is the most common reported allergen food for children in Hong Kong. The prevalence of probable food allergy in Hong Kong was 2.1% (95% CI: 1.65-2.3), while there were 0.4% (0.23-0.57) in Guangzhou and 0.7% (0.48-0.92) in Shaoguan. Positive serology was associated with protection against development of probable food allergy (OR 0.25, P <0.001).

Conclusion: Food allergies are less common in rural China and mainland Chinese cities when compared with Hong Kong. Past infection of hepatitis A was associated with protection against the development of food allergy. The exact environmental factors responsible for such protection remain to be identified.

This study is supported by Hong Kong Research Grant Council GRF Grant CUHK 477110 and the EU through EuroPrevall (FP6-FOOD-CT-2005-514000).

Disclosure of Interest: None Declared
THE USE OF A SYMPTOM QUESTIONNAIRE IN THE DECISION PROCESS OF GASTROINTESTINAL FOOD ALLERGY

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Objectives and Study: Gastrointestinal food allergy (GIFA) can be either non-IgE or mixed IgE and non-IgE mediated. The clinical history and symptoms form the cornerstone for the suspicion of a GIFA. This is confirmed with an elimination diet and challenge. However, symptom improvement following an elimination diet is often difficult to judge and ambiguous. The use of a Likert scale GIFA symptom questionnaire (GIFASQ) to aid the decision process has not been studied in GIFA. We therefore set out to determine the impact on symptom resolution of dietary elimination with or without medication using the GIFASQ.

Methods: This prospective observational study was conducted in a tertiary gastroenterology department. The published GIFASQ was developed from symptoms of 437 children with proven GIFA. Parents completed the questionnaire before commencing the exclusion diet and repeated this after 4 weeks. The GIFASQ measured 9 symptoms individually from 0 (no symptom) to 5 (the most severe) and globally from 0 to 45. If symptoms improvement was ≤25% and the paediatric gastroenterologist criteria agreed, medication was added.

Results: GIFASQ of 54 participants were analysed. The median age was 23,5 months (2-189). Forty seven patients (87%) were managed only with an elimination diet: 4 (8,5%) on a cow’s milk (CM) elimination, 9 (19,1%) on a CM and soy, 8 (17%) on a CM, soy and egg, 9 (19,1%) on a CM, soy, egg and wheat (MEWS), 12 (25,5%) on a MEWS and further targeted restrictions and 5 (10,6%) followed a restricted diet different to those mentioned above. Seven patients needed medication: 1 Sulphasalazine, 1 Sodium Cromoglycate, 3 Sodium Cromoglycate + Ketotifen and 2 Cetirizine + Ketotifen. Thirty eight patients (70%) achieved ≥50% improvement in symptom after intervention. Four patients reached a final score = 0 (total improvement). From the 7 patients on medication, 6 showed further improvement in symptom. Table 1 provides data on symptom improvement for all patients.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N</th>
<th>Deteriorate</th>
<th>No change</th>
<th>a) Partial Improvement</th>
<th>b) Total Improvement</th>
<th>Improvement a)+b</th>
<th>n (%N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>51</td>
<td>1</td>
<td>9</td>
<td>27</td>
<td>14</td>
<td>41 (80%)</td>
<td></td>
</tr>
<tr>
<td>Flatus</td>
<td>44</td>
<td>1</td>
<td>10</td>
<td>18</td>
<td>15</td>
<td>33 (75%)</td>
<td></td>
</tr>
<tr>
<td>Bloating/ Distension</td>
<td>35</td>
<td>1</td>
<td>8</td>
<td>11</td>
<td>15</td>
<td>26 (74%)</td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>35</td>
<td>3</td>
<td>3</td>
<td>18</td>
<td>11</td>
<td>29 (82%)</td>
<td></td>
</tr>
<tr>
<td>Symptom</td>
<td>Before</td>
<td>Improvement</td>
<td>After</td>
<td>Improvement</td>
<td>Total</td>
<td>Improvement</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------</td>
<td>-------------</td>
<td>-------</td>
<td>-------------</td>
<td>-------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>33</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>19</td>
<td>26 (78%)</td>
<td></td>
</tr>
<tr>
<td>Back arching/screaming</td>
<td>32</td>
<td>1</td>
<td>3</td>
<td>12</td>
<td>16</td>
<td>28 (87%)</td>
<td></td>
</tr>
<tr>
<td>Food aversion/refusal</td>
<td>31</td>
<td>5</td>
<td>5</td>
<td>12</td>
<td>9</td>
<td>21 (67%)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>30</td>
<td>0</td>
<td>4</td>
<td>7</td>
<td>19</td>
<td>26 (86%)</td>
<td></td>
</tr>
<tr>
<td>Rectal Bleeding</td>
<td>16</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>11</td>
<td>14 (87%)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** The GIFASQ assesses symptom improvement objectively in suspected GIFA. It is a quick and easy tool that all health care professionals can use in clinical practice in a condition that is notoriously difficult to diagnose. The GIFASQ also helps identify children who only partially respond to an elimination diet and who benefit from the addition of adjuvant medications.

**Disclosure of Interest:** None Declared
Objectives and Study: Hazelnut (*Corylus avellana*) is a common cause of lifetime lasting IgE-mediated food allergy. Symptoms range from mild oral allergy syndrome to severe life-threatening anaphylaxis. We aimed to identify allergenic determinants in children living in the Campania region (Italy) with hazelnut allergy.

Methods: Otherwise healthy children with oral food challenge confirmed hazelnut allergy were prospectively evaluated. Crude protein extracts were obtained from 5 hazelnut varieties, including autochthon, Northern Italy and Oregon (USA) cultivars, with phosphate saline buffer, pH 7.2. The immunoreactive protein components were identified by SDS-PAGE electrophoresis and Western immunoblotting, using patients sera as source of specific IgE. The IgE-binding protein bands were characterized by advanced proteomic strategies and tandem mass spectrometry (MS)-based *de novo* peptide sequencing.

Results: Four subjects were evaluated (2 male, 50%; mean age 39 m). Symptoms were: urticaria (2), angioedema (3), anaphylaxis (2). No significant differences were observed considering the main demographic and clinical characteristics at diagnosis. All children’s sera were immunoreactive to a protein, not previously annotated in database, occurring in hazelnut regardless the variety. The allergen was isolated by combined chromatographic strategies. Only one patient exhibited an additional reactivity to the vicilin-like 7S 48 kDa glycoprotein (Cor a 11). The MS-based characterization provided evidence of a high homology degree between the IgE-binding protein subunit and 11S globulin-like storage proteins expressed in other seeds. The new allergen shares structural traits with the hazelnut 11S globulin-like proteins (Cor a 9) such as the disulfide linkage of two subunits, an acidic (∼35 kDa) and an alkaline (∼21 kDa) one. Interestingly, only the alkaline subunit exhibits antigenic properties.

Conclusion: A previously unrecognized hazelnut allergen was identified. Except for a faint IgE reactivity of Cor a 11 recorded in a single case, the new allergen was the unique IgE-binding protein in our patients. Future study are warranted to better define possible prognostic and immunotherapeutic implications.

References:

Disclosure of Interest: None Declared
USE OF NUTRITIONAL STRATEGIES FOR MANAGEMENT OF OFG AND RAS IN CHILDREN WITHOUT ENTERIC CROHN’S DISEASE

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Objectives and Study: Management of chronic oral and lip inflammation in children can be a challenge. In the absence of an agreed consensus statement, prescribed treatments tend to be variable. We report experience of using a primary dietary algorithm in a multidisciplinary setting from a single tertiary paediatric gastroenterology centre.

Methods: Patients were identified from the paediatric endoscopy and IBD databases. Clinical, laboratory and histopathologic information were recorded. Children with Crohn’s and other systemic inflammatory conditions were excluded from the study.

Results: 13 children (Median age 8.4 yrs, IQR 6 yrs, M:F = 6:7) with OFG and mouth ulceration (n=2) enrolled in the study. Patients were followed up for a median duration of 1.2 years (IQR = 0.2 yrs). Serologic RAST testing was generally unrewarding. After failure of first line topical treatments including mouthwashes & SLS free toothpaste 10 children were given an option of using EEN (exclusive elemental nutrition) or CB (Cinnamon Benzoate free) diet. All opted for CB diet as first choice; 5 achieving long-term remission continuing on a partially restricted CB diet to this date. Off the 5 non responders, 2 failed to respond to treatment with EEN, 1 self-resolved and another opting for steroids initially responded but failed to maintain remission on thiopurines. Off the 3 not offered CB diet, 2 self-settled and the 3rd moved area.

Conclusion: Dietary manipulation is a viable treatment option in children with OFG and related conditions. When given a choice, children with solitary mouth ulcers will avoid the life style compromising EEN with 50% achieving remission on CB diet. EEN & thiopurines, continue to have a role in a limited number of children. We recommed management in a multidisciplinary setting whilst highlighting the need for a larger scale study and an agreed consensus statement for use of diet and other treatments.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Gastroesophageal Reflux (GER) has a variety of etiologies including both anatomic and functional. Among the functional causes DGE appears to be the most important pathophysiological factor. Although some studies have suggested a relationship between GER and FA there have been no studies linking FA with DGE. The purpose of the present study was the evaluation of the role of FA in infants with DGE and GER and in children, adolescents and adults with DGE and DS.

METHODS: Study Population: 24 infants and children (group 1), with chief complain of GER, 58% male and 42% female, age ranging from 1 month to 36 month (medium 9.5 months); 22 children and adolescents (group 2) age 3-17 years with chief complaint of DS and 23 adults (group 3) with DS. We measured the DGE by the “gold standard” Tc99 in all patients that entered in the study. FA and GER were diagnosed respectively by DBPCFC and 24 hours pH probe. DS was diagnosed by typical clinical picture and by upper GI endoscopy and biopsy. All subjects were Caucasian.

RESULTS: All subjects showed as they presented in our clinic, before treatment, with the chief complain of GER or DS, with abnormal variations in mean gastric emptying time (MGET) ranging from 75-250 min (x=100min). Following treatment with hypoallergenic diet all subjects showed improvement in MGET ranging from 22-45 (x=35min). After challenge with milk all patients relapse with the MGET ranging from 45-120 (x=75min).

CONCLUSION: The results of these studies suggest that FA was the origin of DGE in all cases. In infants and children, FA could be responsible for the elevation of MTGE in patients with GER and suggest that food allergy should be considered in the diagnostic work-up of all children with GER. The results also suggest that in children, adolescents and adults, with history DS, FA in these subjects could be responsible for the elevated MGET which in turn leads to DS as a consequence of DGE. All patients with symptoms of GER and DS, therefore, should be carefully examined to evaluate the pathogenic role of FA and to determine whether GER or DS is primary or secondary to FA and DGE.

THE ROLE OF PD-1 IN ISCHEMIA REPERFUSION INJURY OF STEATOTIC LIVER GRAFT

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Objectives and Study: Steatotic livers are associated with decreased hepatic cell survival and elimination of fat improves the ability of the liver to withstand ischemic insults. The critical barrier to progress in treating Non Alcoholic Fatty Liver Disease (NAFLD) is our lack of understanding of the underlying pathophysiologic mechanisms contributing to decreased survival. Emerging data in NAFLD studies suggest that the adaptive immune system is centrally involved and the resultant T cell activation is a balance between stimulatory and inhibitory receptors. The role of PD1 as a critical inhibitory member of the CD28 family is emerging in various clinical scenarios including transplantation tolerance, sepsis, viral hepatitis and autoimmunity. The aim of this study is to determine the role of PD1 in IRI induced injury of a steatotic liver.

Methods: Wild type C57B6 mice were fed a high fat diet (HFD). After 12 weeks, they were exposed to 20 minutes of ischemia by clamping the portal vein and the hepatic artery followed by reperfusion. Splenic and hepatic T cells were isolated and subjected to flow cytometry for CD45, CD3, CD4, CD8, and PD1. Histology was assessed for presence of necrosis and serum ALT was evaluated as a marker of hepatocellular injury. Similarly, PD1 KO mice were also fed a HFD and exposed to IRI followed by histological examination of liver tissue and serum ALT.

Results: The mice fed a HFD showed increased body weight and the presence of hepatic steatosis by oil red O staining at the end of 12 weeks. They also showed increased necrosis and higher serum ALT as compared to their lean littermates, who were fed regular chow. Total splenocytes were significantly increased after IRI in both lean and HFD fed mice. On Day 3 of reperfusion, PD 1 was upregulated on CD4 T cells in splenic and hepatic T cells of steatotic mice fed a HFD. This upregulation was seen earlier in the spleen initiating at 6 hours of reperfusion. CD 8+PD1+ cells in the spleen were increased at 6 hours of reperfusion in lean but not in the HFD mice. No difference in CD8+PD1+ T cells was seen at day 1 or Day 3 in lean or HFD mice spleens. Additionally, PD1 KO mice were protected from IRI, showing much decreased necrosis and lower serum ALT.

Conclusion: Steatotic livers are increasingly susceptible to IRI as compared to normal livers. In fatty liver disease, the CD4+ hepatic and splenic T cells show an increase in PD1+ after IRI, profiling a unique signature which can be targeted for therapeutic intervention for mitigating hepatocellular injury.

Disclosure of Interest: None Declared
COMMON ESPGHAN TOPICS
IMMUNOLOGY INCLUDING FOOD ALLERGY AND INTOLERANCE

PO-G-0182

GASTROINTESTINAL SYSTEM FINDINGS IN PRIMARY IMMUNE DEFICIENCIES AND FOLLOW-UP RESULTS
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Objectives and Study: Primary immune deficiencies (PID) are a group of heterogeneous disorders with unique genetic defects in the immune system. As the largest immune organ of the body, the gastrointestinal system (GIS) comprises one of the most affected systems in PIDs. In this study we aimed to evaluate the endoscopic and histologic features of GIS in PIDs.

Methods: Patients with PID who had undergone endoscopic evaluation in Hacettepe University Pediatric Gastroenterology department were retrospectively evaluated.

Results: The study group consisted of 16 patients (8 females, %50) with PID including 6 patients with combined immune deficiency (2 severe combined immune deficiencies, 2 isolated CD4 deficiencies, 1 ZAP70 deficiency, 1 CD3-TCRαβ deficiency, 43.8%); 4 patients with chronic granulomatous disease (CGD, 25.0%); 2 patients with common variable immune deficiency (CVID)(12.5%), 1 patient with chronic mucocutaneous candidiasis/T cell deficiency (6.25%), 1 patient with hyperimmune globulin M syndrome (6.25%), 1 patient with hyperimmune globulin E syndrome (6.25%). The mean age at diagnosis of PID was 1.89±2.3 years (0.3-8.5) and the mean age at the time of endoscopy was 5.49±4.0 years (0.4-13.4). All patients had undergone esophagogastroduodenoscopy and colonoscopy. The most common GIS symptom was chronic diarrhea (87.5%), followed by bloody diarrhea (18.75%), oral aphthous lesions (6.25%) and perianal abscess/fistula (%6.25). One patient (CGD) was asymptomatic at the time of endoscopy which was performed because of the ongoing elevated acute phase reactants. The duodenal and colonic biopsies of 2 patients (ZAP70 deficiency and CVID) were normal. 2 patients had giardiasis shown in biopsies of duodenal and colonic mucosa (CD4 deficiency and hyperimmune globulin E syndrome). The colonic biopsies of 12 patients (75%) showed active colitis (including the asymptomatic patient) consistent with inflammatory bowel disease (IBD). These patients received prednisolone (n= 10), mesalazine (n=9), azathiopurine (n=4) for treatment of colitis. 3 of these 12 patients received allogeneic stem cell transplantation, 3 of them were unresponsive to treatment, 2 of which had died due to severe infections. 4 of the patients showed partial remission with steroid dependence and only one patient had complete remission with treatment.

Conclusion: Our study shows the presence of IBD like colitis in a diverse spectrum of PIDs. It also demonstrates that the treatment of colitis can be challenging. Understanding the mechanisms of colitis in adaptive and innate immune deficiency disorders may support the immune deficiency model of Crohn’s disease.

Disclosure of Interest: None Declared
EFFICACY OF PROTON PUMP INHIBITOR-BASED TRIPLE THERAPY AND BISMUTH-BASED QUADRUPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION IN CHILDREN

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Objectives and Study: The aim of this study was to assess and compare the efficacies of proton pump inhibitor (PPI)-based triple therapy and bismuth-based quadruple therapy as first-line treatments for Helicobacter pylori (H. pylori) eradication in Korean children.

Methods: We retrospectively reviewed the data of children who had been diagnosed with H. pylori infection at the Seoul National University Bundang Hospital from March 2004 to August 2012. The patients were randomly assigned to receive either triple therapy consisting of omeprazole, amoxicillin, and clarithromycin for 2 weeks (OAC group) or quadruple therapy comprising omeprazole, amoxicillin, metronidazole, and bismuth salts for 1 week (OAMB group). The patients were evaluated for eradication of H. pylori infection at 4 weeks after the completion of the treatment.

Results: Of the 129 children enrolled in this study, 118 (91.5%) were included in the final analysis. The eradication rates in OAC and OAMB groups were 67.7% (42/62) and 83.9% (47/56), respectively, which were significantly different between the 2 treatment groups (p = 0.041). The eradication rates in the OAMB group during the periods 2004–2006, 2007–2009, and 2010–2012 were superior to those in the OAC group.

Conclusion: This study indicated that the 1-week bismuth-based quadruple therapy, compared with the standard 2-week triple therapy, was significantly more successful in eradicating H. pylori infection in Korean children.

Disclosure of Interest: None Declared
APPROPRIATE ORAL FLUID REPLACEMENT AND WATERY STOOLS IN CHILDREN WITH DIARRHEA: A RANDOMIZED CLINICAL TRIAL

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Objectives and Study: To evaluate appropriate fluid load during oral rehydration therapy in children with diarrheal disease.

Methods: Randomized clinical trial at Pediatric University Hospital in Bahia, Brazil. Seventy male children with acute diarrhea and dehydration, aged 2 to 30 months, after rehydration, were randomized into 2 groups for maintenance therapy. Group A received a standard oral rehydration solution (ORS), replacing the equivalent volumes of measured abnormal losses + ad libitum free water, and a diet appropriate for age; Group B received the same ORS but the calculated replacement volume deducted all other fluid intake.

Results: Thirty-four children were allocated into Group A and 36 children were allocated into Group B. The median total fluid intake was 2600 mL (interquartile range [IQR] = 4000 mL) for Group A versus 1900 mL (IQR = 2200 mL) for Group B (P = 0.02). This significant difference in median total fluid intake correlate with a higher ORS intake (median = 782 mL and IQR = 1790 for Group A; median = 172 mL and IQR = 310 for Group B, P < 0.001) in Group A. The median fecal loss was higher in Group A than in Group B (median = 1.64 mL/kg/h and IQR = 1.05 for Group A and median = 1.10 mL/kg/h and IQR = 1.43 for Group B, P < 0.08). Diarrhea cessation occurred earlier (63%) in Group B compared to Group A (incidence density ratio of 1.63 [1.002 to 2.653] 95%, P < 0.05). The Kaplan-Meier curves revealed a median time to diarrhea termination of 44 h for Group A and 32 h for Group B (P < 0.05).

Conclusion: Controlling total fluid volume intake during oral rehydration therapy leads to a more accurate fluid needs. By adjusting replacement methods but using the same ORS, an early cessation of diarrhea was observed, with a median 12 h reduction. This information might be crucial in designing future clinical trials to evaluate fluid therapy in acute diarrhea. Otherwise less rigid ORT and non uniform methods in multi-center studies, might influence in final results and induce potential bias not related to tested fluid therapies.

Disclosure of Interest: None Declared
A PROBIOTIC MIXTURE IN 6-36 MONTH-OLD INDONESIAN CHILDREN WITH ACUTE GASTROENTERITIS

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Objectives and Study: In developing countries, oral rehydration solution (ORS) and zinc are standard therapy for treating acute diarrhea in children. Probiotics are also widely used, although not recommended by WHO. It is recommended to test each (combination of) probiotic(s). Therefore, we tested the efficacy of a probiotic mixture (Lactobacillus (L.) rhamnosus R0011 1.9 x 10^9 cfu and L. acidophilus R0052 0.1 x 10^9 cfu) in the treatment of acute gastroenteritis (GE).

Methods: A randomized double blind clinical trial was performed in children aged 6-36 months old with acute diarrhea with mild to moderate dehydration in the central Jakarta region. Both groups were given standard therapy (ORS and zinc); the intervention group was given the probiotic mixture for 5 days. The outcomes were duration of diarrhea and frequency of defecation. Stool frequency was recorded daily until resolution of diarrhea.

Results: 112 subjects were enrolled (56 in each group). Median duration of diarrhea in the supplemented group was 68.5 hours and in the control group 61.5 hours (P=0.596). Median frequency of defecation 5/day in teh probiotic group and 5.5 in the control group (P=0.795).

Conclusion: Compared to standard treatment, the probiotics mixture failed to shorten the duration of diarrhea or to reduce stool frequency. These data illustrate that each probiotic (mixture) should be tested for its efficacy.

Disclosure of Interest: B. Hegar: None Declared, I. M. I. Waspada: None Declared, H. Gunardi: None Declared, Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals
ESCHERICHIA COLI MODEL OF DIARRHEA IN NEWBORN PIGS

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Objectives and Study: Enterotoxigenic Escherichia coli causes diarrhea in infants worldwide. Reliable animal models of pathogen-induced diarrhea are of importance to investigate preventive dietary effects. E. coli F18 is a common porcine pathogen causing diarrhea in newly-weaned pigs. We have previously shown that artificially-reared newborn pigs deprived of sow’s milk from birth, show high susceptibility to E. coli F18. We hypothesized that neonatal E. coli F18-induced diarrhea is dose-dependent and that bovine colostrum and maternal flora reduces the disease severity.

Methods: Term pigs were delivered by cesarean section. In experiment 1, pigs were fed infant formula (Milex, Arla Foods) and inoculated with either no bacteria (controls, n=8) or a low (n=9), medium (n=7) or high (n=7) dose of E. coli F18 (1x10^7, 2x10^8 and 8x10^9 CFU/d, respectively) for 5 days. In experiment 2, pigs were kept for 8 days and received either no bacteria (controls, n=7), E. coli F18 (2.6x10^11 CFU/d, n=7), E. coli F18 (2.6x10^11 CFU/d) plus maternal flora on day 1 (4x10^7 CFU, n=5), and E. coli F18 (2.6x10^11 CFU/d) plus 50% dietary substitution of the Milex formula with bovine colostrum (n=4). The degree of diarrhea, body weight, amount of mucosa, intestinal permeability, hexose absorption and density of adherent bacteria were determined.

Results: In experiment 1, increasing doses of F18 increased the incidence of diarrhea (p<0.05). Amount of mucosa and intestinal permeability did not differ. In experiment 2, all groups inoculated with E. coli F18 had more diarrhea than control pigs (p<0.05). Co-inoculation with maternal fecal flora or inclusion of bovine colostrum in the enteral formula diet had no effect on diarrhea outcome or any other measured parameters.

Conclusion: Artificially-reared, caesarean-delivered pigs are highly susceptible to diarrhea induced by E. coli F18. The effect is dose-dependent but less affected by the birth colonization (maternal fecal flora) and protective diets such as bovine colostrum. The newborn pig may be a useful model to investigate dietary components preventing E Coli diarrhea in newborn infants.

Disclosure of Interest: None Declared
**SYNBIOTICS' EFFECTS ON IMMUNE SYSTEM OF CHILDREN WITH ACUTE GASTROENTERITIS**

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**Objectives and Study:** The aim of this randomized, double blind study was to compare pro-, antiinflammatory and immunomodulator cytokine levels between the groups of administered synbiotic (bifidobacterium bifidum + inulin) and placebo group, on acute diarrhea.

**Methods:** In this prospective study 40 pediatric patients who admitted with diarrhea to Uludag University Medical Faculty Pediatric Gastroenterology and Emergency Polyclinics were randomly divided into two groups. Group 1; 19 patients (mean age 36 months, 7 male, 12 female) and group 2; 21 patients (mean age 38 months, 12 male, 9 female). There were no differences in terms of age, sex and symptoms between the two groups. Synbiotic had been given orally twice a day to group 1 patients for 7 days, and placebo had been given to group 2 patients for 7 days. At the beginning of the study, stool microscopy, blood count, C-reactive protein, erytrocyte sedimentation rate, lactate dehydrogenase and cytokine (tumour necrosis factor-alpha (TNF-α), interferon gamma (IFN-γ), transforming growth factor-beta (TGF-β), interleukin-10 (IL-10), interleukin-13 (IL-13)) levels were studied for all patients. On the seventh day, the cytokine levels were restudied in group 1 and 2 (Table). Statistical analysis was performed with Pearson’s Chi-square, Fisher’s exact test, Mann Whitney U-test and Wilcoxon’s signed rank test.

**Results:** Six bacterial diarrhea were determined in both groups, and there were no significant differences in other parameters either (p>0.05). Serum interleukin-10 levels on day 7 was increased in group 1 (5.97 vs 14.54), but there was no increase in group 2 (19.86 vs 0.01).

<table>
<thead>
<tr>
<th>Cytokine levels</th>
<th>Group 1</th>
<th>Group 2</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Day 7</td>
</tr>
<tr>
<td>IL-10</td>
<td>5,97</td>
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<tr>
<td>IL-13</td>
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<tr>
<td>IFN-γ</td>
<td>0,41</td>
<td>0,01</td>
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<tr>
<td>TNF-α</td>
<td>1014</td>
<td>823</td>
</tr>
<tr>
<td>TGF-β</td>
<td>203,5</td>
<td>214,8</td>
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</table>

**Conclusion:** This study, gives an idea about the immunomodulator effects of synbiotics with regulating antiinflammatory cytokines in children with acute gastroenteritis.

**Disclosure of Interest:** None Declared
THE PREVALENCE OF HELICOBACTER PYLORI-GASTRITIS IN NEWLY DIAGNOSED CHILDREN WITH INFLAMMATORY BOWEL DISEASE OR CELIAC DISEASE.

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Objectives and Study: Recent studies- mostly concerning adults- have shown that patients with inflammatory bowel disease (IBD) are less likely to be infected with Helicobacter pylori (Hp) compared to non-IBD patients, whereas those with celiac disease (CD) have no significant difference when compared with non-celiac patients. We aimed to study the prevalence Hp-gastritis in newly diagnosed children with IBD or celiac disease in comparison to those with both non-IBD and non-CD patients in Greece.

Methods: All children who underwent first esophagogastroduodenal endoscopy (EGD) between 2002-2011 were retrospectively included. Five groups were studied: patients with Crohn's disease (CrD), ulcerative colitis (UC), IBD-unclassified (IBDU), celiac disease (CD), and non-IBD-non-CD (control group, CG). H.pylori infection was defined by positive culture or by positive histology and CLO-test. Those children with negative or not available culture and only one positive test (histology or CLO) were further evaluated by urea breath test and the positives were also included in the infected group.

Results: We studied 216 children with celiac disease (median age 7.5±4.1 years, 61.1% females), 91 patients with CrD (median age 10.6±3.4 years, 52.8% females), 53 patients with UC (median age 79.8±3.6 years, 64.1% females), 45 patients with IBDU (median age 8.4±4.0 years, 55.6% females) and 955 patients in CG (median age 7.6±4.6 years, 45.8% females). Hp-gastritis was detected in 3 children with CrD (3.3%), 15 children with CD (6.9%) and 181 children from CG (18.9%), whereas it was not found in UC and IBDU groups. Children with Hp-gastritis were 21 times less likely to belong in IBD group (OR: 21.0, 95% ci: 6.6-66.9), and 3.2 times to belong in CD group (OR: 3.2, 95% ci: 1.9-5.6), when compared to CG, independently of gender and age.

Conclusion: Occurrence of Hp gastritis is less frequent in children with IBD or celiac disease compared to controls. Our study confirms an inverse association between H.pylori and IBD. Future studies are needed to determine whether this finding results from a protective role of H.pylori.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: To investigate the features of coinfectious viral agents in hospitalized young children for acute gastroenteritis and to compare the results with those of monoinfection.

METHODS: Between January and September 2012, patients under 4 years of age admitted to the hospital with acute gastroenteritis were enrolled. A stool sample from each patient was screened for enteropathogenetic bacteria and tested by reverse transcription polymerase reaction for presence of norovirus and by latex agglutination for rotavirus. The clinical features of every type of infection were analyzed and compared.

RESULTS: A total of 102 patients (pts) were enrolled with a mean age of 26.3 ± 3 months and a male/female proportion. Rotavirus and norovirus monoinfection were detected in 41 pts (40%) and 40 pts (39%), respectively. Dual viral infections were detected in 21 pts (20%) with rotavirus-norovirus co-infection. Both patients with rotavirus and norovirus monoinfection manifested vomiting (100% vs 71.4%, respectively), diarrhea (93% vs 85.7%, respectively) and fever (78.5% vs 57%, respectively). Intensive diarrhea (> or =5 times/day) was more frequent and serum C-reactive protein concentration was higher in children with rotavirus enteritis. Compared to the patients with only rotavirus infection we didn’t find any statistical difference in severity of symptoms, mean hospital stay, fever and serum C-reactive protein concentrations in patients with co-infection, instead important statistical differences were found among these children and those with norovirus mono-infection with a more intensive vomiting and diarrhea and an higher serum C-reactive protein concentrations in the first group (p<0.001).

CONCLUSION: Rotavirus and norovirus infection were common coinfectious viral agents. Their association do not seem to worsen the clinical features and duration of enteritis. The presence of rotavirus infection seems to be the only risk factor for severe and longer enteritis.

Disclosure of Interest: None Declared
Objectives and Study: Acute gastroenteritis is an important reason of mortality in developing countries. Proper management of dehydration could decrease both mortality and morbidity. Knowledge and practice of the families are important in preventing dehydration. In this study, it is aimed to evaluate the knowledge, attitude and practice of families about acute gastroenteritis management.

Methods: Parents of children who have admitted to paediatric outpatient clinics aged between 6 months-5 years were enrolled. Sociocultural levels of parents, knowledge, attitude and practice about feeding of the child during diarrhoea, fluid intake and usage of oral rehydration fluid (ORF) were questioned by a questionnaire.

Results: 189 families were enrolled. Sociocultural class of the families were high in 79.4% and middle in 20.6%. A great majority (95.5%) of the parents stated that breastfeeding should be continued or increased during diarrhoea. It was known that feeding amount should be same (54.1%) or increased (33%). On the other hand, most of the families (89.2%) thought that a special diet should be given. Of the families questioned, 94.1% knew that fluid intake should be increased and most (93.3%) of them put it in practice. Parents performed similar attitude and practice in these issues. A significant difference was not found between middle and high sociocultural classes. Knowledge on usage of ORF was not sufficient.

Conclusion: This study shows that families are aware about importance of breastfeeding and increasing fluid intake. However, education about appropriate feeding skills and usage of ORF is still needed.

Disclosure of Interest: None Declared
GASTROENTEROLOGY
GI INFECTIONS

PO-G-0191

SELECTIVE DETECTION AND CLINICAL INFORMATION AFTER PROBIOTIC LACTOBACILLUS AND BIFIDOBACTERIUM SUPPLEMENT TO PREMATURE NEONATES
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Objectives and Study: Necrotizing enterocolitis (NEC) is the most common acquired disease of the gastrointestinal tract in premature neonates. Probiotic supplementation Bifiborm® bacteria, Lactobacillus rhamnosus and Bifidobacterium lactis was introduces at the Department of Neonatology, Rigshospitalet to reduce NEC risk and potentially provide benefits for the preterm neonates.

Methods: To groups of preterm infants < 30 weeks of gestation were recruited from a single level III NICU at Rigshospitalet, Copenhagen, Denmark. Probiotic was introduced as a part of treatment to all premature less than 30 weeks of gestation from May 2010. The probiotic product was Bifiform® (Ferrosan A/S, Denmark). Bifiform® contains freze-dried Lactobacillus rhamnosus GG and Bifidobacterium animalis subspecies lactis BB-12. Probiotic was add to 1 ml of mothers milk and given from day 3. The first group was recruited from September 2006 to January 2009; the probiotic group was recruited from May 2010 to October 2011. All patients underwent routine NICU care as determined by the managing service. Faecal samples from the neonates were collected by nurses of the department. Fecal samples were collected at postnatal day 0-5 (sample 1), day 10 (sample 2) and day 30 (sample 3). A specific polymerase chain reaction (PCR) of the Bifiborm® bacteria was designed to detect the Bifiborm® bacteria in fecal samples.

Results: The natural colonization with L. rhamnosus and B. lactis was investigated on fecal samples from the group of neonates how didn’t received probiotic. A total of 461 samples were run 0.7% were found positive for L. rhamnosus, 0.4% were found positive for B. lactis, none of the samples were positive for both. In the group how did received probiotic a total of 247 fecal samples were run 74.1 % were found positive for L. rhamnosus, 34.0 % were found positive for B. lactis, 33.2 % of the samples were positive for both. In the first group 12.7 % developed NEC in the probiotic group 7.1 % developed NEC. NEC incident was reduced but it was not significant p=0.15, the amount of dead was reduced but it was not significant p=0.30.

Conclusion: The results indicate that the two probiotic bacteria L. rhamnosus and B. lactis are not naturally present in the gut of neonates but the probiotic supplementations do reach the gastrointestinal tract and can be detected probiotic. In this study probiotic do not change the outcome of NEC or dead.

Disclosure of Interest: None Declared
THIORPHAN INHIBITS CHOLERA-, BUT NOT E.COLI HEAT STABLE TOXIN-INDUCED ION SECRETION IN HUMAN ENTEROCYTES

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Objectives and Study: Although oral rehydration solutions resolve dehydration due to infectious diarrhea, the need for an additional treatment to reduce intestinal fluid secretion still persists. Cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) represent two of the main intracellular signal transduction pathways stimulating fluid fluxes across intestinal mucosa by Vibrio cholerae and enterotoxigenic E. coli, respectively. Thiorphan (Trp) is an antidiarreal agent whose mechanism of action is still unclear. The aim of this study is to investigate the effects of Trp on transepithelial ion transport in enterotoxin-induced ion secretion.

Methods: Ion transport was investigated by monitoring electrical parameters in human intestinal Caco-2 cells mounted in Ussing chambers and exposed to Trp, in the absence or presence of V.cholerae toxin (CT) or E. coli heat-stable enterotoxin (ST). cAMP and cGMP intracellular concentrations were also determined with commercial ELISA kit.

Results: Trp addition to the mucosal side of enterocytes induced a decrease in Isc (-3,4 µA/cm²), indicating ion absorption. The effect was time and dose-dependent peaking at 1 hour after 10µM Trp exposure. Trp alone reduced cAMP but not the cGMP levels (p<0,05). Preincubation with Trp resulted in a significant reduction of ion secretion (-72,7%) and cAMP production (-66,2%) elicited by CT. ST-induced cGMP production, but not the ion secretion, was reduced with Trp preincubation (-45,3%).

Conclusion: Trp directly promotes ion absorption, through cAMP decrease and consistently reduces cholera-toxin, but not heat stable-toxin-induced secretion. These results demonstrated that Trp act directly on the enterocyte adding new insights in the mechanism of action.

Disclosure of Interest: None Declared
IDIOPATHIC LIVER FIBROSIS AND IL-21R DEFICIENCY

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Objectives and Study: The etiology of liver fibrosis in childhood is often unknown. We followed a consanguineous family with two affected children diagnosed with idiopathic liver fibrosis. Both children presented with chronic cholangitis and hepatic fibrosis leading to liver failure. Further investigations revealed that both children had chronic cryptosporidiosis and subtle evidence of T and B cell dysfunction. We initiated a study to discover the genetic etiology.

Methods: We performed SNP-based homozygosity mapping followed by next-generation exome sequencing (NGS). Functional assays were performed on patients’ peripheral blood mononuclear cells.

Results: Using a combination of homozygosity mapping and NGS we identified a homozygous loss-of-function mutation in the IL21R gene (Patients P1/P2: c.G602T, p.R201L), resulting in aberrant subcellular trafficking of the IL-21R, ligand binding, and IL-21R-mediated signal transduction. Functional assays revealed impaired IL-21-induced B cell proliferation and immunoglobulin class-switch, T cell cytokine production and NK cell cytotoxicity. Patient P1 underwent orthotopic liver transplantation at the age of 4 years, but died shortly thereafter due to infectious complications. Patient P2 was treated by allogeneic hematopoietic stem cell transplantation at the age of 10 years and also died prior to engraftment. Upon identification of the IL21R mutations, an additional kindred with two affected patients (P3/P4) and a distinct homozygous deletion in the IL21R gene was found (c.240_245delCTGCCA, p.C81_H82del).

Conclusion: Our study highlights that “idiopathic liver fibrosis” may be secondary to primary immunodeficiencies (PID). We here identify a novel PID caused by IL-21R deficiency. Early diagnosis is critical to tailor therapy.

Disclosure of Interest: None Declared
**Objectives and Study:** Autophagy is a lysosomal degradation pathway that is essential for cell survival and homeostasis. It is also a component of innate immunity against intracellular pathogens. Vitamin 1,25(OH)₂D₃ (1,25D₃) has been described to induce autophagy thus promoting antimicrobial clearance via the human cathelicidin LL-37. In this study we investigate the role of autophagy and its regulation by 1,25D₃ in Rotavirus (RV)-related enterocyte damage.

**Methods:** Confluent Caco-2 cells monolayers were incubated in glutamine free medium for 24 hours and consequently infected with an inoculum of activated simian RV strain SA11 at a multiplicity of infection of 10 PFU. To assess the role of autophagy during RV infection, cells were pretreated with 1,25D₃ (50nM) at 37°C up to 24 hours. Autophagy was evaluated by western blot and immunofluorescence using an anti-LC3 mAb. Apoptosis was evaluated by western blot using an anti-Caspase3 mAb. LL-37 expression was seen by immunofluorescence with a specific mAb. Epithelial integrity was estimated by transepithelial electrical resistance (TER).

**Results:** RV induced autophagosome formation as judged by immunofluorescence – showing an increase in LC3 puncta at 24 hours post-infection (62% cells with ≥7 LC3 dots per cell vs 40% control cells, p<.05) – and western blot densitometry (1.25±0.1 vs 0.73±0.1 AU, p<.05). LC3+ vesicles did not localize with the lysosomal marker LAMP-2. Pretreatment with 1,25D₃ for 24 h a) reduced LC3-II 24 h post-infection (PI) indicating an increased autophagic flux (0.88±0.1 vs 1.25±0.1 AU); b) induced LL-37 expression at immunofluorescence 6 h PI (74% vs 41% LL-37+ cells, p<.01); c) reduced apoptosis as judged by Caspase3 increase at western blot (1.92 vs 1.48 AU, p<.05); d) reduced the RV-dependent epithelial damage as judged by TER compared with control infected cells (275±6 vs 180.1±2 Ω/cm², p<.0001).

**Conclusion:** Autophagy is involved in response to RV infection in human enterocytes, and its upregulation can reduce RV-related cytotoxic effect. Future research is needed to understand the mechanisms by which the autophagic pathway is modulated in RV-infected cells.


**Disclosure of Interest:** None Declared
Objectives and Study: Oesophageal atresia is a common problem in neonates, with incidence of 1:3000-1:5000 births. The current surgical treatments offer a significant morbidity of 30-40%. Therefore, tissue engineering may provide a safer alternative. The aim of this study was to compare 2 techniques to decellularize a rat oesophagus, for use as a biological scaffold for transplantation.

Methods: Oesophagi were resected from 250-300g Charles Rivers rats (n=10) and decellularized using two different methods. The detergent-enzymatic treatment (DET) comprised of deionized water (24hrs, 4°C), 4% sodium deoxycholate (4hrs, room temperature (RT)), 2000kU DNase-I in 1M NaCl (3hr, RT), and PBSAA (30mins, RT) with the solution being pumped through the lumen. Up to four cycles of DET were performed with samples being taken at the end of each cycle. The second method involved static incubation in 1% sodium dodecyl sulphate (SDS) solution. Samples were taken at 1, 3, 6 and 24 hours. The oesophageal scaffolds were analysed using DNA, collagen and elastin quantification. Samples were analysed with Haematoxylin and Eosin (H&E), Masson’s Trichrome (MT) and Elastin Van Gieson (EVG) stains. Immunofluorescence was performed for laminin, collagen-I and collagen-III.

Results: H&E and DAPI staining that demonstrate no cellular remnants following 1 cycle of DET and 6 hours of SDS respectively. However, histological results show clear loss of microarchitecture in the SDS-treated oesophagus with a poor connective tissue network. Elastic fibers are significantly more disrupted in the SDS compared to the DET-treated oesophagus. The DET-treated oesophagi retained an appropriate microarchitecture and extracellular matrix components.

Conclusion: The best course of decellularization is the DET as it causes the least disruption of the structure and components of the extracellular matrix whilst still removing all cellular remnants.

Disclosure of Interest: None Declared
COMMON ESPGHAN TOPICS
BASIC SCIENCE

PO-G-0196

ABSENCE OF EFFECT OF NASAL CONTINUOUS POSITIVE-AIRWAY PRESSURE ON THE ESOPHAGEAL PHASE OF NUTRITIVE SWALLOWING IN NEWBORN LAMBS
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Objectives and Study: It is currently recommended to start oral feeding in premature infants as soon as possible, often at an age where nasal continuous positive airway pressure (nCPAP) is still required for ventilatory support. While some neonatologist teams routinely initiate oral feeding in premature infants with nCPAP, others refuse to do so, by fear of the cardiorespiratory consequences of laryngeal penetration and tracheal aspiration. Our previous data showed that application of nCPAP up to 10 cmH2O in full-term lambs has no deleterious effect on cardiorespiratory safety, feeding efficiency or on nutritive swallowing-breathing coordination [1]. To our knowledge, no study has focused on the effects of nCPAP on esophageal motility in the neonatal period. Therefore, the aim of the present study was to further assess the effects of nCPAP on oral feeding by assessing its effects on the esophageal phase of nutritive swallowing (nutritive esophagodeglutition).

Methods: Six full-term lambs, aged 2-3 days, underwent esophageal Multichannel Intraluminal Impedance-pH monitoring (MII-pH). Lambs were bottle-fed under two randomized conditions, namely spontaneous breathing and nCPAP 6 cmH2O.

Results: Beyond confirmation of cardiorespiratory safety and unaltered feeding efficiency, analysis of multiple variables measured by impedance monitoring revealed that nCPAP-6 does not alter nutritive esophagodeglutition in any way (nCPAP vs. spontaneous breathing, p > 0.1 for all variables).

Conclusion: Beyond offering some further support to neonatologists pleading for initiation of oral feeding in infants still on nCPAP, the present results set the foundations for similar clinical studies in preterm human infants to confirm the absence of effects of nCPAP on nutritive swallowing.


Disclosure of Interest: None Declared
Objectives and Study: Postnatal gut development from the suckling phenotype to the adult, occurs during the third week of life in the rat, coinciding with the dietary change at weaning. In this study, the role of pancreatic enzymes in postnatal gut maturation, was studied using suckling rats as the model.

Methods: Suckling rats were gavaged at 14-16 days of age with porcine pancreatic enzymes (Creon®, Abbott Laboratories, USA), with microbial-derived pancreatic-like enzymes (amylose, protease and lipase, Sigma-Aldrich, USA) or with water as the control. After this treatment, at 17 days of age, the intestinal permeability in vivo was measured by feeding the macromolecular markers BSA and IgG. Three hours later blood was collected and analyzed for markers, and the visceral and lymphoid organs were dissected, weighed and processed for structural and functional analyses.

Results: The data showed that the exogenously fed pancreatic or pancreatic-like microbial enzyme preparations, accelerated the maturational changes in structure and function in the GI-tract, similar to those normally seen at weaning. This was shown by an increase in gastric acid secretion, changes in the intestinal disaccharidase pattern, with decreased lactase and increased maltase and sucrase activities, replacement of the fetal-type vacuolated enterocytes by the adult-type enterocytes in the distal intestine, and gut “closure” with a cessation of macromolecular transfer to the blood circulation. Enzyme administration also promoted pancreas growth and endogenous enzyme, i.e., amylase and trypsin, production. The obtained effects of the enzyme preparations were confined to the proteases, which in a dose-dependent effect was able to accelerate the GI maturation.

Conclusion: The results suggest that an increased exocrine pancreatic secretion may be involved in the gut maturation of young rats. In addition, the results imply that exposure to a protease (of microbial origin) may be used to provoke gut maturation in, e.g., premature babies.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: It is well known that the perinatal nutritional environment can affect both structure and physiology of a range of organs and tissues, thereby increasing susceptibility to metabolic disorders later in life. During the perinatal period the gastrointestinal tract undergoes profound structural and functional maturation. Experimental studies suggest that alteration of the perinatal nutritional environment may lead to abnormal intestinal development in foetus and neonates. We hypothesized that growth retardation may impair intestinal maturation.

METHODS: Growth retardation was induced by undernutrition during the suckling period in FVB/j mice, by adjusting the litter size to 15 pups per mother on day 4 of life (8 pups per mother in control group). Effects of postnatal undernutrition on the structure and functions of the ileal and colonic epithelium were studied at postnatal day 21 (P21) (weaning).

RESULTS: Pups from large litters had a lower body weight (median 5.4 g vs. 8.8 g at P20; \( p = 0.0002 \)) and a lower growth velocity until P21 (median 0.17 arbitrary unit (au) vs. 0.35 au; \( p = 0.0005 \)). They showed catch up growth after the weaning period with a more important body weight gain until adulthood (median +280.7% vs. +88.2%; \( p = 0.0045 \)). Postnatal undernutrition induced a delay in the maturation of the ileal epithelium characterized by presence of vacuolated villus enterocytes that normally disappeared at P21, abnormal expression of the tight junction proteins, associated with an increase of the paracellular permeability, and no expression at the brush border of the digestive enzymes dipeptidyl-peptidase IV and intestinal alkaline phosphatase. Colonic structure in underfed mice was impaired with a thinner mucosa (median 178.0 \( \mu \)m vs. 197.0 \( \mu \)m; \( p = 0.014 \)), a thinner muscularis externa (median 30.6 \( \mu \)m vs. 43.1 \( \mu \)m; \( p = 0.014 \)), a lower crypt depth (median 164.0 \( \mu \)m vs 177.7 \( \mu \)m; \( p = 0.014 \)), submucosal detachment, and fragile surface epithelium.

CONCLUSION: We conclude that postnatal growth retardation induced by early undernutrition alters maturation of the intestinal epithelium. Long term consequences of such anomalies remain to be assessed.

DISCLOSURE OF INTEREST: None Declared
ABNORMAL PROTEIN GLYCOSYLATION IN LIVER DISEASE CAUSED BY GENETIC DEFECTS
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Objectives and Study: In many conditions of liver disease, such as chronic hepatitis and fibrosis, abnormalities have been identified in serum glycosylation profiles. Such glycoprofiles of total serum proteins are studied as biomarker for use in diagnostics, monitoring disease progression and therapy response. The Congenital Disorders of Glycosylation (CDG) comprise a heterogeneous group of genetics diseases. In the classical presentation of CDG with defects in the Endoplasmatic reticulum, the majority of patients shows involvement of the liver within a multisystem presentation, dominated by neurological symptoms. In the growing group of CDG patients with Golgi glycosylation defects, a relatively large subgroup of patients (n=30) presents with non-syndromal liver disease. The goal of our study program is to unravel the genetic etiology of disease.

Methods: We employed mass spectrometry and exome sequencing.

Results: We developed a novel method for high-resolution glycoprofiling of intact serum transferrin on a C8-chip-QTOF mass spectrometer for high-throughput analysis of protein specific glycosylation. In our cohort of patients, we could distinguish at least four groups of patients with liver disease on basis of specific glycosylation abnormalities. In our whole-exome sequencing program, we have functionally confirmed 1 novel gene defect 1, while for 2 groups candidate genes are listed. For PGM1, the characteristic glycosylation profile lead to the identification of many new PGM1 deficient patients. The clinical phenotype included hepatopathy in all patients with dilated cardiomyopathy and exercise intolerance with increased creatine kinase in some. Guided by mechanistic studies, we could restore protein glycosylation by dietary addition of galactose (in review).

Conclusion: we have firm evidence that the glycosylation abnormalities in patients with non-syndromal liver disease are not a secondary reflection of general disease state but rather originate from a genetic cause. In addition, for the first identified defect in this category, we have been able to design a treatment regime.


Disclosure of Interest: None Declared
COMMON ESPGHAN TOPICS
BASIC SCIENCE

PO-G-0200

GUT MICROBIOTA IN PRETERM INFANTS THROUGHOUT THE FIRST YEAR OF LIFE
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Objectives and Study: Gut microbiota establishment is an important step in the maturation of intestine. Abnormal microbiota has been reported in preterm neonates during hospitalization but long term data are lacking. The objective of the study was to describe the gut microbiota of preterm infants throughout the first year of life.

Methods: Monocentric prospective longitudinal study of 77 preterm infants followed during the first year of life. Fecal samples were collected at 1 week (wk), 1, 3, 6, and 9-12 months of age (mo) and analysed using culture and culture-independent methods.

Results: Aerobic species: staphylococci, enterococci and enterobacteria colonized 2/3 of the preterm infants at 1 mo, but at 3 mo and afterward, almost all preterm infants were colonized by these aerobic genera. Preterm infants born <28 wks GA were less frequently colonized by these genera at 1 mo than infants born at a GA ≥28 wks. Moreover, they exhibited a delayed colonization by Escherichia coli, a usual commensal species in neonates, compared with those born at a GA of 28 to 33 wks GA (mean age of colonization of 31 d vs. 111 d). Anaerobic species: at 1 mo the anaerobic flora comprised mainly clostridia which colonized 80% of the preterm infants, colonization by Bacteroides, bifidobacteria, and lactobacilli being observed in only 1/3 of the infants. At 6 mo almost all infants born at a GA >33 wks were colonized by bifidobacteria and Bacteroides by contrast with those born at ≤33 wks. At 9-12 mo, a delayed in colonization by Bacteroides was still observed in infants born at a GA ≤33 wks.

Conclusion: Our data demonstrate abnormal early but also late gut colonization in preterm infants. Colonization patterns were mainly depending on GA. Other factors influencing this bacterial establishment are discussed. A delayed colonization by bifidobacteria and Bacteroides, known for their health promoting properties, can be observed up to 1 year of life in preterm infants born at a GA <33 wks. The clinical consequences of this prolonged abnormal microbiota warrant further studies.

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Disclosure of Interest: None Declared
COMMON ESPGHAN TOPICS
BASIC SCIENCE

PO-G-0201

DYNAMIC GASTRIC DIGESTION MODEL REVEALS PROTEIN FUNCTIONAL RETENTION IN HUMAN MILK AND INFANT FORMULA
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Objectives and Study: Milk proteins provide physiological functions above and beyond their nutritional value; however, gastric digestion may break down intact proteins thereby diminishing their activity. A key element in assessing protein bioavailability is to understand how the functionality of bioactive proteins from human milk (HM) and infant formula (IF) is retained or introduced during stomach digestion. In this study, we have implemented a novel dynamic gastric model (DGM) to more accurately simulate infant gastric digestion and applied proteomic tools to study the survival of bioactive compounds and support an effort to develop IF functionally closer to HM.

Methods: The DGM can accurately simulate human stomach physiology and protein gastric digestion. HM or reconstituted IF (Enfamil® Lipil®) was added to gastric-enzymatic secretions with the pH titrated over time. Digesta was emptied from the DGM over a 60min period at 12min intervals. Collected digesta were partitioned into an insoluble fraction, including disrupted milk fat globule and casein micellar material with associated proteins, and an aqueous fraction containing solubilized proteins. Soluble proteins from the aqueous fraction were analyzed by in-solution tryptic digestion, Tandem Mass Tag labelling (TMT 6 plex), peptide prefractonation and nano LC-MS/MS analysis using LTQ/OrbitrapXL. Mascot search engine was used for MS/MS ion search and TMT quantification. A nested ANOVA accounting for the data hierarchy including factors of biological subjects, digestion durations and technical replicates was used to assess the statistical significance of differences in digestion kinetics.

Results: Over 400 proteins were quantified at multiple stages of digestion. While a number of carbohydrate metabolism proteins were broken down promptly, significant decreases in aqueous phase abundance were not observed until times exceeding typical gastric digestion periods for the majority of proteins. Conversely, significant increase in the aqueous-phase abundance was observed for some proteins, including extracellular-matrix glycoproteins and lipid transport proteins. Similar results were found for proteins from IF.

Conclusion: Time-resolved quantitative proteomic analysis suggests that gastric digestion may alter partitioning of proteins in milk, providing a mechanism to release proteins from less digestable portions of the milk matrix in a controlled manner. Variations in the kinetics of gastric proteolysis observed may be used to assess protein bioavailability.

Disclosure of Interest: None Declared
ATOPY PATCH TESTS ARE USEFUL TO PREDICT ORAL TOLERANCE IN CHILDREN WITH GASTROINTESTINAL SYMPTOMS RELATED TO NON-IGE-MEDIATED COW'S MILK ALLERGY

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Objectives and Study: Oral food challenge (OFC) is required to establish the persistence or resolution of cow’s milk allergy (CMA). Atopy patch test (APTs) are useful in the initial diagnostic approach in children with non-IgE-mediated CMA. We aim to investigate the benefit of APTs in predicting a reaction to the OFC in children with non-IgE-mediated CMA.

Methods: We enrolled consecutively children with CMA admitted for OFC to reassess their allergy. The APTs were performed using a drop (20 µl) of fresh cow’s milk (CM) containing 3.5% fat placed on filter paper and applied with adhesive tape to the unaffected skin of the child’s back using a 12-mm aluminum cup. Isotonic saline solution was used as negative control to exclude false positive reactions. The occlusion time was 48 h, and the results were read 20 min and 24 h after removal of the cups. Antihistamines and anti-inflammatory agents were discontinued at least 7 days before the test. All tests were performed by the same nursing staff, and the results were read by two expert pediatric allergists blind to the outcome of OFC. Skin findings were recorded on a standardized form. Reactions were judged to be either negative or positive. Positive skin reactions on the APTs site were classified mild (erythema and slight infiltration, +), moderate (erythema plus papules, ++), or severe (erythema plus vesicles, +++). The OFC was performed after 12 months of exclusion diet. Accuracy of APTs and their correlation (Spearman’s Test) with OFC results were calculated.

Results: 172 children (97 boys, 56.4%; age 6.37 months, range 2–12 months) with CMA-related gastrointestinal symptoms were evaluated. Gastrointestinal symptoms at presentation were vomiting (72, 41.9%), chronic diarrhea (117, 68%), abdominal pain (45, 26.2%). At diagnosis 113/172 (65.7%) children had positive APTs to cow’s milk proteins (CMP). After 12 months of exclusion diet 94 children outgrown CMA. The APTs performed immediately before OFC at 12 months showed a sensitivity of 67.95% (95%CI 56.42-78.07), specificity of 88.3% (95% CI 80.03-94.01), PPV of 82.81% (95%CI 71.32-91.1), NPV of 76.85% (95%CI 67.75-84.43) and a LR of 5.80 (95%CI 3.35-10.38). APTs were significantly correlated (p<0.001) with OFC outcomes (r 0.579).

Conclusion: The APTs are a valuable tool in the follow-up of pediatric patients with non-IgE-mediated CMA by contributing in determining whether an oral challenge can safely be undertaken.

Disclosure of Interest: None Declared
GUT MICROBIOTA COMPOSITION OF BREAST-FED INFANTS DIFFERS FROM FORMULA-FED AND IS CORRELATED WITH HUMAN MILK OLIGOSACCHARIDES CONSUMED

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Objectives and Study: Differences in the composition of bacterial genera between breast- and formula-fed infants are currently much debated. Human milk contains a large quantity of structurally-diverse oligosaccharides (HMO) that serve as prebiotics. Herein we tested the hypothesis that the bacterial genera of breast- and formula-fed infants would differ and that HMO modulate the microbiota composition of BF infants.

Methods: Breastmilk samples and fecal samples were collected from breast- (BF; n=16) or formula-fed (FF; n=6) infants at 3-month postpartum. Microbiota was assessed by pyrosequencing of V1-V3 regions of 16S rRNA genes. HMO were measured by HPLC-Chip TOF MS. Distance-based redundancy analysis (DBRDA) and principal component analysis (PCA) were applied to analyze microbiota and HMO composition, respectively. ANOVA was used to compare bacterial genera between BF and FF. Associations between HMO profiles and bacterial genera were modeled by partial least squares (PLS) regression.

Results: DBRDA distinguished the overall microbiota of BF from FF (p=0.005). ANOVA showed that BF had higher relative abundances of Bacteriodes, lower abundances of Clostridium XVIII, Lachnospiracea incertae sedis, Streptococcus, Enterococcus and Veillonella compared to FF (p<0.05). Bifidobacterium predominated in both BF and FF infants with no difference between the two groups. PCA separated HMO into 3 clusters based on the ratio of LNT/2'FL. The most abundant HMO were LNT/LNnT (22.6%), 2'FL (14.5%), LNFP I (9.5%), LNFP II (8.2%) and LDFT (6.6%). PLS regression of HMO and microbiota showed some bacterial genera could be predicted by the HMO profiles. The bacterial genera that were best predicted by the PLS were Bifidobacterium, Bacteroides and Enterococcus. The HMO that contributed most to the prediction of bacterial genera were identified. The best predictors for relative abundance of Bifidobacterium were LDFT, MFLNH III and DSLNT, while 2'FL, LNFP I, LDFT and LSTb were the most important predictors for Bacteroides. For Enterococcus, 2'FL, LDFT and DSLNT were the best predictors.

Conclusion: Diet impacted the human infant fecal microbiota. The microbial composition of BF infants correlated with the presence of HMO in milk. Our results suggest that supplementation of infant formula with defined HMO could promote growth of specific genera, thereby enabling FF infants to reconstitute a microbial ecosystem similar to that of BF infants (Supported by R01 HD061929).

Disclosure of Interest: None Declared
NUTRITION
NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

PO-N-0204

BIFIDOBACTERIUM CECT 7765 ATTENUATES METABOLIC AND IMMUNOLOGICAL ALTERATIONS ASSOCIATED WITH HIGH-FAT DIET INDUCED OBESITY IN MICE
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Objectives and Study: To evaluate the effects of administration of Bifidobacterium pseudocatenulatum CECT 7765 on metabolic and immune alterations in obese mice.

Methods: Adult male wild-type C57BL-6 mice were fed a standard diet or high-fat diet (HFD), supplemented or not with B. pseudocatenulatum CECT 7765 for seven weeks. The assessments included biochemical and immunological parameters, insulin resistance, glucose tolerance, histology of liver, white-adipose and intestinal tissues, immunocompetent cell functions, and microbiota-related features.

Results: B. pseudocatenulatum CECT 7765 reduced serum cholesterol, triglyceride and glucose levels and decreased insulin resistance and improved glucose tolerance in obese mice. This strain reduced serum levels of leptin, interleukin (IL)-6 and monocyte chemotactic protein-1, while increased those of IL-4 in HFD-fed mice. B. pseudocatenulatum CECT7765 reduced liver steatosis and the number of larger adipocytes and number of fat micelles in enterocytes of obese mice. The strain administration increased bifidobacteria and reduced enterobacteria in the gut microbiota and reduced its inflammatory properties in HFD-fed mice.

Conclusion: B. pseudocatenulatum CECT 7765 ameliorates both metabolic and immunological dysfunction related to obesity in HFD-fed mice. Further studies are underway to understand the mode of action of this strain on the peripheral tissues.

Disclosure of Interest: None Declared
THE EFFECT OF ENTERAL SUPPLEMENTATION OF NEUTRAL AND ACIDIC OLGOSACCHARIDES ON THE RESPONSE TO PNEUMOCOCCAL HEPTAVALENT VACCINATIONS IN PRETERM INFANTS.

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Objectives and Study: Recently, we found a trend towards decreased incidence of serious infectious morbidity during the neonatal period after enteral supplementation of neutral and acidic oligosaccharides (scGOS/lcFOS/pAOs) to preterm infants, but no effect on the response to DTaP-Hib vaccinations. The pneumococcal vaccination was introduced in the Dutch vaccination programme in 2006. The aim of this study was to determine the effect of enteral supplementation of scGOS/lcFOS/pAOS on the immune response to heptavalent pneumococcal conjugate vaccine (PCV7) in preterm infants.

Methods: In a RCT, preterm infants with a gestational age <32 weeks and/or birth weight <1500g received enteral supplementation of scGOS/lcFOS/pAOs or placebo (maltodextrin) between days 3-30 of life. Serum samples were taken at 5 and 12 months of age, after the 3rd and 4th PCV7 vaccination, respectively. Samples were analyzed by multiplex immune assay (MIA, Luminex).

Results: In total, 89 preterm infants at 5 months and 85 infants at 12 months were included. Baseline patient and nutritional characteristics were not different between both groups. We found a lower response to pneumococcal vaccinations after 5 months. This effect was not related to gestational age, birth weight or cord blood pneumococcal antibody concentration. After 12 months was no significant difference between both groups had (table 1). At 5 months, >88% of the infants had protective antibody concentrations for all serotypes in the scGOS/lcFOS/pAOS and control group except for type 6B (39% and 72%, p<0,05) and 23F (71% and 79%, p>0,05). At 12 months, >93% of the infants showed protective antibody concentrations.

Table 1. Pneumococcal antibody concentrations of preterm infant at 5 months and 12 months of age.

<table>
<thead>
<tr>
<th>Serotype</th>
<th>4</th>
<th>6B</th>
<th>14</th>
<th>9V</th>
<th>18C</th>
<th>23F</th>
<th>19F</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 months</td>
<td>G/F/A</td>
<td>1.53*</td>
<td>0.25*</td>
<td>2.39*</td>
<td>1.19*</td>
<td>1.88*</td>
<td>0.75*</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.29</td>
<td>0.79</td>
<td>4.52</td>
<td>2.64</td>
<td>3.15</td>
<td>1.88</td>
<td>14.64</td>
</tr>
<tr>
<td>12 months</td>
<td>G/F/A</td>
<td>4.28</td>
<td>3.33</td>
<td>5.76</td>
<td>4.00</td>
<td>4.73</td>
<td>4.62</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.55</td>
<td>5.39</td>
<td>8.14</td>
<td>5.25</td>
<td>5.40</td>
<td>7.36</td>
<td>11.50</td>
</tr>
</tbody>
</table>

µg/ml, G/F/A: scGOS/lcFOS/pAOS, *p<0,01
**Conclusion:** Preterm infants showed at 5 months a temporarily reduced antibody response to pneumococcal heptavalent vaccinations after short-term enteral supplementation with scGOS/lcFOS/pAOS. After the booster vaccination at 12 months there was no significant difference between both groups. At 12 months, more than 93% of the preterm born infants in both groups had protective antibody levels.

**Disclosure of Interest:** J. Van Den Berg: None Declared, E. Westerbeek: None Declared, G. Berbers: None Declared, F. van der Klis: None Declared, H. Lafeber: None Declared, R. van Elburg Industry of: also an employee of Danone Research
IMPACT OF LIPID QUALITY IN PERINATAL PERIOD ON INFLAMMATION

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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) on neuroinflammatory process in early life and on inherent cognitive deficit at adulthood.

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 arachidonic acid (ARA) (0.5%), 2) equilibrated with vegetable lipids (palm, sunflower, rapeseed oil), 3) diet with vegetable lipids deficient in PUFA n-3. After weaning, offspring were fed with the same diet given to their mother during gestation and lactation except pups from deficient diet group. Those animals received either the same diet or dairy lipids diet.

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 peripheral and central cytokines. Spatial memory performance was assessed at adulthood on the other animals.

Results: Our results showed that inflammatory response’s profile depends of dietary fat matrix. Cytokines expression was significatively increased in animals fed with vegetable lipid diet, deficient diet or diet with dairy lipid + DHA/ARA compared to animals fed with diet containing dairy lipids.

Inflammation at PND 14 induced spatial memory alteration at adulthood. Consumption of dairy diet, all the life along or just after weaning, protect against cognitive deficit induced by postnatal LPS.

Moreover mice fed with dairy lipid diet + DHA/ARA developed spatial memory deficit at adulthood in basal and stimulated conditions.

Conclusion: To conclude, our results showed that consumption of dairy lipids diet protect from adult cognitive deficit induced by perinatal inflammation.

Disclosure of Interest: None Declared
MILD HEAT TREATMENT DOES NOT REDUCE THE COLITIS-PROTECTIVE EFFECTS OF BOVINE COLOSTRUM IN PRETERM PIGS

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Objectives and Study: Fresh bovine colostrum (BC) prevents development of necrotizing enterocolitis (NEC) in preterm pigs. Spray drying and pasteurization are required to use BC in clinical settings but this may also reduce its bioactivity. In studies on preterm pigs, we compared raw BC with spray dried and pasteurized BC.

Methods: Preterm pigs were fed total parenteral nutrition for 2 days, followed by two boluses of milk formula (15 mL/kg/3h) and continued enteral feeding with milk formula (FORM, n = 14), fresh BC (COLOS, n = 14), spray dried, powdered BC (POW, n = 8), or spray dried, pasteurized BC (POWPAS, n = 9). Pigs were euthanized after two days of enteral feeding and NEC lesions, intestinal structure, digestive and absorptive functions, microbiota, and tissue protein and mRNA levels of immune factors were analyzed. Finally, we determined the concentrations of some bioactive proteins in the colostrum products and studied treatment-related aggregation of proteins.

Results: POW and POWPAS pigs showed lowered gut NEC severity, IL-1β and IL-8 levels and lactic acid levels, and higher intestinal villus heights, hexose absorption, hydrolase activities (lactase, maltase, peptidases) than FORM pigs (all P < 0.05). These values in POW and POWPAS groups were similar to those in the COLOS group. Intestinal expression of IL1B, IL6 and IL8 and bacterial abundance score were positively correlated with NEC severity (P < 0.05). Spray drying, and especially pasteurization, increased the breakdown of growth factors (TGF-β1 and -β2) and aggregation of milk proteins.

Conclusion: Spray drying and pasteurization affect BC proteins but such treatments do not necessarily decrease its trophic and anti-inflammatory effects on the immature intestine. It remains to be studied if such colostrum products also improve gut maturation in preterm infants.

Disclosure of Interest: A. C. Støy: None Declared, P. Sangild Grant / Resarch Support from: Biofiber-Damino, Gesten, Denmark, K. Skovgaard: None Declared, T. Thymann: None Declared, M. Bjerre: None Declared, D. Chatterton: None Declared, S. Purup: None Declared, M. Boye: None Declared, M. Schmidt: None Declared, P. Heegaard: None Declared
PO-N-0209

HIGHER N-6 POLYUNSATURATED FATTY ACID VALUES IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE
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Objectives and Study: In our previous study we investigated the fatty acid composition of plasma lipid classes in adult patients with inactive inflammatory bowel disease (IBD) (Figler et al, Br J Nutr 2007) and found considerable differences between the long-chain polyunsaturated fatty acid (LCPUFA) status of patients suffering from ulcerative colitis (UC) or Crohn disease (CD). The aim of this cross-sectional study was to investigate the same question in children. Therefore we analysed n-6 and n-3 fatty acid status of twelve children with UC (age: 13.98 [2.54] years; BMI: 21.86 [3.80] kg/m², mean [SD]), twenty-seven with CD (age: 14.62 [2.70] years; BMI: 21.00 [4.00] kg/m²) and thirty-four controls (age: 13.59 [3.49] years; BMI: 20.57 [4.24] kg/m²).

Methods: Fatty acid composition of plasma phospholipid (PL), triacylglycerol (TG) and sterol ester (STE) fractions was analysed with high performance gas-liquid chromatography.

Results: There were no differences among n-3 fatty acid values in the three investigated groups. We found no differences in the values of the n-6 essential fatty acid, linoleic acid (C18:2n-6). In contrast, the values of its principal metabolite, arachidonic acid (C20:4n-6) were significantly higher in all three investigated fractions in UC patients than in controls (Table). Similarly, 20:4n-6 values were significantly higher in UC, than in CD patients in both PL and STE fractions. Values of 22:4n-6 were significantly higher in both PL and TG fractions in UC patients than in controls (PL: 0.57 [0.06] vs 0.52 [0.13] and TG: 0.26 [0.05] vs 0.20 [0.06], UC vs control, % weight/weight, median [IQR]; A: p < 0.01, a: < 0.05) and were significantly higher in UC, than in CD patients in the PL fraction (0.57 [0.06] vs 0.50 [0.15] UC vs CD, % weight/weight, median [IQR]; A: p < 0.01). In the PL fraction of CD patients the values of 22:5n-6 were significantly lower than in both UC patients and controls (0.51[0.17] vs 0.37 [0.17] UC vs CD vs control, % weight/weight, median [IQR]; A: p < 0.01, a: < 0.05).

Table: Arachidonic acid values (% w/w) of plasma phospholipid (PL), triacylglycerol (TG) and sterol ester (STE) fractions in children with colitis ulcerosa (n = 12), Crohn disease (n = 27) and controls (n = 34)

<table>
<thead>
<tr>
<th></th>
<th>Colitis ulcerosa</th>
<th>Crohn disease</th>
<th>Control</th>
</tr>
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<tbody>
<tr>
<td>PL</td>
<td>11.73 (1.75)A  B</td>
<td>9.55 (1.61)A</td>
<td>9.39 (2.44)B</td>
</tr>
<tr>
<td>TG</td>
<td>1.61 (0.61)A</td>
<td>1.34 (0.60)</td>
<td>1.22 (0.44)A</td>
</tr>
<tr>
<td>STE</td>
<td>7.37 (2.61)A,a</td>
<td>6.15 (2.74)a</td>
<td>5.67 (2.80)A</td>
</tr>
</tbody>
</table>

Data are median (IQR), A,B = p < 0.01, a = p < 0.05
Conclusion: 1. Children with colitis ulcerosa have higher plasma values of n-6 long-chain polyunsaturated fatty acids, which are precursors of proinflammatory eicosanoids. These results raise the possibility that supplementation of the diet of children with colitis ulcerosa with n-3 fatty acids may be beneficial.

Disclosure of Interest: None Declared
HUMAN MILK AND BOVINE COLOSTRUM DECREASE INCIDENCE OF NECROTIZING ENTEROCOLITIS IN PIGS
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Reproduction, Faculty of Health and Medical Sciences, University of Copenhagen, Frederiksberg, Denmark

Objectives and Study: Preterm birth and formula feeding predispose to development of necrotizing enterocolitis (NEC) in infants. As mother’s milk is often absent following preterm delivery, artificial milk formula or human donor milk are used as alternatives. We hypothesized that human donor milk may provide similar NEC-preventive effects in preterm pigs, as bovine colostrum.

Methods: Preterm pigs delivered by cesarean section received 2 days of total parenteral nutrition, followed by 2 days of total enteral feeding (15 mL/kg/3h) with bovine colostrum (BC, n=13), human donor milk (HM, n=13) or infant formula (IF, n=14) provided at isoenergetic levels. Following an in vivo hexose absorption test, pigs were euthanized on day 5 and the gastrointestinal tract was collected to record intestinal NEC lesions (macroscopic scores 1-6, NEC defined as score ≥ 3), histopathology (necrotic cells, congestion, hyperemia, subepithelial edema and loss of villi/epithelia), digestive enzyme activities and tissue concentrations of IL-6 and IL-8.

Results: Relative to IF, pigs fed BC or HM showed higher body weight gain (+22 g/d), more intestinal mucosa (+16%), higher activity of six digestive enzymes (+67-175%), higher hexose absorptive capacity (+400%), all P<0.05. This was associated with lower prevalence of histopathologic lesions in the distal small intestine and colon (overall range -41% to -82%) and lower NEC incidence in BC and HM pigs vs. IF (both 7/13 vs.13/14, P<0.05). All parameters were similar between BC and HM pigs, except that BC pigs showed increased crypt depth (+32%) and higher aminopeptidase N activity (+22%) relative to HM pigs (P<0.01). Relative to IF pigs, IL-6 and IL-8 levels were lower in HM pigs (-86 and -29% respectively, P<0.05) and IL-8 tended to be lower in BC pigs (-31%, P=0.06).

Conclusion: Bovine colostrum and human milk are superior to formula with regards to effects on gut structure, function and NEC resistance in preterm pigs. Bovine colostrum may be a relevant nutritional alternative to mother’s milk in sensitive newborn infants if human milk is unavailable. Further studies are required to study the effects of milk from different species, gestational ages, lengths of lactation, and product treatments (e.g. pasteurization, freezing).

Disclosure of Interest: None Declared
EFFICACY OF AN EXTENSIVELY HYDROLYZED RICE BASED FORMULA IN INFANTS WITH COW’S MILK PROTEIN ALLERGY

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Objectives and Study: To assess the tolerance of an extensively rice protein hydrolysate infant formula and of an innovative thickening complex (PAX) (eHRF). The formula complies with EU regulation for infant formula including its protein content and amino acid profile. As secondary objectives, growth and regurgitation scores were evaluated.

Methods: The eHRF was administered to formula-fed infants (mean age: 3.4 ± 1.5 months [0.5-6 months]) during 6 months. The infants were included if there was a diagnosis of cow’s milk protein allergy (CMPA) based on a positive challenge with standard infant formula (except in infants presenting a risk of anaphylactic reaction) and/or a positive skin prick test associated with a clinical history of allergy. Growth was monitored and the CMP-Intolerance-symptom score (a score based on regurgitation, stool, eczema/urticaria, crying, respiratory symptoms) was evaluated during the challenge and after 1 month of feeding the eHRF. Infants were followed up on for a period of 6 months. The preliminary results based on a 1 month observation period are presented here.

Results: 39 infants were included. 2 patients did not have a food challenge because of anaphylaxis risk. 7 patients were included based on a positive SPT (mean wheal 11 mm (range 5 - 25 mm) associated with a clinical history of allergy. 2 patients stopped the study because of food refusal (no taste acceptance). eHRF (Novarice) was given as the exclusive formula and was well tolerated in all 37 infants. No infant dropped out because of symptoms of intolerance. The CMPI-score decreased significantly (table 1).

Table 1. CMPI-score (min - max 0 - 33)

<table>
<thead>
<tr>
<th></th>
<th>Challenge</th>
<th>30 d eHRF</th>
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<tbody>
<tr>
<td>Mean (SD)</td>
<td>13 (5.1)</td>
<td>3.5 (2.3)</td>
</tr>
<tr>
<td>Median</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Q1-Q3</td>
<td>9 - 16</td>
<td>2 - 5</td>
</tr>
<tr>
<td>Min-Max</td>
<td>4 - 24</td>
<td>0 - 8</td>
</tr>
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</table>

Median weight gain was 0.7 kg (Q1-Q3 0.6-0.9 kg) during 1 month. Almost one third of infants were crying more than 5 hours per day when fed milk proteins based formula; crying decreased to less than 1.5 hr/day in 86.5% and none cried > 3 hours/day (based on a 3 days diary average) while fed the eRHF. The severity and frequency of regurgitation (evaluated by a score) decreased by 74% after 1 month.
Conclusion: This eHFR was well tolerated by all infants with a documented CMPA, ie by more than 90% of patients with a 95% confidence interval in accordance with current recommendations. During eHFR feeding, weight gain was within normal range.

Disclosure of Interest: E. De Greef: None Declared, Y. Vandenplas Consultant for: for Biocodex and United Pharmaceuticals
ORAL POLYUNSATURATED FATTY ACIDS AND NON-DIGESTIBLE OLIGOSACCHARIDES SUPPLEMENTATION REDUCES ALLERGEN-INDUCED DERMATITIS IN MICE

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Objectives and Study: Breast-feeding is generally accepted to be the optimal method of nourishing infants as human milk contains the best mixture of essential nutrients and bioactive components. Amongst these, PUFA (polyunsaturated fatty acids) like arachidonic acid (AA) and docosahexaenoic acid (DHA) exert immunomodulatory functions through alteration of metabolite formation and direct interaction with cellular signaling. Non-digestible oligosaccharides beneficially affect the host by stimulating the growth and/or activity of a limited number of bacterial species in the gut. Since little is known about the effect of combined oral administration of PUFA and non-digestible oligosaccharides on barrier integrity and allergic diseases in the skin, we have investigated their impact on severity of allergen-induced dermatitis in mice.

Methods: Skin inflammation was induced by serial epicutaneous OVA-applications in OVA-sensitized mice. In parallel, mice were fed with solid food containing arachidonic acid/docosahexaenoic acid (AA/DHA), galactooligosaccharide/polydextrose (GOS/PDX) or their combination. Skin lesions were assessed by clinical skin score, but also skin barrier parameters, immunohistochemical analyses and local cytokine expression profile.

Results: Both dietary AA/DHA and GOS/PDX significantly ameliorated the severity of allergen-induced dermatitis. The clinical improvement upon oral AA/DHA and GOS/PDX supplementation was associated with a reduction of transepidermal water loss and decreased Ki-67 expression in the skin. Moreover, in GOS/PDX treated mice IFN-γ and TGF-β expression was increased in skin lesions. Lesional CD8+ and mast cells were significantly reduced in all treatment groups, but appeared to be most pronounced in the mice that were treated with the AA/DHA/GOS/PDX combination.

Conclusion: Dietary supplementation of AA/DHA and oligosaccharides (i.e. GOS/PDX), in ranges similar to what can be found in human breast milk, ameliorated the disturbed epidermal skin barrier of allergen-induced dermatitis due to dampening of the local inflammatory response. Taken together, our observations support epidemiological findings indicating that the decline in nursing is promoting allergic pathogenesis and that supplementation of formula with LC-PUFA in combination with oligosaccharides can act in a preventive, but also therapeutical manner in the context of human atopic eczema through specific peripheral immunomodulatory mechanisms.

Disclosure of Interest: C. Weise Grant / Research Support from: Research grant, prebiotics and polyunsaturated fatty acids provided by Mead Johnson Nutrition, D. Ernst Grant / Research Support from: Research grant, prebiotics and polyunsaturated fatty acids provided by Mead Johnson Nutrition, E. van Tol Employee of: Mead Johnson Nutrition, M. Worm Grant / Research Support from: Research grant, prebiotics and polyunsaturated fatty acids provided by Mead Johnson Nutrition
ANTIBIOTICS MARKEDLY AFFECT URINE AND PLASMA METABOLOMES OF PRETERM PIGS SUSCEPTIBLE TO NECROTIZING ENTEROCOLITIS

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Objectives and Study: Antibiotics (AB) treatment is commonly used to prevent and treat necrotizing enterocolitis (NEC), a severe microbiota-dependent gut disorder in preterm infants. Neonatal AB treatment affects the intestinal and plasma proteome and protects against NEC, at least short term. We hypothesize that reduced bacterial colonization following AB treatment would also affect the plasma and urine metabolomes and help to explain how AB may induce NEC protection in neonates.

Methods: Preterm pigs, used as a model of infants, were given broad-spectrum antibiotics (n=11) or control treatment (saline, n=13) from just after birth by caesarean section. After five days, urine and blood plasma were collected and their metabolite profiles were analyzed with ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) using a non-targeted approach. Potential metabolite candidates for biomarkers with significantly different abundance in urine or plasma between AB and control group were identified based on mass spectral information and verified with commercial chemical standards.

Results: AB treatment prevented NEC development, relative to control (0/11 versus 11/13, P < 0.001). The principal component analysis (PCA) of metabolomes showed a significant effect of the AB treatment on both urine and plasma metabolomes. Twenty and eight putative markers were identified based on mass spectra in urine and plasma, respectively. The most notable feature of differentiated metabolome is the significantly lower abundance of bacterial metabolic products and/or intermediates of amino acids in the AB pigs, which reflects that a major part of the microflora is eradicated while the intestinal permeability is still intact. These metabolites include indolylacryloylglycine and 3-methylidioxyindole from metabolism of tryptophan, 3-phenyllactic acid and phenylacetylglucose from phenylalanine and tyrosine, 2-aminoadipic acid from lysine. Besides, 3-methyladipic acid and pimelic acid from the metabolism of long-chain fatty acids showed lower abundance in the AB piglets relative to the control ones.

Conclusion: The close relations among AB treatment, NEC disease, and identified metabolites make it possible to test the metabolite signature in urine and/or plasma as biomarkers of NEC in preterm neonates. Metabolites such as 3-phenyllactic acid and 2-aminoadipic acid, bacterial metabolic intermediates, have a potential to indicate the progression of NEC which could be important for timely clinical interventions. More research is required to understand how the affected metabolites relate to gut microbial colonization and NEC pathology.

Disclosure of Interest: None Declared
SHORT-TERM INTRAVENOUS FISH-OIL EMULSIONS IN PEDIATRIC ONCOLOGIC PATIENTS - EFFECT ON LIVER PARAMETERS

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Objectives and Study: Pediatric oncologic patients often need parenteral nutrition (PN) during chemotherapy. Long-term use of soybean-based lipid emulsions is associated with progressive liver disease and cholestasis, while fish oil based emulsions have been shown to have anti-cholestatic effects. We studied the potentially hepatoprotective effects of short-term use of SMOF lipids (soybean oil, MCT, olive oil, fish oil) in children undergoing chemotherapy.

Methods: 15 pediatric oncologic patients treated with SMOF lipids were retrospectively analyzed in respect to bilirubin and liver parameters, and compared to a historical cohort who had received standard soybean-based fat emulsions. For statistical comparison the time-points baseline, PN14 and post (day+7) were chosen.

Results: None of the study patients developed cholestasis. Within the SMOF-lipid group there were no differences in the laboratory parameters between baseline, PN14 and post. In the control group γGT levels increased significantly during PN (PN14 vs. baseline, 63.00 vs. 26.43 U/l, p < 0.05). When comparing both groups a rise in γGT at PN14 did not reach significance (50.00 U/l vs. 63.00 U/l, p = 0.503). In the SMOF lipids group LDH decreased to significantly lower levels compared to controls (-32.75 U/l vs. +29.57 U/l, p < 0.05).

Conclusion: An advantage of novel fish oil-based parenteral fat emulsions can be shown even after short-term PN. In children undergoing chemotherapy, while bilirubin levels stayed within normal limits, the use of soybean-based fat emulsions but not SMOF lipids led to significantly increased γGT levels.

Disclosure of Interest: None Declared
POSSIBLE PREVENTION OF FOOD ALLERGIES IN CHILDREN WITH SHORT BOWEL SYNDROME: A RETROSPECTIVE PEDIATRIC STUDY
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Objectives and Study: Short bowel syndrome (SBS) is the major cause of intestinal failure (IF). Patients often require parenteral nutrition (PN) for a variable period of time to survive. There is no consensus on the optimal feeding formula for the SBS infants during the weaning from PN. The common practice is to strictly wean with a semi-elemental diet. Aim of this study was to retrospectively analyze the risk of reactions (food allergy) in a population of children with SBS weaned from PN with an hydrolyzed formula (HF) or with an amino-acid based formula (AA).

Methods: The clinical records of children with IF because of SBS on PN were retrospectively evaluated. The following data were recorded: anthropometric data, age at start and mean duration of PN, residual small bowel length, familial history of atopy, possible development of allergy. We also collected results of allergy tests of patients who had allergic reactions.

Results: Forty-seven children with SBS (26 males; mean age of 4,53 ± 3,85 years), studied at the Department Pediatric from 2000, were retrospectively evaluated. Nine of 47 children (20%) had residual bowel ≥ 100 cm with a mean duration of 3.3 ± 1.8 months of PN. This group was weaned from PN with HF and no allergic reaction was reported. Thirty-eight of 47 (80%) had residual bowel ≤ 100 cm and required a mean duration of 17,36 ± 6,7 months of PN. In this group 22/38 children were weaned from PN with AA and 16 with HF. Twelve of 38 children had adverse events. None of the 22 children weaned with AA did develop allergic reactions; instead in 10/16 (62.5%) (p<.0001) children who were weaned with HF, Cow’s milk allergy (CMA) was diagnosed. In 18/38 children we found familiar history of atopy. Among these children, 6 who were weaned with HF developed CMA, while 12 children who were weaned with AA did not develop CMA. The analysis of age at start and mean duration of PN between allergic and non allergic children demonstrated non statistically significant differences.

Conclusion: Children with SBS have increased risk of developing food allergies. The reduced length intestinal residual (≤ 100 cm) is a risk factor for the development of allergic reactions. Also a familial story of atopy plays a role. However an exclusion diet based on AA exerts a positive role.

Disclosure of Interest: None Declared
**Objectives and Study:** The basic principle of management children with atopic dermatitis (AD) at the period of marked clinical onsets is the elimination of the food-items having the causative significance which were revealed during the clinical examinations and also of food items with high sensitizing activity. Prescription the hypo-allergic diet it’s quite important to replace all the eliminated food-items properly and to keep the nutrition on the balance. The aim of this study was to estimate nutrition status of children with atopic dermatitis.

**Methods:** We have analyzed the conditions of the actual nutrition of 87 children aged from 3 to 6 years who had the atopic dermatitis and who had passed a lot of time on the eliminating diets. Dietary analysis was undertaken using a proprietary dietary analysis program. The concentration of vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B6 (pyridoxine), vitamin A (retinol) and vitamin E (tocopherol) was defined in the blood serum.

**Results:** We have established that just 11% of sick children received the nutrition that was adequate to their age-related needs (in respect to the key nutrients such as proteins, fats, carbohydrates and energy density). The food value of the ration could be both excessive (in 19,2 % of cases) and insufficient (16,3% of cases). The fair quality of patients have the shortage of the proteins (24,8%) and the excess of the carbohydrates (29,2%). The actual nutrition of all examined children was deficient for one or few examining vitamins, while the evidence of the lack of certain vitamins reached 65,5% of the age-related physiological needs. The mean values of the actual consumption of vitamins by the AD-patients were reduced: they were 2,3 times less than the recommended standards of consumption for the vitamins B_{1} and E, 1,8 times less for the vitamin A, 1,7 times less for the vitamins B_{2} and B_{6}. Only 5 patients (6%) had the appropriate provision with all vitamins, and in the blood serum of 33 patients (38%) the content of 5 analyzed vitamins was lower then the inherent to their age indexes.

**Conclusion:** The cause of unbalanced diet of 25 (28,7%) children in researched group was restriction of ration without adequate replacement by other source of nutrients. Addition causes were a failure of appetite (18,4%) or it’s selectivity, sometimes rejection of any products and food neophobia

**Disclosure of Interest:** None Declared
Objectives and Study: Food protein-induced gastrointestinal allergy (FPGIA) is an immune mediated reaction, and can be either non-IgE or mixed IgE- and non-IgE-mediated. The cornerstone for management of FPGIA is dietary exclusion of the offending allergen, which predisposes children to nutritional inadequacies. Hypoallergenic formulas (HF) contribute significantly towards micronutrient intake, however older children are often transitioned to milk alternatives (i.e. oat milk) on the grounds of the child eating a varied diet. We therefore set out to determine the micronutrient intake of children with FPGIA with or without a HF.

Methods: A prospective observational study was conducted at Great Ormond Street Hospital for Children, specialist tertiary referral centre. Patients diagnosed with FPGIA following an exclusion diet completed a 3-day semi-quantitative food diary of current intake. Micronutrient intake of children on an exclusion diet where HF was used as a milk substitute, were compared to those on an exclusion diet without HF.

Results: Food diaries of 51 participants (33 boys) were analysed. The median age was 21.6 months (3.6-190.8). The most common combination of foods excluded were cow’s milk, hen’s egg, soya, wheat and other targeted foods (38.6%); cow’s milk, hen’s egg, soya, and wheat (18.2%); cow’s milk, hen’s egg and soya (18.2%); and cow’s milk and soy (15.9%). Hypoallergenic formula was used in 23 (45.1%) children; the median age of children consuming a HF was 10.8 months (3.6-54) and median age of those without HF was 62.4 months (6-190.8). Significant differences in micronutrient intake were found, with intakes below the lower reference nutrient intake for zinc (12.5% with HF vs 44.4% without, p=0.016), selenium (0% with HF vs 33.3% without, p=0.002) and for children under 4 years (n=31) intakes were less than 66% of the Recommended Nutrient Intake for vitamin D (30.4% with HF vs 75% without, p=0.043). Children receiving HF had significantly higher intakes for zinc (p=0.003), selenium (p=0.011), iron (p=0.049) and vitamin D (p<0.001). There was no significant difference between the groups for calcium, vitamin A, or vitamin C intake.

Conclusion: Children that have transitioned onto nutritionally incomplete milk substitutes are at risk of low intakes of essential nutrients zinc, selenium, iron and vitamin D. Although concerns regarding calcium intake in this cohort are often considered, it seems that this is adequately addressed by the fortification of calcium in non-dairy milk alternatives. Our findings highlight the concern that diet alone may not provide all essential nutrients for children not on a HF.

Disclosure of Interest: None Declared
INFLUENCE OF GESTATIONAL AGE AND STAGE OF MILK SECRETION IN CYTOKINE EXPRESSION PROFILE OF HUMAN MILK

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Objectives and Study: Breast milk (BM) is considered as the reference for infant’s nutrition. The complex composition of BM may exert specific effects on their immunological competence, particularly during the first months of lactation when breast milk is the sole source of food. The role of several bioactive components of BM such as cytokines, chemokines, growth factors and hormones is poorly known, but they might be implicated in the immune response development.

The aim of our study was to detect a spectrum of cytokines, chemokines, hormones and growth factors (GF) in BM samples and analyze the influence of perinatal factors such as gestational age and stage of milk secretion.

Methods: Longitudinal prospective study of characterization of cytokines, chemokines, hormons and growth factors in BM samples from healthy mothers by Protein array (Ray Bio® Human Cytokine Array G6. Ray Biotech, Inc) consisting of 60 different antibodies directed against them.

Results: Interleukin-6 (IL-6/CXCL6), Epidermal growth factor (EGF), angiogenin, B lymphocyte chemoattractant (BL/CXCL13), Monocyte chemotactic protein 1 (MCP-1/CCL2), Insulin-like growth factor-binding protein (IGFBP-1 and IGFBP-2) and Transforming growth factor beta 1 (TGF-β1) were the most common proteins found in term and preterm BM samples along all the stages of milk secretion, reaching the highest concentrations in all the groups. We identified several proteins scarcely reported in the literature, such as: a) GF: Fibroblast growth factor (FGF 6 and 7); b) chemotactic factors: B lymphocyte chemoattractant/CXCL13, Macrophage inflammatory protein (MIP)-1D/CCL9/10, MIP-3a/CCL20, Pulmonary and activation-related chemokine (PARC)/CCL18, Thymus and activation regulated chemokine (TARC)/CCL17; c) anti-inflammatory factors: Macrophage-derived chemokine (MDC)/CCL22. Moreover, Bone morphogenetic proteins (BMPs-4 and 6) and Ciliary neurotrophic factor (CNTF) have not been described previously. The cytokine profile was not influenced by lactation time, however we observed an overall decreasing tendency of cytokine levels over the milk secretion. Gestational age had an impact on cytokine composition of BM, observing a wider spectrum in preterm samples but higher concentrations in term samples.

Conclusion: Antibody array could serve as a fast, high-throughput and sensitive tool for cytokine profile characterization. Our study is the first to provide the influence of perinatal factors on cytokine, chemokine, growth factors and hormones in human milk.

Disclosure of Interest: None Declared
VALIDATION OF BIOIMPEDANCE BODY COMPOSITION ASSESSMENT IN CHILDREN BY DUAL-ENERGY X-RAY ABSORPTIOMETRY


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Objectives and Study: To validate the BIA measurer TANITA BC-418 for its clinical and epidemiological use to assess body composition in children, having Dual-energy x-ray absorptiometry (DXA) as the reference.

Methods: Cross sectional validation study in which 7 years-old children from the Spanish subsample of the EU Childhood Obesity Project, were measured to determine their body composition through anthropometry, BIA and DXA. Main outcome measures were: total body fat, total body lean, trunk fat and trunk lean masses [Kg] assessed through BIA (BIA outputs) and DXA. Fat mass index (FMI) [Kg/m²] was calculated. Predictive equations for the composition of total body and trunk were derived from raw impedance and anthropometric measures in linear regression models; results obtained from these predictive equations (BIA regressions) were compared to DXA as well.

Results: Results from 171 (84 boys) 7 years-old children were obtained. BIA outputs and DXA results showed very small differences for total body lean mass (1%), moderate differences for total body fat mass (13%) and high differences for trunk fat and trunk lean masses (>30%). BIA regressions results showed differences <5% for total body and of 20% for trunk composition as compared to DXA. Sensibility and specificity to correctly classify children in the highest quartile of FMI were 88.4% (74.1, 95.6) and 96.9% (91.7, 98.9) for BIA outputs and 92.9% (79.4, 98.1) and 97.7 (92.8, 99.4) for BIA regressions, respectively.

Conclusion: TANITA BC-418 octopolar bioelectrical impedance analyzer measurements of body composition may be valid for epidemiological use. At individual level, measurements should be interpreted with caution but could still be useful to support diagnose and monitoring in childhood overweight and obesity. The validation of predictive equations from raw impedance measurements in specific populations may increase the precision of the technique.

Disclosure of Interest: None Declared
NUTRITIONAL STATUS AND NUTRITIONAL RISK IN SCHOOLS FOR CHRONICALLY ILL OUTPATIENT CHILDREN

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Objectives and Study: Studies in hospitalized children show that children with an underlying chronic illness have a higher risk for malnutrition than healthy children. In the Netherlands a number of chronically ill primary-school children attend special schools and a number of these schools run their own feeding program. This study aimed to investigate the prevalence and risk of malnutrition of children with a chronic illness in the outpatient setting.

Methods: Design: prospective observational cohort study.
Setting: special primary schools for chronically ill children
Participants: a total 642 children from 9 schools aged 4.2-13.4 years (median 9.9 y) were included, 60% male, 72% white.
Main outcome measures: SD-scores < -2 for weight for height (WFH) and height for age were considered to indicate acute and chronic malnutrition respectively, whereas an SD-score > 2 for WFH was used to indicate overweight. The risk of malnutrition was obtained with the STRONGkids screening tool1.

Results: Overall 29% of the children had an impaired nutritional status; 3% had acute malnutrition, 14% chronic malnutrition and 16% had acute and/or chronic malnutrition. Thirteen percent of the children were overweight. Median HFA SD-scores were -0.61SD and median WFH SD-scores were 0.46 SD. There were no differences in nutritional status between boys and girls and between White and non-White children. Children who had been chronically ill since birth had the highest prevalence of acute and chronic malnutrition. The risk of malnutrition measured with the STRONGkids instrument showed that 41% of the children were at an increased risk (39% moderate risk, 2% high risk). Children with a moderate or high risk had significantly lower SD-scores for WFH and HFA than children with low risk.

Conclusion: This study in a large group of chronically ill primary-school children attending special schools shows that 29% of the children had an impaired nutritional status. The STRONGkids screening tool indicated 41% of children to be at risk for malnutrition and could discriminate between groups. The high proportion of children with impaired nutritional status or at nutritional risk underlines the need for special feeding programs at these schools.


Disclosure of Interest: None Declared
EFFECT OF PREMATURITY ON FAT MASS DISTRIBUTION AND BLOOD PRESSURE AT PREPUBERTAL AGE: A FOLLOW-UP STUDY

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Objectives and Study: Preterm infants may be at risk for altered adiposity. Excess of intra-abdominal adipose tissue is a risk factor for metabolic syndrome. Aim was to evaluate if body composition was altered and blood pressure was elevated in a cohort of children born preterm followed up to prepubertal age.

Methods: Observational, longitudinal study. Thirty-two children born preterm underwent growth, skinfold thicknesses (1) and body composition assessment by means of an air displacement plethysmography system (COSMED, USA) at term corrected age and at prepubertal age (5.5±0.3 y). Blood pressure was also measured at prepubertal age. Inclusion criteria were birth weight <1500 g, gestational age <32 weeks. Exclusion criteria were presence of congenital diseases, chromosomal abnormalities, necrotizing enterocolitis or surgical diseases. Thirty-seven healthy children born at term were recruited as a reference group.

Results: Mean birth weight (g), length (cm), head circumference (cm) and gestational age (weeks) of children born preterm were 1064±306, 36.3±3.9, 29.6±2.3 and 29.6±2.3, respectively. At term corrected age children born preterm were lighter (2461.2±499 g vs 3158±445 g, p<0.0001) and shorter (45.6±3.5 cm vs 49.0±2.3 cm, p<0.0001) than children born at term. Fat free mass at term corrected age was lower in children born preterm (2109.6±402 g vs 2878.1±267 g; p<0.0001), whereas fat mass was higher than their counterparts (14.6±4.0% vs 9.0±3.2%; p=0.02 or 392.6±157 g vs 293.6±130 g; p<0.0001). No difference in the abdominal skinfold thicknesses was found between the two groups. At prepubertal age weight (kg) of children born preterm was similar to that of children born at term (19.38±5.2 vs 19.86±2.41) whereas height (cm) of children born preterm was lower (109.7±6.6 vs 112.3±4.1, p=0.04). No difference in % of fat mass (18.5±6.9 vs 19.8±5.6, respectively) and in fat free mass (15.8±3.2 Kg vs 15.9±1.9 Kg) was detected between the two groups. Abdominal skinfold (mm) was larger in the preterm group as compared to the term group (6.9±3.6 vs 5.3±2.8, p=0.022). Diastolic pressure (mmHg) was higher (62.9±6.99 vs 57.5±7.9, p=0.004) in the preterm group as compared to the term group whereas no difference in systolic pressure was detected.

Conclusion: Children born preterm, although showing a recovery of total body fat free mass at prepubertal age, show a tendency towards a greater intra-abdominal adiposity and increased values of diastolic pressure, which might have adverse consequences for later health.


Disclosure of Interest: None Declared
THE EFFECT OF MILK PROTEIN INTAKE AND IGF1 GENE VARIANTS ON GROWTH PATTERNS IN CHILDHOOD IS MEDIATED BY IGF-I CONCENTRATIONS IN INFANTS AT AGE 6 MONTHS – FURTHER EVIDENCE FOR THE PROTEIN PROGRAMMED ACCELERATED GROWTH HYPOTHESIS.


Objectives and Study: Previous research have shown that a higher protein intake early in life is one of the mechanisms of accelerated postnatal growth, resulting in later obesity risk. Whereas the effect of protein intake on growth and on IGF-I concentrations on later obesity risk have been shown previously an explicit test of intermediation via IGF-I levels of the hypothesized effect of protein intake on growth pattern is lacking.

Methods: In an European randomized clinical trial of 1090 term, formula-fed infants were assigned to receive cow’s milk-based infant and follow-on formulae with lower (LP: 1.25 and 1.6g/100mL) or higher (HP: 2.05 and 3.2g/100mL) protein contents for the first 12 months of life; a comparison group of 588 breastfed infants (BF) was included. BMI was assessed biannually from birth to age 6 yrs and was standardized to WHO-growth-standards. Genetic variants of the IGF1 gene (rs1520220) was analyzed. Serum levels of total and the molar-ratio IGF-I/IGF-BP3 at age 6 months were regressed on the SNP and feeding-groups in 500 infants; its indirect effects on identified BMI-growth via IGF-I mediation were assessed by a combination of path analysis and longitudinal growth-mixture-modeling.

Results: Three BMI-growth-pattern-classes could be identified. A normative growth class of “ideal growth” according to WHO-standards (Class 3: 63%); a class of rapid weight gain in the first 2 life years (Class 2: 32%) and an accelerating growth class during the first 6 years (Class 1: 5%). IGF1-SNP rs1520220 significantly increased the molar-ratio IGF-I/IGF-BP3 and total IGF-I by ~1.3ng/mL per allele. The molar-ratio IGF-I/IGF-BP3 and the concentration in total IGF-I were increased in HP and in LP fed infants (~2.7 & ~1.9 ng/mL and ~2.3 & ~1.7 ng/mL, respectively). Infants with a 10 ng/mL increase in the mediating IGF-I levels or a 10-fold increase in the molar-ratio showed a 8-, respectively 10-fold risk to have a BMI-growth-trajectory of persistently accelerating growth (class 1) in childhood then those breastfed.

Conclusion: The effect of milk protein intake and genetic variants of the IGF1-gene on type of growth patterns is mostly mediated by IGF-I axis serum levels. Thus, the results of these mediation models give further, explicit empirical evidence for the protein programmed accelerated growth hypothesis.

Disclosure of Interest: None Declared
IS THE INCREASED N-6 FATTY ACID INTAKE CONTRIBUTING TO THE INCREASE OF OBESITY AND DIABETES WORLDWIDE?

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Objectives and Study: Holman and others (see review by Lands in Progr Lipid Res 2008) showed our need for essential fatty acids (EFA) was low and Ailhaud et al. (Progr Lipid Res 2006) hypothesized that high intake of n-6 fatty acids early in life might be hazardous for later health in adults. The prevalence of obesity and diabetes are increasing worldwide and the causes are multifactorial, including life-style changes like physical activity, food availability and quality. The obesity increase worldwide parallels the extension of Western diet, characterized by exchange of saturated fat for vegetable oils, rich in n-6 fatty acids. The quality of fat influences gene expression in the developing child both in uteri, and postnatally by the breast milk, and might thereby program for diseases later in life. The aim of this study was to reevaluate and compromise data from a series of own studies in order to investigate if the food changes might be related to the obesity and diabetes epidemics.

Methods: In series of experiments in rodents high saturated fatty acid/ low EFA were given during pregnancy or lactation and in other series different ratios of n-6/n-3 fatty acids during pregnancy and lactation, all other factors in diets being the same to controls. All animal were given standard chow after weaning and followed to adult life regarding anthropometry, insulin-glucose homeostasis, leptin and gene expression in liver. Lipids and fatty acids were controlled with HPLC and GLC.

Results: Later development of obesity was related to EFA deficiency during pregnancy, while the same deficiency only during lactation resulted in resistance to high-fat induced obesity, increased glucose tolerance and persistently changed PPAR expression in the liver of adult animals [1-3]. We also noticed that a ratio of n-6/n-3 fatty acids of around 10:1 during pregnancy and lactation resulted in obesity, high insulin, high blood pressure and increased serum triglycerides in the male adult offspring [3,4]. In comparison animals given a low n-6/n-3 ratio of fatty acids during pregnancy and lactation had lower adipocyte size and were lean as adults [5].

Conclusion: Our studies imply different long-term effects regarding obesity and related symptoms by high saturated fat/low EFA diet if given during late pregnancy or only during lactation. Furthermore the ratio of n-6/n-3 fatty acids during pregnancy and lactation also influenced later obesity. Our series of animal experiments support the hypothesis by Ailhaud et al. that high n-6 fatty acid intake during perinatal period might contribute to the obesity and diabetes epidemics.

References: [1]

Disclosure of Interest: None Declared
ASSOCIATION BETWEEN BMI AND SLEEP DURATION: A CASE-CONTROL STUDY
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Objectives and Study: The primary objective of this study was to compare the duration of sleep of two groups of children, respectively normal weight and obese.

In this observational case-control study were recruited a total of 132 subjects, mean age of 9.4 (2.1) years (70 females and 62 males), 66 normal-weight and 66 obese children, matched for sex and age (± 1 year).

Methods: The condition of normal weight and obesity were defined according to the International Obesity Task Force. Blood sampling was performed in the morning (8.00am ± 1 h) to assess fasting lipid profile, blood glucose, insulin, liver function and C-reactive protein (CRP). The sensitivity and insulin resistance have been studied by calculating HOMA index (Homeostasis Model Assessment) and QUICKI (Quantitative Insulin-Sensitivity Check Index).

Data of total energy expenditure, duration of physical activity, duration of intensity more than three metabolic equivalents (METs, 1 MET = 1 kcal / kg / hour or equal to the oxygen consumption of a subject at rest, ie 3.5 ml / kg / min), number of steps and sleep duration were recorded by BodyMedia SenseWear Pro2 Armband, obtaining the daily average values from the monitoring of the subjects for seven days.

Results: Table 1. Comparison between obese subjects and normal weight in term of total energy expenditure, duration of physical activity, count of steps, duration of sleep.

<table>
<thead>
<tr>
<th></th>
<th>Obese children (n=66)</th>
<th>Normal weight children (n=66)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Median</td>
<td>Min-Max</td>
</tr>
<tr>
<td>Total energy expenditure</td>
<td>2183.5 (471.9)</td>
<td>2149.0</td>
<td>1332.0-3426.0</td>
</tr>
<tr>
<td>(Kcal/die)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of physical activity</td>
<td>132.7 (93.7)</td>
<td>109.5</td>
<td>18.0-483.0</td>
</tr>
<tr>
<td>&gt; 3 METs (min/die)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steps (steps/die)</td>
<td>11265.5 (4553.1)</td>
<td>10639.5</td>
<td>3494.0-23167.0</td>
</tr>
<tr>
<td>Duration of sleep (min/die)</td>
<td>394.6 (69.2)</td>
<td>397.0</td>
<td>245.0-521.0</td>
</tr>
</tbody>
</table>
Normal-weight children, compared to obese children, showed higher QUICKI index (0.37 [0.02] vs 0.31 [0.03]; P < 0.001), whereas the average HOMA, which is an insulin-resistance index, was 1.3 (0.6) compared to 5.6 (5.4) of the obese subjects (P < 0.001).

A multiple linear regression analysis performed in the group of obese children has shown positive and independent association between sleep duration and number of steps per day (P=0.026).

**Conclusion:** The promotion of correct physical activity in children could help in maintaining optimal weight both directly, by increasing energy expenditure, and indirectly, by promoting sleeping and possibly reducing adverse effects of sleep deprivation on metabolism.


**Disclosure of Interest:** None Declared
ADIPONECTIN LEVELS IN EARLY INFANCY ARE NUTRITIONALLY REGULATED AND CORRELATE WITH GROWTH

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Objectives and Study: The adipokine adiponectin regulates insulin sensitivity, glucose and fatty acid metabolism. Lower circulating adiponectin is seen in adults and older children with greater adiposity, and in small-for-gestational age (SGA) infants showing rapid weight gain. However, there are few data in early infancy, especially in non-SGA infants, where the physiological role of adiponectin is less clear. Our aim was to explore the relationships between adiponectin and leptin levels in human breast milk (HM) and infant capillary dried blood spots (DBS), and early infancy growth.

Methods: The Cambridge Baby Growth Study (CBGS) is a prospective birth cohort, with detailed infant anthropometry from birth to 2 years, antenatal and postnatal exposures. 3 month DBS samples, and a small pilot subgroup at 12 months, were processed for adiponectin and leptin levels using DELFIA immunoassays. Mothers collected hindmilk at 4-8 weeks postnatally, pooled over 2-4 weeks. Radioimmunoassay was used to calculate HM adipokine concentrations.

Results: Mean±SD DBS adiponectin was much higher at 3 months in 307 non-SGA infants (143 male) [13.3±4.9 (4.1-32.1) ug/ml] than at 12 months (N=63) [4.4±1.6 (1.5-9.0) ug/ml]. Even among the age 3 month samples, adiponectin was inversely related to exact age (B ≈ 0.1, p<0.0005).

Infant nutrition: 3 month DBS adiponectin was higher in exclusively breast fed versus mixed or formula milk-fed infants (p=0.01), independent of body size. DBS adiponectin was also positively related to HM adiponectin [Mean±SD HM 27.8±7.1ng/ml (N=631)]. In contrast 3 month leptin was unrelated to nutrition type or HM leptin levels [5.2±8.9 (0.0-73.2) ng/ml].

Infant growth: 3 month adiponectin was inversely related to birth-weight, length and skinfold thickness, and to 3 month weight and length. In multivariate models adjusted for age, the strongest determinant of 3 month adiponectin was infant length. DBS adiponectin was positively associated with 3 month DBS branched chain amino acids.

In contrast, 3 month DBS leptin levels [2.9±2.1 (0.6-20.0) ug/ml] were positively related to body size and adiposity, but unrelated to HM leptin levels. Neither HM adiponectin nor HM leptin correlated with infancy body composition.

Conclusion: Circulating adiponectin and leptin levels can be quantified from DBS using immunoassay. 3 month adiponectin and leptin levels showed divergent associations with body size. Adiponectin levels were higher in smaller, shorter infants, appeared to decline with age and be nutritionally regulated. In contrast, leptin was positively associated with adiposity. HM adipokines were not associated with infancy growth.

A FOLLOW-UP STUDY ON SERUM LEPTIN LEVELS IN INFANCY AND ANTROPOMETRY IN CHILDHOOD.


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Objectives and Study: Leptin is present in breast milk and plays an important role in the central regulation of energy balance, exerting an anorexigenic effect and inhibiting the synthesis of fatty acids and triglycerides and increasing the oxidation of fatty acids, affecting body composition. We have previously reported that breast fed infants have a higher leptin serum level that formula fed ones, but the link with childhood obesity is still not well defined. The aim of this study was to evaluate serum leptin levels in infants in the first 18 months of life according to kind of feeding, and to investigate the relationship between serum leptin levels in infancy and body mass index (BMI) in childhood.

Methods: We studied 89 AGA healthy subjects recruited in early infancy to investigate leptin serum concentration. These subjects have been evaluated at 9 years for anthropometric parameters and BMI calculation. Of this population, 48 were exclusively BF at least six months and 41 exclusively FF. Serum leptin has been determined at enrollment using radioimmunoassay kit, Statistical analysis: Mann-Whitney test, Spearman correlation, Multivariate linear regression model with BMI at follow-up as an dependent variable; statistical significance was set at p<0.05

Results: In this samples of infants we observed a higher serum leptin level in breast-fed infants than in formula-fed ones (p<0.005). When the follow-up sample was divided according to kind of feeding, we observed statistically significant differences for weight (p=0.000), length (p=0.005) and BMI (p=0.001) at follow-up with lower values in children who were breast-fed than those who were formula-fed in infancy. We highlight a cut-off serum leptin level of 2.7 ng/ml (median serum leptin level in breast-fed infants), and we observed that infants with serum leptin levels lower than this value have a significantly higher BMI in childhood. Using a multivariate regression model has been showed that infants, with serum leptin levels higher in infancy, had a BMI at follow-up that was lower than 1.35 Kg/m², compared to those in infants with leptin levels lower.

Conclusion: the data from this study showed higher serum leptin levels in breast-fed infants than formula-fed ones, confirming our previous observations (1). Considering the values of leptin during infancy and BMI at follow-up, we observed that children with lower concentrations of leptin had a BMI significantly higher in the third childhood. Interestingly, we identified a leptin cut-off value of 2.7 ng/ml, below which infants had higher BMI in childhood. It represents a further evidence in supporting the protective role of breastfeeding in infancy against the development of overweight and obesity.

References: Savino F et al Acta Paediatr 2005

Disclosure of Interest: None Declared
**Objectives and Study:** Accelerated growth during the first six months post-term of small-for-gestational age (SGA) preterm infants and preterm infants with postnatal growth restriction is related to increased fat mass during infancy and adulthood, which may be associated with adverse metabolic consequences. We compared growth, body composition, and nutritional intake until six months post-term between appropriate-for-gestational-age preterm infants with and without growth restriction at term age (AGA GR+ and AGA GR-, respectively) and SGA preterm infants.

**Methods:** In 83 AGA GR- infants (weight and length at birth and term age ≥-2 SDS), 15 AGA GR+ infants (weight and length at birth ≥-2 SDS and weight and/or length at term age < -2 SDS), and 33 SGA infants (weight and/or length at birth < -2 SDS) weight and length were measured at birth, term age, and six months post-term. Lean mass (LM; g) and fat mass (FM; g) were measured by whole-body dual-energy x-ray absorptiometry (Hologic QDR4500A) at term age and six months post-term. Protein intake (g/d and g/kg/d) and energy intake (kcal/d and kcal/kg/d) between term age and six months post-term were calculated.

**Results:** During the first six months post-term, higher protein and energy intakes per kg per day resulted in higher gain in weight and length SDS in AGA GR+ and SGA infants compared to AGA GR- infants. Regarding body composition, gain in LM was higher and gain in FM was lower in AGA GR+ and SGA infants (Table 1). At six months post-term, LM was similar but FM remained lower in AGA GR+ and SGA infants compared to AGA GR- infants.

**Table 1. Nutritional intakes, growth, and gain (Δ) in lean mass (LM) and fat mass (FM) between term age and six months post-term.**

<table>
<thead>
<tr>
<th></th>
<th>AGA GR-</th>
<th>AGA GR+</th>
<th>SGA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protein (g/kg/d)</strong></td>
<td>2.40 (0.39)*.#</td>
<td>2.69 (0.41)</td>
<td>2.56 (0.67)</td>
</tr>
<tr>
<td><strong>Protein (g/d)</strong></td>
<td>18.41 (4.16)</td>
<td>18.53 (3.27)</td>
<td>17.6 (2.67)</td>
</tr>
<tr>
<td><strong>Energy (kcal/kg/d)</strong></td>
<td>95.6 (12.8)*.#</td>
<td>107.5 (9.4)</td>
<td>102.7 (15.2)</td>
</tr>
<tr>
<td><strong>Energy (kcal/d)</strong></td>
<td>760.1 (132.0)</td>
<td>781.8 (96.8)</td>
<td>774.6 (109.3)</td>
</tr>
<tr>
<td><strong>ΔWeight SDS</strong></td>
<td>0.29 (1.33)*.#</td>
<td>1.46 (1.50)</td>
<td>1.17 (1.53)</td>
</tr>
<tr>
<td><strong>ΔLength SDS</strong></td>
<td>0.66 (1.26)*.#</td>
<td>1.18 (1.75)</td>
<td>1.21 (1.23)</td>
</tr>
<tr>
<td><strong>ΔLM (g)</strong></td>
<td>2252 (618)+*.#</td>
<td>2898 (587)</td>
<td>3055 (581)</td>
</tr>
<tr>
<td><strong>ΔFM (g)</strong></td>
<td>1722 (764)*.#</td>
<td>1263 (834)</td>
<td>1441 (772)</td>
</tr>
</tbody>
</table>
* AGA GR- versus AGA GR+, P<0.05
# AGA GR- versus SGA, P<0.05
‡ AGA GR- versus AGA GR+, P=0.05
* AGA GR- versus AGA GR+, P=0.07

**Conclusion:** Post-term nutrition in preterm infants seems to have an impact on body composition at six months post-term. During the first six months post-term, careful monitoring of the postnatal effects of specific nutritional intakes on body composition is strongly recommended in order to prevent risk of adiposity and metabolic consequences in later life.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Waist-to-height ratio (WHtR) is a simple and rapid screening tool, which has been shown to be a better screening tool than waist circumference (WC) and body mass index (BMI) for adult cardio-metabolic risk factors. A simple boundary value (0.5) is used for men and women of different ethnic groups. More recently, the same boundary value has been proposed also for children.

The objective of our study was to compare BMI, WC and WHtR with respect to their power to predict cardio-metabolic risk factors in paediatric patients.

**Methods:** A cross-sectional population-based study was conducted among Caucasian children aged 10-16 years old. A multi-stage stratified cluster random sampling method was employed to select 502 subjects. Measurements of height, weight, WC and blood pressure were taken and fasting blood samples of plasma glucose, HDL-cholesterol and triglycerides were obtained. BMI and WC standard deviation score (SDS) were calculated according to national references. The main outcome was the presence of, at least, 2 of these cardio-metabolic risk factors: fasting glucose >100 mg/dl, HDL-cholesterol <40 mg/dl, triglycerides >110 mg/dl and systolic or diastolic blood pressure >p90th.

**Statistical Analysis:** Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. We also calculated a ROC curve for BMI, WC and WHtR and compare de area under the curve (AUC) between them using Hamley-McNei test.

**Results:** Mean age was 12.82±0.17 years and 54.6% (274) of the participants were boys. In the study population, 10.2% of subjects were obese, 27.5% were overweight, 25.5% had abdominal obesity and 24.4% had a WHtR >0.5. There was no difference in the prevalence of obesity, abdominal obesity or WHtR between sexes.

In men, WHtR showed the highest sensitivity (72.41%) and NPV (95.92%). BMI showed the highest specificity (91.25%), but a very low sensitivity (37.93%). WHtR had the highest AUC [0.838 (95%CI 0.771-0.906)], and it was significant higher than BMI (p<0.001) and WC (p=0.001).

In women, WC had the highest sensitivity (86.67%) and NPV (98.79%), but with lower specificity than WHtR. Again, BMI showed the highest specificity (93.84%) and a very low sensitivity (33.33%). WHtR had the highest AUC [0.859 (95%CI 0.7607-0.9572)], and it was also higher than BMI (p<0.001) and WC (p=0.043).

**Conclusion:** WHtR is a better screening tool than BMI and WC for detecting cardio-metabolic risk factors in Caucasian children between 10 and 16 years old.

**Disclosure of Interest:** None Declared
NUTRITION ASSESSMENT AND CHANGES OF MICROELEMENTS IN PICU HOSPITALIZED CHILDREN

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Objectives and Study:
To provide theoretical basis for clinical rational nutrition support of critical ill children, and assess nutritional status of critically ill children and investigate the impact of primary diseases and nutritional status on levels of microelements. The correlation of microelements’ levels with severity of illness and clinical outcomes will also be discussed.

Methods: Children hospitalized in PICU in Beijing Children’s Hospital (BCH) from 2010.11.1 to 2011.1.31 were enrolled in our study. Prospective clinical study method is applied in this study. Anthropometric parameters such as height/length, weight, body mass index, mid upper arm circumference and skinfold in all enrolled children were measured. Blood concentration of microelements is tested at admission, and retested on the 7th day and the 14th day after admission. Clinical records including primary diseases, mechanical ventilation rate, LOS and survival rate on the 28th day. Diagnosis of malnutrition and obesity were collected.

Results: 196 cases were enrolled. Overweight or obesity occupy 8.7% (17/196). The prevalence of malnutrition is 21.9% (43/196), and 23.2% (38/164) in children aged 0-5 years old. Children aged 0-5 years old and 15.6% (5/32) in children older than 5 years old. Normal nutritional status group has lower mechanical ventilation rate and higher survival rate on the 28th day than malnutrition group (17.6% VS. 34.9%, 94.9% VS. 83.7%, P < 0.05). The rate of low blood iron level at admission is 60.2% (118/196), 58.2% (114/196) with low blood zinc. Patients with respiratory illness have highest rate of zinc deficiency (P<0.05). With increasing of LOS, the levels of zinc raised (P<0.05). No copper deficiency occurred. Level of blood copper fluctuated during hospital stay (P<0.05). Levels of copper in was a little higher in survivors (P<0.05). No statistically difference was found between survivors and non-survivors about the levels of iron and the rates of zinc deficiency.

Conclusion: The prevalence of malnutrition in children admitted to PICU was 21.9%. Compare to past studies, no significant improvement was observed in malnutrition in critically ill children. Malnutrition group has higher mechanical ventilation rate and lower survival rate on the 28th day, suggesting that malnutrition correlates with severity of diseases and clinical outcomes. Low of levels of iron and zinc in peripheral blood (60.2%, 58.2%) existed in children admitted to PICU, but zinc rise with increasing of LOS. Copper level fluctuate through hospital stay. Levels of microelements had correlation with primary diseases but little with patients’ nutrition status. No significant correlation between levels of microelements and clinical outcomes.

Disclosure of Interest: None Declared
Objectives and Study: To determine the correlation between brachial perimeter and other anthropometric indicators in nutritional assessments applied to 0-5 year old children with edema, ascites, and/or visceromegaly.

Methods: A descriptive, observational, and transversal study carried out with samples collected from 100 patients consisting of children 0-5 year old, with edema, ascites and or visceral over-growth (visceromegaly), who were hospitalized at the National Institute of Pediatrics (NIP), in Mexico City. Measurement of weight, height, cephalic perimeter (CP), brachial or paramesobrachial perimeter (BP or PMBP), tricepal fold were made. The assessment of weight/height (W/H), weight/age (W/A), height/age (H/A), cephalic perimeter (CP), and paramesobrachial perimeter (PPMB) were made using Z-score, Quaker Arm Circumference measuring stick (QUAC) method for brachial perimeter, and Kanawati McLaren index. Eutrophic greater or equal to -1 of standard deviation (SD), mild malnutrition of -1 to 2 SD, moderate of -2 to -3 SD, and mild severe of -3 SD

Results: The principal clinical characteristics found were: liver over-growth (Hepatomegaly) in 79% of the cases, and spleen over-growth (splenomegaly) in 39%. In accordance with Z-score (WHO), W/A measurement showed that 86% of the patients were found with malnutrition, for H/A it was 74%, and for W/H it was 64% while for PMBP it was 90%. With the QUAC method 87% was found with malnutrition while Kanawati McLaren index showed 81% of malnutrition in all patients studied. All the anthropometric indicators detected severe malnutrition between 31 to 51%

Conclusion: The applicability of the most used habitual indicator for the assessment of acute malnutrition grade (Weight/height) in clinical situations in children with ascites, edema, and/or over-growth of visceral (visceromegaly) decreased due to the fact that it is affected by weight; underestimating the malnutrition grade of such patients. Based on this, we suggest the use of PMBP and QUAC method as well as Kanawati McLaren index in this group of patients.

Disclosure of Interest: None Declared
ASSOCIATION BETWEEN CORD BLOOD LC-PUFA COMPOSITION AND BMI UP TO AGE 10 YEARS IS INDEPENDENT OF LATER LC-PUFA COMPOSITION. RESULTS FROM THE LONGITUDINAL LISAPLUS STUDY.

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Objectives and Study: Studies suggested that n6 and n3 long-chain polyunsaturated fatty acids (LC-PUFAs) in blood are associated with body mass index (BMI). Pregnancy and lactation may be critical periods for growth development. In this study, we examined whether n6 and n3 LC-PUFA levels in serum cord blood are associated with BMI up to the age of 10 years, after accounting for LC-PUFA composition at 2, 6, and 10 years.

Methods: This analysis included 408 children from the German LISAplus birth cohort study. BMI was measured at 2, 6 and 10 years. Fatty acid composition was measured in cord blood and in blood collected at 2, 6 and 10 years. Associations between n3 and n6 LC-PUFAs in cord blood and BMI were assessed using linear mixed models. Models were adjusted for sex, age, birth weight, maternal BMI before pregnancy, time of follow-up (2, 6, and 10 years), and PUFA composition as well as total sum of fatty acids at follow-up. Furthermore, two interaction terms were included in the model (between time of follow-up and maternal BMI and between LC-PUFA in cord blood and time of follow-up).

Results: In the fully adjusted model, both n6 LC-PUFA and n3 LC-PUFA concentrations in cord blood were not consistently associated with BMI over time. However, there was a significant interaction between n6 LC-PUFA levels in cord blood and time of follow-up with respect to BMI (p=0.0278). A negative effect was observed at 2 years, no effect was observed at 6 years and a positive effect was observed at 10 years. The effect of n3 LC-PUFA was in the opposite direction, and did not reach significance (p=0.1449).

Conclusion: BMI up to 10 years of age may be influenced by n6 LC-PUFA composition in cord blood. However, this effect appears to vary with age, thereby highlighting the importance of considering age when examining associations of fatty acids on BMI.

Disclosure of Interest: None Declared
Objectives and Study: Objectives and Study: Obesity is a major health problem that is associated with high morbidity and mortality rates. The prevalence of obesity in children and young adolescents is increasing worldwide. It is important to identify subjects at risk to become obese at an early time point. Up to now, however, there are no good markers available that can predict whether a subject will become obese. The aim of this study is to identify early biomarkers reflecting the susceptibility of an individual to become obese later in life and thus could potentially identify high-risk groups. This was studied in an established humanized animal model for hyperlipidemia with mild obesity.

Methods: Male ApoE*3Leiden mice were fed a standard chow diet until 12 weeks of age which is comparable to the age of young adolescent humans. Subsequently, mice were fed a high fat diet (HFD) for another eight weeks to induce obesity. Blood collected prior to and during HFD feeding was extensively analyzed by lipidomics and proteomics. Blood parameters were correlated to endpoints of obesity including body weight gain, body composition, adipose tissue quality and quantity.

Results: All mice responded to HFD but showed considerable variation in body weight gain (between 2.6 and 11.8 gram). The circulating levels of four specific cholesteryl esters correlated significantly with body weight gain, body composition, adipose tissue quality and quantity, prior to and during HFD feeding.

Conclusion: Early predictive biomarkers for the development of obesity can be identified in a humanized mouse model. Such markers may open up new strategies for dietary counseling or nutritional intervention while monitoring the development of obesity in early life. Follow-up studies are aimed at evaluating a broader array of potential biomarkers and confirm their validity.

NUTRITIONAL STATUS AND CLINICAL OUTCOME IN 327 INFANTS UNDERGONE CARDIAC SURGERY

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Objectives and Study: To identify the nutritional status in infants with congenital heart disease (CHD) before operative correction, and to evaluate its impact on the clinical outcome in these patients.

Methods: Infants admitted to the Department of Cardiac Surgery of Xinhua Hospital from Jun.1 2010 to Dec.12 2011, were investigated retrospectively. Patient history, anthropometry measurement at admission, biochemistry tests, and clinical outcomes (length of hospital stay (LOS), length of ICU stay, days on ventilation, death) and other detailed information were collected from medical record. Malnutrition was defined as Weight for age z-score (WAZ) ≤ –2, and parameters were compared between patients with or without malnutrition.

Results: There were totally 327 infant patients (189 boys, 138 girls) included in this study, with an average age of 5.9 months (47d-12 m), and 104 were with cyanotic CHD. The weight-for-age z scores of all the infants at admission were -0.94±1.54, and 87 infants were malnourished (WAZ ≤ –2). 302/327 infants (92.45%) were found with serum levels of pre-albumin lower than normal reference at the time of admission, while low albumin levels were only found in 5 cases. WAZ score was positively correlated with infant age (r=0.244, p=0.001), but negatively correlated with LOS (r=0.185, p=0.009), ICU stay(r=0.245, p=0.01) and days on ventilation (r=0.219, p=0.012). Infants with WAZ ≤ –2 had delayed enteral nutrition starting time post-operation (1.8±1.4 vs. 1.2±0.6, p=0.003), more frequent parenteral nutrition support (47/87 vs.65/220, p=0.001), obviously longer LOS and ICU stays (see table below).

Table. Comparison of clinical outcome between infants with different nutrition status

<table>
<thead>
<tr>
<th></th>
<th>Malnutrition (WAZ≤ –2)</th>
<th>Non-malnutrition (WAZ&gt; –2)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=87</td>
<td>N=240</td>
<td></td>
</tr>
<tr>
<td>LOS(d)</td>
<td>23.1±13.9</td>
<td>17.9±8.6</td>
<td>0.003</td>
</tr>
<tr>
<td>ICU stay (d)</td>
<td>10.5±8.9</td>
<td>6.2±4.6</td>
<td>-0.001</td>
</tr>
<tr>
<td>Days on Vent (d)</td>
<td>4.9±6.2</td>
<td>2.9±3.8</td>
<td>0.013</td>
</tr>
<tr>
<td>Death (%)</td>
<td>6 (6.9%)</td>
<td>6(2.5%)</td>
<td>0.062</td>
</tr>
</tbody>
</table>

* By mann-whitney U test or χ² test
**Conclusion:** Malnutrition is common in infants with congenital heart disease before corrective operation, especially in smaller infants. Nutrition status may be related to the clinical outcome in the period after cardiac surgery, and better nutrition strategy should be stressed in this clinical situation.

**Disclosure of Interest:** None Declared
EVALUATION OF MALNUTRITION RISK IN HOSPITALIZED CHILDREN AND ADOLESCENTS
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¹University Children's Hospital Ljubljana, Ljubljana, Slovenia

Objectives and Study: Malnutrition is an important prognostic factor in many progressive diseases. The present nutritional status can be assessed with anthropometric measurements. However, to predict and prevent development of malnutrition different tools can be used to evaluate the risk of its development. We studied the risk of malnutrition in children hospitalized in our university children's hospital using STRONGkids questionnaire.

Methods: A hundred and 20 children aged from 1 month to 18 years hospitalized on June the 29th 2012 were included in the one day cross-sectional study. Eighty four (70%) had chronic disease conditions and 36 (30%) were hospitalized due to acute illness only. According to age patients were divided into three groups: 1 month to 1 year, 1 year to 5 years, and 5 to 18 years. Children or their parents were interviewed using STRONGkids questionnaire.

Results: We found high risk of malnutrition in 34 (28.3%), moderate risk in 50 (41.7%) and low risk in 36 (30%) children. However, no children with high risk and 15 (41.7%) children with moderate risk of malnutrition were found among those with acute illness alone, while in the group of chronically ill children 34 (40.5%) patients were at high risk and 35 (41.6%) patients were at moderate risk of developing malnutrition (p < 0.0005, Chi-square). In contrast to acute or chronic nature of the disease, the age of the patient had no influence on nutritional risk. In the youngest, the middle and in the oldest group high/moderate/low risk of malnutrition were found in 17.2%/51.4%/31.4%, 32.1%/42.9%/25%, and 33.3%/35.1%/31.6% of children, respectively.

Conclusion: More than 20% of children hospitalized in our university children's hospital were at high risk for malnutrition development. There were no children at high risk among those with acute illness only, but over 40% of children with chronic diseases were at high risk of developing malnutrition.

Disclosure of Interest: None Declared
MOZART OR BACH? THE EFFECT OF CLASSICAL MUSIC ON ENERGY EXPENDITURE IN PRETERM INFANTS
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Objectives and Study: We have recently shown that W.A Mozart music significantly lowers resting energy expenditure (REE) in healthy preterm infants (1). Whether or not this effect is specific to Mozart is unknown. The objective of this study is examine whether J.S. Bach music has a lowering effect on REE in preterm infants similar to that of Mozart music.

Methods: A prospective, randomized clinical trial with cross-over in 12 healthy, appropriate weights for gestational age, gavage fed, metabolically stable, preterm infants. Infants were randomized to a 30-minute period of either Mozart or Bach music or no music over 3 consecutive days. REE was measured every minute by indirect calorimetry and averaged over three 10-minute periods.

Results: Three REE measurements were performed in each of 12 infants at age 20 15 days. Mean gestational age was 30 2 weeks and mean birthweight was 1246 239 g. REE was similar during the first 10 minutes of all 3 randomization periods. During the next 10-minute period, infants exposed to music by Mozart had a trend toward lower REE than when not exposed to music (P=0.07). This trend became significant during the third 10-minute period (P=0.005, Paired Wilcoxon). In contrast, music by Bach or no music did not affect significantly REE during the whole study. On average, the effect size of Mozart music upon REE was a reduction at 20-30 minutes of approximately 4.5% from baseline.

<table>
<thead>
<tr>
<th></th>
<th>Mozart music</th>
<th>Bach music</th>
</tr>
</thead>
<tbody>
<tr>
<td>No music baseline</td>
<td>81.67 ± 12.80</td>
<td>81.67 ± 12.80</td>
</tr>
<tr>
<td>First 10 minutes</td>
<td>78.83 ± 9.25</td>
<td>79.49 ± 10.67</td>
</tr>
<tr>
<td>10-20 minutes</td>
<td>75.87 ± 10.20</td>
<td>79.82 ± 11.81</td>
</tr>
<tr>
<td>20-30 minutes</td>
<td>75.36 ± 10.88</td>
<td>79.68 ± 15.0</td>
</tr>
<tr>
<td>P</td>
<td>0.041*</td>
<td>0.59*</td>
</tr>
</tbody>
</table>

*Last period compared to first period

Conclusion: In the current study, similar to our previously published one (1) we confirmed that Mozart music has a reducing effect on REE. The effect size was also similar, in that in the current study we found an average reduction of REE of 7.7% within 10-30 minutes, while in the previous one the reduction ranged 7.3 to 12.2%.
Contrary to our hypothesis, we found that exposure to Bach music had no significant lowering effect on REE. This would suggest that the effect that we observed with Mozart music is more a "Mozart effect" than a universal "music effect". The exact mechanism of this "Mozart effect" requires further investigation. We speculate that the Mozart effect must be taken into account when incorporating music in the therapy of growing preterm infants, since not all types of music may have similar effects upon REE and growth.


**Disclosure of Interest:** None Declared
INCREASED GROWTH AND SURVIVAL OF NEONATES FOLLOWING IMMEDIATE BACTERIAL COLONIZATION OF THE INTESTINE
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Objectives and Study: To see the metabolic and growth promoting effect of intestinal microflora on neonatal mice

Methods: Naturally inhabiting commensal intestinal bacteria were isolated from mouse fecal samples and taxonomically classified through morphological observation, biochemical typing, and/or 16S rDNA typing. The isolated Probiotics, Bacteroidetes, Firmicutes, or a combination of the Bacteroidetes and Firmicutes groups (B/F) were fed to germ-free (GF) neonatal mice immediately after birth, and the effect on growth was monitored periodically by measuring the change in body weight.

Results: The immediate colonization of neonatal mice with the Bacteroidetes, Firmicutes, or combined groups resulted in an increased gain in body weight compared to the non-colonized, GF controls. The Firmicutes group of bacteria most significantly increased the body weight of neonatal mice compared to GF control [34.55\(\pm\)0.86 g (Firmicutes) versus 27.7\(\pm\)0.88 g (GF); \(n=13\text{–}15\); \(p<0.05\)]. Unexpectedly, the colonization with a group of probiotics bacteria was fatal to the neonates. These results suggest that the immediate intestinal colonization of low birth weight infants with the Firmicutes group of bacteria could be an ideal therapeutic treatment for boosting proper development and growth of the infants.

Conclusion: In conclusion, these studies are showing that the Firmicutes group of bacteria has an excellent potential as a therapeutic agent for weight gain of neonates but application of probiotics in an attempt to activate weight gain of neonate should be reconsidered.

Disclosure of Interest: D. Pandeya Employee of: Nepalese Army Institute of Health Sciences, S. Hong: None Declared
Objective and Study: We conducted growth assessment in premature infants fed with fortified human milk (FHM), as well as comparative assessment of the group fed with specialized milk formula adapted for preterm infants (PF).

Methods: A prospective analysis included 100 preterm infants, gestational age <34 GW. Infants were divided into two groups: group I (n=50) fed with FHM (Nestle FM 85) and group II (n=50) on the PF diet (preNAN Nestle) if lactation has not been established for a period of 4 weeks. Anthropometric growth parameters were analyzed, body weight (g/day), body length and head circumference (cm/week) along with the analysis of the energy, protein and volume intake. Average time to achieve full enteral intake (days) was determined.

Results: Initially tested groups did not differ with respect to gestational age and anthropometric parameters at birth. Infants fed with FHM reach complete enteral intake earlier compared to the group fed with formula (p <0.05). Difference in energy, protein and volume intake between the groups was not statistically significant. Anthropometric parameters of growth in children on the diet FHM and PF are equalized.

Conclusion: Anthropometric parameters of growth in infants on FHM diet and PF diet are equal, though group on FHM diet achieved complete enteral intake significantly earlier.


Disclosure of Interest: None Declared
DEVELOPMENT OF A 1-DAY BIPHASIC 13C-SUCROSE/GLUCOSE BREATH TEST FOR THE DIAGNOSIS OF CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY OR SUCRASE INSUFFICIENCY

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Objectives and Study: Congenital sucrase-isomaltase deficiency (CSID) is an autosomal-recessively inherited disorder causing symptomatic maldigestion of sucrose (SUC). More than 43 CSID variants have been identified with >8 of the exonic amino acid exchanges causing hypomorph or null alleles.1 The diagnosis requires EGD with biopsy for sucrase assay and CSID is probably under diagnosed. Practical screening tests do not yet exist. Sucrose-only breath tests (BT) have been proposed, but not perfected. Our goal was to advance the development of an easy and accurate 1 day(d) 13C-stable isotope substrate-based screening BT.

Methods: Eleven children (11m-15y; 6m/5f) with proven CSID (sucrase<7 EU/g) underwent 13C-SUC BT (20 mg in excipient) and repeat testing on d2 with comparative 13C-glucose (GLU) dosing to critically adjust for habitus. Oxidation results were expressed as a change in isotopic enrichment ratio between the reference GLU and the test SUC substrates [13C-Sucrose Coefficient of Glucose Oxidation (SCGO)] in 13 children (8m-13y, 4m/9f) who underwent EGD with biopsy for clinical reasons (BxCs) showed normal sucrase activity (>25 EU/g) and BT. It was postulated that the 60’ or 75’ time-points might be best. Thirty-four, healthy, asymptomatic and historically SUC-tolerant children (ASTC) underwent 2d/2-stage 13C-SUC/GLU BT and results were compared with data from the BxCs. A sub-set of 19 ASTC repeated BT using a modified 1d-biphasic 13C-SUC/GLU BT in which the second, serial 13C-GLU substrate was super-dosed (5X) to negate any residual SUC effects. Delta enrichment measures attributed to the GLU were adjusted (X/5) before the SCGO was calculated. The results between the 2d and 1d test methods were compared and the best diagnostic time-point and cut-off were determined based on 99% confidence interval (C.I.).

Results: The CSID patients had very low 2d/2-stage 13C-SCGO for both 60’ & 75’ time-points (0.25±0.19 vs. 0.36±0.29, NSD) and CSID differed from BxCs (60’:1.31±0.31; 75’:1.31±0.27; p<0.01). 13C-SCGO enrichment values for BxCs did not differ from those obtained from ASTC at 60’ (1.31±0.31 vs. 1.02±0.52, p=0.08), but improved at the 75’ time point (1.27±0.27 vs. 0.95±0.36, p<0.01). Among the 19 ASTC who also completed the 1d-biphasic 13C-SUC/GLU BT, SCGO values for 60’ were 1.13±0.63 vs. 0.99±0.26 (p=0.42); and for 75’ were 0.99±0.43 vs. 0.99±0.13 (p=0.85). Using the 75’ test outcomes as reference values, the lower limit SCGO cut-off is ≤ 0.75 (99% C.I 1.00±0.24), the test sensitivity and specificity to diagnose CSID was 100%.

Conclusion: The 13C-SCGO 75’ cut-off was defined as <0.75, the 1d-biphasic BT has improved accuracy over the 2d serial test and is convenient for non-invasive testing of mucosal sucrase activity.


Disclosure of Interest: A. Opekun, M.S., P.A.-C Grant / Resarch Support from: QOL Medical, LLC (Florida USA) and US PHS P30 DK56338 through the Texas Medical Center Digestive Disease Center and the USDA/ARS Children’s Nutrition Research Center
POSTNATAL AMNIOTIC FLUID FOR NEC PREVENTION: EXPERIENCE FROM PRETERM PIGS
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1Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Frederiksberg, 2Department of Large Animal Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, 3Department of Animal Science, Aarhus University, Tjele, Denmark

Objectives and Study: Opposite to infant formula, maternal colostrum and milk are rich in bioactive components and protect against necrotizing enterocolitis (NEC) in preterm neonates. Amniotic fluid (AF) contains similar bioactive components including growth, immunomodulatory and antimicrobial factors that stimulate prenatal intestinal development and maturation. We hypothesized that postnatal AF feeding would protect against NEC. We tested the effects of minimal enteral nutrition (MEN) with AF during parenteral nutrition, AF supplementation during full enteral formula feeding or both in our preterm pig model of formula-induced NEC.

Methods: In 3 experiments, a total of 76 preterm pigs were delivered by cesarean section on day 105 of gestation (term day 115) and allocated to 5 treatment groups to test the effects of porcine AF (pAF) and human AF (hAF) as MEN in the parenteral nutrition period (2 d) and in the following enteral formula feeding period (2 d): -/-, -/pAF, pAF/-, hAF/-, pAF/pAF. In an additional experiment, a group of pigs (n=27) received AF as MEN and was euthanized already after the parenteral period: -/0, pAF/0, hAF/0. After euthanasia, the gastrointestinal tracts were evaluated for macroscopic NEC lesions, and mucosal morphology, nutrient uptake capacity and brush-border enzyme activities were analyzed. The effects of pAF and hAF on intestinal epithelial proliferation and migration were tested in vitro in IEC-6 cells.

Results: NEC incidence was decreased in pAF/pAF (2/10) compared with -/- pigs (18/40), whereas no effects were observed in -/pAF (7/14) and pAF/- (6/12) pigs. Body weight was increased in pigs receiving AF (pAF or hAF) in the MEN period (pAF/pAF, pAF/-, hAF/-, pAF/0, hAF/0) compared with -/- (P<0.05), whereas -/pAF did not affect body weight. No clear effects of postnatal AF supplementation compared with -/- were identified on mucosal morphology, galactose absorption or brush-border enzyme activities. In vitro, pAF and hAF increased proliferation up to 20% and migration up to 150% at a concentration of 15% AF (P<0.01) in IEC-6 cells.

Conclusion: Postnatal feeding with AF reduced NEC susceptibility in preterm pigs when given as MEN and during subsequent enteral formula feeding, but not when given solely as MEN or during enteral formula feeding. The structure and function of the intestine were not improved by postnatal AF feeding, which indicates other mechanisms of function, possibly via inflammatory pathways or the gut microbiota. To fully elucidate the potential of postnatal AF feeding in NEC prevention further studies are needed.

Disclosure of Interest: None Declared
EFFECTS OF THE NEW SYNTHETIC BUTYRATE DERIVATE N-(1-CARBAMOYL-2-PHENYL-ETHYL) BUTYRAMIDE ON INNATE IMMUNITY IN NEONATES

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Objectives and Study: Butyrate is a major short chain fatty acid produced by intestinal microflora involved in immunity modulation. The low palatability and stability limit a wide therapeutic use of this substance in the clinical practice. We have recently obtained a high palatable and stable synthetic butyrate derivate, N-(1-carbamoyl-2-phenyl-ethyl)butyramide (BuBull). In this study we evaluated the effect of BuBull on intestinal innate immunity development in neonatal age.

Methods: Not breast milk at term neonates observed in 2 neonatal Units from June 2012 to September 2012 were considered eligible for this pilot study. Enrolled subjects were randomly allocated to receive BuBull supplementation (10 mg/d) of formula milk or placebo, for the first 28 d of life. At the enrollment (0-3 d of life) and at 28 d of life fecal beta-defensins and fecal secretory-IgA concentrations were measured by an ELISA technique.

Results: We enrolled 30 neonates (birth weight 3010±250 g, gestational age 39.3±1.2 w, Cesarian section 22%): 15 received BuBull and 15 placebo. The two groups were similar at the baseline regarding main clinical characteristics and fecal concentrations of Beta-Defensins (123.2±0.14 vs 177.0±102.5 pg/ml; p=0.226) and sIgA (4.1±0.9 vs. 52.6±79.2 mcg/ml; p=0.162). At 28 days of life neonates receiving BuBull supplementation showed higher fecal concentrations of Beta-Defensins (153.9±115.7 vs. 49.5±0.31 pg/ml, p=0.049) and of sIgA (155.2±91.6 vs. 53.3±0.2 mcg/ml, p=0.049) compared with placebo.

Conclusion: The new synthetic butyrate derivate is effective in stimulating innate immunity at intestinal level in neonates. Results of our study open new therapeutic perspectives for this compound in the prevention of infectious diseases in the neonatal period. Our data support the utility of BuBull as new ingredient for infant formula.

Disclosure of Interest: None Declared
HEAT TREATMENT OF MILK REDUCES INTESTINAL FUNCTION AND RESISTANCE TO NECROTIZING ENTEROCOLITIS IN PRETERM PIGS

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Objectives and Study: In preterm infants, exclusive feeding with mother’s own milk improves intestinal health and resistance to necrotizing enterocolitis (NEC) relative to infant formula. Donor milk may be less effective because it is obtained at a relatively late stage of lactation, and pasteurization could reduce its bioactivity. We have previously shown, using a preterm pig model that fresh unpasteurized bovine colostrum may support gut function and protect against NEC. Part of this beneficial effect may be explained by lack of heat treatment. Hence, we hypothesized that freeze-dried bovine milk powder would show improved bioactivity in preterm pigs, relative to a milk powder produced by pasteurization and spray-drying of bovine milk.

Methods: Seventy-four caesarean-delivered preterm pigs were given parenteral nutrition plus minimal enteral nutrition for two days followed by two days of total enteral nutrition. In experiment 1 (Expt1), freeze-dried bovine mature milk (BM, \(n=13\)) was compared with fresh bovine colostrum (BC, \(n=14\)) and powdered infant formula (IF, \(n=13\)). In experiment 2 (Expt2), heat-treated whole milk powder (WMP, \(n=15\)) was compared with freeze-dried BM (\(n=9\)) and IF (\(n=10\)). The four diets were iso-energetic.

Results: In Expt 1, BM decreased NEC incidence and NEC severity in the small intestine relative to infant formula (\(P<0.05\)). Similar to BC, BM significantly improved gut structure (mucosal weight, villus height) and functions (barrier function, nutrient absorption, digestive enzyme activities, colon fermentation), relative to the IF group. Compared with BC, BM was less effective in increasing lactose digestion and absorption, lactase activity and decreasing colon fermentation and tissue IL-8 concentrations. In Expt 2, the processed milk (WMP) showed reduced intestinal NEC resistance, mucosal weight, lactose digestion and lactase activity, relative to BM.

Conclusion: Avoiding heat-treatment of bovine mature milk improves NEC resistance and intestinal structure and functions in preterm pigs, relative to infant formula and whole milk powder. The effects were in most cases similar to those of fresh bovine colostrum although differences were observed with some parameters. Processing of bovine milk (e.g. pasteurization, spray-drying) may significantly reduce the milk bioactivity and this could be particularly detrimental for sensitive newborns, such as preterm infants. Based on these results, we suggest that future efforts should be focused on optimizing thermal treatments of milk to retain beneficial effects.

Objectives and Study: To determine whether increased individual dietary intervention given by pediatric dietitian may impact on growth parameters in preterm infants with birth weight between 1500 and 2000 g at term and at four months corrected age.

Methods: Thirtythree preterm infants with a birth weight (BW) between 1500 and 2000g were randomized to an intervention by enhanced dietary intervention or a control group following the routine nutrition protocol in our neonatal intensive care unit. The intervention includes follow-up by pediatric dieticians who individualize the dietary regimen according to the study protocol. The main difference between intervention and control groups was earlier and higher intake of protein and energy during hospital stay and individual fortification in order to obtain optimal weight gain. When infants in the intervention group were discharged from hospital, they continued the ongoing dietary intervention until four months corrected age, whereas the infants in the control group followed the departments’ standard nutrition program.

Results: The preliminary results showed no differences regarding day of lowest weight (4.2 days vs 3.9, intervention vs control) and percentage weight loss (6.5 vs 6.7) after birth. At term (40 weeks gestational age, GA) there were significant differences in mean (SD) weight (3568 g (311) vs. 2993 g (354)) (p<0.001) and in length (50.5 cm (1.5) vs. 49.2 cm (1.6)) (p<0.05) between the two groups and no significant difference in head circumference. At four months corrected age significant differences were found between the intervention (7042 g (776), 63.7 (2.3) and 42.2 (1.1)) and control (6219 g (810), 62.0 (2.1) and 41.1 (1.4), respectively for weight (p<0.01), length (p<0.05) and head circumference (p<0.05)).

Conclusion: Infants with birth weight between 1500 and 2000 g improve growth when given individualized dietary follow up by a dietitian and nutritional support aiming to reach the in utero growth rates for weight, length and head circumference.

Disclosure of Interest: None Declared
DOES HIGH ENERGY INTAKE REDUCE THE RISK OF GROWTH RESTRICTION AT DISCHARGE IN VERY LOW BIRTH WEIGHT INFANTS?

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Objectives and Study: Extravuterine growth restriction/retardation (EUGR) in very low birth weight (VLBW) infants indicates that the nutrients requirements have not been adequately met intrauterine growth. On the other hand, too much energy may potentially increase the risk of congenital heart disease later in life. The aim is to compare the incidence of EUGR in VLBW infants according to different energy intake of Chinese nutritional guideline.

Methods: We retrospectively studied 252 VLBW infants (130 boys and 122 girls) from Shanghai Children's Medical Center in Shanghai from January 1, 2001 to December 31, 2010. Growth restriction was defined according to weight or head circumference (HC) ≤10th percentile of the growth value expected based on estimated postmenstrual age. When admission, these infants were grouped small gestation age (SGA) and appropriate gestation age (AGA). At discharge, they were divided into 2 groups: “high energy intake” (median energy intake of PN >70Kal/kg/d) and “low energy intake” (median energy intake of PN ≤70Kal/kg/d).

Results: VLBW infants with SGA had a significantly higher rate of EUGR compared with VLBW infants with AGA (82.5% vs 59.4% by weight, 75.8% vs 35.1% by HC). Between “high energy intake” and “low energy intake”, there is no significance for SGA, but the same finding for EUGR. Higher incidence of EUGR was not associated with lower energy intake. According to logistic regression, 3 factors were related to EUGR by weight: gestational age at discharge, birth weight and length of hospital stay; the following 3 factors were related to EUGR by HC: time to regain birth weight, HC at birth, weight at discharge. In this study, during the first 28 days, there were the same trend of the growth curve between boys and girls, and the same between SGA and AGA.

Conclusion: High energy intake cannot reduce the risk of growth restriction at discharge in very low birth weight infants according to Chinese nutritional guideline. It is crucial to determine the optimal energy intake for VLBW infants.

Disclosure of Interest: None Declared
Objectives and Study: Temporal changes leading to moderate or severe acute malnutrition in infants is poorly understood although it remains a tremendous problem in many developing countries. Our objective was to develop a prospective study of nutritional depletion using a pig model. We specifically aimed to describe changes in growth parameters and blood profile measurements as well as end stage markers of function and structure of the gut and liver.

Methods: Four-week old pigs were weaned from their mothers and given ad libitum access to either pure maize flour (maize, n=12) or a nutritionally optimized diet (reference, n=12). Weekly blood samples and growth parameters including body weight (BW), crown-rump length (CRL), thoracic circumference (TC) and length of the metatarsus (LM) were collected. Blood was sampled weekly for haematology and biochemical profiling. After 7 weeks, pigs were euthanized and intestinal and hepatic morphology, brush border enzyme activity and triglyceride content of the liver were measured.

Results: Relative to reference group, body weight of maize-fed pigs was reduced from 2 weeks onwards with final bodyweights of 8.2 kg vs. 29.7 kg at 7 weeks (P<0.001). Similar patterns were seen for CRL, TC and LM. Blood alanine aminotransferase (ALAT) and bilirubin levels were increased in maize pigs from week 3 and 1, respectively (P<0.001), while albumin levels were reduced from week 1 (P<0.05) and dropping to 20 g/L in week 7 (P<0.001). After 4 weeks haemoglobin concentration, mean cell volume and hematocrit were reduced in the maize pigs (P<0.01) with increasing clinical signs of anemia throughout the study period. There was lower villous height and crypt depth in maize-fed pigs (P<0.001) and lower brush border activity of lactase and aminopeptidase A (P<0.05). Activity of sucrase, maltase, aminopeptidase N and dipeptidylpeptidase IV were not affected. Liver triglyceride content tended to be higher in maize pigs (P=0.05) and was associated with histopathological changes in hepatic tissue.

Conclusion: Feeding pure maize for 7 weeks induces severe stunting and mild to moderate wasting. Changes in levels of blood cells, ALAT, bilirubin and albumin were evident from an early stage. Malnutrition induces gut atrophy but largely maintains mucosal function in terms of digestive enzyme activity. Hepatic fat infiltration and increasing levels of ALAT, bilirubin and decreased levels of albumin suggest progression of liver disease which is commonly seen in children with severe acute malnutrition. This model provides information about changes during the course of malnutrition, which is helpful to device refeeding strategies to restore normal physiological function after malnutrition.

Disclosure of Interest: None Declared
FINDING THE CSID PATIENT: A POTENTIAL NEW DIAGNOSTIC PARADIGM BASED ON GENETICS AND FUNCTIONAL BREATH TESTING

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Objectives and Study: Congenital sucrase isomaltase deficiency (CSID) is a rare genetic disorder that results in chronic diarrhea and abdominal pain due to a lack of sufficient sucrase enzyme needed to digest dietary sucrose. The “gold standard” for diagnosing CSID is a disaccharidase assay via small bowel biopsy, which requires a costly and invasive procedure. Due to the variance in clinical practice and symptomatology similar to other gastrointestinal disorders, less invasive screening diagnostics are needed for CSID.

Methods: Relevant published, unpublished, and retrospective data were aggregated to develop two methods in identifying and diagnosing a new CSID patient. It was desired for the first method to be a genetic test to evaluate the sucrase-isomaltase (SI) gene for variants and the second needed to verify that the genetic variants resulted in functional sucrase deficiency.

Results: The SI gene was sequenced in 33 previously diagnosed CSID patients and suspected pathogenic variants were identified. Intracellular research confirmed some of the suspected pathogenic variants to cause ineffective delivery of the protein sucrase-isomaltase outside of the cell needed for activity in the lumen. As a result, a list of 37 common CSID genetic variants was developed and collectively, these variants have an allele prevalence of 1.2% of sequenced European Americans in the Exome Variant Server. Also, 80% of these CSID patients were found to be variant homozygous or compound heterozygous while the rest of the patients were true heterozygotes. These results suggested that the prevalence of CSID may be greater than previously estimated and that CSID may also be an autosomal dominant disorder. A sucrose hydrogen breath test is useful for showing functional sucrase deficiency, but is less accurate. Instead, a new $^{13}$C-sucrose breath test was chosen as the second method that measures sucrase activity from the oxidation ratio of ingested sucrose relative to glucose over a 3-hour timeframe. Genetic testing in combination with the $^{13}$C-sucrose breath test warrants further investigation as a new, noninvasive, diagnostic paradigm to identify a CSID patient.

Conclusion: Findings demonstrate the need for a prospective study in children to assess the prevalence of the identified 37 common CSID genetic variants in children experiencing chronic diarrhea or chronic abdominal pain. Children who have one or more of the 37 common CSID genetic variants could also be tested for functional sucrase deficiency via a new $^{13}$C-sucrose breath test. From this work, clinicians may be able to use genetic testing and/or the $^{13}$C-sucrose breath test in the future as a screening tool to identify new CSID patients.

Disclosure of Interest: S. Chong: None Declared, H. Elser Employee of: QOL Medical, LLC
FEEDING AND GROWTH ASSESSMENT IN INFANTS WITH CONGENITAL HEART DISEASE USING A NEW COMPOSITE SCORING SYSTEM
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Objectives and Study: Children with congenital heart disease may suffer with feeding problems and fail to thrive. This can adversely affect the underlying cardiac condition and timings of any interventional treatments. The aims of this study are:

Methods: Children (< 1 yr of age) with a confirmed diagnosis of congenital heart disease, admitted to the paediatric cardiology wards were prospectively recruited to the study. Following cardiac and GI clinical assessments all had a 2D echo and Doppler assessment. Anatomical complexity was defined using the 32nd Bethesda classification. The validated Southampton Congenital heart disease severity scoring system was modified for paediatric use (PCHDIS– Paediatric Congenital Heart Disease Index Southampton). PCHDIS scores, HR index & RR Indices were correlated with GI symptoms.

Results: Over the course of 2 years, 60 infants were enrolled in the study (Median age = 0.08 yrs, 65% males). More than 60% of the children had severe heart disease (eg; hypoplastic left heart) with 38.3% having had previous cardiac surgery. Infants had a median respiratory rate of 44 (IQR 37-55); nearly 60% with oxygen saturations < 93. Low saturations were significantly related to severity/complexity of heart disease (p=0.0) and LV change (p=0.03).
66.7% had one or more GI problems of NGT feeding, low weight percentile and gastro-oesophageal reflux. A high proportion of children (45%) were NG fed with 15% reported to have GOR. The median weight at recruitment was z=-0.2 (Height z=+0.17) with no significant loss compared to the birth weight (WR, p=0.7). Infants passed up to 7 stools a day (5%) with 35% having one stool a day (Median = 1 stool a day).
Low albumin levels were significantly related to complex/severe heart disease (p=0.002), however severe heart disease wasn’t predictive of GI symptoms like GOR, frequent stools, need for NGT feeding, low birth weight or low weight at admission
The RR Index correlated significantly with weight on admission, body surface area, serum Albumin (<0.01) and number of Stools per day (p=0.04) whereas HR Index didn’t correlate with number of stools per day.

Conclusion: PCHDIS and HR and RR indices are effective tools for use in paediatric cardiac studies and day to day clinical practice. We conclude and recommend that medical management particularly the gastrointestinal needs, should be tailored to each individual child rather than assumed on the basis of severity of heart disease.

Disclosure of Interest: None Declared
DIETARY N-3 POLYUNSATURATED FATTY ACIDS AFFECT COGNITION, MOTOR SKILLS, AND HIPPOCAMPAL NEUROGENESIS IN DEVELOPING MICE


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Objectives and Study: Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are critical nutrients that play important roles in development of brain and visual functions. The n-3 long-chain PUFA docosahexaenoic acid (DHA) is especially important during the last trimester of pregnancy and the early postnatal period where it rapidly increases in the brain and eyes. The objective for this study was to assess the impact of dietary n-3 PUFAs during development on cognition, motor functions, brain metabolism, and hippocampal neurogenesis in mice.

Methods: On day 0 of gestation, 4-month-old female C57BL/6J mice were fed either n-3 PUFA deficient or n-3 PUFA adequate diets. After weaning, the male pups remained on diets and were tested at postnatal day (PND) 30 and 60. Sensorimotor integration was assessed using rotarod and pre-pulse inhibition. The Morris water maze (MWM) was used to examine spatial learning and memory on PND 60. Brain metabolism was determined by phosphorus magnetic resonance spectroscopy ($^{31}$P MRS) prior to collection of brains for biochemical and immunohistochemistry (IHC) analyses to measure fatty acid content, neurogenesis and synaptic connections.

Results: At PND 30, the adequate group performed better than the deficient group (p ≤ 0.01) in accelerated motor performance trials. In the pre-pulse inhibition test at PND 60, both groups showed a habituation effect for the startle pulses (p ≤ 0.01) but the adequate group showed a lower startle reaction to the pulses than the deficient group (p ≤ 0.05). There were no differences between the groups during acquisition of the MWM at PD60; however, the adequate group showed memory for the platform location. $^{31}$P MRS analysis revealed no differences in phosphocreatine, ATP, phospho-mono/di esters or inorganic P between the diet groups. IHC of the hippocampus demonstrated significantly fewer doublecortin positive neurons in the adequate group, suggestive of accelerated neural development. There was no difference in the postsynaptic marker PSD-95 between the groups.

Conclusion: Dietary n-3 PUFAs improve both cerebellar (PND 30) and cortical (PND 60) functioning. The behavioral effects did not seem related to markers of brain metabolism, but rather to accelerated maturation of the hippocampus. These data further strengthen the importance of dietary n-3 PUFAs for brain development and function.

VITAMIN D STATUS DURING PREGNANCY AND ADIPOSIITY IN WOMEN AND THEIR NEONATES

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Objectives and Study: Low vitamin D (25(OH)D) status has been linked to adiposity because (25(OH)D) and its metabolites are fat soluble, which leads to greater sequestration in more adipose tissue (1). However little is known of the effects of low 25(OH)D status in pregnancy on neonate body composition. The objective was to determine 25(OH)D status of pregnant women and how it affects body fat percentage (BFP; %) of the mother and neonate.

Methods: 128 healthy, (mean (SD)) 30.6 (4.2) years old pregnant women and their singleton neonates were included in study performed from May 2011 to June 2012. In the 32nd (3) week of pregnancy, serum was collected and frozen at -20 °C until 25(OH)D was measured by liquid chromatography-tandem mass spectrometry. 25(OH)D was season-standardized (46° N latitude) based on the equation: 25(OH)D = baseline + amplitude × sine (angular frequency × day of year + phase shift) (1) and compared to existing recommendations (2). Body height, body mass and three skinfold thicknesses were measured in the 32nd (3) week of pregnancy and one month after delivery. The same measurements were obtained from neonates at birth and one month after birth. Body mass index (BMI; kg/m^2) and BFP (from skinfolds) were calculated for women and their neonates. Data were analysed by t-test. The study was approved by the Slovenian Ethics Committee and is part of a project entitled “My-Milk” (www.moje-mleko.si; registered at ClinicalTrials.gov as NCT01548313).

Results: The serum 25(OH)D concentration of pregnant women was 29.9 (10.4) μg/l. 109 women (85%) had recommended 25(OH)D serum concentrations (20-70 μg/l), 15 (12%) had 25(OH)D insufficiency (10-20 μg/l) and 4 (3%) had 25(OH)D deficiency (<10 μg/l). In women with low 25(OH)D serum concentrations trend in higher body mass during pregnancy (p=0.115) was noted, but no other effects on their body composition was found. The neonates from women with high 25(OH)D serum concentrations have higher BMI at birth (p=0.041) and tend to have higher birth mass (p=0.0786), and higher BFP (p=0.0973) at age of one month.

Conclusion: The majority of pregnant women (85%) had recommended 25(OH)D serum concentration. These women tended to have lower body mass, but their neonates had higher BMI at birth and tended to be more adipose one month after birth.

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Disclosure of Interest: None Declared
SPECIFIC FERMENTATION OF INFANT MILK FORMULA INCREASES ITS PROTEASE INHIBITION CAPACITY
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Objectives and Study: Human milk contains functional proteins such as b-casein, cystatins, α1-anti-trypsin, and α1-anti-chymotrypsin, which are protease inhibitors. Protease inhibitors are pivotal in intestinal health by protecting the gut against digestive and bacteria-induced tissue proteases as these proteases can induce intestinal injury. Additionally, specific protease inhibitors improve gastric survival of functional whey proteins that could stimulate intestinal growth and development, and immunity. Interestingly, fermentation of milk proteins has been reported to generate bioactive peptides with, for example, immunomodulatory properties that promote human health. Furthermore, an infant milk formula (IMF) fermented by Streptococcus thermophilus 065 (ST065) and Bifidobacterium breve C50 (BbC50) (Lactofidus™), has previously been reported to improve gut comfort in infants with minor digestive problems. In this context, we aimed to investigate the protease inhibition capacity of the fermented IMF in comparison with unfermented IMF.

Methods: To determine the digestive protease inhibition capacity of both IMFs, the caseinolytic activity of pancreatin (a mixture of digestive proteases) was analyzed in the presence of fermented or unfermented IMF. A similar approach was used to analyze the capacity to inhibit bacteria-induced tissue proteases of both IMFs, by using papain and a chemical substrate. Results are given as Mean ± SD.

Results: The fermented IMF significantly decreased the total protease activity (caseinolytic activity of pancreatin) compared to the unfermented IMF (28.9% ± 2.65 vs 45.0% ± 2.51, p<0.05). Moreover, the fermented IMF also significantly inhibited the papain activity compared with the unfermented IMF (3.40% ± 0.90 vs 16.37% ± 1.69, p<0.01).

Conclusion: Fermentation of IMF by ST065 and BbC50 significantly increases its protease inhibition capacities. This may protect the gut against protease activity and contribute to the intestinal health of infants.

**Effect of Bovine Colostrum on Adaptation after Intestinal Resection in Newborn Pigs and Human Infants**

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**Objectives and Study:** Minimal enteral nutrition may stimulate gut adaptation following intestinal resection, whether this depends on the nature of enteral diet is unknown. Bovine colostrum contains trophic and immuno-modulatory factors and may stimulate adaptation better than a standard formula. We hypothesized that minimal enteral nutrition could stimulate intestinal adaptation in neonates, and that bovine colostrum was superior to a milk-formula.

**Methods:** Experiment 1: Three-1 d-old piglets subjected to resection of 50% of the intestine were given total parenteral nutrition (CONTROL, n=9) or parenteral nutrition supplemented with minimal enteral feeding of bovine colostrum (COL, n=5) or formula (FORM, n=6) for 7 days. Effects were assessed by a 24-hour nutrient balance study as well as intestinal histological and functional endpoints. Experiment 2: Feasibility of using bovine colostrum for humans was assessed by randomizing newborn infants subjected to intestinal resection to receive colostrum (n=5) or not (n=5) as minimal enteral nutrition. Clinical symptoms and biomarkers of allergy were collected.

**Results:** In experiment 1 relative wet weight absorption was higher in COL versus CONTROL pigs (52.5 ± 5.80% and 22.7 ± 6.80 %, p < 0.05). Relative Na⁺ absorption was higher in COL and FORM versus CONTROL (-447 ± 65%, -655 ± 76% versus -916 ± 82%, p< 0.05).

In experiment 2, colostrum was well tolerated and did not induce allergy in infants.

**Conclusion:** Minimal enteral nutrition improved gut adaptation with limited effects of type of diet. Bovine colostrum was well-tolerated in newborn piglets and infants after intestinal resection.

**Disclosure of Interest:** None Declared
OBJECTIVES AND STUDY: To compare the main metabolic pathways of long chain polyunsaturated fatty acids (LC PUFA) - intensity of lipid peroxidation (LPO), antioxidant activity (AOA) and spectrum of fatty acids - in blood of preterm infants fed formula enriched in LC PUFA and infants who received non-enriched formula.

METHODS: 37 premature infants with a birth weight of 1750-2720 g, gestational age of 33-37 weeks were observed in Moscow children’s hospital № 8 comparatively with 50 healthy full-term children. Premature infants were divided into two groups: I group received within 16-17 days the formula enriched accordingly to ESPGHAN recommendations by arachidonic and docosahexaenoic acids (DHA), II group received similar formula non enriched with LC PUFA. General clinical assessment of children performed daily, the level of malondialdehyde (MDA) by reaction with thiobarbituric acid, AOA by the method of LPO suppression in the egg yolk lipoproteins and spectrum of fatty acids by gas liquid chromatography in the cord blood and in 14 days - in the venous blood.

RESULTS: The reduction in the level of MDA and AOA (46% and 58%, respectively, p <0.05), the amount of ω-6, particularly arachidonic acid (p<0,05), ω-3 LC PUFA - DHA and docosapentaeenoic acid and accumulation of eicosapentaeenoic acid (EPA) ω-3 (p<0,05) was shown in the blood of premature infants compared to full-term infants. Feeding children in the I group by a formula with LC PUFA partially normalized the spectrum of fatty acids: the level of ω-6 linoleic acid significantly increased and the accumulation of EPA was reduced. While LPO tended to normalize, AOA remained reduced. Feeding children in the II group led to a further reduction of the arachidonic acid level and accumulation of EPA in the blood. The levels of MDA and AOA continued to decline.

CONCLUSION: The reduction of blood LPO and AOA level and the phenomenon of accumulation of EPA at reduction of blood ω-6 fatty acids level in the premature infants was shown. Feeding premature infants for 14 days by a formula enriched with LC PUFA can partially normalize the spectrum of fatty acids and LPO level, which may contribute to the normalization of defense mechanisms and processes of premature babies normal development but does not fully restore the level of LC PUFA, especially ω-3, which could be linked to low levels of antioxidant activity of blood.

DISCLOSURE OF INTEREST: None Declared
PREMATURITY REDUCES FUNCTIONAL ADAPTATION TO INTESTINAL RESECTION IN PIGLETS
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Objectives and Study: Necrotizing enterocolitis and congenital gastrointestinal disorders in infants often require intestinal resection, with subsequent risk of short bowel syndrome (SBS), especially with a dysfunctional colon. Intestinal adaptation is an important prognostic factor and we hypothesized that adaptation to resection is diminished in preterm versus term neonates. To test the hypothesis, we studied adaptation in a novel model of SBS using preterm and term piglets with a jejunostomy.

Methods: Term or preterm two-day-old piglets were subjected to 50% distal intestinal resection with placement of a jejunostomy. For 4-5 days, resected piglets were given parenteral nutrition with gradually increasing doses of enteral nutrition. Samples of intestine were collected at birth, 2 and 6-7 days to measure structural parameters and digestive enzyme activity.

Results: Preterm and term piglets showed similar increase from birth to 2 days in intestinal weight and digestive enzyme activities (sucrase, maltase, and peptidases). At 6-7 days, the remnant intestine had a similar density (g/cm) and mucosal mass in both groups. Villous height, crypt depth, enzyme activities (sucrase, maltase, DPPIV) and hexose uptake capacity were greater in term versus preterm pigs (all P<0.05). Clinically, preterm piglets were more vulnerable to resection in terms of hypoglycemia, respiratory distress, dehydration and circulatory instability. Consequently, more preterm than term pigs were euthanized prior to the end of the protocol (8/14 vs. 2/10, P=0.13).

Conclusion: Studies on intestinal adaptation after resection in neonates is feasible using preterm and term piglets, but extensive clinical care is required, especially for resected preterm pigs. Physiological instability and developmental immaturity may explain that intestinal functional adaptation after resection is less pronounced in preterm versus term neonates.

Disclosure of Interest: None Declared
BREAST MILK MACRONUTRIENTS AND INFANCY GROWTH

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Objectives and Study: The suggested benefits of human breast milk (HM) intake on later obesity and metabolic risks may relate to slower weight gain of breast-fed infants through lower total calorie intake or specific HM nutritional content. Previous studies of HM macronutrients are small, and few have addressed growth outcomes.

Methods: The Cambridge Baby Growth Study (CBGS 2000-2010) is a prospective birth cohort with detailed infant anthropometry from birth to 2 years [weight, length and skinfold thicknesses (adiposity), expressed as standard deviation scores (SDS)]. Data are available on antenatal, postnatal exposures and uniquely over 600 mothers collected hindmilk at 4-8 weeks postnatally, pooled over 2-4 weeks.

Triglyceride (fat) and lactose (carbohydrate) concentrations were measured in homogenised HM samples using 1H-NMR spectra. Protein was measured by precipitation and freeze drying. Total calorie (TC) content was calculated using Atwater conversions and %macronutrients (of TC) determined. Relationships between TC and %macronutrient contents, and growth in term infants were investigated.

Results: In 613 HM samples, fat content (mean±SD) was: 2.7±1.5g/100mls, carbohydrate:8.4±0.7g/100mls, protein:1.9±0.4g/100mls. TC content was 66.0±14.4kcal/100mls. HM of mothers exclusively breast-feeding vs. mixed feeding was more calorific (68.0±14.7 vs. 62.9±13.4kcal/100mls, p<0.0005), with greater %fat; less %carbohydrate and less %protein. TC and %macronutrient contents were unrelated to maternal BMI, social deprivation score, gestational age, or infant sex.

Subsequent analyses were adjusted for nutrition type (exclusive breast-fed vs. mixed), sex and birth weight SDS. TC content was inversely related to 12 month adiposity (p=0.01), and 3-12 month adiposity gain (p=0.03). HM %fat was inversely related to infant 3-12 month weight gain and adiposity gain, whereas %carbohydrate was positively related to weight gain and adiposity gain, and %protein was unrelated to growth (table 1). There were no associations with height gain.

Table 1: Associations between HM %macronutrients and infancy growth, adjusted for nutrition type, infant sex & birthweight SDS

<table>
<thead>
<tr>
<th>% of TC content</th>
<th>%Fat</th>
<th>%Carbohydrate</th>
<th>%Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>12m weight</td>
<td>P=0.2</td>
<td>P=0.2</td>
<td>P=0.9</td>
</tr>
<tr>
<td>3-12m weight gain</td>
<td>-ve, p=0.04</td>
<td>+ve, p=0.02</td>
<td>P=0.8</td>
</tr>
<tr>
<td>12m SF</td>
<td>-ve, p=0.003</td>
<td>+ve, p=0.001</td>
<td>P=1.0</td>
</tr>
</tbody>
</table>
Conclusion: In HM samples from a large UK cohort, we show that TC content is greater in HM from mothers exclusively breast-feeding. Independently, HM %fat was inversely related to later infant adiposity, whilst %carbohydrate was positively related to later adiposity. These findings may help to understand mechanisms underlying the benefits of HM.

COMPARISON OF TWO EXTENSIVELY HYDROLYSED FORMULAS


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Objectives and Study: According to guidelines, the recommended treatment of cow’s milk protein allergy (CMPA) is a strict elimination diet with an extensive (cow’s milk based) hydrolysate. Whether the best option is a whey or a casein hydrolysate is a matter of debate. Therefore, we compared the efficacy of an extensive whey to that of an extensive casein hydrolysate both enriched with (different) probiotic strains, in a double-blind, randomized, trial.

Methods: Efficacy was assessed with the help of a novel clinical score. The score encompasses crying, regurgitation, stool consistency, atopic eczema, urticaria and respiratory symptoms. The score ranges from 0 to 33. The primary hypothesis of the trial was to show non-inferiority between the whey and casein hydrolysate in means of the score. The inclusion criterion of the trial was a clinical suspicion of CMPA because of a score > 12. Specific and total IgE and skin prick test were performed at baseline. The composition of the gastrointestinal flora was analysed at baseline and after one month.

Results: 116 infants with a clinical score of > 12 were included. There was a statistical and clinical significant decrease of the score during the first month: -8.32 in the whey and -7.82 in the casein hydrolysate group. The treatment difference at one month was -0.879 (95% CI -2.79, 1.03) and is below the predefined non-inferiority margin of +3, confirming that the whey hydrolysate is non-inferior to the casein hydrolysate. An open challenge was performed in 85 (74%) infants and was positive in 59/85 (69%); there were less late reactions in the whey (8/41 (20%)) than in the casein hydrolysate group (18/44 (41%), p = 0.037). No significant differences were found between both groups for total and specific IgE, and for the skin prick tests. No significant differences were found in the items composing the score: crying, regurgitation, stool consistency, atopic eczema, urticaria, respiratory symptoms. The whey hydrolysate, which was enriched with bifidobacteria, did lead to more bifidobacteria, enterobacteria and total bacteria but to less lactobacilli. The casein hydrolysate, which was enriched with lactobacilli, resulted in higher lactobacilli levels. The whey hydrolysate leads to better growth (weight and weight for age z-scores); the casein hydrolysate leads to smaller head circumferences.

Conclusion: In daily practice, the clinical score of ≥12 is a useful tool to select infants with a high risk of IgE and non-IgE mediated CMPA. The extensive whey and casein hydrolysates are equally effective in the treatment of CMPA.

NUTRITION
NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

PO-N-0255

BIFIDOGENIC EFFECT OF A STARTER FORMULA CONTAINING BOVINE MILK OLIGOSACCHARIDES AND THE BIFIDOBACTERIUM LACTIS PROBIOTIC

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Objectives and Study: The gut microbiota composition of formula-fed and breast-fed (BF) infants differs. Strategies to promote an intestinal microbiota similar to the one found in BF infants include the addition of probiotics and/or prebiotics to infant formula (IF). The objective of this study was to evaluate whether an IF supplemented with bovine milk oligosaccharides (BMOs) in combination with *Bifidobacterium lactis* NCC2818 (CNCM I–3446, *B. lactis*) induces a microbiota equivalent to the one found in BF infants.

Methods: Seventy-six healthy full-term infants aged <14 days were randomly assigned to receive for 3 months a control IF (CTRL; n=37, starter IF with protein 1.8g/100kcal, whey/casein ratio 70/30) or an identical experimental IF with BMOs (5.7g/100 g) and *B. lactis* NCC2818 (1.10^7 cfu/g) (EXPL, n=39). Infants who were exclusively BF were studied as a reference group (n=39). The primary outcome was fecal microbiota (appraised at 1.5 and 3 months). The secondary outcomes were growth until 3 months and stool pH.

Results: Fecal lactobacilli levels were equivalent in the EXPL and BF groups [absolute difference of 0.0163 log_{10}(cfu/g), p<0.0001, margin of 1 log_{10}(cfu/g)] and higher than CTRL. Higher levels of bifidobacteria were observed in the EXPL compared to CTRL [10.84±0.26 versus 10.03±0.92 log_{10}(cfu/g) and 10.23±0.9 for BF group]. *B. bifidum* levels were equivalent in the EXPL and BF groups [difference of 0.0595 log_{10}(cfu/g), p=0.019, margin of 0.5 log_{10}(cfu/g)]. In the EXPL, *B. lactis* was detected in 75.0 and 57.1% of infants at 1.5 and 3 months, respectively, compared with 0% and 7.7%, respectively, in the CTRL. All anthropometric parameters (weight gain, length and head circumference) did not differ between groups from inclusion until 3 months. At 6 weeks, the incidence of hard stools was higher in the CTRL compared to the EXPL (Odds ratio 7.22; 98.34%CI; (1.16; 45.04), p=0.01). Stool pH was lower in the EXPL compared to the CTRL (6.03±0.9 vs 6.55±0.84, p=0.06) and closer to that of BF infants (5.37±0.53).

Conclusion: In infants fed an IF supplemented with the synbiotic (BMOs + *B. lactis*), stool pH was closer to that of BF infants, and levels of bifidobacteria and lactobacilli were increased. Weight gain and all anthropometric measurements were similar in the three groups.

THE DEGREE OF MEET OF THE INFANT’S NEEDS IN PROTEIN, CALCIUM, MAGNESIUM, ZINC AND IRON DURING EXCLUSIVE BREASTFEEDING.

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Objectives and Study: Breastfeeding is optimal food for all babies in conditions of mother’s adequate health and nutrition status. WHO recommends exclusive breastfeeding up to 6 months of age. To determine the degree of the infant’s requirements in protein, calcium, magnesium, zinc and iron during exclusive breastfeeding we assessed the levels of protein, Ca, Mg, Zn, and Fe in 186 milk samples from 74 mothers. Human milk samples were collected from health mothers in 1 and 6 months of lactation. All samples were stored in a freezer at -80°C. We use the following WHO’s recommendation concerning dietary intakes for 6 month’s breast fed infants: in protein – 12,7 g/day (2,1 g/kg/day), in Ca – 300 mg/day, in Mg - 26 mg/day, in Zn – 1,1 mg/day, in Fe – 4,3 mg/day (taking into account the high biological availability of these nutrients from human milk).

Methods: Analysis of the protein was based on the Kjeldahl method. Protein content were calculated from total nitrogen x 6,38. Ca and Mg were analyzed by complexonometric method. Zn, and Fe content was assessed by atomic-absorbtive method.

Results: The level of protein in 1 month of lactation was 13,7±1,9 g/L. Protein level in 6 months was 11,2±2,4 g/L. (p<0,05). The Ca, Mg, Zn, and Fe average concentrations found in 1 month of lactation were: 275,7±77,7 mg/L, 34,1±7,3 mg/L, 1,8±0,3 mg/L, 1,1±0,5 mg/L. For the milk samples taken in the 6 months of lactation the results were: 266,5±54,1 mg/L, 33,5±5,2 mg/L, 1,7±0,3 mg/L, 0,9±0,3 mg/L respectively. Taking into account the physiological needs of the infant in the estimated nutrients we calculate, that human milk practically completely meets the needs of the infant in the protein, calcium, magnesium and zinc in the age of 6 months. At the same time the infant's needs in the iron in that period are met only on 20%.

Conclusion: Exclusive breastfeeding does not meet the infant’s needs in the iron at the age of 6 months, which is an increased risk of iron deficiency anemia in the future. For the prevention of this condition infants should begin introduction of complementary foods before 6 months.

Disclosure of Interest: None Declared
ENERGY AND MACRONUTRIENTS IN BREAST MILK FROM MOTHERS OF EXTREMELY PREMATURE INFANTS.
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Objectives and Study: Breast milk (BM) is the preferred basis of nutrition for infants, including those born prematurely. To meet nutritional requirements for extremely preterm infants, it is necessary to add human milk fortifier (HMF) to BM. Information about energy and protein contents of BM is therefore desirable to avoid risk of undernutrition or overnutrition of the preterm infant. However, data of nutrient composition in BM from mothers of extremely preterm infants are scarce. The aim of this study was to describe the composition of energy and macronutrients over time in BM from mothers who delivered extremely preterm infants.

Methods: Information of analysed BM samples from Swedish mothers giving birth prematurely before 27 weeks of gestation during 2004-2007 was obtained from hospital records. All analyses of energy density and macronutrient content of BM were performed using infrared analysis (MilkoScan 4000). BM samples were divided into two groups, early BM (0-28 postpartum days) and mature BM (29-119 postpartum days). Mean and standard deviation (SD) were used to describe the nutrient content in the mother’s milk and Paired Samples T-test was used in statistical analysis between early and mature BM.

Results: In total, 820 BM samples from 252 mothers were analysed (Table 1). Fat content showed the highest variability between mothers (10th-90th percentile; 2.9 - 5.0 g/100 mL), which was also reflected in variable energy content (10th-90th percentile; 61-85 kcal/100 mL). Protein content (10th-90th percentile; 1.2-2.4 g/100 mL) decreased significantly over time (p<0.001), reaching its lowest level after 28 days post partum.

Table 1. Energy and macronutrient contents over time in BM samples from mothers of extremely premature infants in Sweden.

<table>
<thead>
<tr>
<th>Content per 100 mL BM</th>
<th>Early BM Postpartum Days</th>
<th>Mature BM Postpartum Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>73±10</td>
<td>73±9.0</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>2.1± 0.4</td>
<td>1.7±0.4</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>3.9±1.0</td>
<td>4.0±0.8</td>
</tr>
<tr>
<td>Lactose (g)</td>
<td>6.6±0.4</td>
<td>6.9±0.3</td>
</tr>
</tbody>
</table>

Mean±SD
**Conclusion:** Our study provides information of energy and macronutrient contents in early and mature BM from mothers of extremely preterm infants. BM fat and energy content was highly variable between mothers and protein content decreased significantly during the first 28 days post partum. Weekly analyses of BM macronutrient content during the first 28 postpartum days of BM would therefore allow a more individualized nutritional support to this vulnerable group of infants.

**Disclosure of Interest:** None Declared
IRON STATUS IN BREAST-FED INFANTS DEPENDING ON TIME OF SOLID FOOD INTRODUCTION
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Objectives and Study: There are different recommendations on the time of weaning in infancy. WHO recommends an exclusive breast feeding till 6 months of age. However the question of iron status of breast-fed infants at 6 months of life is still unclear. The goal of this research was the evaluation of iron status of infants depending on time of weaning food introduction

Methods: Methods. 103 healthy term infants were under our observation, among then 62 were breast-fed (BF), 41 - formula fed (FF). In breast In BF infants solid food was started at 4, 5 or 6 months. FF infants started solid food at 4 or 5 months. Before weaning and at 6 months analysis of capillary blood has been performed with Hematoanalyser Sysmex XT-2000i, and Archetect1000i.

Results: Hb level before weaning did not differ between groups with median 122 g/l. However the delay of solid food introduction has been associated with a tendency to decreasing of red blood cells size and significant decrease of Hb erythrocytes level (MCH) in infants starting solid food at 6 months. MCH at 4 months in BF infants was 27,2* (26,0-28,6) pg, in FF infants** - 27,7 (27,0-28,5) pg, at 5 months MCH in BF infants was 26,6* (25,5-27,0) pg, in FF infants** - 26,5 (25,7-27,1) pg. At 6 months in BF infants - 25,9* (24,7-26,4), (* - p < 0,05, p** < 0,004).

Ferritin level at 4 months in BF infants was 150,3* (80,5-157,4) ng/ml that was significantly higher than in FF infants - 54,1 (30,4-80,5) ng/ml, that confirm important role in BF in prevention of iron deficiency. However at 5 months there was a dramatic decrease of ferritin level till 46,6* (32,6-99,0) ng/ml in BF infants, which did not differ from ferritin level in FF infants - 46,5 (32,1-76,3) ng/ml. In exclusively BF infants at 6 months was the lowest concentration of ferritin level - 27,8* (16,4-45,0) ng/ml. (** - p < 0,05).

Conclusion: This investigation has shown high iron provision in BF infants at 4 months and moderate iron status at 5 months. Significant decrease of iron indices at 6 moths indicate the depletion of iron stores in BF infants. BF infants should start solid food enriched with iron not later than 6 months of age.

Disclosure of Interest: None Declared
Objectives and Study: Mineral absorption has been reported to be more efficient from human milk compared to infant milk formula (IMF). Therefore, mineral concentrations in IMF have been increased to meet daily requirements. The minerals Calcium (Ca) and Magnesium (Mg) are of particular importance for healthy bone growth and development of infants. Adequate Ca and Mg absorption from IMF is therefore of utmost importance. In addition, Ca which is not absorbed in the small intestine is delivered to the colon. This is thought to be related to hard stools and, in this way, may cause gut discomfort. Interestingly, an IMF (Lactofidus™) fermented by Streptococcus thermophilus 065 (ST065) and Bifidobacterium breve C50 (BbC50), has previously been reported to improve gut comfort in infants with minor digestive problems. To investigate potential differences in Ca and Mg absorption, the fermented IMF and a standard non-fermented IMF were tested in a piglet model.

Methods: Three week old piglets served as a model for three month old infants. The digesta of six piglets were collected at the terminal ileum. The complete IMFs were provided for a period of two days in a Latin square design. Chromium (Cr) oxide was added as a non-absorbable marker to adjust for ileal flow. Digesta were collected for eight hours and analyzed for Cr, Ca, and Mg. Apparent mineral absorption was calculated as percentage of total dietary mineral intake. Results are given as mean ± SEM.

Results: Apparent small intestinal Ca absorption from the fermented IMF was 30 ± 1% higher compared to a standard, non-fermented IMF. The absorption of Mg from the fermented IMF was 88 ± 13% higher compared to a standard, non-fermented IMF.

Conclusion: Ca and Mg are better absorbed in the small intestine from the fermented IMF compared to the standard non-fermented IMF in a piglet model. This could be beneficial for skeletal growth and development, and may improve gut discomfort via softening of stools.

LACTASE FROM A SPECIFIC FERMENTED MILK FORMULA RETAINS ACTIVITY AFTER IN VITRO GASTRIC AND SMALL INTESTINAL DIGESTION
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Objectives and Study: Lactose constitutes a significant energy source for small infants. The digestive system of infants is, however, still developing and digestive capacity may not always be sufficient for complete digestion of macronutrients. Lactose, which is not digested by the small intestine, is fermented by colonic microbiota. This can result in bloating, intestinal cramps, and diarrhea. An infant milk formula (IMF) (Lactofidus™), fermented by \textit{Streptococcus thermophilus} 065 (ST065) and \textit{Bifidobacterium breve} C50 (BbC50), has been reported to improve gut comfort in infants with minor digestive problems. Interestingly, this fermented IMF contains natural lactase activity. This lactase activity could aid lactose digestion in the small intestine of infants and improve gut comfort. To test lactase survival during gastrointestinal digestion, the fermented IMF was tested \textit{in vitro}.

Methods: The fermented IMF, and an unfermented control IMF, were digested \textit{in vitro} using the dynamic TNO gastrointestinal model (TIM-1) that simulates gastric and small intestinal digestion. The model's conditions (gastric pH, enzyme loads) were adjusted to mimic those of infants below twelve months of age. Gastrointestinal digestion was simulated over a period of six hours by the addition of luminal gastric and pancreatic enzymes. At the end of the small intestinal compartment ileal effluent was continuously collected. Total lactase activity was measured in the IMF and in the ileal effluent. Lactase survival is expressed as percentage of dietary intake and represents the results of 3 or 4 independent experiments.

Results: As expected no lactase activity was detected in the unfermented IMF before and after digestion (n=3). After simulated gastrointestinal digestion the natural lactase activity in the fermented IMF was still $13.2 \pm 0.8\%$ at the end of the small intestine (mean ± SEM, n=4).

Conclusion: Lactase activity naturally present in the fermented IMF is very robust against digestive degradation as part of the activity survives gastric and small intestinal digestion. This proves that the lactase activity from the IMF could substantially contribute to lactose digestion throughout the entire gastrointestinal tract. Moreover, this could result in more complete lactose digestion at the end of the small intestine and, in this way, may promote gut comfort in infants with digestive problems.

NUTRITION NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

PO-N-0261

NUTRIENT INTAKE OF ITALIAN BREASTFED INFANTS IN THE FIRST 6 MONTHS OF LIFE
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Objectives and Study: Few data exist on energy and macronutrient intake in breastfed children during the first months of life. The objective of this study was to quantify human milk supply over a longitudinal period of six months and to quantify milk nutrient contents in a subsample.

Methods: 174 Italian breastfed children were followed using double weighing before and after breastfeeding and three-day food protocols from birth to age six months. Children had to be exclusively breastfeed for at least three months of life. From a sub-sample of thirty mothers breast milk samples were collected at child ages one (T1), two (T2), three (T3), and six (T6) months, and were analyzed for the contents of protein, carbohydrates, total lipids and fatty acid composition (FA). To assess dietary intake from breastmilk in those children without milk samples, energy and macronutrient intake was calculated on the basis of the median breastmilk content of the sub-sample in each month (T1, T2, T3, T6). We compared the variation of human milk content over time by Skillings-Mack test. Mean intake of human milk, energy, fat, carbohydrates and protein was determined.

Results: Of 174 breastfed children enrolled into the study 136 (78%) infants filled in at least one three-day food protocol within the first six months of life and complied with double weighing of all milk feeds. The number of evaluable food protocols declined from 127 infants at one month to 82 at six months of age. None of the measured parameters in human milk changed significantly from age one to age six months, except protein, which decreased from a mean of 1.4 g/ml (SD 0.2) to 1.0 g/ml (0.2). Energy content of breast milk ranged from 62 (13) to 68 (13) kcal/100ml. The inter-mother variation in human milk was relatively low for monosaturated fatty acids and protein. However, for the latter the variation increased during the first six months of life. The variation was large for most other parameters, especially for fat content and eicosapentaenoic and docosahexanoic acids.

Macronutrient intakes of all breastfed children were not significantly different between the BFms and the BF group at any time point. Median human milk intake decreased from 616 at T1, over 728 at T3 to 503 ml/day at T6. Average energy and protein intake per day increased from 426 (SD 105) kcal and 8.7 (2.0) g at T1, respectively, to 579 (128) kcal and 13.5 (5.9) g at T6.

Conclusion: These data provide a reference range of nutrient intakes in breastfed infants and may provide guidance for defining optimal nutrient intakes for infants that cannot be fully breastfed.

Disclosure of Interest: None Declared
PO-0262

THE POSSIBILITY OF PROLONGING OF BREASTFEEDING FOR FULL-TERM INFANTS WITH CEREBRAL ISCHEMIA.

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Objectives and Study: The maternal milk is very important for all neonates especially for infants with acute or chronic hypoxia - cerebral ischemia, who can not be fed from the mother's breast in the first days after birth because of the severity of their condition. The aim of our study was to identify the opportunities to support and prolong breastfeeding for these patients. 86 lactating women were enrolled in our study. The group №1 (the comparison group) included mothers (n = 32) of healthy infants with 9-10 points concerning Apgar score and breastfeeding in the first 30 minutes after birth. 30 mothers, delivered the infants with mild and moderate severity hypoxia (5-8 points in Apgar score), were enrolled in group №2. These infants began to feed from the mother's breast on 3-5 days after birth. The group №3 included mothers of the infants with severe hypoxia (less than 5 Apgar score) and breastfeeding on 5-15 days after birth. The period of observation and advising in all aspects of breastfeeding was 12 months.

Methods: All women were need to comply the complex of necessary recommendations included the observance of correct technique of feeding, feeding on demand (unless contraindicated), regular pumping the breast milk in rhythm feeding (with contraindications to the breastfeeding), application of various methods of stimulation of lactation.

Results: At 6 months 65.5% of infants of the 1 group, 66.6% of infants of the 2 group, and 75% of infants of the 3 group were breast-fed. By 12 months 59.4% of infants of the 1 group, 40% of infants of the 2 group, and 50% of infants of the 3 group continued to receive breast milk in any quantity. The analysis of the possible impact of different reasons for the duration of lactation showed that the main factor affecting the duration of lactation was the breast-feeding on demand and regular pumping breast milk in the rhythm of feeding (r=0.75). The second most important factor was the presence of a harmonious type of relationship between mother and baby (r = 0.66). The day of initiation of breastfeeding and the child's severity were less significant factors for the successful lactation. (r=0.48, r=0.43 respectively).

Conclusion: Thus, it was found that the organization of successful and prolonged breastfeeding for infants with cerebral ischemia is possible. The duration of breastfeeding of these patients may be approximated to that of healthy infants in the case of performing mothers all necessary recommendations to support lactation.

Disclosure of Interest: None Declared
LONG TERM NUTRITIONAL OUTCOME OF CHILDREN FED AN AMINO-ACID FORMULA.
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Objectives and Study: Cow’s milk protein allergy (CMPA) sometimes needs formulas with nitrogen based on amino-acids (AAF) at a level higher than in infant formulas. This study assessed the long term consequences of an AAF-based elimination diet on the biological and clinical parameters of CMPA children.

Methods: A telephone survey (Nov2011–Feb2012) analyzed retrospectively consecutive (2004-2010) patients diagnosed with CMPA (digestive/cutaneous/respiratory symptoms) in a food allergy reference center (Cohort Arsène, n°DC-2009-955). Children were enrolled if having adhered to dietetic recommendations, and fed with ≥500mL/day of AAF (Neocate®) or extensive whey hydrolysate-based formula (eWHF, Pepti-Junior®) for ≥6mo.

Results: From a longitudinal data set of 515 children, 131 responded to enrolment criteria, 102 fed with an AAF and 32 fed with an eWHF. AAF had been started before age of 6mo (Infant formula age, AAF1) in 41 (2.9±1.6mo, mean±SD), between 6 and 12 months (≈ Follow-on, AAF2) in 42 (7.5±1.6mo) and after 1yr (≈3rd age, AAF3) in 20 (21.7±12.9mo) and eWHF before age 6mo in 20 (3±1.09mo, eWHF1). Formula was given for 17.75±9.7mo (AAF1), 26.21±23.6 (AAF2), 15.43±10.3 (AAF3) and 19.94±12.8 (eWHF1). At survey, BMIs (percentile) were in males: 42.85±28.79 (AAF1), 42.73±29.37 (AAF2), 25.63±18.49 (AAF3), 44.17±30.07 (eWHF1); in females: 31.91±38 (AAF1), 31.54±24.95 (AAF2), 33.85±22.68 (AAF3), 64.16±26.07 (eWHF1, p0.04 vs AAF1). Ferritin / hemoglobin levels were within the normal range: in males 26.7±13.6 / 11.64±0.6 (AAF1), 30.6 ±14.1 / 11.98±0.8 (AAF2), 31.7 ± 9.8 / 12.38±0.75 (AAF3), 34.3 ±12.28 / 11.05±0.55 (eWHF1); in females 27±17 / 12.7±0.4 (AAF1), 26.5±0.5 / 12.6±0.4 (AAF2), 35±8.6/ 11.6±0.6 (AAF3), 11.36±1.8 / 35.12±30.3 (eWHF1).

Conclusion: This study suggests that the long term use of AAF (>500mL/D for more than 6 mo) results in appropriate anthropomorphic and iron status parameters.

Disclosure of Interest: D. Colson Grant / Research Support from: Nutricia Nutrition Clinique, B. Michaud: None Declared, P. Soulaines: None Declared, C. Dupont: None Declared
IMPACT OF THE BABY-FRIENDLY HOSPITAL INITIATIVE ON BREAST-FEEDING: COMPARISON OF THREE MATERNITIES

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Objectives and Study: to evaluate the impact of the baby-friendly hospital initiative (BFHI) on breast-feeding

Methods: practices at birth, rate and duration of breast-feeding, were compared in three maternities which are differently involved in the process of BFHI: labelled (A), on demand to be labelled (B), not involved (C).

Results: At birth, mothers are more frequently informed on breast-feeding in maternities A (88%) and B (86%) than in maternity C (79%) (p<0.05), and have a skin-to-skin contact for a longer time (A=120 min; B=60 min; C=5 min; p<0.001). The child stays more often close to his mother in maternities A (100%) and B (90%) than in maternity C (86%) (p<0.02). Complement bottles were less frequently offered in in maternities A (10%) and B (9%) than in maternity C (51%) (p<0.001).

Duration of breast-feeding is higher in maternities A (2.5 months) and B (2.5 months) than in maternity C (0.5 month) (p<0.01). Percentage of breast-feeding at 3 months was higher in maternities A (54%) and B (62%) than in maternity C (30%) (p=0.01). Mothers were more often satisfied with their breast-feeding practice in maternities A (75%) and B (85%) than in maternity C (52%) (p=0.01).

Factors that were associated with duration of breast-feeding were encouragement from the father, information on breast-feeding during pregnancy, contact with associations for breast-feeding, absence of complement bottle at maternity.

Conclusion: Practices at birth, rate and duration of breast-feeding are significantly improved when maternities are involved in the BFHI process. Widespread of BFHI in France is important for promotion of breast-feeding.

Disclosure of Interest: None Declared
**NUTRITION**

*NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES*

**PO-N-0265**

"EARLY ESTABLISHMENT OF GUT MICROBIOTA AND FEEDING PRACTICES IN INFANCY"

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**Objectives and Study:** The aim of this study was to investigate the influences of early feeding practices on the establishment of gut microbiota in infants.

**Methods:** Feecal samples were collected from 100 children recruited in the H2G2 birth cohort in 2008-2009. Samples were taken during the first week of life and at 4 and 12 months of age. Families were asked about feeding practices in a questionnaire during first week of life, at 4 and 12 months of age. A 3-day feeding dairy was completed by the parents at 4 and 12 months of age. Gut microbiota were sequenced with metagenomic technique.

**Results:** The influence of feeding patterns on the taxonomic composition and gene-function composition of infant gut flora at 4 months of age are both significant. The alpha diversity of babies breast-feeding at 4 months of age is significantly lower than the babies not being exclusively breast fed, indicating the diverse type of additive to formula that might incur a diversity increase in the gut microbiome. Two different species of bifidobacterium were enriched in exclusively breast fed infants and formula fed babies respectively. Formula fed infants tend to have more pathogens. Lactobacillus genus is enriched in infants being exclusively breast fed. The major species of Lactobacillus enriched in the microbiota in exclusively breast fed babies are the *Lactobacillus rhamnosus*, Lactobacillus paracasei and Lactobacillus casei. There was no significant influence of the introduction of solid food at 4 or 12 months of age on the composition of the intestinal microbiome. Complete stop breast-feeding at one year of age did significantly influence the phylogenetic composition of intestinal microbiome.

**Conclusion:** Early feeding practices have profound influences on the early establishment of gut microbiota. The introduction of solid food did not alter the composition of infant microbiota, but the stop of breast-feeding in one year old infants lead to a composition shift of infants microbiota toward a more adult-like one.

**Disclosure of Interest:** None Declared
THE EFFECT OF INULIN-TYPE FRUCTANS ON APPETITE, ENERGY INTAKE, AND BODY WEIGHT IN CHILDREN AND ADULTS: SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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Objectives and Study: Experimental studies have documented that inulin-type fructans (ITF) modulate the secretion of gastrointestinal peptides involved in appetite regulation and lipid metabolism. The aim of this review was to systematically evaluate the effects of ITF supplementation on appetite, energy intake, and body weight in children and adults.

Methods: The MEDLINE, EMBASE, and Cochrane Library databases were searched in October 2012, with no language restriction, for randomized controlled trials (RCTs) that compared the effects of supplementation with well-defined ITF with placebo or no intervention.

Results: For the pediatric population, 4 RCTs met the inclusion criteria. One RCT involving 14 infants aged 5 to 24 weeks found a similar body weight in infants fed infant formula supplemented with inulin (0.25 g/kg/d) compared with infants fed unsupplemented formula for 3 weeks [mean difference (MD) 0.1 kg/3 weeks, 95% CI -0.19 to 0.38]. One RCT conducted in term neonates (n=62) showed no effect of formula supplemented with ITF (oligofructose + inulin 0.4 g/dl and 0.8 g/dl) on body weight and energy intake after the 28-day study period (data not available). One RCT (n=56, aged 16 to 46 weeks) found no significant difference in changes in weight between children fed fructooligosaccharides (FOS)-supplemented infant cereal (0.75 g FOS per serving of cereal) or placebo for 28 days (MD 0.02 kg, 95% CI -0.1 to 0.14). One RCT involving 97 adolescents aged 9 to 13 years found a reduced increase in body weight in the ITF (oligofructose + inulin 8 g) group compared with the control (maltodextrin) group for 1 year (MD -1.3 kg, 95% CI -2.41, -0.19).

For the adult population, 13 RCTs met the inclusion criteria. Four RCTs (n=112) found no effect of ITF supplementation on appetite sensations. Eleven RCTs (n= 325) found no effect of ITF supplementation on daily energy intake or energy intake during a meal tolerance test. Among 4RCTs that assessed the effect of ITF supplementation on body weight, only one RCT (n=35) found that compared with placebo, FOS (0.14 g/kg, 120 days) significantly reduced body weight (MD -16.10 kg (95% CI -21.9 to -10.3)). In 2 RCTs, no significant differences between groups in changes in body weight were found. Of 3 RCTs that compared changes in body weight after ITF supplementation, one (n=38) showed a significant reduction in body weight after oligofructose consumption (21 g/day, 12 weeks)(MD -1.48 kg, 95% CI -1.72 to -1.24).

Conclusion: Limited data suggest that long-term administration of ITF may have an effect on weight reduction. The mechanism by which ITF influence body weight is still unclear. Further studies are warranted.

Disclosure of Interest: None Declared
EFFICACY OF PROBIOTIC TREATMENT IN PATIENTS WITH ALLERGIC CONJUNCTIVITIS
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Objectives and Study: The term 'allergic eye disease' describes a spectrum of clinical conditions, ranging from the common, milder conditions of seasonal and perennial allergic conjunctivitis (SAC, PAC), to the rare and more severe diseases, vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC). These latter two diseases can involve the cornea, leading to impaired vision. Although there is an underlying allergic mechanism, each of these ocular surface conditions involves different cellular responses and much effort has been made to identify the molecular pathways, which could be used as potential targets for therapeutic intervention. Currently available drugs, in particular for chronic forms of disease, are inadequate and there is an urgent need for safer, more localized and effective treatment. Probiotics have been shown to improve allergic inflammation. The aim of this study was to evaluate the efficacy of Lactobacillus Acidophilus eye-drops and capsules in controlling signs and symptoms of AKC.

Methods: 18 patients (mean age 4.8±2.4; 5 girls, 13 boys) with mild to moderate AKC were included in the study. Lactobacillus Acidophilus diluted in saline solution (1 x 10^7 CFU/ml) was administrated as eye-drops 4 times daily for 4 weeks in both eyes. In addition 9 patients used Lactobacillus Acidophilus capsules (1 x 10^7 CFU) twice a day. Clinical signs (conjunctival hyperemia, chemosis, secretion, Trantas dots, superficial punctuate keratitis) and symptoms (itching, photophobia, burning, tearing) were evaluated and scored from 0 to 3 at baseline, after 2 and 4 weeks of treatment. Total sign (TSI) and symptom (TSyI) indices were calculated.

Results: In the 15 patients who completed the study, symptoms were significantly improved after both 2 weeks (TSyI: baseline 7.7 ±0.6 vs 3.9±1.0; p < 0.05) and 4 weeks (TSyI: baseline 6.4 ±0.8 vs 3.2 ±1.1, p < 0.05) of treatment. A significant improvement of clinical signs was observed after 3 weeks of treatment (TSI: baseline 8.6 ±1.4 vs 3.2 ±1.4, p < 0.05) but not after 2 weeks of treatment. In particular, photophobia was significantly reduced at 2 weeks, while at 4 weeks the scores for chemosis, secretion, Trantas dots, conjunctival hyperemia and chemosis were significantly lower compared to baseline. All patients with the positive clinical effects additionally received probiotic with Lactobacillus Acidophilus per os.

Conclusion: Our study showed that 1-month treatment with probiotic eye-drops improves signs and symptoms in patients with AKC. Additional use of Lactobacillus Acidophilus per os support the positive clinical effects of topical Lactobacilli on AKC patients.

Disclosure of Interest: None Declared
THE RELATIONSHIP BETWEEN SERUM OSTEOCALCIN AND BODY COMPOSITION

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Objectives and Study: Growing evidence suggests that overweight and obesity may cause osteoporosis fracture in children and adolescents, but the exact mechanism is still not clear. Here we examined such a relationship between serum osteocalcin and body composition in obese children and adolescents.

Methods: Seventy-nine, aged 7 to 12 years, who visited the obesity clinic of our hospital were recruited for this study. Weight, fat mass (FM), body fat percentage (BF%), lean body mass (LBM), visceral fat area (VFA), free fat mass (FFM) were assessed by bioelectrical impedance analysis with InBody 720 for subjects in upright position after bladder emptying. Fat mass index (FMI), free fat mass index (FFMI) and obesity degree were calculated by application of the following formulas: FMI = FM (kg)/height (m)²; FFMI = FFM (kg)/height (m)²; Obesity degree = [(actual weight (kg) - ideal weight (kg)) × 100%]/ideal weight (kg). Serum osteocalcin level (OC) was measured in serum by ELISA.

Results: No statistical significant association was found between obesity degree and serum osteocalcin level (r = -0.29, p = 0.052), but serum osteocalcin levels were negatively correlated with BF% and VFA (r = -0.24 and -0.46 respectively, p < 0.05). There were positive correlation between LBM, FFM, FFMI and serum osteocalcin levels (r = 0.24, 0.23 and 0.31 respectively, p < 0.05). In addition, serum osteocalcin levels were significantly decreased in severe obesity (44.46 ± 9.73 μg/ml) and moderate obesity (48.72 ± 10.82 μg/ml) subjects compared to those mild obesity (55.43 ± 12.4 μg/ml) and overweight (54.36 ± 11.96 μg/ml) subject (p < 0.05).

Image:

Summary of participants' characteristics at baseline, classified by obesity degree

<table>
<thead>
<tr>
<th>Groups (M/F)</th>
<th>Overweight (4/4)</th>
<th>Mild obesity (8/5)</th>
<th>Moderate obesity (19/4)</th>
<th>Severe obesity (24/11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>19.06 ± 0.98</td>
<td>19.68 ± 0.48</td>
<td>23.35 ± 2.14</td>
<td>28.55 ± 4.55</td>
</tr>
<tr>
<td>Obesity degree (%)</td>
<td>16.51 ± 2.14</td>
<td>24.33 ± 2.28</td>
<td>41.84 ± 4.89</td>
<td>71.42 ± 17.88</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>28.25 ± 4.96</td>
<td>28.72 ± 4.65</td>
<td>36.09 ± 4.28</td>
<td>41.00 ± 4.28</td>
</tr>
<tr>
<td>BF% (%)</td>
<td>82.77 ± 21.03</td>
<td>80.93 ± 13.27</td>
<td>77.95 ± 15.17</td>
<td>70.44 ± 21.19</td>
</tr>
<tr>
<td>FMI (kg/m²)</td>
<td>15.50 ± 3.73</td>
<td>15.93 ± 3.08</td>
<td>18.05 ± 3.02</td>
<td>19.43 ± 4.18</td>
</tr>
<tr>
<td>VFA (m²)</td>
<td>23.56 ± 12.19</td>
<td>33.56 ± 23.65</td>
<td>76.30 ± 26.46</td>
<td>93.41 ± 43.76</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>25.43 ± 4.46</td>
<td>25.18 ± 3.63</td>
<td>30.45 ± 5.86</td>
<td>37.39 ± 12.17</td>
</tr>
<tr>
<td>FFMI (kg/m²)</td>
<td>13.68 ± 1.28</td>
<td>13.81 ± 0.8</td>
<td>14.92 ± 1.15</td>
<td>16.74 ± 2.29</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>23.89 ± 4.25</td>
<td>23.67 ± 3.43</td>
<td>28.66 ± 5.52</td>
<td>35.27 ± 11.47</td>
</tr>
<tr>
<td>OC (μg/ml)</td>
<td>55.43 ± 12.4</td>
<td>54.36 ± 11.96</td>
<td>48.72 ± 10.82</td>
<td>44.46 ± 9.73</td>
</tr>
</tbody>
</table>

Data are shown as means ± the standard deviation. P-values are calculated by one-way analysis of variance.

* p < 0.05 for comparison between the four groups.
Conclusion: The BF%, VFA were inversely related to serum osteocalcin levels, however positive correlations were found between LBM, FFM, FFMI and serum osteocalcin levels in obese and overweight children. These results show a correlation between obesity and bone metabolism, and the mechanism of adipose tissue influence on bone metabolism needs further research.

References:

Disclosure of Interest: None Declared
PRIMARY PREVENTION OF ALLERGIC DISEASES IN INFANTS BY ADMINISTRATION OF BIFIDOBACTERIA TO PREGNATAL MOTHERS AND INFANTS AND EFFECTS ON FECAL MICROBIOTA

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Objectives and Study: Intervention to modulate intestinal microbiota in infants may be an useful method for preventing allergy, and some clinical studies have demonstrated the efficacy of probiotics. In the present study, we investigated the effects of probiotic treatment to pregnant women and their infants on prevention of allergic diseases in infants and on their intestinal microbiota.

Methods: In an open trial, we gave lyophilized powder containing two bifidobacterial strains (Bifidobacterium longum BB536 and Bifidobacterium breve M-16V) prenatally to 119 mothers for one month and postnatally for 6 months to their infants. Another 41 mother-infant pairs were not administrated as a control group. Development of allergic symptoms was diagnosed by doctors at 4, 10, 18 and 36 month after birth. Fecal samples were collected from mothers before probiotic administration and at delivery, and from infants at each diagnosis. Fecal microbiota were analyzed using Roche 454 GS FLX.

Results: Analysis among infants upon to 18 month old demonstrated that probiotic administration resulted in a significantly lower prevalence of infantile eczema/atopic dermatitis at 10 and 18 month, as compared to the control group. Analysis of fecal microbiota using samples from 64 mother-infant pairs showed that the proportion of Proteobacteria including Enterobacteriaceae was significantly lower in administrated mother at delivery, as compared to the not-administrated control. Actinobacteria including Bifidobacteriaceae was significantly lower and Proteobacteria was tended to be higher in fecal microbiota at 4 month from infants who developed infantile eczema/atopic dermatitis at each 4 and 10 month. Further, there was a positive correlation of Proteobacteria between mother at delivery and infant at 4 month.

Conclusion: These data suggest the efficiency of these bifidobacterial strains in primary prevention of allergic disorders and mechanisms for a possible of modification of microbiota. We are following-up allergy development in children until 3-yr old.

COLIFORMS AND INFANT COLIC: FISH ANALYSIS OF FECAL SAMPLES OF BREASTFED AND FORMULA FED INFANTS.
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Objectives and Study: Several lines of evidence point towards a possible role of the microbiota in different diseases. Among them, infantile colic, which are among the most common clinical presentations in the first few months of life, have been recently associated to the composition of colonic microbiota. Whereas it has been demonstrated that the faeces of breast-fed colicky infants have more coliforms compared to healthy infants1, data about colonic microbiota in formula-fed infants suffering for colic is scanty. The aim of this study was to compare the amount of coliforms in the faecal microbiota of breast-fed and formula-fed colicky infants, and of healthy breast-fed babies.

Methods: Between January 2010 and January 2012, 32 exclusively breast-fed healthy infants, and 54 infants (28 breast-fed and 26 formula-fed) suffering from infantile colic according to Wessel’s criteria, have been recruited in the Department of Paediatric and Adolescence Science – Regina Margherita Children Hospital – Turin. Faecal samples have been collected and immediately frozen until the analysis of coliforms concentration. Coliforms were quantified by means of FISH technique using a FITC fluorescent polynucleotide probe, specific for the 16S rRNA of Enterobacteriaceae. Positive bacteria were quantified in an epifluorescence microscope at the appropriate wavelength, 30 to 100 microscopic fields being counted and averaged in each slide. Differences in means among the three infant groups were evaluated using one-way ANOVA, followed by Tukey’s post hoc comparisons. For all comparisons, P values < .05 were considered statistically significant.

Results: The faeces of both breast-fed and formula-fed colicky infants presented a significantly higher number of coliforms (p < 0.05), compared to healthy infants. Furthermore, among the colicky subjects, coliforms were more numerous (p < 0.05) in the faeces of formula fed infants than in breast fed ones [mean ± sd = 6.96 ± 2.40 vs 7.63 ± 1.67 log10 (cells/g)].

Conclusion: FISH analysis of coliforms suggested the presence of more concentrated coliforms in faeces of colicky infants than in healthy babies, and higher numbers in formula-fed than in breast-fed ones.


Disclosure of Interest: None Declared
DNA METHYLATION IN THE HUMAN PLACENTA AND ITS ASSOCIATION WITH HIGH MATERNAL BODY MASS INDEX


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Objectives and Study: Changes in epigenetic profile in response to perturbations within the in utero environment could contribute to modifications in feto-placental function that, ultimately, place the resulting individual at increased risk of metabolic disease in later life. This results from associations of the methylation pattern of genes expressed in the placenta with changes in gene expression which could impair placental function. Furthermore, whilst the use of genome-wide methylation arrays enables more detailed examination of human epigenomics, this can lead to controversial interpretations. The present study, therefore, aimed to examine the influence of maternal body weight on the epigenomic profile in the human placenta followed by the determination of the expression of genes identified to be differentially methylated.

Methods: Term placental samples as part of the PREOBE study* were collected from 3 groups of pregnant women with normal glucose tolerance, according to pre-pregnancy BMI classified as normal weight (BMI<25 kg/m\(^2\); n=5), overweight (25≤BMI<30 kg/m\(^2\); n=4), and obese (BMI≥30 kg/m\(^2\); n=5). Illumina Infinium HumanMethylation450 BeadChip array was used to examine genome-wide DNA methylation patterns and annotation data were analysed using NIMBL software. Gene centric plots were generated for novel genes which were most differential methylated and their expression was determined by QPCR.

Results: The greatest difference in methylation was found in placenta sampled from overweight mothers in which there were more than 200 differentially methylated CpG sites, an adaptation that was largely absent in placenta sampled from obese women. Methylation of the promoter regions for both FAM3B and Wnt2 was raised in placenta of overweight women, but this adaptation was only accompanied with comparable changes in FAM3B gene expression. Conclusion: Placenta of overweight women show greater adaptation in their global methylation profile than those of women who are obese although this is not consistently directly related to changes in gene expression. The global-methylation response, therefore, with increasing maternal BMI suggests that enhanced maternal overweight may result in adverse fetal outcomes.


Disclosure of Interest: None Declared
UNDERNUTRITION CAUSES CARDIAC DYSFUNCTION IN A PIGLET MODEL


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Objectives and Study: The association between undernutrition and cardiac function in pediatric patients is still poorly understood. A possible link is important for an estimated 60 million children up to 5 years of age that are suffering from undernutrition. The objective of this study was to investigate cardiac function with respect to undernutrition, using an experimental piglet model.

Methods: Four-week old piglets were given ad libitum access to either a low-nutrient diet consisting of pure maize flour (MAIZE, n=12) or a control diet (CON, n=12) for 7 weeks. Temporal changes in plasma levels of pro-atrial natriuretic peptide (proANP) and troponin T (TNT) were measured as markers for cardiovascular disease. Echocardiography was performed at 7 weeks when cardiac tissue was collected for analysis of Na/K ATPase density. For comparison, echocardiography was also performed on a reference control group consisting of pigs with a body weight similar to maize-fed pigs without undernutrition.

Results: Body weight was lower in MAIZE relative to CON pigs (-72%, P<0.001). There was an initial decline in proANP for both MAIZE and CON pigs during the first 3-4 weeks, then a marked increase in MAIZE pigs at 5-7 weeks, relative to CON pigs (P<0.05). Likewise, mean TNT tended to be higher in MAIZE (P=0.07) suggesting myocardial damage. Echocardiography, as indicated by the myocardial performance index, showed left ventricle dysfunction in MAIZE relative to both weight- and age-matched control pigs. Heart to body weight ratio was similar between groups but the heart had a flabby appearance in the MAIZE group. Myocardial Na/K ATPase levels were 50% higher in MAIZE vs. age-matched control pigs (P<0.01).

Conclusion: Undernutrition in a piglet model causes adverse cardiac remodeling and dysfunction. The results suggest that assessment of cardiac function is important in undernourished patients and that proANP may be a relevant plasma biomarker of cardiac dysfunction.

Disclosure of Interest: None Declared
DEFICIENCY OF TRACE ELEMENTS AND MINERALS IN GIRLS WITH A RESTRICTIVE TYPE OF ANOREXIA NERVOSA

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Objectives and Study: To investigate the prevalence of deficiencies in trace elements (copper and zinc) and minerals (calcium, phosphor and magnesium) and its possible clinical risk factors (age, BMI z-score, duration of amenorrhea and the rate and degree of weight loss) in girls (≤18 years) with a restrictive type of anorexia nervosa (AN) at the time of diagnosis.

Methods: Medical files of 84 girls with AN and of a control group of 90 girls with chronic fatigue syndrome (CFS), diagnosed at UZ Brussel in the last 10 years were reviewed. Of the girls suffering from AN, 75/79 had a Tanner stage ≥M2, 5/53 used oral contraceptives and 42/48 pubertal girls without contraceptives had secondary amenorrhea or oligomenorrhea. Serum values of zinc, magnesium, copper, calcium and phosphor were measured by routine laboratory techniques.

Results: The median (range) age of AN patients (15.4y (13.0-18.7)) was significantly (p=0.01) higher than CFS subjects (15.9y (12.8-18.3)). Median (range) zinc and magnesium levels were significantly (respectively p=0.03 and p<0.01) higher in the AN group (respectively 83.5 µg/dl (56-141) vs 79.0 µg/dl (53-128) and 2.1 mg/dl (1.8-2.5) vs 2.0 mg/dl (1.7-2.5)). The median (range) serum level of calcium was also significantly higher (p<0.01) in the AN group than in the control group (9.3 mg/dl (8.1-10.2) vs 9.2 mg/dl (8.2-9.9)). Girls diagnosed with AN had significantly (p<0.01) lower median (range) copper serum levels than girls with CFS (respectively 77.0 µg/dl (47-163) vs 108.0 µg/dl (40-244)). All differences in serum levels remained significant after correction for age. No significant difference was found in median serum phosphor levels (p=0.21). Copper deficiency (serum Cu <80 µg/dl) was significantly (p<0.01) more prevalent in girls with AN than in girls with CFS (respectively 55.4% vs 18.7%). Deficiencies of the other studied minerals and trace elements were not statistically different between both groups (p-values ranging from 0.07 to 1.00). In the AN girls serum copper (p=0.52; p<0.01) and magnesium levels (p=-0.27; p=0.01) correlated significantly with BMI z-score. None of the serum trace element and mineral levels correlated with age, duration of amenorrhea or rate or degree of weight loss.

Conclusion: Copper deficiency is the most frequent trace element deficiency in girls with a restrictive type of anorexia nervosa, especially those with the lowest BMI z-score, putting them at risk for developing leukopenia. Although serum mineral levels can be falsely elevated in AN because of associated dehydration, systematic supplementation of trace elements and minerals, at least at the moment of diagnosis, does not seem to be indicated in AN girls.

METABOLIC SYNDROME IN MODERATE/SEVERE OBESE CHILDREN: AN EFFECTIVE TREATMENT.
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Objectives and Study: The prevalence of childhood obesity and its metabolic consequences has dramatically increased in the last two decades urging physicians to early detect, treat and possibly prevent metabolic syndrome (MS). Unfortunately, the standard treatment of severe obesity (diet and aerobic exercise) is unsuccessful. The principal aim of the study is to evaluate the efficacy of a multidisciplinary hospitalization program for children affected by moderate/severe obesity in order to identify and to treat MS.

Methods: 103 children (63 M) followed at our outpatient for severe obesity (BMI over the 95th percentile) were hospitalized for 6 days. During hospitalization, laboratory examinations and clinical evaluations were performed in order to identify obesity related complications; and a multidisciplinary treatment based on the educational integrated therapy (by nutritionist and psychologist) addressed to modify behaviours and habits which caused and/or nourished the complications was started. MS was identified on the basis of the presence of following parameters: central obesity, hypertension, dyslipidemia, impaired glucose tolerance (3 or more of these risk factors). One year follow up, characterized by clinical evaluations every three months (by pediatrician), and by educational program (by nutritionist and psychologist), was addressed to all patients, while blood examinations were repeated after 6 months only in the subjects affected by MS.

Results: Mean age of the population was 11,5 ± 2,7, mean BMI z-score 2.6 ± 0.4. MS was present in 41,7% (N = 43) of the population. After 6 months mean BMI z-score was 2.2 ± 0.4 and only 7,7% of the sample was still affected by MS.

Conclusion: The important reduction of MS (-34%) after 6 months of the treatment shows that the combined role of the multidisciplinary hospitalization program initially and of the educational integrated program secondly are important to: 1) identify MS (otherwise not surely identified); 2) address specific treatments; 3) modify unhealthy behaviours.

Disclosure of Interest: None Declared
LUNCH AT SCHOOL, AT HOME OR ELSEWHERE: WHERE DO ADOLESCENTS GET IT AND WHAT DO THEY EAT? – RESULTS OF THE HELENA (HEALTHY LIFESTYLE IN EUROPE BY NUTRITION IN ADOLESCENCE) STUDY

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Objectives and Study: Considering the potential nutritional role of a proper lunch for dietary intake and the large number of children and adolescents worldwide staying at school over midday information on their lunch pattern is of public health relevance. Objective of this analysis was to describe and evaluate potential differences in characteristics and lunch-time food intake of European adolescents who get lunch at school, at home or elsewhere.

Methods: HELENA was a multi-centre study conducted between 2006 and 2007 in 10 European cities. The overall aim was to obtain reliable and comparable data on nutritional and health-related parameters in a sample of > 3000 European adolescents (12.5-17.5 years). For this analysis 891 adolescents (47% male) with plausible data on lunch-time food intake obtained from two 24h recalls and on lunch location were considered. Food intake was compared to the Optimized Mixed Diet (OMD), a food and meal based total diet concept for children and adolescents. Analyses were performed stratified by lunch location (school, home and elsewhere).

Results: Adolescents who get their lunch elsewhere are the oldest and characterised by the highest numbers of smokers and breakfast skippers. Those getting lunch at home have the highest values for BMI-SDS and the lowest values for familial affluence and physical activity. The number of breakfast skippers is the lowest in the adolescents participating in school meals. However, the numbers of those who have lunch on only one of the two recall day is also the highest in this group. Although lunch-time energy intake is nearly in line with the recommendations at all lunch locations, lunch-time food intake of European adolescents is suboptimal compared to the OMD: the intakes of vegetables and potatoes reached only 11% and 31% of the recommendations; meat intake exceeded the recommendations by 28% at all lunch-locations. At school, participants had lower intake levels for sweets and higher intake levels for potatoes; at home more drinks and vegetables are consumed when compared with the other locations. Food intake of participants getting lunch elsewhere is characterised by the smallest amounts of potatoes and the highest amounts of bread and sweets.

Conclusion: Lunch-time food intake of European adolescents is not in line with the food and meal based recommendations of the OMD regardless of lunch location. Data suggest that participants getting their lunch elsewhere have the unhealthiest lifestyle characteristics and lunch pattern. Furthermore, schools do not seem to reveal all their potential to offer a healthy lunch for everyone yet.

Disclosure of Interest: None Declared
ASSOCIATION BETWEEN CESAREAN SECTION AND INCREASED BODY MASS INDEX IN SCHOOL CHILDREN
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Objectives and Study: To assess the association of caesarean section (CS) with increased body mass index (BMI) and obesity in school children from two Brazilian cities with distinct socioeconomic backgrounds.

Methods: Two birth cohorts respectively born in 1994 in Ribeirao Preto (RP), a wealthy city in Southeast, and in 1997/98 in São Luis (SL), a less wealthy city in Northeast, were evaluated. After birth, 2846 pairs of mothers-newborns were evaluated in RP and 2542 in SL. In 2004/05, 790 children aged 10/11yrs were randomly reassessed in RP and 673 at 7/9yrs in SL. Information on type of delivery; maternal and child characteristics; socioeconomic position; and anthropometric measurements were collected after birth and at school age. Obesity was defined as BMI ≥ 95th percentile at school age.

Results: Obesity rate was 13.0% in RP and 2.1% in SL. CS was associated with obesity and remained significant after adjustment only in RP [OR=1.74 (95%CI 1.04;2.92)]. The association between CS and BMI remained significant after adjustment in both cities. In RP children born by CS had BMI 0.31kg/m² (95%CI 0.11;0.51) higher than those born by vaginal delivery. In SL BMI of children born by CS was 0.28kg/m² higher (95%CI 0.08;0.49).

Conclusion: A positive association between CS and increased risk of high BMI was demonstrated in areas with different socioeconomic status in a middle-income country. The results pointed out that CS may be associated with obesity in areas with high rates of CS.

Disclosure of Interest: None Declared
BARIATRIC SURGERY IN OBESE ADOLESCENTS: A PRELIMINARY EXPERIENCE WITH A MULTIDISCIPLINARY APPROACH.
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Objectives and Study: Surgery for severe obesity has been shown to be efficacious in adults. Very few studies have documented the efficacy of bariatric surgery in adolescents. We reported our preliminary experience with a multidisciplinary approach for the treatment of severely obese adolescents, who achieved no results by a dietetic and behavioural protocol.

Methods: In a 12 months period from our ambulatory for the treatment of severe obesity (26 subjects) 3 patients were selected for bariatric surgery. The inclusion criteria were: no adequate success to various dietetic and behavioural treatments, high rate of comorbidities related to obesity, high motivation to the surgery and distrust to the dietetic/behavioural intervention, low self-esteem and body esteem, and other psychological correlates such as: obesity stigma, reduced level of quality of life, social isolation, no adequate scholastic success. Their age varied between 15 and 17 years old. In all the cases patients weight was higher than 140 kgs. All the patients were evaluated preoperatively by a multidisciplinary team (pediatrician, nutritionist, psychologist, paediatric surgeon) and operated by a mixed team of adult and pediatric surgeons.

Results: One patient underwent to the positioning of a Bioenteric Intragastric Balloon (BIB), through an endoscopic procedure lasted 30 minutes, the other two underwent to a malabsorbitive surgical procedure, lasted about 4 hours, because one of them refused the positioning of a BIB, the other one was affected by Prader-Willi Syndrome, which alters the centre of satiety regulation as a result of hypothalamic-pituitary abnormalities. The weight loss after 4 months was more than 20 kgs, and after one year was more than 30 kgs in Prader-Willi patient and in the other ones. One of the patient treated surgically showed iron deficiency, treated with infusion. All the patients showed higher self- and body-esteem, improved social relationships and higher level of quality of life.

Conclusion: This study confirms that bariatric surgery is efficacious also in adolescents, especially when the recruitment process is very selective according to multidisciplinary criteria, and when the follow up is very frequent and managed by the multidisciplinary team (pediatrician, nutritionist and psychologist), with the aim of educate them towards correct nutritional habits and healthy lifestyle. More long-term and bigger sample studies seem to be necessary in order to have a wider vision on this emerging topic.

Disclosure of Interest: None Declared
CONCLUSIVENESS OF THE COCHRANE REVIEWS IN NUTRITION: A SYSTEMATIC ANALYSIS
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Objectives and Study: Cochrane reviews (CRs) are systematic studies of relevant randomized controlled trials (RCTs). The aim of this study was to assess the conclusiveness of the CRs in the field of Nutrition. Hypotheses: 1) the majority of CRs is inconclusive; 2) the majority of CRs recognizes the need for further and better studies; 3) the ability to reach a conclusion is dependent upon both the number (N) of studies performed and the N of patients enrolled.

Methods: All 87 CRs in Nutrition were analyzed for N of: RCTs found, RCTs included for analysis & patients enrolled. The stated need for further studies, reason(s) for it, and conclusiveness were noted. CRs classification: 1) a strategy/drug “better” than alternative; 2) no significant differences between strategies/drugs; 3) inadequate studies quality, thus no decision; 4) not enough data, thus no decision. The first 2 categories were defined “conclusive”, and the last two “inconclusive”. Conclusiveness was determined on the basis of the main outcome (and not secondary outcomes). Kruskal-Wallis was used to test differences between “conclusive” and “inconclusive” studies, and linear regression analysis to study correlation between % of conclusive reviews and year of publication.

Results: 56/87 CRs (64.4%) were conclusive. The average N of available RCTs, % of articles included, average N of RCTs retained in analyses, and total N of patients were significantly higher in conclusive CRs. The need for further studies was similar in conclusive and inconclusive CRs. Publication year did not affect the % of conclusive CRs.

<table>
<thead>
<tr>
<th>Mean±SD (median, range)</th>
<th>“Conclusive” CRs (n=56)</th>
<th>“Inconclusive” CRs (n=31)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Available articles</td>
<td>40.7±56.0 (19, 1-260)</td>
<td>16.2±20.2 (12, 0-110)</td>
<td>0.002</td>
</tr>
<tr>
<td>% of included articles</td>
<td>46.6±25.7 (45.9, 1.81-100)</td>
<td>30.8±32.0 (19.6, 0-100)</td>
<td>0.014</td>
</tr>
<tr>
<td>Retained articles</td>
<td>12.1±12.8 (8, 1-62)</td>
<td>4.7±7.4 (1, 0-27)</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients enrolled</td>
<td>5577±21626</td>
<td>1930±6290</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
**Conclusion:** The majority of CRs in the field of nutrition is conclusive. Most CRs ask for further studies. The ability to reach a conclusion is affected by the patient N and the N of RCTs included.

**Disclosure of Interest:** None Declared
THE PREVALENCE OF UNDER-NUTRITION IN HOSPITALIZED CHILDREN WITH SURGICAL PATHOLOGY
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Objectives and Study: Acute under-nutrition in hospitalized children has a high prevalence (from 6 to 40%) in the world. It is particularly relevant for children in the surgical department as under-nutrition is associated with high risk of infectious complications, prolonged wound healing, changes in the functions of the intestine. No data on the under-nutrition prevalence in children with surgical pathology in Russian Federation is available. The aim of this pilot study was to determine the prevalence of under-nutrition in children with surgical pathology.

Methods: 40 previously operated patients (15 girls and 25 boys) with surgical pathology (portal hypertension, short bowel syndrome, pectus excavatus; biliary, esophageal and anal atresia), at age from 4 months to 16 years were included into the study. Clinical assessment and anthropometric measures were performed. Anthropometric data were assessed using WHO criteria (program “WHO Anthro” and “WHO Anthroplus”). Acute under-nutrition was defined as ≤ -2 SD weight-for height and chronic under-nutrition as ≤ -2 SD height-for age. In children older 5 years with under-nutrition bioimpedance analysis was done.

Results: According to WHO criteria, a total prevalence of under-nutrition in children entered for surgery, was 40%. Chronic under-nutrition was observed in 9 (22.5%) patients, and acute in 7 (17.5%) patients. There was severe under-nutrition in 57.1% in the group of children with acute under-nutrition. In 8 patients Z-score weight-for height was -1-2 SD, that enables to include these patients in risk group of nutritional deficiency developing and in this case requires the need of nutritional support. Bioimpedance analysis data showed that the most sensitive criterion for the presence of under-nutrition is active cell mass decrease.

Conclusion: Under-nutrition in children with surgical diseases has a high prevalence. Bioimpedance analysis is an additional sensitive method to detect developing nutritional deficiency.

Disclosure of Interest: None Declared
NUTRITION RISK SCREENING AND CLINICAL OUTCOMES ANALYSIS IN 1201 HOSPITALIZED SURGICAL PEDIATRICS BY USING MODIFIED STAMP
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Objectives and Study: To evaluate the impact of nutritional risk defined by modified Screening Tool for Assessment of Malnutrition in Pediatric (STAMP) on clinical outcomes in hospitalized surgical pediatrics.

Methods: In this retrospective cohort study, totally 1201 hospitalized surgical patients were recruited from August 2010 to June 2011 in Shanghai Children’s Medical Center. Data were collected on the STAMP Score at admission or post operation, application of parenteral nutrition (PN) and enteral nutrition (EN), nosocomial infection, cure rate, hospital length of stay (LOS), ICU stay and hospitalization expenses. To evaluate the nutrition risk on operation, the National Nosocomial Infection Surveillance risk index (NNIS) was adopted as grading how the operation implicate the nutrition status, and added as a part of the STAMP score.

Results: The patients were classified in two groups according to the STAMP score: ≥ 4 defined into ‘at high nutritional risk’ (HNR group, n=301), and < 4 defined into ‘at low nutritional risk’ (LNR group, n=900). The nosocomial infection rate was significantly higher in the HNR group than that in the LNR group, LOS and ICU stay were longer. There were higher PN & EN application rate in the HNR group than that in the LNR group. However, the cure rate and hospitalization expenses had no significantly differences between the two groups.

Conclusion: The modified STAMP score can be effectively used as the nutrition risk assessment tool for hospitalized surgical pediatrics. Higher modified STAMP score implies to poor clinical outcomes. Modified STAMP score also has beneficial to be a predictor in the perioperative nutrition support.

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Objectives and Study: Recent retrospective studies have shown that early body size and growth in infancy are related to bone mass in late adolescence. However, if this is correlated to food patterns, D-vitamin and bone markers are not studied prospectively. The objective was to study prospectively the correlation between food patterns, D-vitamin and bone markers in a cohort of healthy Swedish children.

Methods: A population-based longitudinal birth cohort with 300 children recruited 2008 and 2009 in south-western Sweden was followed with anthropometric measurements and blood sampling at birth (B), 4 months (4m), 12 months and 36 months of age. At visits to the child health centre, parents were asked to complete a food questionnaire. Measurements of weight, height, head and waist circumference were recorded using a standard procedure. 25-hydroxyvitamin (25OHD), propeptide of human collagen type I (PINP) and osteocalcin were measured with IDS-iSYS-technique.

Results: Individual levels of 25OHD were remarkable stable over all the studied period (20-50% variance), whereas PINP varied widely (50-500% variance), with highest levels at 4 months of age (mean (SD) at B 1253 ng/ml (517) and 4m 1874 ng/ml (514), p<0.05). This increase was also seen for osteocalcin (B 58 (28) and 4m 95 (39), p<0.05). Interindividual differences were large: Neonatal 25OHD ranged between 18-117 ng/ml, osteocalcin between 18-152 ng/ml and PINP 192-3685 ng/ml. We will show correlations to food patterns and vitamin addition, but did not find significant correlations to the season when sampling was performed.

Conclusion: Vitamin D levels were found to be remarkable stable during the first years of life, corresponding to familiar food patterns. The large differences in markers of bone remodeling may instead reflect differences in physical activity.

Disclosure of Interest: None Declared
Objectives and Study: Eating disorders are the third most common chronic disease in adolescents. The number of adolescents with eating disorders is increasing continuously. In essence, anorexia nervosa (AN) is a psycho-emotional disorder. The malnutrition that develops as an outcome in AN carries great risks of different physical complications with permanent consequences. The development of anorexia nervosa in the very sensitive period of adolescence, when the majority of bone mass is gained, can result in low bone mineral density and development of osteoporosis. The aim of this study was to evaluate the level of bone mineral density (BMD), serum values of insulin-like growth hormone (IGF-I), bone markers (osteocalcin-OC and C-telopeptid of type I collagen-CTX) and their relationships with the duration of the disease and the duration of amenorrhea.

Methods: We examined 90 adolescent girls with AN mean age 15.4±2.9 years (8.11-21.7), 69 of them with secondary amenorrhea (SA) average duration 8,8±10.18 months (2-49) and the rest of them with primary amenorrhea. According to the duration of the disease the patients were divided into two groups. Group A (≤12 months) and Group B (>12 months). We used the Pearson linear correlation test to compare the two groups.

Results: We found significant negative correlations between the level of Z-score and the duration of the disease (r= -0,257; p=0,0149), between the level of Z-score and the duration of amenorrhea (r= -0,385, p=0,0011) in the group of girls with SA and negative correlation between IGF-I and bone resorption markers serum values (r= -0,49; p=0,008).

Concentration of bone markers, IGF-I and body mass index did not differ significantly among the groups.

Conclusion: The disease duration as well as the duration of amenorrhea significantly affected bone mineral density. Lower IGF-I concentrations correlated with higher bone resorption markers and decreased mineralization, which suggests the importance of IGF-I in the ethiopathogenesis of osteoporosis. No difference was ascertained in the values of bone markers, which could potentially be the result of a significant age difference among the groups.

Disclosure of Interest: None Declared
INTAKE PATTERN OF INFANT COMPLEMENTARY FEEDING IN TWO POPULATIONS IN NORTHERN SPAIN
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Objectives and Study: Nutrition during the first months of life has an important role in early infant health and later body composition and metabolic programming. The relative impact of complementary feeding has not been elucidated. Our aims are both to describe the pattern of complementary feeding intake in two populations of infants in Northern Spain and explore their associations with infant anthropometry.

Methods: Longitudinal observational study in 245 healthy infants (133 males), enrolled at 6 months of age and controlled until 9 months, as part of a larger study about complementary feeding and body composition in two cities in Northern Spain. Structured 24-h feeding recall questionnaires were performed to assess patterns and amounts of food intake (breastfeeding, formula, fruit, cereal, yogurt and porridge of vegetable and meat or fish (PVMF)). Perinatal and family sociocultural characteristics were also registered. Anthropometric variables (weight, length, body circumferences and skinfold thicknesses) were measured at 6 and 9 months of age under standardized methodology.

Results: Anthropometry at 6 and 9 months and their changes during this period were adequate. Concerning food intake, breastfeeding was maintained at 6 months of age in 42.3% of infants and in 27.4% at 9 months. The percentage consuming each food group at 6 and 9 months were, respectively: formula 80.6% and 76.6%; cereals 79% and 77.4%; fruit porridge 58% and 68.5%; PVMF 33% and 80.6%; and yogurt 1.6% and 22.6%. Cereals and fruit are the favourites for complementary feeding initiation. The amount of food intake at 9 months was: formula 472 ±190ml; cereals 26±16g; fruit porridge 192±70g; PVMF 259±108g; and yogurt 131±35g. Infants who were breastfed consumed less amounts of both infant formula and PVMF; at 6 months we found positive relationship between cereals and infant formula intake (r=0.227) and cereals and PVMF (r=0.321); and, at 9 months, between fruit and cereals (r=0,303) and fruit and PVMF (r=0.233) (p<0.05). No relationship has been found between the amount of any food intake and infant growth during this period.

Conclusion: Prevalence of breastfeeding is high in the north of Spain and complementary feeding introduction is consistent with the latest ESPGHAN recommendations. The majority of infants are already consuming all food groups at 9 months of age. Infants who are breastfed consume less amounts of both infant formula and PVMF. There is a positive clustering association between the foods ingested but, no relationship has been found between amounts of food intake and infant growth during this period.

Disclosure of Interest: None Declared
SURVEY OF PRACTICES IN UK CENTRES LOOKING AFTER PAEDIATRIC PATIENTS ON HOME PARENTERAL NUTRITION

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Objectives and Study: Home parenteral nutrition (HPN) is a specialist service and its use has increased significantly over the past decade (1). This survey aims to capture the variation in practice across centres looking after paediatric patients on HPN in the UK, and to share expertise by describing this variation.

Methods: We performed a survey of practices in all centres looking after patients on HPN. Responses were collected and collated electronically. The survey was developed by a multidisciplinary team including a Gastroenterologist, Pharmacist, Nurse Specialist and Dietician. Questions included free text spaces. The name of the centre was included to allow combination and comparison of responses from within each unit.

Results: We received 24 responses to our survey from 17 centres. Of these 6/17 (35%) had less than 5 patients on HPN, 5/17 (29%) had 5-10 patients on HPN and 6/17 (35%) had more than 10 patients on HPN. Intralipid was the most commonly used lipid in children requiring PN for <28days. 11/17 centres used Intralipid, 3/17 used SMOF, 2/17 used ClinOleic, 1/17 used another lipid emulsion. In children requiring PN for > 28 days SMOF was used in 13/17 (76%) centres, Intralipid in 2/17, Clinoleic in 1/17 and other in 1/17. All (17/17) centres used SMOF for children with liver disease. 9/17 centres used lipid free days (days when no lipid was given in parenteral nutrition), of those 4/9 centres increased carbohydrate on fat free days. 10/17 centres used aqueous and lipid phase in a single bag, 7/17 used separate lipid and aqueous phase. 71% (12/17) of the centres used Taurolock, 3 used it in all patients, 9 used it in patients with multiple line infections and in addition two centres used Taurolock occasionally as part of treatment for line infections. 4 used Hep 100 and 8 used citrate. 9 centres reported choosing to withdraw Taurolock and 3 centres reported choosing to flush it. 12 centres responded to a question on the use of alcohol in central lines, of those 3 never used alcohol for lines, 2 used it for blocked lines, 5 used it for infection prophylaxis and 2 centres used alcohol for treatment of line infection.

Conclusion: This survey provides an important review of practice at 17 centres looking after patients on HPN. There is significant variation in practice in the UK. Collaboration between centres and reporting these details may help identify differences in outcome. There is need for a national guideline to be developed using the best evidence available, although the lack of high quality evidence in this field means that expert opinion is likely to form the basis of many aspects of care.

References:

Disclosure of Interest: None Declared
INCREASE OF DHA CONTAINING GLYCEROPHOSPHOLIPID SPECIES IN PLASMA AND RED BLOOD CELLS DURING A 4 WEEKS DHA SUPPLEMENTATION

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Objectives and Study: Docosahexaenoic acid (DHA) and other long chain-polyunsaturated fatty acids (LC-PUFA) are important for early development of neurological, visual and immune function. Plasma and red blood cell (RBC) fatty acid compositions are commonly used as biomarker for LC-PUFA status. We studied the effect of DHA supplementation on individual glycerophospholipid (GPL) species in plasma and RBC.

Methods: Thirteen young healthy adults with a mean BMI of 21.9±1.6 kg/m² were supplemented with 510 mg DHA/d for 29 days. Fasted blood samples were taken at baseline and at 9 time points during supplementation. GPL species were analysed by liquid chromatography/tandem mass spectrometry. Repeated measures ANOVA was used for comparison of species with significant increase (paired t-test, P ≤ 0.01).

Results: In plasma, percentages of all measured DHA-containing GPL species increased significantly, except for lyso-PC(22:6), without significant differences between species. Relative increases were found for lyso-PE(22:6) 58±31% (mean±SD), PC(16:0/22:6) 84±33%, PC(18:0/22:6) 97±34%, PC(18:1/22:6) 78±34%, PE(16:0/22:6) 76±37% and PE(18:0/22:6) 91±38%. All species showed steep initial increases with a less steep slope after 4–9 days of supplementation.

In RBC, phosphatidylcholine (PC) species with DHA (PC(16:0/22:6) 90±41%, PC(18:0/22:6) 85±36%) increased comparable to DHA-containing GPL species in plasma. PC(18:0/22:6) showed a constant increase over the study period while PC(16:0/22:6) showed an initial steep increase similar to plasma species. Phosphatidylethanolamine (PE) and phosphatidylserine (PS) species showed a significantly smaller increase (PE(16:0/22:6) 23±12%, PE(18:0/22:6) 18±12%, PE(18:1/22:6) 13±9%, PS(18:0/22:6) 18±13%, PS(18:1/22:6) 25±17%). Nonetheless, the slowly changing PE and PS species contributed more than 90% to total GPL DHA in RBC, even after supplementation.

Conclusion: DHA supplementation did not affect DHA distribution between GPL species in plasma. Dietary DHA leads to a fast increase of DHA-containing GPL-species that are available quickly for tissue uptake. The rapid change of DHA-containing PC species in RBC appears to reflect a fast, fatty acid chain length dependent exchange of RBC and plasma PC. Nonetheless, DHA percentage of RBC GPL is a valid biomarker of long-term DHA status as RBC DHA largely occurs in species with slow rates of exchange.

Disclosure of Interest: None Declared
A NUTRITION-RELEVANT COGNITION-BEHAVIOR MODEL IN NEWBORN PIGLETS
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Objectives and Study: Nutrition is important for early maturation of the gut and the brain. Lack of mother’s milk or specific nutrients, may inhibit infant brain development, but the most sensitive stages of development and the responsible diet factors remain unknown. We hypothesized that preterm and term newborn pigs can be used to document diet-related neurodevelopmental functional and structural outcomes.

Methods: Clinical variables and brain-related functions were followed in preterm and term newborn piglets after different nutritional regimens. Term pigs were sow-reared for 3 days and fed formula for 4 weeks with a standard or low protein level (46 or 23 g/L, n=36). Clinical variables, physical activity, and a visual discrimination test were used to investigate neurodevelopmental outcome. Preterm pigs were delivered at 90% gestation and fed increasing doses of bovine colostrum or infant formula until day 12 of life (n=8).

Results: Newborn term pigs are mobile and have open eyes within a few minutes of birth. Feeding a low protein diet to 3-20 d-old term pigs reduced the body weight gain (7 vs. 15 g/kg/d, P<0.05), but this did not affect the number of trials taken to reach competent visual discrimination in the test cage (70±3 vs. 60±10 trials, P=0.67). Competence was defined as 80% correct learning responses in 10 consecutive trials. No differences were observed in total brain weight (46.7±0.8 vs. 46.6±0.7 g), relative to controls. Preterm, low birth weight piglets (700-900 g) showed signs of neurodevelopmental immaturity during the first days after birth as reflected by delayed and unstable locomotion, slow eyelid opening and poor sucking reflexes. Colostrum-fed preterm pigs were more active (67 vs. 55% activity time during the first 12 days, P<0.05) and developed sucking reflexes earlier, relative to formula-fed pigs (78 vs. 168 h, P<0.05). One week-old preterm pigs showed explorative behavior in the visual discrimination test cage, and some limited capacity to understand the test at 3 weeks of age. Magnetic resonance imaging (MRI) of the brain showed increased brain myelination in 12 d-old vs. newborn preterm pigs (each n=2), but both groups had markedly less myelination than term pigs of a similar postnatal age.

Conclusion: The newborn pig may be a suitable model to study diet effects on infant neuronal development. Moderate protein undernutrition does not affect cognitive performance in term pigs. Preterm pigs show impaired and diet-dependent behavioral characteristics that may reflect their immature brain structure and function.

Disclosure of Interest: None Declared
STABILITY ASSESSMENT OF TOTAL NUTRIENT ADMIXTURES WITH HIGH GLUCOSE CONCENTRATIONS
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Objectives and Study: To meet the energy needs of fluid-restricted patients, it is possible to increase glucose concentrations of all-in-one parenteral nutrition emulsions. The purpose of the present study was to examine the influence of various concentrations of glucose on TNAs for fluid-restricted patients.

Methods: Five formulations were designed with 5 different glucose concentrations containing the same amounts of fat emulsion, complex amino acid solution, and ions. Final glucose concentrations of admixtures were 5% (G5), 10% (G10), 15% (G15), 20% (G20), and 25% (G25), respectively. The analyses were carried out immediately after preparation (0 h) and at 12h, 24h, 48h and 72h after preparation. Two methods were selected to determine fat globule size: optical microscopy and electron scanning microscopy. Complementary evaluation included visual inspection, measurements of pH and osmolarity. All nutrient admixtures were stored at room temperature (25±2°C).

Results: (1) There was no observable alteration in colour and phase separation in any nutrient admixture. (2) Lipid globules diameter appeared to be no significantly altered (P > 0.05) in any of the analyzed formulations from 0 to 72 hours (table). (3) The pH of all the nutrient admixtures was between 6.08 to 6.37 at the recommended range within 72 hours. (4) At 0 hour, the mean osmolarities for G5-G25 were 611.3mOsm/L, 839.1mOsm/L, 1105.0mOsm/L, 1384.0mOsm/L, and 1621.0mOsm/L, respectively. Within 72 hours, a constant level was observed in osmolarity in each group (P > 0.05).

Table. Average lipid globules diameter in TNA under different glucose concentrations (Mean±SD, μm)

<table>
<thead>
<tr>
<th>Groups</th>
<th>0h</th>
<th>12h</th>
<th>24h</th>
<th>48h</th>
<th>72h</th>
</tr>
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<tr>
<td>G5</td>
<td>0.348±0.052</td>
<td>0.353±0.098</td>
<td>0.315±0.078</td>
<td>0.322±0.041</td>
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<td>G10</td>
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<td>0.319±0.054</td>
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<td>G15</td>
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<td>G20</td>
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<td>0.319±0.044</td>
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<td>G25</td>
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<td>0.328±0.040</td>
<td>0.321±0.042</td>
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</table>

Conclusion: Lipid emulsions of TNA were stable in the presence of 5-25% glucose concentrations. However, more than 20% glucose concentrations in the experimental TNAs presented high osmolarities, which were out of the recommended range for central infusion in paediatric patients.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Bone marrow transplantation (BMT) is often used in the treatment of various diseases. Parenteral nutrition (PN) plays an important role in the supportive care of children undergoing BMT. The study aimed to assess lipid peroxidation, fatty acid profiles and liver function of an olive-based (OO) lipid emulsion compared with a MCT/LCT (M/L) emulsion in paediatric BMT patients, and to observe the incidence of oral mucositis and diarrhea in the duration of PN for these patients.

METHODS: Prospective observational study in 20 paediatric BMT patients (age 1-18 years) who expected to require PN support for at least 7 days. All the patients were randomly assigned to receive either OO (10 patients) or M/L (10 patients) lipid emulsions within PN. Both groups had similar basal characteristics and received a similar energy load (OO vs M/L, 19kcal/kg/d vs 20kcal/kg/d). Clinical and routine laboratory parameters, plasma fatty acids profile, plasma lipids, total superoxide dismutase (T-SOD) and malondialdehyde (MDA) concentration were recorded at baseline and at the end of PN. Frequency and quantity of defecation, and oral mucositis were recorded every day. Diarrhea was evaluated by the Hart and Dobb Grade.

RESULTS: No significant differences were found for liver enzymes and plasma lipids. At study end, the OO group showed higher antioxidant enzyme activities, namely, an increased serum T-SOD with a reduced serum MDA level; however, no differences were found between the two groups after PN (OO vs M/L: T-SOD, 21.9±15.3u/ml vs 20.9±8.2u/ml, P>0.05; MDA, 14.4±7.5nmol/ml vs 22.3±14.9nmol/ml, P>0.05). The baseline fatty acids levels in the two groups were similar, while the OO group exhibited higher levels of C18:1n-9 (P>0.05) and C18:2n-6 (P>0.05) compared to the M/L group at the end of PN. Meanwhile, the OO group showed higher values of C20:5n-3 (6.10±1.99 vs 10.79±4.92, P=0.033) and C22:6n-3 (46.40±13.51 vs 67.10±18.50, P=0.026). Six (60%) and seven cases (70%) developed oral mucositis in the OO group and the M/L group, respectively. The Hart and Dobb Grade for diarrhea was 3.5 in the OO group compared to 3.7 in the M/L group (P=0.748).

CONCLUSION: OO lipid emulsion and M/L lipid emulsion were well tolerated and maintained essential fatty acids. OO lipid emulsion was trended to lower in the peroxidation status with a higher polyunsaturated fatty acids (C20:5n-3 and C22:6n-3).

DISCLOSURE OF INTEREST: Y. Feng Grant / Resarch Support from: AFINS grant by Project HOPE, L. Hong Grant / Resarch Support from: AFINS grant by Project HOPE, B.-H. Zhang: None Declared, L.-Y. Pan Grant / Resarch Support from: AFINS grant by Project HOPE
Objectives and Study: Iron deficiency is the most common nutritional disorder in the world. Young children are particularly vulnerable to the consequences of iron deficiency because of the rapid growth and development of their brain. Many studies have evaluated iron intake and status in young children in Europe, but no systematic review of these studies exists to date. Therefore, the aim of this study was to determine the prevalence of inadequate iron intake and biochemical iron deficiency (anaemia) in young European children aged 6-12 months and 12-36 months.

Methods: Computerised searches for relevant articles were performed in May 2012. Additionally, data gathered by the ‘NutriPlanet tool’ were used, a data collection tool developed by Danone Research that consists of an extensive literature review and interviews with experts in the field of nutrition. The probability approach was used to estimate the prevalence of inadequate iron intake.

Results: A total of 7,279 citations were screened and 46 studies were included in this review. In children aged 6-12 months, most studies showed average intakes around 8-9 mg/d compared to the Recommended Nutrient Intake (RNI) of 11 mg/d, leading to an estimated prevalence of inadequacy of 21% - 44%. In children aged 12-36 months, average iron intakes were close to the RNI of 7 mg/d and the estimated prevalence of inadequacy ranged from below 10% to around 20%.

The prevalence of biochemical iron deficiency varied widely between studies and was influenced by children’s characteristics, such as socioeconomic status and type of milk consumption. Two to 25% of children aged 6-12 months were found to be iron deficient, with a higher prevalence found in those who were socially vulnerable and those drinking mainly cows’ milk. In children aged 12-36 months, reported prevalence rates of iron deficiency varied between 3% and 48%. Prevalence of iron deficiency anaemia in both age groups was found to be especially high in Eastern Europe, up to 50%, whereas the prevalence in Western Europe was generally below 5%.

Conclusion: Average iron intakes are below recommendations in all studies in European infants aged 6 to 12 months, and in the majority of studies in young children aged 12 to 36 months. Iron deficiency is a relatively common nutritional deficiency among young children in many parts of Europe, whereas iron deficiency anaemia is especially common in Eastern Europe. To prevent iron deficiency (anaemia), public health programmes should focus on iron malnutrition, e.g. by educating parents on the importance of iron-rich foods and by iron-fortification of common infant and toddler foods.

A SURVEY OF DIETARY INTAKE IN A COHORT OF RUSSIAN INFANTS AND YOUNG CHILDREN AGED 6-36 MONTHS

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Objectives and Study: Feeding during the early years is important for health in the short and long term. As food habits are established, achieving nutritional adequacy can be challenging. The National Infant Feeding Program in Russia (2009) provided new nutritional recommendations for infants; guidance for feeding the young child has increased in recent years. The aim of this study was to provide contemporary dietary intake in young Russian children aged 6-36 months; these data are currently lacking.

Methods: A regionally diverse cohort (n=2050) based on official birth data was recruited. This was made up of 462 infants 6-12 months, 794 children 12-24 months and 794 children of 24-36 months. Dietary assessment was undertaken by a 3-day estimated diet diary. The field work was undertaken by a clinical research organisation. Dietary analysis was undertaken using a proprietary dietary analysis program.

Results: Dietary intakes were broadly similar to previous Russian national data from the 1990s but it was apparent that feeding practices in infants have improved. The National Infant Feeding Program is likely to have contributed to this. Food intake and nutrient analysis in the young children showed areas of concern. Only 46% of children aged 12-24 months, and 35% aged 24-36 months eat vegetables (other than potatoes) daily. Regular meat intake (≥5 times per week) was seen in only 22% and 20% of children aged 12-24 months and 24-36 months respectively. Intake of “inappropriate” or ‘non-core’ foods including mayonnaise, chips, sausages, soft beverage is high (23-50%). More than 75% of young children eat sweets regularly. This food behavior resulted in lower than recommended intakes of key nutrients. The recommended nutrient intakes (RNI) for calcium, iron, vitamin D were not met for more than half of the young children. Lower than RNI intakes for iron were seen in 78% of children 12-24 months and 7% of children 24-36 months. Comparative analyses of consumers of iron fortified foods versus non-users showed that these food contributed 17-35% of daily iron intakes in the young children. The BMI of 10% children 12-24 months is higher than 97th percentile. Less than 30% mothers expressed a concern about their child’s diet.

Conclusion: Apparently low intakes of iron, calcium and vitamins D, and excessive salt are the main nutritional issue in this Russian cohort of young children. This study suggests a role for fortified foods for improving iron intake. Education program for parents appear important to improve the dietary practices and more work is required for this for children over 12 months.

Disclosure of Interest: A. Surzhik Employee of: sponsor , T. Borovik: None Declared, I. Zakharova: None Declared
LONG-TERM GROWTH IN SHORT BOWEL SYNDROME
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Objectives and Study: It is our impression that children with short bowel syndrome and previous dependence on long-term (> 27 days) parenteral nutrition frequently have poor growth when weaned from parenteral nutrition support. The aim of this study was to review the long-term growth and weight gain of these children from at least six months after weaning from parenteral nutrition (PN).

Methods: Case notes were reviewed of all children with short bowel syndrome who had been dependent on parenteral nutrition for at least 28 days after surgical resection (or birth if congenital short bowel) and who had weaned off parenteral nutrition for at least six months. The records of all patients who had presented over a 10-year period since 2001 were selected. Clinical details recorded included age, sex and aetiology of short bowel syndrome. Anthropometric details recorded were height, weight and BMI. Growth measurements used were for the UK-WHO growth charts. Short stature was defined as height for age below 2nd centile.

Results: 21 children aged 1-15 (mean 5.8) years, 13 male, were identified from medical records of 102 patients treated for SBS and had been reviewed in the previous few weeks. Selected patients either had congenital short bowel, n=2 or underwent small intestinal resection n=19. Diagnoses were necrotising enterocolitis in 11 cases, intestinal atresia in 5, volvulus in 3, and gastroschisis in 2 cases. Mean length of remaining small intestine was 49cm (range 18-120 cm). the ileo-caecal valve had been excised in 12 cases.
Patients had been dependent on PN for 10 weeks -12.8 years, median 1.8 years. Median time since weaning from PN was 2 (0.5-9.5) years, and follow up 2 (0.5-9.5) years.
Twelve or 57% cases had weight below the 2nd centile with four cases or 19% below the 0.4th centile.
Ten of 21 patients or 48% had short stature i.e. height below 2nd centile. In six cases or 29% height was less than the 0.4th centile.
The BMI was in the normal range for 20 of the 21 children, or 95% according to the UK-WHO growth chart.

Conclusion: Short stature is common in children with short bowel syndrome affecting about 50% of all cases requiring parenteral nutrition for more than 28 days. It does not appear to be secondary to a poor nutritional state since BMI was in the normal range.
It is essential that children with short bowel syndrome and previous dependence on 'long-term parenteral nutrition have long-term follow-up in a specialist gastroenterology clinic to ensure full growth potential is achieved.

Disclosure of Interest: None Declared
PO-N-0292

LONGTERM OUTCOME OF PAEDIATRIC INTESTINAL FAILURE: TWO DECADES OF AUSTRALIAN AND GLOBAL EXPERIENCE
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Objectives and Study: To describe the clinical outcome of children with long-term intestinal failure (IF) recruited in the 19-year-old Victorian Home Parenteral Nutrition (HPN) program at the Royal Children's Hospital, Melbourne and compare this data with international long-term pediatric intestinal failure literature.

Methods: Retrospective medical record review and analysis of all children with primary IF assessed for HPN between 1992 and 2010. Results reported in context of previously published long term follow up studies of pediatric intestinal failure.

Results: 51 patients were identified. Diagnoses included 42 short bowel syndrome (SBS), 5 chronic intestinal pseudo-obstruction syndrome (CIPOS), and 4 congenital enteropathies. Survival probabilities at 1, 2, 3, 5, and 10 years were 94%, 88%, 86%, 86%, and 86%, respectively; probabilities of PN dependency at 1, 2, 3, 5, and 10 years were 67%, 60%, 49%, 38%, and 29%, respectively. 26 (51%) patients had HPN.
Predictors for PN weaning in SBS were small bowel length (SBL) (hazard ratio [HR] 1.21 for every 10% increase in length, p=0.026) and presence of ileoceleal valve (ICV) (HR 2.87, p=0.015). The minimum anatomy for SBS patients who weaned PN was 4% SBL (~6cm at Gestational Age 35 weeks (GA35)) with ICV and 12% SBL (~17cm at GA35) without ICV.
Central Venous Access Devices (CVAD) lasted for a median of 117 days (mean 561 days ≈ 18.4 months). Overall sepsis rate was 8.13 episodes per 1000 CVAD days with large variations in sepsis rates for individual patients ranging from 0-24.8 episodes per 1000 CVAD days. Frequency of catheter-related bloodstream infection (CRBSI) and loss of vascular access decreased with increasing PN duration and age, and HPN (all p<0.001); SBS patients had higher CRBSI rates (p<0.001).
59% of children developed intestinal failure associated liver disease (IFALD) based on LFT and liver biopsy with 23% of these patients went onto develop end-stage liver failure. IFALD was associated with prematurity (p=0.014) and sepsis (p=0.018); and SBS patients had more severe IFALD (p=0.008). IFALD was the only significant predictor of mortality.

Conclusion: This Australian study reports a high survival rate of long term paediatric PN of 84% over 19 years. Potential for PN weaning was higher in SBS than in non-surgical causes of IF. SBL, ICV and colon are important factors for PN weaning in SBS. Our results shall be presented in the context of current international literature.

Disclosure of Interest: None Declared
DIETARY PATTERNS AND NUTRIENT INTAKES OF PRESCHOOL CHILDREN WITH PICKY-EATING BEHAVIORS
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Objectives and Study: Picky eating behaviors are common in preschool children. Picky eaters (PEs) typically consume a limited food variety and resist trying new foods. These eating behaviors may be associated with a dietary pattern lacking in nutrients and an increased likelihood of being underweight. Conversely, PEs who prefer sweets and/or fatty foods may be at an increased risk of obesity. The objective of this study was to identify the dietary patterns and nutrient intakes of preschoolers in China and Hong Kong (HK) with picky-eating behaviors and compare their intakes to HK Food Pyramid (FP) and Chinese Recommended Nutrient Intake (RNI).

Methods: Data were analyzed from baseline 3-day food records of participants in a multicentre, randomized controlled trial of a nutritionally balanced milk formula among 153 preschoolers aged 3.8 ± 0.7 years who were described by parents as PEs and with weight-for-height ≤25th percentile. The Nutrition Data System Research database was used for diet analysis.

Results: Median daily energy intake was 996 kcal, while the corresponding age-specific Chinese RNI is 1300-1450 kcal. Energy contribution patterns were consistent with FP recommendations with grains and cereals providing the largest proportion of daily energy (32.6%); whereas, meat, poultry, fish, shrimp, eggs and dry beans combined and dairy products provided 22.6% and 19.1% of daily kcals, respectively. Despite the FP recommendation to “eat less”, sweets provided 10.0% and fats and oils contributed 6.2% of daily energy intakes. A small percentage of PEs consumed FP recommended daily serving amounts: 2.1% for grains and cereals, 7.0% for vegetables, 6.3% for dairy products, 20.3% for meat and alternatives and 46.9% for fruits. The median nutrient intake of PEs, as a percentage of the Chinese RNI were calcium 62.5%; iron 62.6%; zinc 52.4%; vitamins A 81.7%; C 59.7%; and D 37.1%. The mean (SD) daily intake of dairy products was 231.0 ± 285.6g, which is less than half of the FP recommended intake. Fiber intake was only 7.3 ± 3.5g/day.

Conclusion: In China and Hong Kong, PEs were more likely to consume a dietary pattern with less than the recommended amounts of all major food groups, but more sweets and fats, which may increase the risk of inadequate intake of energy, nutrients and fiber. Further research is needed to characterize the eating habits of preschoolers with PE behaviors.

Disclosure of Interest: None Declared
SURVEY OF DENTAL HEALTH IN CHILDREN WHO ARE ON HOME PARENTERAL NUTRITION

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Objectives and Study: Administration of Home Parenteral Nutrition (HPN) in adults is known to be associated with poor oral health¹. Little is known about the incidence of dental problems in children who are on long term home parenteral nutrition. The aim of the study is to determine the presence of dental problems in children who are on long term home parenteral nutrition.

Methods: Long term HPN was defined as administration of HPN for a period of more than 3 months. Information about the duration of PN, methods of enteral feeding, breast and bottle feeding in infancy, frequency of dental visits, dental problems, frequency of brushing and use of tooth paste were collected by emails, questionnaires and telephone consultations.

Results: Dental health on twenty five children who were on HPN were analysed. The age group of study population was 1-18 years with a median age of 5.5. The average duration of PN administration was 4.3 years. Just under half had oral feeding concomitantly. 76% of patients have had breast and bottle feeding in infancy. 56% of children reported dental problems. 28% had teeth staining, 8% had gum infection, 16% had teeth decay and delayed dentition. 96% of children brushed regularly and 68% reported using tooth paste. 64% visited dentist on 2-12 monthly intervals.

60% of adults on HPN are reported to have problems with oral health¹. In England, 41-54% of children have tooth decay and 67% of children have non carious dental condition³. Micronutrient supplementation is known to improve oral inflammation⁴. Children on HPN are regularly monitored and supplemented with micronutrients and thereby deficiency is uncommon in them. This also could possibly explain the lesser incidence of dental problems on children who are on HPN.

Conclusion: Children on HPN have better dental health when compared to England’s national statistics on children and adults on HPN.

Children’s dental health in England 2003

Disclosure of Interest: None Declared
INTAKE OF FISH AND SUPPLEMENTS IN PRE-PREGNANT AND PREGNANT SLOVENIAN WOMEN
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Objectives and Study: Women of child bearing age should aim to achieve an average dietary intake of at least 200 mg docosahexaenoic acid (DHA)/day (1). We studied the DHA intake in pre-pregnant and pregnant Slovenian women from dietary intake and omega-3 supplements (fish oil and other supplements (capsules or tablets), all containing DHA) in association with socio-demographic variables. We also studied the intake of other supplements (folic acid and mineral/vitamin supplements).

Methods: Pregnant women (n = 270) aged (mean (SD)) 30.6 (4.2) years in the 32nd (3) week of pregnancy from three regions (Ljubljana, Nova Gorica and Maribor) were included from May 2011 till October 2012. Dietary habits one year before and during pregnancy were evaluated by food frequency questionnaire, containing 31 food items grouped into four categories (fish: marine fish, seafood, fish products and freshwater fish) and supplements (omega-3, folic acid and other mineral/vitamin supplements). The following statistical methods were used: t-test for paired samples, ANOVA, and Fisher exact test. The study was approved by the Slovenian Ethics Committee and is part of the project entitled “My-Milk” (http://www.moje-mleko.si/en/; registered at ClinicalTrials.gov as NCT01548313).

Results: The consumption of one or more meals of fish and fish products per week before and during pregnancy, reported 68.9% and 62.3% of women. Women consumed more DHA from fish before than during pregnancy (mean (S.E.)) (194.9 (11.2) vs. 165.4 (10.0) mg DHA/day (p<0.05). Pregnant women consumed on average (mean (S.E.)) 80.8 (5.8) mg DHA/day with omega-3 supplements. The dietary DHA intake before and during pregnancy was not correlated either with education either with geographical region either with age. The intake of one or more dietary supplements during pregnancy reported 94.7% of women. The supplement intake was not correlated with the education or age. The most commonly used supplements were mineral/vitamin supplements (94.4%), folic acid (91.7%) and omega-3 supplements (35.9%).

Conclusion: The consumption of DHA in Slovenian pregnant women meets the recommended value (mean (S.E.)) (246.2 (11.6) vs. at least 200 mg DHA/day) due to consumption of omega-3 supplements additionally to fish. Encouragements to increase the DHA intake from fish during pregnancy would be of benefit.

Disclosure: Study was supported by the Slovenian Research Agency (Research Project N° J4-3606).


Disclosure of Interest: None Declared
SAFETY AND EFFICACY OF TWO FORMS OF PARENTERAL IRON IN CHILDREN – REGIONAL EXPERIENCE
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Objectives and Study: Iron deficiency anaemia is a common finding in gastroenterology patients as a result of dietary insufficiency, malabsorption and occult or overt gastrointestinal bleeding. Due to poor tolerance of oral iron supplementation some patients require parenteral administration. There is limited experience with use of parenteral iron in the paediatric population with gastrointestinal disease.

To evaluate two centres’ experiences of safety and efficacy of IV Iron hydroxide dextran complex (Cosmofer®) and IV Iron isomaltoside 1000 (Monofer®) at 8-12 weeks after treatment in children with gastroenterological conditions.

Methods: Children (< 16 years) received Cosmofer® at centre 1 and Monofer®at centre 2 over a two year period. Data abstracted included primary indication, underlying diagnoses, dosing and administration, laboratory values before and after therapy, and adverse reactions. The decision for parenteral iron was made on an individual basis. The total iron deficit was calculated using the Ganzoni formula in both groups with maximum dose of 20mg iron/kg as single infusion in the Monofer® group. In the Cosmofer® group, doses were split and a test dose over 1 hour given prior to infusion over 5 hours. Monofer® is a rapid one-visit total dose intravenous iron preparation that can be given over 1 hour without test dose. The main indication in both groups was malabsorption from short gut, and inflammatory bowel disease. There is no difference in licensing between either of the preparations except Cosmofer® licensed for > 14 years and Monofer® for >18 years old.

Results: There were 13 infusions of Cosmofer® (11 children) and 9 of Monofer® (8 children). The groups (Chart) were comparable except the Cosmofer® group smaller in age/wt. and received less iron. Mann Whitney test was used to evaluate statistical difference for pre and post haemoglobin rise in both groups (p<0.01). One patient from each group experienced allergic reaction within few minutes of infusion but made fully recovery. There were no delayed effects reported on follow up.

<table>
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<th>Cosmofer</th>
<th>Monofer</th>
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<tbody>
<tr>
<td>No. of children</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>% Male</td>
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</tr>
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<td>Age in years Median</td>
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<td>12.3 (5.58-14.5)</td>
</tr>
<tr>
<td>Weight kg Median</td>
<td>19 (6.36-37)</td>
<td>32.9 (18.7-56.4)</td>
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<tr>
<td>Increase from baseline in Hb and MCV (8-12 weeks)</td>
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</tr>
<tr>
<td>Hb (g/dl) Median</td>
<td>2.35 (0 to 5.5)</td>
<td>3.65 (0.1 to 5.7)</td>
</tr>
<tr>
<td>MCV (fl) Median</td>
<td>4.5 (-4 to 17)</td>
<td>7.9 (-1.3 to 17.2)</td>
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Conclusion: In children with gastrointestinal disease who are intolerant of oral iron, parenteral therapy is effective in correcting anaemia. The best formulation of parenteral iron is uncertain, and serious allergic reactions were observed with both preparations used. Monofer offers the potential advantage of a single, rapid infusion and simple dose calculation.

Disclosure of Interest: None Declared
IS GENDER A RELEVANT FACTOR MODIFYING THE POLYUNSATURATED FATTY ACID COMPOSITION OF SERUM AND ERYTHROCYTE MEMBRANE LIPIDS IN ALL AGE GROUPS?

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Objectives and Study: To systematically review published data on the role of gender in determining the fatty acid composition of different biomarkers reflecting fatty acid status.

Methods: The MEDLINE, Scopus and Cochrane Library CENTRAL databases were searched for trials showing fatty acid compositional data separately in both genders. There was no age limitation; the minimal number of participants was set at fourteen. We used formal inclusion/exclusion criteria and applied standard operation procedures for data extraction and meta-analysis.

Results: We evaluated 51 publications, dated from 1975 to 2011. Only one study was carried out in children before puberty and two studies investigated children older than 12 years of age. Meta-analysis showed significantly lower values of both arachidonic acid and docosahexaenoic acid in total plasma lipids (32 and 33 studies) and in plasma phospholipids (21 and 23 studies) in men than in women. Primary analysis of the phospholipid fraction showed the mean difference in arachidonic acid to be 0.42% weight/weight (95% CI: 0.18% to 0.65%, n = 7769) and in docosahexaenoic acid to be 0.37% weight/weight (95% CI: 0.24% to 0.51%, n = 8541), while in the values of LA and ALA there was no gender difference.

There were not enough studies to perform a meta-analysis in the age group 0-12 years. Results of studies carried out in children are controversial.

Conclusion: 1. Gender distribution should be regarded as significant potential confounding factor in every study investigating fatty acid compositional data in adults. 2. Though similar consideration might be true also for children, at the moment there is no evidence making it imperative to divide the pediatric participants of fatty acid supplementation studies into boys and girls.

Disclosure of Interest: None Declared
Objectives and Study: To compare the outcomes and complications between Percutaneous Endoscopic Gastrostomy (PEG), Laparoscopic Gastrostomy (LAPG) and open gastrostomy (OG) in children.

Methods: Retrospective review of 369 patients from July 1998 to December 2010 who had their gastrostomies inserted at a single tertiary institution. Patients who were lost in follow-up were excluded from this study.

Results: Out of 369 patients, 260 patients underwent LAPG, 86 PEG and 23 open gastrostomy (OG) procedures. The PEG and LAPG groups were comparable for age, gender and indication for insertion. The early complication rate for PEGs was 10.5%, and 2.7% for LAPGs (p=0.006). The late complication rate was 41.9% for PEGs and 43.1% for LAPGs, (p=NS). The overall complication rate for PEG was 54.7% and it was 44.6% for LAPG (p=NS). Major complications occurred only in the PEG group; gastro-colonic fistula (2), peritonitis (1), and “buried bumper syndrome (1)”. The overall complication rate for OG was 78.3% (p =0.01, when this was compared to LAPGs and PEGs together). There were no early complications in the OG.

Conclusion: The findings support current literature that PEGs have a higher overall complication rate than LAPGs, although the difference was not statistically significant. PEGs also had a significantly higher early complication rate than LAPGs and the only major complications occurred in the PEG group. Both PEGs and LAPGs were significantly superior to OG in terms of complication rates. Data from future prospective studies is needed to corroborate the findings.

Disclosure of Interest: None Declared
MATERNAL SUPPLEMENTATION WITH FISH OIL AND VISUAL DEVELOPMENT OF CHILDREN: DIFFERENTIAL EFFECT DEPENDING ON GENDER

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Objectives and Study: Docosahexaenoic acid (DHA) has putative roles that relate to visual function, including signal transduction and neurotransmission, therefore, DHA deficiency during pregnancy could be related to delay in the cognitive and visual development. However, many controversies can be found in the scientific literature regarding visual acuity and DHA supplementation and they can be attributed to the multiple factors and different conditions of the studies such as gestational age, mother’s diet, timing, way of the supplementation, and newborn’s sex. The aim of the current study was to elucidate the effect of DHA supplementation on visual development of the newborn, taking into account the gender of infants.

Methods: 80 women were randomly assigned to one of the following intervention groups: A) Control Group (n=40): They received 2 glasses/day of the control dairy drink, and B) Supplemented Group (n=40): The women received 2 glasses/day of the fish-oil supplemented dairy drink (400mg DHA/day). Dietary intervention began in the sixth month of pregnancy and concluded at the end of breastfeeding. During all this time women from both groups received a controlled diet under the supervision of a dietician. At 2.5 and 7.5 months of life of infants (n=54), pattern-reversal visual evoked potentials (VEPs) were measured at different angles (2°, 1°, 30’, 15’, 7.5’). The results are expressed as latency (P1, in miliseconds).

Results: There were no differences between groups in latency. However, when only boys (n=27) were considered, latency at 7.5 months was significantly lower in group B (P<0.05 at 7.5’). In addition, when considered just the supplemented group (n=28), latency at 7.5 months was significantly lower in boys compared to girls (P<0.05 at 15’ and also at 7.5’).

Conclusion: The effects of a dairy drink enriched in DHA on visual development of children depend on the gender being more evident in boys than in girls. More studies are needed to further elucidate these differences and the mechanisms involved.

MODE OF IRON ADMINISTRATION DOES NOT AFFECT IRON ABSORPTION IN HEALTHY, SWEDISH INFANTS

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Objectives and Study: Iron supplements and iron fortification of formula and cereals have reduced the prevalence of iron deficiency during infancy (1). Providing iron supplements to iron-replete infants may have adverse effects on growth (2). We have observed that iron given as drops significantly increased serum ferritin but not haemoglobin (Hb) concentrations, whereas the same amount of iron given in fortified foods resulted in a significant increase in Hb, but not in S-ferritin (3). We therefore investigated if the mode of iron administration (supplementation vs. fortification) and the amount consumed (high vs. low intake) affects iron absorption or utilization in iron-replete 6 mo-old infants.

Methods: Healthy, full-term, predominantly formula-fed infants (n=72) were randomized at 6.1±0.3 mo of age to: high-iron infant formula (HI: total iron intake 6.6 mg/d), low-iron formula (LI: total iron intake 1.3 mg/d) or iron drops and formula with no added iron (DI: total iron intake 6.6 mg/d) for a total of 45 days. Iron absorption was measured using stable isotopes (57Fe-labeled formula or iron drops, 58Fe given intravenously) (4).

Results: At baseline, S-ferritin, S-Fe and S-transferrin were similar in all three groups. However, Hb was significantly higher in the DI group compared to the HI group (p=0.039). The change in Hb until day 45 did not differ significantly between groups (p=0.058). At day 45 S-ferritin was significantly lower and there was a significant decrease in S-ferritin from baseline to day 45 in the LI group compared to the other 2 groups (p=0.020 and p=0.018, respectively). The geometric mean iron absorption was 6.8% for the HI group, 7.4% for the LI group and 7.7% for the DI group. There were no significant group differences in the iron absorption or Hb incorporation.

Conclusion: These preliminary data show no difference in either absorption or incorporation of iron, whether given as iron-fortified infant formula or as iron drops. Low-iron formula (2.3 mg ferrous sulphate/L) was insufficient to maintain iron stores in these healthy 6 mo-old infants.


Disclosure of Interest: None Declared
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DIETARY GANGLIOSIDE CONSUMPTION INCREASES MONOUNSATURATED GANGLIOSIDES GM3 AND GD3 IN HUMAN PLASMA

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Objectives and Study: Gangliosides are glycolipids that influence epithelial cell properties including cell signaling and infectivity of micro-organisms. For example, ganglioside decreases pathogenicity of E. coli and Giardia lamblia. Endogenous production of ganglioside is accomplished by tissues and small amounts of ganglioside are also available from dietary sources. Ganglioside attenuates inflammatory signaling cascades in acute inflammation of the bowel and thus perhaps in disorders like Crohn’s disease and ulcerative colitis. The uptake of ganglioside has been described in human intestinal epithelial cells and infant intestinal epithelium. Uptake of ganglioside has also been demonstrated in animal tissues including intestine, retina, brain and plasma. Previous literature has reported the ganglioside profile of human plasma, but little is known about uptake of ganglioside from diet. Compositional data regarding the fatty acid tail of gangliosides is also lacking. In the present study, the composition of ganglioside species in human plasma is presented in response to ganglioside feeding.

Methods: Subjects consumed one gram of a ganglioside-enriched milk fraction containing GD3 and GM3 daily for eight weeks. Fasting blood samples were drawn at baseline and weeks two, four, six, and eight. Plasma was collected and subjected to a Folch extraction to isolate gangliosides. Extracts were injected onto a C18 column where gangliosides were separated by reverse-phase chromatography prior to detection using an Agilent 6430 triple-Quad LC/MS operated in multiple reaction monitoring mode. The cells were screened against a database of 120 mono-, di- and trisialylated gangliosides.

Results: Plasma level of monounsaturated GM3 was higher at week eight than at baseline in subjects that consumed ganglioside. Average level of monounsaturated GM3 increased by about 8% between baseline and week eight. Plasma level of monounsaturated ganglioside GD3 increased at each time point throughout the study until peaking at week six. The average increase in monounsaturated GD3 among subjects that consumed ganglioside between baseline and week eight was approximately 49% (p < 0.05).

Conclusion: This study demonstrates bioavailability of dietary ganglioside. Consumption of ganglioside increases ganglioside detection in human plasma suggesting that oral intake of ganglioside could be used to alter inflammatory processes.

Disclosure of Interest: None Declared
THE PREDICTIVE VALUE OF ELF TEST IN PATIENTS WITH BILIARY ATRESIA
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Objectives and Study: Biliary Atresia (BA) is the commonest cause of serious liver disease in childhood. The primary treatment is surgical with the Kasai procedure. Where this is successful in clearing jaundice most children will subsequently survive without transplant into adult life. Where the Kasai procedure is unsuccessful, the only treatment is liver transplantation. There is a need for non invasive test to predict prognosis in individuals with BA. The extended liver fibrosis (ELF) test has been widely validated for staging hepatic fibrosis in adult patients and in some sub-groups of paediatric liver disease. Our aim was to determine whether serial changes in the ELF test or its components are predictive of long term outcome (and therefore survival with/without transplant) following the Kasai procedure.

Methods: 39 patients with BA presenting to a single centre between 2007 and 2011. ELF and its components were measured at time of Kasai (baseline), 3 months later and at 1 year. At baseline liver biopsy was performed, and analysed by degree of fibrosis as well as ISHAK score. Outcome was classified as survival with or without transplantation at 18 months.

Statistics used were multivariate and univariate logistic regression.

Results: All are alive and 13 have undergone transplant at age <18 months. At baseline the only factor predictive of requiring transplantation was age at surgery (p=0.048). None of ELF, its components or baseline bilirubin were predictive of outcome.

At 3 months bilirubin level, ELF and 2 of its components (Hyaluronic acid and TIMP1) were predictive of outcome. Following multivariate analysis bilirubin was the only significant predictive factor (p=0.001).

In those surviving without transplant there was a significant fall in ELF from baseline mean of 12.16 to 10.65 and p<0.005.

Conclusion: In biliary atresia: ELF at the time of Kasai is not predictive of early outcome. ELF at three months post Kasai is predictive of early outcome but does not improve on conventional measures. ELF levels fall significantly following successful Kasai.

Serial ELF measurements have prognostic value for the early outcome of biliary atresia. Longitudinal studies of serial ELF measurements in biliary atresia are necessary.

Disclosure of Interest: None Declared
Objectives and Study: Transient elastography (Fibroscan) has been approved as a non-invasive novel method for measurement of hepatic fibrosis easily applied in variety of chronic liver disease such as biliary atresia. A few years ago, TE probe for children (S1, S2 probe) was introduced instead of for adults (M probe). We prospectively investigated the feasibility and reliability of S probe in a single disease (biliary atresia) compared with M probe.

Methods: One hundred biliary atresia patients were enrolled in this study. Three liver stiffness measurement (LSM) values were obtained in every each patient using S1, S2 and M probe. Patients were divided into two groups as small (≤45cm) and large (>45cm) thorax perimeter groups. The 3 probes were statistically compared in each other and the relation between LSM values and AST to platelet ratio index (APRI) were analyzed.

Results: In ≤45cm group, inter-class correlation coefficient (ICC) was highest between S1 probe and S2 probe (S1 and S2: 0.979, S1 and M: 0.769, S2 and M: 0.824). On the other hand, ICC was highest between S2 and M in >45cm group (S1 and S2: 0.767, S1 and M: 0.636, S2 and M: 0.895). The LSM measured by S1, S2, M was 20.66±17.88kPa, 15.15±12.61kPa, 12.37±10.13kPa respectively and showed significant difference each and all. Correlation coefficient between ARPI and LSM of S1,S2 and M probe in ≤45cm group was 0.646, 0.638, 0.493 respectively and 0.677, 0.630, 0.616 respectively in >45cm group.

Conclusion: Although there is a tendency of overestimation of LSM, S probe could be applied usefully in monitoring hepatic fibrosis in pediatric biliary atresia patients. The standardization of LSM values measured with each prove is needed.

Disclosure of Interest: None Declared
THE ROLE AND SIGNIFICANCE OF PHOSPHORYLATED MYOSIN REGULATORY LIGHT CHAIN IN SMOOTH MUSCLE OF THE COMMON BILE DUCT IN PANCREATICOBIILIARY MALJUNCTION ACCOMPANIED BY BILE DUCT DILATATION IN CHILDREN
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Objectives and Study: In this study, we examined the content of phosphorylated myosin regulatory light chain (P-MLC20) and myosin light-chain kinase (MLCK) in the smooth muscle of the common bile duct of pediatric patients with pancreaticobiliary maljunction (PBM) and bile duct dilatation (BDD), and provided evidence for their potential role in regulating the pressure of the common bile duct in PBM patients.

Methods: Twenty-one specimens of the common bile duct from pediatric patients with PBM and BDD were collected. P-MLC20 was examined with immunohistochemistry. The expression of P-MLC20 and MLCK was also examined with Western blot. Twenty-one specimens of the common bile duct from pediatric patients without PBM and BDD were used as controls.

Results: In the PBM group, the mean optical density (MOD), mean labeling intensity (MLI) and minimum qualifying scores (MQS) of P-MLC20 were 115.6856 ± 58.1634, 21.7125% ± 9.6555 and 21.3531 ± 6.5255, respectively. In the control group, MOD, MLI and MQS were 96.5581 ± 9.7859, 11.1813% ± 3.6208 and 10.7819 ± 3.5323, respectively. There was no significant difference of MOD between the two groups (P>0.05), whereas there was a significant difference in MLI and MQS between the two groups (P<0.05). The expression of P-MLC20 and MLCK, as determined with Western blot, was also significantly higher in the PBM group than that in the control group (P<0.05).

Conclusion: P-MLC20 is associated with increased contractile force of the smooth muscle of the common bile duct in pediatric patients with PBM and BDD. The enhanced expression of P-MLC20 probably operates in the smooth muscle of the common bile duct of pediatric patients with PBM and BDD via by the MLCK pathway.

Disclosure of Interest: None Declared
MIR-200B IS A POTENTIAL MAKER FOR MONITORING PROGRESSION OF LIVER FIBROSIS IN BILIARY ATRESIA
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Objectives and Study: Biliary atresia (BA) is an infantile obstructive cholangiopathy that characterized by obliteration or fibro-obliteration and obstruction of the extrahepatic biliary system. This disease affects approximately 1 of 17,000-19,000 live births in Europe. Liver fibrosis is regarded as a major contributor of morbidity and mortality in biliary atresia (BA). Owing to poor understanding of the mechanisms that involved in progression of liver fibrosis in BA, there are no defined-diagnostic marker and effective antifibrotic therapies currently. Here, we are going to investigate that expression and possible function of miR-200b in the liver fibrosis of BA.

Methods: Histological and Masson's trichrome staining staining studies were used to determine the grades of liver fibrosis. Real time-PCR was performed to analyze the level of miR-200b in the liver tissues of BA. Transforming growth factor-β1 (TGF-β1) was used to activate LX-2 cells prior to transect with miR-200b mimics/inhibitors.

Results: A total of 18 children were enrolled in this study, who were clinically diagnosed as biliary atresia (BA). The grades of liver fibrosis were classified into I,II,III and IV according to masson's trichrome staining. After determined the amounts of miR-200b in BA, we found that expression of miR-200b was strongly elevated in fibrotic liver of BA and significantly correlated with progression of liver fibrosis. Furthermore, we demonstrated miR-200b not only inhibited significantly growth of HSCs, but also attenuated expression of alpha-smooth muscle actin (α-SMA).

Conclusion: This study suggested that miR-200b have potential values for monitor the progression of liver fibrosis in BA.

Disclosure of Interest: None Declared
HEPATOLOGY

PO-H-0306

ASSESSMENT OF RISK OF BLEEDING FROM ESOPHAGEAL VARICES DURING MANAGEMENT OF BILIARY ATRESIA IN CHILD
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Objectives and Study: The management of esophageal varices (EV) in children suffering from biliary atresia (BA) remains controversial. Recent studies in children proposed initiating a prophylactic treatment in patients with severe (Grade III) EV and/or EV associated with red color signs. Our study was aimed at assessing the risk of bleeding from EV in a series of BA patients, identifying risk factors for bleeding in order to develop a predictive model of bleeding.

Methods: This was a retrospective study including 83 eligible BA patients. Clinical, ultrasonographic, endoscopic, and laboratory parameters were studied from the beginning of medical management up to the occurrence of upper gastrointestinal bleeding. In patients not presenting any bleeding, data were analyzed until liver transplantation, endoscopic treatment of EV was performed or last follow up. Risk factors were investigated using univariate and multivariate statistical analyses. Methodology was originally based on machine learning and "ensemble" feature selection methods. We therefore builded a large number of models (10,000) using randomly constituted sub-cohorts of patients. This ensemble approach is highly robust and generally offers good predictive performance.

Results: Out of 80 available endoscopic data patients, 73(91%) developed EV, of which 31% were Grade I, 37% were Grade II, and 23% were Grade III. Red color signs were observed in 27% of patients and hypertensive gastritis in 62%. There were a total of 7% gastro-esophageal varices and 2% isolated gastric varices. Seventeen out of 83 patients (20%) presented gastrointestinal bleeding, with a median age of 9.5 months (6-50 months). All bleeding was treated endoscopically using variceal ligation in five patients and sclerotherapy in 12 patients of less than 7 months of age.

In univariate and multivariate analyses, high-grade EV, red color signs on endoscopic examination, and low fibrinogen levels, at first endoscopy, were identified as risk factors for bleeding. When tested in more than 10,000 different models, these three variables appeared to play the most significant role in predicting bleeding.

Conclusion: Our study confirmed that grade III EV and red color signs are risk factors for bleeding in patients followed up for BA. We identified low fibrinogen levels as an additional risk factor. The relevance of these three factors to predict bleeding from EV requires validation in a prospective study. These prospective studies must also include analysis of fibrinogen supplementation impact on variceal bleeding risk.

Disclosure of Interest: None Declared
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PRIMARY SCLEROSING CHOLANGITIS IN CHILDREN: A RETROSPECTIVE REVIEW OF TWO ITALIAN CENTERS.
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Objectives and Study: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and progressive bile duct fibrosis. There are few data on pediatric PSC. The aim of this study was to characterize a pediatric population with PSC.

Methods: We performed a retrospective chart review of 30 pediatric patients (pts) with PSC, followed in two Italian centers (Policlinico Umberto I of Rome and University Federico II of Naples) between 1994 to 2012. PSC was diagnosed according to the criteria reported by Lazaridis et al, including the presence of typical abnormal bile ducts at cholangiography (MRCP), compatible biochemical findings and/or histologic features.

Results: The mean age at diagnosis was 8.6±4.8 years. At presentation 17 pts (56%) were asymptomatic and PSC was suspected based on abnormal liver test detected during routine medical evaluation (31%) or routine screening in 6 pts (35%) with IBD; 3 pts presented hepatomegaly and 2 pruritus. IBD was found in 11 pts (36%): 9 ulcerative colitis (UC) and 2 unclassified inflammatory bowel disease (IBDU). Diagnosis of IBD was contemporary, previous or following in 6, 2 and 3 pts respectively. Other associated diseases were overlap syndrome/autoimmune hepatitis (AIH) in 4 pts, mental retardation and Graves’ disease in 1 pt. 4 pts without histologic features of AIH had positive autoimmune markers and responded to UDCA monotherapy. MRCP revealed both extrahepatic and intrahepatic, isolated intrahepatic and no biliary involvement (small duct PSC) in 11 (36%), 12 (40%) and 5 (16%) pts, respectively. Liver biopsy, performed in 18 pts (60%), showed histologic features of PSC and moderate fibrosis in 5 pts, advanced fibrosis in 12 pts, micronodular cirrhosis in 1 pt. In 4 pts there was also interface hepatitis. 4 pts (13%) had also portal hypertension. All pts were treated with UDCA; 7 pts also received immunosuppressants. The median follow-up was 93 months (range 24-144 months). None of pts required liver transplantation. 2 pts performed colectomy and 1 of these presented pouchitis.

Conclusion: In our study, most of children with PSC asymptomatic at presentation had advanced fibrosis. All pts had biochemical evidence of biliary disease (increased serum GGT and/or ALT) and radiologic findings typical of PSC. IBD was present at the diagnosis of PSC in 20% of pts, mostly UC. Small duct PSC was observed in 16% of cases. As reported in the literature, pediatric PSC involves the intrahepatic bile ducts and incidence of overlap syndrome with AIH is higher than in adults. Levels of transaminasis normalized after therapy with UDCA in all pts; in 1 pts nonadherent to therapy, liver enzymes increased.


Disclosure of Interest: None Declared
ALAGILLE SYNDROME IN POLISH PATIENTS – CLINICAL FEATURES

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Objectives and Study: Alagille syndrome (AGS) is a multiorgan disease inherited in an autosomal dominant pattern with a diverse expression of symptoms. There are five major features of the disease: chronic cholestasis, characteristic facial features, cardiovascular abnormalities, ophthalmologic anomalies and skeleton defects. These are often accompanied by other minor features, such as renal and extracardiac vascular problems, growth retardation and hypercholesterolemia. The frequency of major and minor symptoms presented in different publications varies significantly (Alagille et al. 1987; Emerick et al. 1999, Subramaniam et al. 2010). The aim of our study was to estimate frequency of major and minor features in our patients with AGS.

Methods: A retrospective review of clinical data of 50 patients with AGS was performed. Median follow up time was 11.7 ± 5.8 years.

Results: Cholestasis was present (by definition) in all cases (100%). Neonatal cholestasis, as the first symptom of AGS, was observed in all but seven cases (86%). In the remaining seven children, biochemical cholestasis was revealed after the cardiological diagnosis. The characteristic for AGS cardiac abnormalities were found in 80% (40/50). The eye anomalies - posterior embryotoxon or retinopathy - were present in 90% (45/50). Butterfly vertebrae were diagnosed in 49% (23/47). Characteristic facial features were present in 100% (50/50). Among minor symptoms, growth retardation was found in 86% (31/36) and hypercholesterolemia in 87% (41/47) of patients. Additionally, in 10 patients renal problems were diagnosed and in five - extracardiac vascular abnormalities were found.

Conclusion: The incidence of major AGS features in the examined group falls within the results reported by foreign specialists. Our data are most compatible with these of Emerick et al. (1999). The high incidence of embryotoxon posterior in our group makes this feature especially important in the diagnostic process. The diagnostics of renal and extracardiac vascular abnormalities require more attention as they may seriously affect the course of the disease.

Disclosure of Interest: None Declared
BILIARY TRACT AND LIVER ULTRASONOGRAPHIC FEATURES: IMPLICATIONS FOR DIAGNOSIS OF BILIARY ATRESIA IN INFANTS.
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Objectives and Study: Biliary atresia (BA) is characterised by progressive fibro-obliteration and obstruction of the extrahepatic biliary tree. It is the most common neonatal cholestatic disorder, occurring in approximately 1 of 18000 (European countries) live births and is the main indication for liver transplantation in paediatric age (1). Diagnosis of BA is challenging because no single diagnostic test, short of laparotomy, is diagnostic. Numerous ultrasonographic (US) features have been described as useful pointers to the diagnosis of BA, such as abnormalities in the shape and wall of the gallbladder and the triangular cord (TC) sign (2). Although US can show signs of liver cirrhosis in patients with decompensated liver function, correlation between liver echostructure and histological findings in patients with BA has not been fully investigated. In the present study we evaluated US features of liver and biliary tree, including the presence of TC, and the correspondence between hepatic echostructure and liver histological aspects in infants with BA.

Methods: 35 consecutive infants (19 males, range age at entry 14 days-17 weeks) with BA, confirmed by intraoperative cholangiography, were retrospectively evaluated at the Paediatric Liver Unit of University Federico II, between 1999 and 2011. US evaluation, performed at a mean age of 63.1±34.9 days, was carried out by a pediatric radiologist with experience in gastrointestinal US and focused on the extrahepatic and intrahepatic bile ducts, characteristics of gallbladder and liver, and presence or absence of TC sign. Liver biopsies were examined with particular regard to the presence and severity of fibrosis.

Results: On US, the gallbladder was not seen in 11 (31%) cases; in the remaining 24 patients gallbladder was regular in 6 and irregular in 18. The TC was identified in 9 (26%) out of 35 patients. Liver biopsy showed signs of cirrhosis or fibrosis in all cases. On the other hand, liver echostructure appeared normal in 21 (60%) patients; only in 14 infants liver parenchyma appeared more echogenic and coarse than normal.

Conclusion: Although the TC was visualized in only a fourth of infants with BA, concomitant presence of abnormalities of gallbladder and TC were identified in 83% of patients with BA. A low correspondence between liver echostructure and presence and severity of fibrosis at liver biopsy was identified; therefore a severe liver disease in infants with BA cannot be excluded only on the basis of US findings.


Disclosure of Interest: None Declared

HEPATOLOGY
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MAGNETIC RESONANCE CHOLANGIO-PANCREATOGRAPHY IN THE DIAGNOSIS OF PAEDIATRIC HEPATOBILIARY DISEASE - A LARGE SINGLE CENTRE EXPERIENCE

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Objectives and Study: MRCP is a relatively new imaging modality of the hepatobiliary tract in children. We reviewed the clinical indications for MRCP in 64 children presenting with a range of clinical problems and how the findings affected patient management.

Methods: In this large retrospective case series we reviewed 64 children aged 0-19 years undergoing MRCP over a nine-year period in a regional tertiary gastroenterology centre. The indications for MRCP, MRCP findings, final diagnosis and patient management were noted from the records.

Results: The most common indication was for patients with suspected cholangiopathy (26/64) and pancreatitis (14/64). Amongst the children with suspected cholangiopathy 22 out of the 26 had other known auto-immune diseases: inflammatory bowel disease (n=20), systemic lupus (n=1) and auto-immune enteropathy (n=1). Twenty-four patients also underwent a liver biopsy which showed chronic hepatobiliary disease in all. All these patients also had auto-immune features with elevated levels of IgG (range 6.7-54.8) and/or positive auto-immune serology indicative of an immune mediated cholangiopathy. The majority of the biopsies showed non-specific features of biliary inflammation and none showed the classical small duct 'onion skin' appearance of primary sclerosing cholangitis (PSC) as is typical in adult patients. A final hepatological diagnosis was made following MRCP. Patients were classified as follows: small duct SC (histological features of cholangiopathy but with normal MRCP), AIH (histological features of AIH and normal MRCP), auto-immune SC (AISC) (histological features of cholangiopathy with or without features of AIH, positive auto-antibody screen and abnormal MRCP) and PSC (histological features of cholangiopathy without positive auto-antibodies and with abnormal MRCP). In our patient group MRCP was abnormal in the majority of patients. Ultrasound imaging of the biliary tract was only abnormal in one of the patients with abnormal MRCP.

Conclusion: MRCP is a safe and sensitive imaging tool in children to diagnose changes of SC, extrahepatic biliary obstruction and pancreatic abnormalities. MRCP was diagnostic in the majority of patients with suspected cholangiopathy, where ultrasound imaging was normal and liver histology non-specific. The correct diagnosis of cholangiopathy is essential as it affects patient management. We recommend MRCP for all children with unexplained histological changes of biliary inflammation.

Disclosure of Interest: None Declared
EVALUATION OF THE MENTAL FUNCTIONING AND QUALITY OF LIFE IN TRANSPLANT-FREE PATIENTS WITH BILIARY ATRESIA

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Objectives and Study: Most of the children with biliary atresia (BA), even after initial good response to hepatopportoenterostomy (HPE), are liver transplant candidates. The aim of the study was to assess the mental functioning and the level of life quality (QoL) in pediatric transplant-free survivors after HPE.

Methods: 22 children (15 girls and 7 boys aged from 4 to 18 yrs (11.5±3.6yrs) at least 4 years after HPE with stable liver function were included in the study. PELD/MELD scores varied from -11 to 10. The most common issue was portal hypertension, 20 patients presented with splenomegaly and 8 developed esophageal varices requiring endoscopic interventions. 6 children had cardiac anomalies with no clinical symptoms. The level of mental functioning was diagnosed by using The Child Behavior Checklist(CBCL) and Youth Self Report (YSR). The KINDL was used for QoL assessment. Questionnaire consisted of 4 subscales: psychological well-being, physical state, social relationship and functional capacity in everyday life. Additionally strategies for coping with stress were being investigated by “How Do You Cope?” Questionnaire. It evaluates three strategies: active coping, focus on emotions and seeking social support. Statistical analysis was based on the Pearson’s correlation coefficient.

Results: In the study group problems in mental functioning were not observed. The results obtained in each subscales CBCL/YSR were rated within the normal range. However the greater the intensity of the emotional difficulties in the group the lower level of the subjective sense of quality of life. The results are shown in the graphs below. When dealing with stress patients mainly used an Active coping strategies and Seeking social support. No significant gender and age differences were found.

Conclusion: In transplant-free patients with biliary atresia HRQoL is related to mental functioning. The anti-stress strategies in this group are based on the model of active coping and seeking social support.

Disclosure of Interest: None Declared
INFLAMMATORY BOWEL DISEASE (IBD) ASSOCIATED WITH PRIMARY SCLEROSING CHOLANGITIS (PSC) HAS A DISTINCT PHENOTYPE IN CHILDREN?

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Objectives and Study: PSC is strongly associated with IBD mainly with the features of ulcerative colitis (UC). Aim of this study is to describe the features and the outcomes of the IBD associated with PSC (IBD-PSC) and compare them to a group of UC patients without PSC.

Methods: Retrospective analysis of 27 patients (mean age 17.8 ± 5.2 yr) with IBD-PSC with a follow-up of at least 5 years, followed in 2 pediatric liver centres. IBD was confirmed endoscopically and histologically in all. PSC was diagnosed on histological and imaging criteria (Endoscopic Retrograde Cholangiography and/or cholangioMR): 22 had typical PSC and 5 small duct PSC. Histological overlap features were present in 10/27 patients (37%). The control group consisted of 20 UC patients (mean age 18.7 ± 3.3 yr) without evidence of liver disease.

Results: According to the sex distribution, there was no difference between IBD-PSC and control UC group. In the majority of patients with IBD-PSC (14/27; 52%) the diagnosis of both conditions was contemporary. Diagnosis of PSC preceded the appearance of intestinal symptoms in 7 (25.9%) and followed the diagnosis of IBD in 6 patients (22%). Patients with IBD-PSC tended to be younger, at the time of diagnosis, compared to the UC group (9.1 yr, vs 11.6 yr; ns). Concerning symptoms, 60% of IBD-PSC patients had gastrointestinal symptoms compared to 100% of UC. Endoscopic pancolitis was significantly more frequent in IBD-PSC patients (91% vs 50% p<0.05) as well as rectal sparing (30% vs 0% p<0.05). The presence of backwash ileitis in both groups was not significantly different. Clinical severity of the IBD was significantly milder in IBD-PSC compared with UC (p<0.001), however without significant difference on histological score. Autoimmune features including serum autoantibody (ANA 81% vs 20%; ASMA 66% vs 0%; p-ANCA 44% vs 5%; p<0.01) as well as the presence of other autoimmune diseases (chronic arthritis, diabetes type 1, celiac disease) (26% vs 0% p<0.05) were significantly more frequent in PSC-IBD than in UC patients.

Conclusion: A mild-asymptomatic pancolitis with rectal sparing associated with autoimmune features is the most common IBD phenotype in paediatric IBD-PSC patients, suggesting the existence of a specific IBD phenotype in paediatrics patients with PSC.

Disclosure of Interest: None Declared
THE ROLE OF NEONATAL BLOOD TRANSFUSIONS IN ADULTS WITH HEPATITIS C

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Objectives and Study: Around 50% of adult patients with chronic hepatitis C have reported an unidentified transmission route (1). During the 1960s and early 70s, blood transfusions were commonly used in the treatment of Rh-immunization and other forms of neonatal anemia. During the late 1970’es, with the introduction of alternative strategies, the number of treatments with blood transfusions for Rh immunization declined (2). The aims of this study were to investigate if neonatal blood transfusions were more common in a group of patients with diagnosed hepatitis C infection and reported unknown transmission route compared to a group with known transmission route, and secondly to investigate the natural disease progress in patients thus defined as neonatally infected

Methods: Questionnaires were sent to 230 patients with chronic hepatitis C born in Sweden 1960-75, of whom 96 (47%) had reported unknown transmission route. 25 declined participation, thus the medical records of 205 (89%) of the patients were studied regarding the occurrence of neonatal blood transfusions. The clinical, virological and histopathological characteristics of those found to be transfused in the neonatal period were also studied.

Results: Four out of 205 (1.95%; 95% confidence interval 0.53%- 4.92%) patients with hepatitis C had received blood products as neonates. Three of them had reported unknown transmission route. One of the 4 hepatitis C patients who had been neonatally transfused had cirrhosis, while two had mild histopathological findings on liver biopsy. Three of them, including the patient with liver cirrhosis, had undergone successful treatment for hepatitis C.

Conclusion: Neonatal blood transfusions do only explain a minority of hepatitis C cases with unknown transmission route. However, the finding that cirrhosis occasionally can develop in early adulthood in patients with neonatally acquired infection and that successful antiviral treatment is possible in such patients is of clinical importance. We therefore suggest that all patients treated in neonatal intensive care units prior to the introduction of blood donor screening for hepatitis C in the early 1990’es need to be actively targeted in look-back studies. This would identify infected young and middle aged adults who could benefit from antiviral treatment.


Disclosure of Interest: None Declared
DOES PREDNISOLONE IMPROVE OUTCOME IN NON-A-E HEPATITIS?
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Objectives and Study: Non-A-E hepatitis (NA-EH) is a leading cause of acute liver inflammation in children. It has a presumed infective aetiology, is associated with aplastic anaemia (AA), and may lead to acute liver failure (ALF) requiring liver transplantation (LT). Diagnosis is based on clinical features and exclusion of other causes of hepatitis. Anecdotal evidence and small studies of prednisolone treatment for acute liver failure are inconclusive. We aim to describe the outcome of non-A-E hepatitis and assess the effect of prednisolone on clinical course.

Methods: A retrospective analysis of consecutive children (<16 years) transferred to a supraregional liver centre, subsequently diagnosed with NA-EH from 2001 to 2012. ALF was defined as INR > 1.5 (PT > 18) or presence of encephalopathy. Children received a trial of prednisolone (2mg/kg maximum 40mg) according to clinical judgement and evolving unit experience. Children were listed for supra-urgent liver transplantation when they fulfilled strict criteria, which include severity of coagulopathy and encephalopathy.

Results: 25 children, M16: F9 median age 8.1 years (range 1.1 – 15.66 years) were identified. Six children without ALF recovered without LT; two had received prednisolone. Of 19 with ALF, 10 reached listing criteria and underwent successful LT (median age 7.25 years, range 1.83 yr – 15.83 yr). Three had received prednisolone, of whom two were listed for LT within 24 hours and the third within 3 days of treatment. Of seven undergoing LT without prior prednisolone, admission INR was median 3.2 (range 1.5 – 10.1) and interval to listing was median 2 days (range 1-11). Five were listed within 2 days, and the other two 6 and 11 days after admission. Nine with ALF recovered without LT (median age 11.91 yr, range 6y – 14.6 yr), of whom six had received prednisolone. Median INR before treatment was 1.8 (range 1.7 – 2.2). In three who recovered spontaneously, all had peak INR of 1.6. Nine children (36%) developed AA. One had low platelets at onset of liver dysfunction. In eight, features of AA developed after onset of NA-EH. In two AA developed after LT and in six after improvement with steroids (5) or spontaneous recovery (1).

Conclusion: Prednisolone may have a beneficial role in the treatment of children with ALF due to NA-EH if started early and before encephalopathy ensues. Prednisolone treatment and immunosuppression after LT do not prevent subsequent aplastic anaemia.

Disclosure of Interest: None Declared
PO-H-0315

OUTBREAK OF ECHOVIRUS 11 FULMINANT NEONATAL HEPATITIS IN BELGIUM DURING SPRING 2012
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Objectives and Study: Nonpolio enterovirus infections are common during summer and fall. Among neonates clinical presentation varies from asymptomatic viral shedding and non-specific febrile illness to sepsis-like syndrome and severe liver, cardiac or cerebral diseases. Echovirus 11 is the most frequent cause of serious neonatal morbidity and mortality, often presented as fulminant hepatitis, infection of the central nervous system, or both. Newborn EV infections may be acquired after birth or vertically, more likely at the time of delivery through contact with maternal blood, fecal material, vaginal or cervical secretions. Mortality rates are greater for infections that appear during the first week of life, probably through vertical transmission, in comparison to later infections.

Methods: We report four cases of echovirus 11 neonatal infections that occurred between April and June 2012.

Results: The four children were admitted during the first week of life, day 4 to 6, with sepsis-like syndrome. All the cases were biologically characterized by marked transaminase elevation (GOT >> GPT), hemolytic anemia, thrombocytopenia, and severe coagulopathy. Diagnosis was confirmed by positive polymerase chain reaction on blood, stool or cerebrospinal fluid samples. Three neonates were born by vaginal delivery. Among them one child deceased after one month because of hemodynamic instability due to a major capillary leak syndrome, and was the only one having been treated with corticoids (day 2 to day 10). All three received supportive treatment associated to intravenous immunoglobulins (IVIG) within 7 days of admission (1 to 2g/kg). The fourth case was born by caesarian delivery and was also treated with early IVIG administration. Contact history was only documented in this last patient (diarrhea in her siblings one week before her birth). Three children presented an inversion of portal blood flow at liver doppler, which is a marker of portal hypertension commonly reported in fulminant hepatitis. Whether this will be associated to long-term sequellae remains to be determined.

Conclusion: This study shows that outbreak of enterovirus is still associated with severe infection and fulminant hepatitis in newborns. Clinical presentation is aspecific although early diagnosis and rapid treatment is mandatory to avoid fatal evolution. There was rationale to administer IVIG, and positive outcome in 3 patients out of 4 might have been favoured by this treatment.

Disclosure of Interest: None Declared
Objectives and Study: Few cases of chronic hepatitis secondary to Hepatitis E Virus [HEV] in immunosuppressed children are described. We screened our paediatric liver transplant population for chronic HEV infection [cHEV] using HEV-RNA detection. Furthermore, we describe the first case of successful treatment with ribavirin [RBV] for cHEV in this population.

Methods: Medical charts of 267 children after orthotopic liver transplantation [OLT] were screened retrospectively for unexplained chronic elevation of liver enzymes. Patients [Pts] thus identified were screened for HEV-RNA by nested PCR as described previously (1). Stored frozen plasma samples [SPS] were used for analysis in a few cases.

In the single identified HEV-RNA positive Pt, 7 SPS from before and 6 samples since diagnosis of cHEV were tested for HEV-RNA to characterize the clinical course of infection. Testing for HEV antibodies was done by MP-Assay (MP Biomedicals).

Results: 22 Pts (11 female) fulfilled the above mentioned criteria. Median age at screening was 6.7 years [y] (1.4-17.2). Pts had undergone a total of 28 OLTs at a median age of 1.4y (0.4-16.7). Median follow up was 50.3 months [m] (4.22-144). Pts had experienced a total of 52 acute cellular (ACR) and 2 chronic rejections. Out of 22 Pts, one patient with cHEV was identified.

The 10y old Pt with cHEV [PtHEV] underwent 3 OLTs. Shortly after 3rd OLT he developed chronically elevated liver enzymes. Several liver biopsies showed features of ACR. Immunosuppression [IS] was steadily increased without success. In subsequent liver biopsies, features compatible with chronic viral hepatitis became increasingly prominent and hepatic fibrosis increased. Anti-HEV-IgG remained negative, but HEV-RNA analysis revealed HEV viremia. IS was reduced without success for 2m. We therefore started RBV at a dose of 15mg/kg bodyweight per day for 6m.

Retrospectively analyzed SPS from PtHEV revealed a HEV viremia since 6m after 3rd OLT and 31m before diagnosis of cHEV.

In summary we report a prevalence of cHEV of 1 in 22 Pts with chronic graft hepatitis out of 267 children after OLT. We describe a clinical course of cHEV with viremia over 33m, associated with progressive liver fibrosis, but without detectable anti-HEV-IgG. We present in this Pt the first paediatric case of RBV therapy for cHEV. Treatment with RBV was tolerated and led to clearance of viremia within 42 days. 3 month after discontinuing RBV treatment PtHEV is still negative for HEV RNA.

Conclusion: Chronic Hepatitis E infection, which is a rare but important differential diagnosis for graft hepatitis, can only be reliably detected by HEV-RNA screening and can successfully be treated with ribavirin.


Disclosure of Interest: None Declared
Objectives and Study: Long-term outcome of children with AIH is not well known.

Methods: Retrospective analysis of 124 patients (92 girls; age at onset: 10m-15y) seen from 1973 to 2004. Presenting features, acute hepatitis (80) or fortuitous finding of liver injury (44), preceded diagnosis by 0-12y (median: 4m). Median ALT and gammaglobulins were 15xN and 3g/dl respectively with abnormal prothrombin in 86 children. 60 children had type 1 AIH and 64 type 2. 75 children had cirrhosis. 121 children were treated: with prednisone and/or azathioprine (112) or with cyclosporine (9); 3 patients with fulminant liver failure were listed for urgent liver transplantation (OLT).

Results: Presence of cirrhosis was correlated with an interval > 1 month between first signs and diagnosis (p<0.01), but not with age at onset or AIH type. ALT normalized in 93% after a mean treatment of 5 m. Prothrombin did not normalize in 16 patients: 1 died before the era of OLT, 3 are alive with native liver and 12 underwent OLT. Early death or early OLT occurred in 8 children, 7 with AIH 2. One or more relapse occurred during treatment in 74 patients (61%) independently of age at onset of treatment, cirrhosis, or type of AIH, but significantly (p<0.00001) related to poor compliance with treatment. Treatment was tentatively stopped after a mean period of 7y in 58 patients; 35 relapsed after a mean of 18m (2m-20y); relapse was severe in 2 leading to death or OLT. At the end of follow-up (median 14y, range 8-31y) 110 patients are alive (%), 95 with native liver: 21 (12 AIH 2) are off therapy after a mean duration of treatment of 7.5 y (3.5-21) with a median follow-up after the end of treatment of 6y (1-27); 74 are still under therapy after a mean duration of treatment of 12 y (8-26). 22 patients underwent OLT at a median age of 16y (range 0.9-36) for early liver failure (6) or complications of cirrhosis (16); 15 of them are alive. Fourteen patients died (11%) because of complications of cirrhosis in the era before OLT (2), complications of OLT (7), pulmonary hypertension, fulminant hepatitis, acute autoimmune hemolytic anemia, macrophage activation syndrome and car accident (1 each).

Conclusion: Treatment of AIH is associated with long term survival with native liver in an high number of patients even though the risk of death is present at any stage in the history of a child with AIH. Urgent treatment, early identification of poor responders (mostly type 2) and assiduous control of compliance with medication are essential to limit the incidence and worsening of cirrhosis and its late complications. Treatment can be stopped in a proportion of patients, but prolonged follow-up is necessary to detect late relapses and manage complications of cirrhosis and possible extra-hepatic autoimmune conditions.

Disclosure of Interest: None Declared
RETHINKING ON HYPO-RESPONSIVENESS TO HEPATITIS B VIRUS VACCINATION IN CHILDREN WITH CELIAC DISEASE: A SYSTEMATIC REVIEW

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Objectives and Study: Several immunogenetic factors can be associated with Hepatitis B surface antibody (HBsAb) response to Hepatitis B Virus (HBV) vaccination. Among the various candidate genes that have been implicated, human leukocyte antigen phenotype DQ2 is particularly worth of attention, being strongly linked to Celiac Disease (CD). We aimed to verify how strong is the literature evidence of the association between HBV vaccine response and CD status. In our work the need of adding HBV vaccination hypo-responders (HBsAb titers <10 U/L) to the categories at increased CD risk, recently proposed by the ESPGHAN as requiring specific CD antibodies testing (Husby et al, JPGN 2012), is discussed.

Methods: We have performed a systematic literature review of the articles reporting response to HBV vaccination in naïve CD patients on a gluten-containing diet.

Results: 10/10 pediatric studies (≈ 444 naïve CD children) published from 2007 (Park et al, JPGN 2007) to 2012 (Urganci et al, JPGN Nov 2012) reported a percentage of HBV vaccine hypo-responders (mean value 58.3%) significantly lower than that observed in controls (mean value 84.8%). HBsAb response after an intramuscular or intradermal booster normalized following starting a proper gluten-free diet (GFD) in 5/5 studies.

Conclusion: The high prevalence of HBV infection in industrialized, and in most developing countries as well, requires pediatric gastroenterologists' alertness to poor HBV vaccine response in naïve CD patients. This condition might indicate undiagnosed CD requiring patient investigation, with a possible correction achievable by an appropriate booster program during a strict GFD, should the patient result affected. Moreover, every new diagnosis of CD in a previously HBV-vaccinated patient need re-evaluation of HBsAb titers in order to take appropriate action in case of non-response to avoid possible poor protection against HBV during risky procedures.

Our results suggest the need to add individuals who are hypo-responder to HBV vaccination to the list of categories at increased CD risk recently proposed by the ESPGHAN as requiring specific CD antibodies testing (Husby et al, JPGN 2012).

Disclosure of Interest: None Declared
Objectives and Study: Autoimmune hepatitis (AIH) is a generally unresolving inflammation of the liver of unknown cause. Onset is frequently insidious with nonspecific symptoms, but the clinical spectrum is wide, ranging from an asymptomatic presentation to an acute severe disease. The diagnosis is based on histologic abnormalities, characteristic clinical and laboratory findings. AIH characterizes by aggressive course in children. Immunosuppressive treatment should be instituted promptly to avoid progression to cirrhosis. Relapse after discontinuation of immunosuppressive therapy occurs in 70-80% of children with AIH. This study aims to investigate the clinical characteristics, diagnostic criteria and treatment response of AIH in children.

Methods: In study were included children with AIH admitted to our department in a five year period (2006 to 2011). We observed 61 children with AIH, 29 male (47.5%), 43 female (70.4%), and mean age 10.5±2.5 years. Criteria for AIH were: serum aminotransferases (ALT, AST) level 5 times above normal; elevated immunoglobulin G (IgG); titer autoantibodies >20. Liver histology was presented interface hepatitis, plasmacytic infiltration, rosettes from hepatocytes.

Results: The definite AIH and probable AIH according to the AIH Scoring system were 60.7% and 39.3% before treatment, and 78.7% and 21.3% after treatment withdrawal, respectively. In 17.7% the onset was insidious or chronic and acute in 82.3%. At the time of diagnosis, liver cirrhosis was diagnosed in 56.4%. The mean of ALT and AST were 1081±268.5 IU/L and 1095.3 ±313.2 IU/L, respectively. The level of IgG was at least 1.5 times above normal in 96.8%. The positive results for ANA, SMA and anti-LKM1 were 49.4%, 32.9%, and 22.3%, respectively. Liver biopsy was performed in 61 children (100%), histological criteria of AIH predominate in all children, and in addition, 17 (29.5%) children hadsigns of destruction and proliferation of bile ducts. As an initial therapy, corticosteroid alone was given in 20 children (32.7%), and corticosteroid with azathioprine was in 41 children (67.3%). Remission was observed in 77.1% of patients (47/61); these children receive maintenance immunosuppressive therapy now. Orthotopic liver transplantation was performed in 18% (11/61). Immunosuppressive therapy was completely discontinued in 4.9% (3/61); these children had not of histological evidence of inflammation in re-biopsy liver after 3 years therapy.

Conclusion: Clinical features AIH in children in compares to adult are characterized by more aggressive and rapid progression of liver disease to liver cirrhosis. AIH must be considered in all children with acute or chronic hepatitis of undetermined cause and it has diverse clinical features that can delay its diagnosis and the institution of potentially lifesaving therapy.

Disclosure of Interest: None Declared
EFFECT OF CHRONIC ACTIVE HERPES VIRUS INFECTIONS ON THE COURSE OF CHRONIC HEPATITIS C IN CHILDREN

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Objectives and Study: Effect of chronic active herpesvirus infections (CAHI) on the course of chronic hepatitis C (HCV) in children not enough was studied now. The aim of this study was to investigate the effect of CAHI on the course of HCV in children.

Methods: We observed 31 children with HCV, 20 female, 11 male, mean age 10.7 ± 1.2 years. Antibodies to herpes simplex virus types 1 and 2 (HSV1-2) and herpes virus type 6 (HHV6) were examined in all children. The DNA of these viruses was determined by PCR in blood cells and liver biopsy. In the biochemical tests were determined the levels of ALT, AST, GGT and AP.

Results: CAHI were diagnosed in 24 children (77.4%) with HCV. Children with HSV1-2 had levels of ALT and AST 110.8±14.3 and 145.5±13.5 IU/L respectively; the children without HSV1-2 had levels of ALT and AST 66.1±5.7 (p<0.01) and 52.9±4.1 IU/L (p<0.001). Children with HHV6 had ALT and AST 141.8±26.1 and 196.8±12.8 IU/L respectively; the children without this infection had ALT and AST 63.4±5.6 (p<0.001) and 52.2±3.9 (p<0.001). The levels of GGT and AP in children with HSV1-2 were 56.7±5.4 and 267.0±18.0 IU/L respectively; the levels of GGT and AP in children without HSV1-2 were 20.1±1.6 (p<0.001) and 208.0±18.4 (p<0.05). And children with HHV6 had GGT and AP 34.1±3.6 and 268.0±30.4 IU/L respectively; the children without this infection had GGT and AP 26.4±2.4 and 207.7±13.5 IU/L (p<0.05). All children were receiving Ursodeoxycholic acid (Ursosan) for three months at a dose of 10 mg/kg/day. After three of treatment ALT and AST were 54.2±4.1 and 52.4±2.8 IU/L respectively; and GGT and AP were 36.4±2.4 and 177.0±1.4 IU/L respectively.

Conclusion: HSV1-2 and HHV 6 is cause high cytolitic and cholestatic activity in children with HCV and using Ursodeoxycholic acid leads to a reduction in markers of cytolysis and cholestasis

Disclosure of Interest: None Declared
THE OUTCOME OF CHRONIC HEPATITIS B IN CHILDREN WITH AND WITHOUT MALIGNANCIES: A TWELVE YEAR-FOLLOW-UP.
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Objectives and Study: The aim of the study is to evaluate the outcome of chronic hepatitis b (CHB) in children cured of pediatric malignancies and compare results with children diagnosed CHB without malignancies. This study was conducted in a case-controlled and comparative manner.

Methods: Twenty four children (15 boys and 9 girls) with malignancy, at the follow-up of pediatric gastroenterology outpatient clinic because of CHB between the dates of january 2000 –september 2012, were enrolled in the study (group 1). The mean age at the diagnosis was 10.89±2.67 years. Of these patients, five (20.8 %) had solid tumors, 19 (79.1%) had diagnosed leukemia/lymphoma. All patients were in remission and none had received chemotherapy for at least 12 months. Group 2 was formed with twenty five children (11 girls and 14 boys, mean age; 8.11±3.69 years) diagnosed CHB without hematologic or oncologic disorder between the same dates. Fifteen patients from group 1 and 21 patients from group 2 were prescribed recombinant interferon (5 MU/m²/day three times a week for 24 weeks) and lamuvudine (maximum 100 mg for at least 1 year) therapy. The data from the patients’ records were compared between two groups of patients according to first findings at diagnosis, response to therapy, liver biopsy findings and last disease status.

Results: The hepatitis B e antigen (HBe Ag) seroconversion rate was found 1.5 % (3 patients) in group 1 and 6 % (15 patients) in group 2 and the difference is found significant (p<0.01). Two patients who treated in group 1 and twelve patients who treated in group 2 had showed seroconversion to anti HBe. Liver biopsy findings (hepatitis activation index and fibrosis score) and response to therapy did not show any difference statistically between two groups. Loss of hepatitis B surface antigen (HBsAg) occurred in one patient in both group 1 and 2.

Conclusion: The children cured of malignancies with CHB showed low HBeAg seroconversion rate. Although initial liver biopsy findings and response to therapy did not differ between two groups the course of CHB could be more severe in children with cancer.

Disclosure of Interest: None Declared
CELIAC DISEASE-ASSOCIATED AUTOIMMUNE HEPATITIS IN CHILDHOOD: LONG TERM RESPONSE TO TREATMENT

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Objectives and Study: Celiac disease (CD) is common in patients with autoimmune liver disease. The pathogenetic role of gluten in triggering the autoimmune process is uncertain, and the long-term response to treatment of patients with autoimmune liver disease coexistent with celiac disease has not been explored in details. The aim of this study was to analyze the long-term response to immunosuppressive treatment in children with autoimmune hepatitis (AIH) associated with CD.

Methods: Retrospective and prospective evaluation of 77 patients with AIH. All patients included in the study were serologically screened for CD. In case of seropositivity, a small bowel histological evaluation was performed and the diagnosis of CD was confirmed on the basis of the presence of a modified Marsh grade \(\geq 2\). All patients with AIH were administered an immunosuppressive treatment. All patients with a coexistent CD also started a gluten free diet. Patients were regularly followed-up by clinical and biochemical evaluation and compliance with the treatment and with the gluten-free diet (GFD) was assessed.

Results: Among 77 patients with autoimmune hepatitis, 16 (13.7 \%) had celiac disease. All of the patients were treated with immunosuppressive therapy based on prednisone \(\pm\) azathioprine and/or cyclosporine. The mean period of follow-up was 111 months; discontinuation of therapy was attempted in 11 of the 16 patients with AIH and coexistent CD while in remission: 5 patients experienced relapses; 6 patients (37.5\%) could definitively stop immunosuppressive treatment with a mean period of treatment-free sustained remission of 89 months (range 26-174). In the same period, treatment discontinuation, attempted in 20 of 61 patients with autoimmune hepatitis without celiac disease, was successful in 9 (14.7\%). When comparing the success rate of treatment discontinuation in the two group of patients a significantly higher number of children with AIH and coexistent CD could stop the immunosuppressive treatment without relapse (\(p = <0.05\)).

Conclusion: Our experience confirms the need for serological screening for CD of all patients with AIH. Moreover AIH coexistent with CD may represent, at least in children, a particular subgroup of AIH with a potentially more favorable prognosis and the possibility to safely withdraw immunosuppressive therapy suggesting a possible long-term adjuvant effect of gluten free diet. An earlier attempt to stop the therapy in children with AIH coexistent with CD might also warrant consideration in future studies.

Disclosure of Interest: None Declared
UNEXPECTED GENOTYPES AND NOVEL RECOMBINANT HBV IN AFRICAN CHILDREN LIVING IN AUSTRALIA

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Objectives and Study: Little is known about the natural history of African chronic hepatitis B (CHB) infection, particularly in children. Migration from Sub-Saharan Africa, where HBV is hyperendemic, is contributing to a rising incidence of CHB infection in Australia. HBV genotypes exhibit variation in natural history, clinical outcomes and treatment response. African CHB is typically associated with unique genotypes such as A1 and E. A1 is strongly associated with early-onset hepatocellular carcinoma, with minimal outcome data for genotype E. We aimed to delineate the molecular virology of HBV in African children living in Australia not previously studied in this region.

Methods: Children of African origin with CHB were recruited at the Royal Children's Hospital Melbourne. Population based sequencing of either the complete HBV genome, or the polymerase gene/basal core promoter (BCP)/precore (PC) region was performed. The HBV (sub)genotype was assigned through phylogenetic analysis, and known mutations that are associated with clinical disease progression identified. INNO-LiPA was used to interrogate mixed infections, and genomic recombination events identified using SimPlot software.

Results: 63 treatment-naive African children with CHB were included. African countries represented included Sudan, Liberia, Ethiopia, Sierra Leone, Kenya, Egypt, Somalia, Tanzania and Guinea. Median age was 12.5 years (range 2.8-17.9). 37 genomic-length sequences have been assembled. Genotype E predominated (43/63, 68.3%); and genotype D (17/63, 26.7%; subgenotype D7/D3/D2), and subgenotype A1 (3/63, 4.7%) were also identified. Three patients had mixed HBV infection with genotypes A/E (1/3) and D/E (2/3). 57.1% (36/63) patients were HBeAg negative; the majority associated with canonical BCP/PC mutations. Low genetic diversity (<2%) was observed within genotype E. Recombination events were seen in 4 patients with (sub)genotype D7/E in atypical breakpoint regions.

Conclusion: HBV genotypes in African children with CHB living in Australia largely reflected their country of origin, with unexpected genotypes (D7) and recombination events identified. Importantly, the emergence of E, D7 and A1 (sub)genotypes, has important ramifications for patient monitoring and treatment guidelines in our region. BCP and PC mutations were present in these children, reinforcing the need for natural history studies to monitor the emergence of HBeAg-negative disease in this important group. Ongoing molecular analysis and longitudinal natural history studies will have important global significance for these lesser-studied variants.

Disclosure of Interest: None Declared
ADOPTIVE IMMUNOTHERAPY WITH EBV-SPECIFIC CYTOTOXIC T-LYMPHOCYTES (CTLs) IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS WITH LOW GRADE, EBV-RELATED POST-TRANSPLANT LIMPHOPROLIFERATIVE DISEASE (PTLD)

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Objectives and Study: PTLD is a severe complication of transplantation, linked in most cases to EBV infection. In immunosuppressed patients, infected lymphoblastoid cells can proliferate and eventually lead to PTLD. One possible therapy, now clinically validated, is to infuse virus-specific lymphocytes expanded and activated \textit{in vitro} in order to enhance the cytotoxic response.

Methods: 5 (4 girls) liver transplanted children with a diagnosis of polyclonal EBV-related B-cell PTLD (2 polymorphic and 3 “Early Lesions”) were treated with EBV-specific CTLs in our Institution. Median age at diagnosis was 5 years and 5 months (range: 4 y 6 m - 15 y 8 m) and median time from liver transplant (OLTx) was 3 years and 7 months (range: 3 y 4 m – 5 y 6 m). All patients showed adenotonsillar and gastrointestinal PTLD with positive EBER staining. At diagnosis they were symptomatic (nasal obstruction due to adenotonsillar hypertrophy) and the IFN-\gamma secreting EBV specific ELISPOT assay was low (median value 0,49 for ml of blood, range: 0 – 1,14, normal > 2). They were previously treated with change of immunosuppression from Tacrolimus to Rapamycin. EBV-transformed B lymphoblastoid cells (LCLs) and EBV-CTL were generated from peripheral blood mononuclear cells (PBMC). For CTLs, PBMC were stimulated with autologous irradiated LCL and expanded by rounds of restimulation with IL-2. EBV-CTLs, before infusion, were examined for immunophenotype, sterility, potency and EBV specificity. Treatment protocol consisted in one or two blocks of 3 monthly infusions at a median dose of 1,5x10^6/Kg CTL cells followed by complete histological reassessment.

Results: Infusions were well tolerated and no adverse reactions were recorded. A check of aminotranspherasases activity, performed one week after each dose of CTL showed no abnormalities. Histological reassessment after 6 infusions documented downgrading of polymorphic PTLD to “Early Lesions” in two patient and complete regression in one. EBER staining after CTL treatment showed an improved picture with no or very few positive cells in all patients.

Conclusion: Adoptive immunotherapy with EBV specific CTL cells is feasible and safe in liver transplanted children with polyclonal, EBV related B-cell PTLD. The major benefits are expected in the long term since some CTLs could persists as memory cells and grant a durable, increased immunization against EBV-infected B-cells.

Disclosure of Interest: None Declared
Objectives and Study: Increased rates of rejection and graft loss in adolescents have led to development of transition programmes. In order to develop our own transition-programme we evaluated opinions of adolescents (pre-transfer), their parents and young adults (post-transfer) from our liver transplant cohort.

Methods: All adolescents liver transplanted at our centre (aged 12-19y) and their parents as well as adults liver transplanted in childhood (aged 17-41y) were asked to respond to a self-designed, standardized questionnaire regarding existing transition programmes. Adults were asked to respond with their current view to transition but also with their anticipated adolescent perspective from before transfer. We compared clinical outcome from responder and non-responder groups and we correlated clinical outcome with responses to the questionnaire.

Results: 57 adolescent pre-transfer patients (33 male; 24 female; mean age 14,7y) and their parents were asked, 38 (67%) of both replied. Of 138 asked adult post-transfer patients (57 female; 81 male; mean age 24,64y) 54 (39,1%) replied. Significant less female adults replied, although they graded their transfer significant worse and more disturbing than male adults.

We found no differences for clinical outcome in responder and non-responder group and given responses did not differ depending on clinical complication rate.

Adolescents were generally sceptical towards transition programmes, but current view of adults differed significantly to this with strong support for introduction of transition-programmes including education, activities, specialised days for outpatient review and training for assuming responsibility. Adults documented an even greater interest in transition programmes then parents of adolescents.

In summary expectations and views of adolescents were not met by already existing transition programmes. In contrast liver transplanted adults agreed with suggestions from such programmes. Different perceptions in and between the groups appeared to be independent from clinical complication rates but not from gender.

Conclusion: We conclude that transition programmes need to be developed in close collaboration with adolescent patients who may either not be aware of problems and risks of transition or oppose external guidance.

Disclosure of Interest: None Declared
FIFTY CONSECUTIVE PEDIATRIC LIVER TRANSPLANTS WITHOUT GRAFT LOSS OR MORTALITY: POSTOPERATIVE COMPLICATIONS ARE DOMINATED BY CALCINEURIN INHIBITOR-ASSOCIATED SIDE-EFFECTS

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Objectives and Study: Until recently, the postoperative course of pediatric liver transplantation (pLT) was complicated most frequently by surgical complications such as arterial or portal vein thrombosis and severe infections. Presently, graft loss in the first year after pLT occurs in 28% of cases, mortality is 15-17% (European Liver Transplant Registry, ELTR.org). The objective of this study is to demonstrate a shift in pLT-related complications to a dominance of calcineurin inhibitor(CNI)-associated side-effects in a pLT program preventing first year graft loss and mortality.

Methods: Single center analysis of postoperative complications by retrospective chart review in 50 children (31 boys, 19 girls) who underwent pLT between 2005 and 2011. Most common indications were biliary atresia in 52%, acute liver failure in 10%. Age at pLT ranged from 21days -19y, body weight (bw) was 3.6 kg -79 kg (median: 9.9 kg), 16 patients with bw < 7 kg. Immunosuppressive regimen was based on tacrolimus and tapered prednisolone. Full-size post-mortem grafts were transplanted in 28%, split grafts (left-lateral, left lobe or right lobe) or living-donation grafts in each 36%.

Range of PELD was 0- 41 (median: 16.0).

Results: 57 (74%) out of 77 complications in 50 patients were associated with CNI-treatment.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Reference (%)</th>
<th>UKT 05 -11 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival Patient / Graft</td>
<td>83-85 / 73-75 (ELTR)</td>
<td>100 / 100</td>
</tr>
<tr>
<td>Complication Biliary anastomotic strictures</td>
<td>5-34 (Sunku B et al., 2006)</td>
<td>28</td>
</tr>
<tr>
<td>Complication Thrombosis: PVT / HAT</td>
<td>8.7 / 6.7 (Yilmaz A et al., 2007)</td>
<td>2 / 2</td>
</tr>
<tr>
<td>Complication Stenosis of HV and VC</td>
<td>8.7 (Yilmaz A et al., 2007)</td>
<td>8</td>
</tr>
<tr>
<td>Complication Acute rejection</td>
<td>20-40 (Clavien et al., p. 304)</td>
<td>6</td>
</tr>
<tr>
<td>Complication Sepsis</td>
<td>13.3 (Ikegami T et al., 2012)</td>
<td>6</td>
</tr>
<tr>
<td>Complication CNI-associated Hypertension</td>
<td>40-80 (Clavien et al., p. 402)</td>
<td>62</td>
</tr>
</tbody>
</table>
Impaired renal function | 32 (Campbell KM et al., 2006) | 28
---|---|---
CMV infection | 16.1 (Bedel et al., 2012) | 12

PVT= Portal vein thrombosis, HAT= Hepatic artery thrombosis, HV= Hepatic vein, VC= Vena cava

**Conclusion:** In pLT postoperative care in a single center, a significant shift towards CNI-associated complications was observed while simultaneously graft loss and mortality were avoided. This indicates that future management of pLT patients needs to increasingly focus on alternative methods of immunosuppression/ immunomodulation and improving quality of life while maintaining excellent outcome measures.

**References:** Sunku B et al., 2006, Liver Transpl; Yilmaz A et al., 2007, Pediatr Transplant; Clavien et al., p. 304, 402; Ikegami T et al., 2012, J Am Coll Surg; Campbell KM et al., 2006, Curr Opin Organ Transplant; Bedel et al., 2012, Liver Transpl

**Disclosure of Interest:** None Declared
OBJECTIVES AND STUDY: The early period after liver transplantation has been associated with low- to normal-range kinetic and serum levels of immunoglobulins. However, data remain sparse, with existing studies limited to adults or case reports of children. The aim of the present study was to evaluate the occurrence and risks of hypogammaglobulinemia in the first 28 days after liver transplantation in a serial pediatric cohort.

METHODS: A retrospective 10-year chart review was conducted of all patients who underwent liver transplantation at a forth-level pediatric medical center.

RESULTS: Of the 57 children with complete information, 17 (29.8%, mean age 6.8±5.2 years) had hypogammaglobulinemia (11 IgG, 1 IgG+IgA, 1 IgG+IgM, 4 IgG+IgA+IgM), detected at 2 to 25 days after transplantation. Abdominal fluid was drained for 5 to 42 days; the amount drained until detection of hypogammaglobulinemia measured 27 to 668 ml/kg. Children who had hypogammaglobulinemia had a significantly higher infection rate than those who did not (0.9 vs 0.17 episodes/patient, p<0.01).

CONCLUSION: Hypogammaglobulinemia is not rare in the immediate post-liver-transplantation period in children, and it may place patients at increased risk of infection. Further studies are needed to delineate the rate of occurrence, risk factors, and clinical implications of hypogammaglobulinemia in this patient population.

Disclosure of Interest: None Declared
HEPATITIS B SURFACE ANTIBODY DISAPPEARANCE IN PEDIATRIC LIVER TRANSPLANTED PATIENTS

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3Rabin Medical Center, Petah Tikva, 4Rambam Medical Center, Haifa, Israel

Objectives and Study: Hepatitis B virus (HBV) is one of the most common etiologies for liver disease worldwide. Chronic HBV frequently progress to cirrhosis and liver failure with or without hepato-cellular carcinoma. Universal vaccination against hepatitis B was implemented in Israel in 1992, with vaccination compliance of 95% of the population. Prior works showed that up to 10 % of vaccine recipients fail to respond with adequate anti-hepatitis B surface antibodies (anti-HBs) levels after a primary series of vaccinations. In addition, anti-HBs levels are expected to decline with time. This has important implications for populations under immunosuppressive treatment.

AIMS: To determine HBV immunity in pediatric liver transplant patients and to observe HBsAb status under immunosuppressive therapy.

Methods: A retrospective electronic chart review of pediatric liver transplanted patients, who were followed up at the liver-intestinal transplantation unit at the Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Medical Center of Israel (SCMCI) between 01/1995-12/2011. Charts were reviewed for HBV serology and immunization status. Immunization for HBV (HBsAb positivity) was defined by HBsAb titer > 10mIU/ml.

Results: We retrieved 100 liver transplanted pediatric patients’ records. Prior to Transplantation data regarding HBV immunity was available for 41 patients (41%), all of them were negative for HBsAg or HbcAb. Out of these, only 28 patients (68.3%) were HBsAb positive. During follow up, eleven patients (39.3%) lost their protective antibodies. Median time for antibodies disappearance was 51 months (range: 15-114 months). Only 8/28 patients (28.5%) kept their immunity during the follow up period.

Conclusion: Conclusions: Our data suggest that loss of HBV immunity during follow up of pediatric liver transplantation patients is common. Whether this loss of response differs from the general population needs to be determined. Regardless of the cause, major attempt should be made to assess HBV immunity status prior to transplantation and during follow up.

Disclosure of Interest: None Declared
Objectives and Study: Liver transplantation in childhood is an effective treatment for end-stage liver diseases. Many of these liver diseases developed portal hypertension which decreases the quality of life and increases morbidity and mortality in transplant waiting. Transjugular intrahepatic portosystemic shunt (TIPS) is a technique that allows setting up communication between the portal and suprahepatic systems through the liver parenchyma in order to ease portal hypertension that causes gastrointestinal bleeding. We presented the results and follow-up in 7 patients who underwent TIPS in our liver transplant program.

Methods: 7 patients underwent TIPS (coated stents Viatorr 8 mm diameter) from 2009 to 2011. Six patients had cirrhosis of different etiologies and another patient developed portal vein thrombosis after liver transplantation with cavernoma formation. The indication of the procedure was refractory bleeding after medical and endoscopic treatment. Average waiting time to TIPS implantation was 14.8 days (1-30 days). Mean patient age was 10.4 years (5.7-16 years), average patient weight was 31.6 kg (14-60 kg) with a mean procedure follow-up of 10 months.

Results: One patient developed transient mild encephalopathy and the one with portal vein thrombosis and cavernoma complicated with acute TIPS occlusion that was resolved with coaxial stent implantation. Three of the cirrhotic children were transplanted after 7.5, 9 and 10 months with TIPS patency verification at the moment of surgery. In the remaining four patients, patency of TIPS was verified by doppler ultrasound at 1, 3, 5 months and there was no need of liver transplant. None of the patients complicated with gastrointestinal bleeding after a mean follow up of 10 months.

Conclusion: TIPS is an effective procedure in the treatment of recurrent variceal bleeding due to portal hypertension. There is controversy in size device but technical development makes the procedure increasingly feasible. TIPS decrease portal hypertension in chronic liver diseases and can postpone liver transplantation and reduce morbidity and mortality in the waiting list.

Disclosure of Interest: None Declared
Objectives and Study: Close-knit post-operative monitoring is of paramount importance for children following liver transplantation. Recently, point-of-care (POC) blood testing devices for liver enzymes and C-reactive protein have become available, allowing for home testing. For this, we developed a customized information and communication system and investigated its application feasibility and acceptance.

Methods: Families of children aged 6-36 months following live-related liver transplantation (biliary atresia, n=2, bile salt excretion pump deficiency, n=1) and live-related liver-kidney transplantation (primary hyperoxaluria, n=1) were selected depending on stable liver function tests on discharge and their place of residency (Libya, Bulgaria, Uzbekistan and Azerbaijan). They participated in a pilot study of using a commercially available POC blood testing device (Alere Cholestech LDX). Local health care providers were asked to agree to fortnightly standard hospital based laboratory investigations alternating with home based POC determination of ALT, AST and hs-CRP.

The POC device was connected to a tablet computer running a specially developed software that reads the test results from the device, stores them in a database and displays them in comprehensive graphs for the parents. The results are transferred via Internet connection to a secure server and can be accessed by the specialist from any place at any time. In addition, the software assesses the child’s resp. parents’ quality of life using standard questionnaires (PedsQL 4.0).

Results: The system has worked reliably in all four children, transferring altogether 38 POC measurements. Blood tests remained stable throughout the observation period except one episode of raised CRP which led to the consultation of a local specialist and had occurred in EBV seroconversion. Detected advantages and problems: 1. transmission failures (n=3) due to insufficient Internet connection, yet all measurement values were stored locally; 2. time and effort for transplant physician; 3. provides high patient satisfaction; 4. communication with local health care provider important and risky: patient may fall in-between responsibilities; 5. total costs amount to approximately 4000/200 Euros for prototypes/consumables for a three-month period. Patients and parents report an improving quality of life and a perceived feeling of safety due to the possibility to perform blood tests regularly and comfortably at home.

Conclusion: POC monitoring following liver transplantation appears feasible and leads to increased patient satisfaction. It is time consuming and expensive. Further prospective investigations are necessary to evaluate if the technology is cost effective and improves patient outcome.

Disclosure of Interest: None Declared
PATIENT SURVIVAL AND CLINIC ATTENDANCE OF PAEDIATRIC LIVER TRANSPLANT RECIPIENTS FOLLOWING TRANSFER FROM PAEDIATRIC TO ADULT HEALTHCARE SERVICES.

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Objectives and Study: The success of liver transplantation has transformed outcomes for children with liver disease. 85% now survive into adulthood resulting in increased numbers transferring to adult services which requires an effective transition process. The determinants of successful transition for liver transplant recipients are unknown. The objective was to measure patient survival and clinic attendance in paediatric liver recipients from two national paediatric liver units in the UK who have transferred to adult care.

Methods: A multi-centre retrospective case-note review of 109 patients transferred from paediatric to adult care between July 2006 and September 2011. Data which included clinic attendance and patient survival was collected from case-notes 1 year prior to transfer (T-12m), and annually up to 5 years post-transfer (T+1 – T+5).

Results: 109 case-notes were reviewed. The median age at transfer was 18.6 years (range 16.1-23.0). 9 (8%) patients have died since transfer. The median time to death after transfer was 2.2 years (range 0.6-4.9).

Scheduled follow-up appointments between T-12 and T+5 and non-attendance (DNAs)

<table>
<thead>
<tr>
<th></th>
<th>T-12</th>
<th>T+1</th>
<th>T+2</th>
<th>T+3</th>
<th>T+4</th>
<th>T+5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of appointments</td>
<td>179</td>
<td>207</td>
<td>151</td>
<td>102</td>
<td>52</td>
<td>24</td>
</tr>
<tr>
<td>Percentage DNA</td>
<td>14.53%</td>
<td>20.77%</td>
<td>24.5%</td>
<td>16.67%</td>
<td>9.62%</td>
<td>12.50%</td>
</tr>
</tbody>
</table>

*Based upon data from 64/109 patients

Conclusion: The preliminary data show patient deaths were highest in the first two years following transfer as were DNA rates, suggesting this may be a crucial period for young people in the transition process. Further analysis is needed to quantify the occurrence of non-adherence, graft loss and rejection. In addition to the case-note review, a qualitative study is being undertaken to explore stakeholder experiences of transition.

Disclosure of Interest: None Declared
EARLY DETERIOATION OF PELD SCORE IN YOUNG CHILDREN WITH BILIARY ATRESIA PREDICTS POOR OUTCOME
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Objectives and Study: The Pediatric End-stage Liver Disease (PELD) score is designed to prioritize children with biliary atresia for liver transplantation, based on the severity of chronic liver disease. High scores at listing predict poor outcome, including death. Periodic calculation of the PELD score in children awaiting liver transplantation may be an important additional predictor of pre-transplantation mortality. We aimed to determine the PELD change or cut-off score in young children with biliary atresia (BA) on the waiting list that could assist clinicians in identifying those with a high risk of dying before transplantation.

Methods: A national cohort of children younger than 5 years with BA, screened for liver transplantation between 2000 and 2012 was retrospectively analyzed. PELD scores and change scores were calculated at listing and then 2-monthly until death or liver transplantation.

Results: A total of 71 children with BA-associated end-stage liver disease were included, of which 12 (17%) died before transplantation. At the time of listing the optimum PELD score cut point to differentiate high from low risk patients was 21 points. In children with a PELD score of 21 points or more mortality risk before transplantation increased to 40% (10/25), whereas a score of 20 points or below reduced this risk to 4% (2/46). Two months after listing, when 47 patients were still waiting for a donor liver, the optimum cut point to differentiate high from low risk patients was 24 points. Children with a score of 24 or more had a 56% (9/16) risk of death, whereas a score of 23 or below gave a 0% risk (0/31; 95% confidence interval (CI) 0 to 9%). A deterioration of PELD score of 5 points or more in the first two months after listing indicated a 50% (9/18) risk of death before transplantation, whereas a change score of 4 points or less reduced mortality to 0% (0/29; 95% CI 0 to 10%).

Conclusion: Periodic calculation of the PELD score in young children with BA-associated end-stage liver disease awaiting transplantation facilitates recognition of those with a high risk of pre-transplantation demise. Earlier listing of BA patients and/or adaptation of priority rules on the waiting list could help to decrease mortality and thus increase the prognosis of BA.

Disclosure of Interest: None Declared
LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN PATIENTS WITH TYROSINEMIA TYPE 1

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Objectives and Study: It is known that specific 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione (NTBC) treatment along with a tyrosine free or depleted diet reduces the need for liver transplantation (LTx) for patients with tyrosinemia type 1. However, it is not known, whether these precautions or treatments reduce the risk for developing hepatocellular carcinoma (HCC) in patients with tyrosinemia type 1. Here we report 6 patients with tyrosinemia type 1, who underwent LTx and had HCC in explanted liver.

Methods: Retrospective analysis of an inception cohort. Tyrosinemia type 1 patients transplanted in our institution during a ten year period have been analyzed by reviewing the data in patient files.

Results: Between 2002 and 2012, 27 patients have been diagnosed with tyrosinemia type 1 in our institution. Four of those patients had liver transplantation due to HCC. Another patient had aLTx with the diagnosis of neonatal hepatitis, where she had HCC in explanted liver and was diagnosed with tyrosinemia type 1 after the LTx. Median age at diagnosis was 2 years (10 months – 9 years). Mean age at the time of LTx was 4.8 years (9 months – 14.4 years). Median time after the diagnosis to LTx was 2.2 years (5 months – 5.8 years). All patients, but one, have been on NTBC treatment right after the diagnosis. Compliance to diet was excellent in 3, poor in one patient. The last patient with the diagnosis after the LTx has obviously never been on a diet. All, but one, patients have been referred for LTx because of suspected HCC with increasing alpha-fetoprotein (AFP) levels and liver nodules on imaging. Prior to LTx, mean AFP level was 1998 ng/ml (46-60.500 ng/ml) (normal value<13 ng/ml). All patients had living-donor LTx. Median follow-up time after LTx was 39 months (12-89 mo). None of the patients have an HCC recurrence during follow-up.

Conclusion: Although efficient medical treatment may provide satisfactory metabolic control and prevent secondary liver failure, LTx continues to be a significant treatment option for patients with tyrosinemia type 1. In case of malignancy, which necessitates timely LTx, living donors may provide feasible grafts also in the setting of tyrosinemia in parts of the world, where cadaveric donor shortage still exists.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Acute liver failure (ALF) is a clinical syndrome from a variety of causes resulting from rapid loss in hepatocyte function. One of the major causes of mortality in patients with ALF is the development of cerebral edema and emergency liver transplantation is often the only life-saving treatment. Severe cerebral edema on a computed tomography scan is associated with either early mortality or permanent neurological deficits. The aim of this retrospective cohort is determine to frequency of posttransplant neurological outcome and related factors.

METHODS: Patients data were collected from medical records and clinic charts. ALF was defined according to PALF group criteria. Hepatic encephalopathy was graded according to the West Haven criteria. Screening for cerebral edema was done with a computed tomography (CT) scan only if there were focal neurological findings or seizures. Invasive intracranial pressure monitoring was not used. Statistical analysis was performed with SPSS version 16.0.

RESULTS: 154 liver transplants performed between August 2009 and October 2012 at this institution and 24 children underwent living donor liver transplantation for acute liver failure. The median age, PELD and weight was 3.5 year (0.1-18), 37.8 (18-66), 15 kg(4-62), respectively. The most common etiology was cryptogenic (n=8, 33.3%); followed by viral infection (n=6, 25%), toxic (n=5, 20.8%) and metabolic liver disease(n=5, 20.8%). Preoperatively, all patients had encephalopathy (gr2-3 n=8; gr3-4n=16), 5 had seizure activity, 6 had radiological evidence of cerebral edema. Posttransplant brain injury developed in 7 patients (%29.1). Of these 7 patients, 3 had brain death, and 2 had hydrocephaly with seizure and two patient had temporary deafness and blindness. Seizures responded to antiepileptic therapy and antiepileptic drug discontinued end of posttransplant 1st year. Deafness and blindness was gradually improved and both patients were well after 6 month of transplantation. The rate of early mortality which related to brain injury was 17%. Four of the 7 patients with neurological complications or death had radiological evidence of pretransplant cerebral edema. One recipient with a neurological complication did not have imaging pre-transplant, and another two had had a normal CT scan. One and 2 year patient survival was 80% and %80 respectively. Univariate analysis by Cox regression analysis found that preoperative convulsion and age were associated with worse patient survival.

CONCLUSION: Despite living donor is shortened to waiting time for liver transplantation, neurologic complication may continue to be problem posttransplant period. We still need to neurologic markers which able to predict brain damage more accurately.

DISCLOSURE OF INTEREST: None Declared
OUTCOMES AFTER LIVING DONOR LIVER TRANSPLANTATION FOR PEDIATRIC ACUTE LIVER FAILURE:
SINGLE CENTER EXPERIENCE
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Objectives and Study: Acute liver failure continues to be associated with a high mortality rate, and emergency liver transplantation is often the only life-saving treatment. The ability to urgently perform liver transplantation within 48 to 72 hours is crucial to reducing the waiting list mortality rate and complications. In countries in which deceased organ donation is uncommon, living donors have been used, but clinical experience is limited in children with ALF. We report our center’s experience with urgent living donor liver transplantation, patient and graft survival, and major complications.

Methods: Patients data were collected from medical records and clinic charts. ALF was defined according to PALF group criteria. Hepatic encephalopathy was graded according to the West Haven criteria. The treatment of ALF included, as required, mechanical ventilation, broad-spectrum antibiotics with antifungal prophylaxis, antiedema therapy, renal replacement therapy, and nutritional support. The standard immunosuppressive regimen was included tacrolimus, and prednisone.

Results: 154 liver transplants performed between August 2009 and October 2012 at this institution and 24 children underwent living donor liver transplantation for acute liver failure. The median age, PELD and weight was 3.5 year (0.1-18), 37.8 (18-66), 15 kg(4-62), respectively. The most common etiology was cryptogenic (n=8, 33.3%); followed by viral infection (n=6, 25%), toxic (n=5, 20.8%) and metabolic liver disease(n=5, 20.8%). The median waiting time was 1.6 (range 6 hours-10 days). Mortality rate was 20% and all of them died within first 2 month. The causes of mortality were sepsis (n=1), brain death (n=3) and primary nonfunction (n=1). Posttransplant complications included neurological problems (29.1%), biliary problems (n=1, 4.1%), aplastic anemia (n=1, 4.1%), bone marrow hypoplasia(n=2, 8.2%) and isolated thrombocytopenia (n=1, 4.1%). One patient underwent bone marrow transplantation. All of the hematological problems developed in patients who diagnosed as cryptogenic. The cumulative patient survival rates 1 month ,1 and 2 years after LT were 87%, 80%, and 80%, respectively. There was two acute rejection episode which responded to including to mycophenolate to immunosuppressive regimen. Univariate analysis by Cox regression analysis found that preoperative convulsion, age and weight were associated with worse patient survival.

Conclusion: Living donor liver transplantation for pediatric acute liver failure may provide optimal time for transplantation. The survival rate is getting closer to survival in nonurgent liver transplantation. Patient should be closely monitorized for posttransplant neurologic and hematologic complications.

Disclosure of Interest: None Declared
Objectives and Study: Cholesterol ester storage disease (CESD) is a rare autosomal recessive disorder due to late onset lysosomal acid lipase (LAL) deficiency. There are relatively few documented clinical reports hence the clinical phenotype is not well defined and its natural history uncertain. We describe a series of 4 cases seen in a single centre.

Methods: Patients presented between the ages of 1 and 13 with either organomegaly (n=4) and/or abdominal pain (n=3). At presentation all had hepatomegaly and one had splenomegaly. All had abnormal transaminases and three had hyperlipidaemia. All were confirmed to have LAL deficiency and were compound heterozygotes for 2 pathogenic mutations in the LIPA gene.

Results: Three have residual abdominal pain suggestive of gastro-oesophageal reflux with partial response to drug treatment. Three developed biliary dyskinesia which responded to surgery. All were treated with a low fat diet which resulted in resolution of diarrhoea where present. Three were treated with statins with a good initial lipid lowering effect. During a mean follow up of 11 years; two developed new onset splenomegaly, of whom one subsequently died following a road traffic accident at the age of 16. The other remains well age 22 and continues on statin treatment. One underwent liver transplantation aged 9 due to hepato-pulmonary syndrome and remains well with normal lipid levels six years on. The final subject also remains well aged 15 with persistent hepatomegaly and good lipid control on statin treatment.

Conclusion: In summary CESD has a heterogeneous clinical presentation with hepatomegaly being a uniform feature in our series. There is a high incidence of biliary and abdominal symptoms. Hyperlipidaemia usually responds to statin therapy. Splenomegaly develops commonly and liver disease appears progressive. Liver transplantation is highly successful where indicated.

Disclosure of Interest: None Declared
DO WE OFTEN MISS THE DIAGNOSIS OF LYSOSOMAL ACID LIPASE DEFICIENCY IN OBESE PATIENTS?
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Objectives and Study: Lysosomal acid lipase deficiency, or cholesteryl ester storage disease (CESD), is the “benign” form of the very severe Wolman disease of infants. Symptoms are a moderately enlarged liver, high transaminases, high cholesterol, “steatosis” on ultrasound (US), and often non specific abdominal pain and diarrhea. If the patient is obese, the putative diagnosis will be “non alcoholic fatty liver disease” (NAFLD). The liver biopsy (LB) shows a major steatosis and foamy macrophages. The diagnosis is made on enzyme assay and molecular biology. We report 2 cases, diagnosed on LB (for suspicion of auto-immune hepatitis), in order to discuss the possible missed diagnosis in obese children, and raise the awareness of clinicians treating these patients.

Methods: P1, 13-year-old boy, non obese, frequent abdominal pain, elevated liver tests while operated on for appendicitis: AST 95, ALT 130 IU. Anti-smooth muscle antibodies 1/1600. US: hyperechogenic hepatomegaly.
P2, 7 year-old girl, non obese, frequent “colics”, firm hepatomegaly 2-3 cm, elevated transaminases for 3 years (+/- 80-100 IU). Hypercholesterolemia 6.6-7.8 mM, HDL cholesterol 0.7 mM (N > 1). Antinuclear antibodies 1/400. US: hyperechogenic liver.

Results: P1. LB: micro- and macro-vacuolar steatosis in 80% hepatocytes, foamy portal macrophages and Küpffer cells, no inflammation, fibrosis F3. Total cholesterol 7 mM. Treatment with cholestyramin, normalization of cholesterol, decrease of transaminases (50 and 90 IU 8 y after diagnosis). Muscle pain with statin. LB after 5 y: unchanged. No portal hypertension. Diagnosis on enzyme assay and genetics.
P2. LB: panlobular steatosis, foamy macrophages, fibrosis F1. Treatment with cholestyramin, normalization of cholesterol, unchanged transaminases. Diagnosis on enzyme assay and genetics.

Conclusion: The evolution of “late onset” lysosomal acid lipase deficiency is not benign, with complications of hypercholesterolemia, and an already significant fibrosis in P1. A case of hepatocarcinoma, and a few cases of patients needing liver transplantation were reported. In these 2 children, symptoms were mild, the most significant being hepatomegaly. They were not obese and the ultrasound was very unusual for a childhood liver disease. Auto-antibodies were probably secondary and led indirectly to the diagnosis. As they are not constant in previous cases, the same symptoms in an obese child would have been suggestive of NAFLD, without probably an indication for LB. It is thus important in the differential diagnosis of NAFLD to look for mild symptoms such as abdominal pain and diarrhea, and a nearly constant low HDL cholesterol. Beside the symptomatic treatment of hypercholesterolemia and the screening for fibrosis, a specific enzyme therapy will soon be available.

Disclosure of Interest: None Declared
TRANSALDOLASE DEFICIENCY: A SEVERE MULTI-ORGAN NEONATAL DISEASE WITH A HIGHLY VARIABLE PROGNOSIS
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Objectives and Study: Transaldolase deficiency is an inborn error of the pentose phosphate metabolism, responsible for a multi-organ neonatal disease: liver and renal failure, haemolytic anemia, thrombocytopenia, cutis laxa, hypertrichosis, micropenis. We report the long term follow-up of the 2 surviving brothers of a consanguineous Turkish family with 4 affected siblings, and 2 other boys with a severe early evolution. We emphasize the occurrence of the disease in several ethnies, the variable severity, the role of early diagnosis and treatment, as the neonatal disease can recover and a chronic organ dysfunction slowly develop.

Methods: P1, 13 y-old, 3rd child; the 1st one (girl) died of liver failure at age 6 m, the 2nd pregnancy (boy) was terminated for hydrops fetalis. P2 is 8 y-old, 4th child. P3 was born from consanguineous Cambodian parents, P4 from consanguineous Saudi parents.

Results: P1 recovered from neonatal liver failure and haematological abnormalities. Like P2, he has a normal growth (1.6 m, 44 kg) and neurological development, mild cutis laxa and telangiectasia. The liver is normal, ultrasound and biology as well. He has a chronic renal failure (creatinin 160 microM). He has testicular insufficiency, initiated puberty without treatment. P2 had the same early evolution than P1. He has also an atrial septal defect. He developed cirrhosis and portal hypertension. Liver function is normal, ALT 90, AST 76, GGT 21 IU. He has a tubular dysfunction, normal creatinin. He has also a micropenis and hypogonadism. P3 was small for gestational age (37 GW, 2450 g), had also a ventricular septal defect and a portosystemic fistula. He had neither renal failure nor tubular dysfunction, but renal calcifications. The neonatal liver failure was moderate (lowest PT 30%). He failed to thrive, developed ascites and died of multi-organ failure after an infection at age 2.5 m. P4 had a severe liver (PT 10%) and renal (anuria) failure. He died at 1 week of age. The diagnosis was confirmed with biochemistry and molecular biology, with different mutations across the 3 families.

Conclusion: Transaldolase deficiency is a rare multi-organ disease, increasingly recognized in all ethnic groups. In our experience, the diagnosis at birth is easy, with constant typical dermatological features, liver failure of variable intensity, anemia and thrombocytopenia. The prognosis is variable in the same family. Neurological development on the long term is normal. A supportive therapy should be organized rapidly, in order to allow for a possible recovery of the neonatal liver, renal and haematological disease. Organ transplantation will probably be discussed in the future. A prenatal diagnosis can be offered.

Disclosure of Interest: None Declared
HEPATIC GLYCOGENOSIS: A SERIES OF FIVE CASES
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Objectives and Study: The aim of this study is to describe the histological findings of needle core liver biopsies in a case series of five patients with poorly controlled type 1 diabetes who presented with hepatomegaly and raised transaminases. Non-alcoholic fatty liver disease (NAFLD) has been well described in patients with diabetes, particularly type II diabetes. However, case studies have been published recently describing unique pathological changes on liver biopsies in patients with poorly controlled type I or insulin dependent diabetes mellitus. We report the clinical and pathological features of five cases where patients presented with a history of poor diabetic control, type 1 diabetes and hepatomegaly. Histological examination of the liver biopsies showed hepatic glycogenosis, a pathologic overloading of hepatocytes with glycogen.

Methods: A descriptive study reviewing the folders and histology obtained from liver biopsies of five patients with poorly controlled type I diabetes and hepatomegaly.

Results: Patients with Type 1 diabetes mellitus with significant hepatomegaly and raised liver enzymes were identified. The case series comprised four males and one female with ages ranging between 15 and 18 years at time of presentation with hepatomegaly. All five patients had high HBA1C levels (range 11-14%) and recurrent admissions with diabetic ketoacidosis. All five patients underwent diagnostic needle core liver biopsies between 2003 and 2010.

Histological sections from needle core biopsies in four out of the five cases revealed GH with maintained hepatocyte architecture. Glycogen infiltration was demonstrated on Periodic Acid-Schiff (PAS) stain and confirmed in one case using electron microscopy. Only one case in the series demonstrated mild non-alcoholic steatosis.

Table 1: Pathological Features of the Liver Biopsies

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<th>Glycogenic distension</th>
<th>Glycogenated nuclei</th>
<th>Perivenular fibrosis</th>
<th>Portal fibrosis</th>
<th>Steatosis</th>
<th>Mega mitochondria</th>
<th>Apoptosis and inflammation</th>
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**Conclusion:** Hepatic glycogenosis is a rare and under-recognised condition occurring in poorly controlled type 1 diabetes. Clinically, Hepatic glycogenosis cannot be distinguished from NAFLD by history, physical examination or ultrasound. Liver biopsy is essential to differentiate between the two conditions as it impacts management and long term outcome. In contrast to NAFLD, Hepatic glycogenosis does not progress to fibrosis or liver cirrhosis and is completely reversible with good glycaemic control is achieved.

**Disclosure of Interest:** None Declared
Objectives and Study: Neonatal haemochromatosis (NH) is a severe liver disease associated with intra and extrahepatic iron overload. Recently, maternal alloimmunity has been reported as the aetiology for NH, called gestational alloimmune liver disease (GALD).

Methods: We report the case of 3 siblings that developed acute liver failure (ALF) during the early neonatal period.

Results: Case 1 was a mildly premature newborn with low weight for gestational age. On the third day of life she presented cytolysis, coagulopathy, hyperammonemia with elevated serum ferritin. Multi-organ failure developed and liver histology showed important pericellular fibrosis, macrovesicular steatosis in regenerative nodules, biliary stasis, hepatocitary and kupffer cell iron overload. Salivary gland biopsy was not contributive and the patient did not present intracranial iron overload in MR images. She deceased on day 19 and post mortem liver immunostaining was positive for membrane attack complex (MAC) leading to the diagnosis of GALD associated NH. No autopsy was allowed. For the next pregnancy, the mother received prophylactic intravenous immunoglobulins to prevent possible recurrent GALD. She gave birth to a full term boy. On the third day of life he also presented ALF with coagulopathy, elevated serum ferritin and edema of lower limbs. He was initially treated with exchange transfusion and immunoglobulins, but failed to improve and was referred for liver transplantation at day 4 of life. Galactose exclusion, as routinely implemented in our referral centre for neonatal liver disease, led to rapid recovery. Genetic and enzymatic studies confirmed homozygocy for Classic Galactosaemia (CG). The same mutations were retrospectively found in stored liver tissue from fatal case 1. Because GALD could not be absolutely excluded, the mother was again treated with immunoglobulins for a third pregnancy. She gave birth to a healthy girl. CG was genetically and enzymatically confirmed and she was fed with soy milk formula. An accidental ingestion of lactose containing milk formula occurred on the seventh day of live, leading to rapid life threatening liver failure, that recovered progressively with liver support treatment.

Conclusion: These 3 familial cases of CG illustrate that ALF can occur after a single dose of lactose containing milk. Therefore, galactose should be excluded from the diet of any infant with severe liver disease, until CG is ruled out. Severe metabolic conditions such as galactosaemia can be associated with elevated ferritin levels, intrahepatic siderosis and positive MAC immunostaining, which is thus, not specific of GALD.

Disclosure of Interest: None Declared
HEPATOLOGY

PO-H-0341

PROTOCOL BASED MANAGEMENT OF METABOLIC LIVER DISEASE IN CHILDREN AT A TERTIARY CARE SPECIALIZED CENTER
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Objectives and Study: Inborn errors of metabolism, where hepatomegaly and/or abnormal liver function form part of the clinical disease, are collectively referred to as “Metabolic liver disease (MLD)”. Dietary exclusions, antioxidants and chelation therapy with immunoglobulins can offer good outcome in some of the treatable MLDs. Liver transplantation (LT) for MLD shows markedly improved outcome. Diagnosing in the acute situation is often problematic on account of inadequate availability of investigations, failure to identify metabolic defect and lack of definitive diagnostic tests. Indian literature has a dearth of MLD mention especially in acute liver disease setting amongst children. Although in children with chronic liver disease, an Indian tertiary care center reported 18.9% cases of MLD, half of which were Wilson’s disease (WD). There are about 1000 MLDs making the laboratory work up very exhaustive as well as expensive and moreover most enzyme assays are not available in India. Protocol based approach to screen for MLDs (with an emphasis on those which are curable or have palliative /LT therapeutic option) should improve the identification rate. Aim: To study the prevalence and the spectrum of Metabolic liver disease (MLD) identified with protocol based screening in Pediatric Hepatology Unit at a Tertiary care specialized center.

Methods: An age and presentation appropriate protocol based approach was used to screen the children with encephalopathy, acute liver failure, cholestasis, hepatomegaly and chronic liver disease (Protocol 1-5 respectively) presenting to the Pediatric Hepatology unit.

Results: Of the total 288 cases 56 (19.4%) were MLD and cryptogenic or indeterminate cases were 5%. 1 of the 6 children in protocol 1 was identified as Primary lactic academia. 13 of the 42 (31%) of the protocol 2, 7 of 62 (11.3%) of the protocol 3, 17 of 18 (94%) of protocol 4 and 18 of 160 (11%) of protocol 5 were MLD. In total there were 26 WD of which 3 were transplanted, 7 died/ left and 16 survived on medical management. There were 8 glycogen storage disorder and all were type 3. There was one female child with urea cycle defect who presented with ALF. One child with cirrhosis was identified as hereditary fructose intolerance. Seven children with cholestasis and pruritus were found to be having PFIC type 3. There were three siblings who were found to be having Chanarin Dorfman syndrome (nonlysosomal lipid storage disorder). Of the neonatal cholestasis 2 each had galactosemia and tyrosinemia type 2 and one had cystic fibrosis. One more baby had lysosomal lipid storage disorder.

Conclusion: Protocol based approach can more effectively identify MLD in a developing world setting and would also help in reducing the cryptogenic or indeterminate liver disease.

Disclosure of Interest: None Declared
A-METHYL-ACYL-COA RACEMASE DEFICIENCY PRESENTING WITH TRANSAMINAEMIA AND GALLSTONES IN 3 SIBLINGS

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Objectives and Study: α-Methyl-acyl-CoA racemase (AMACR) deficiency is a rare peroxisomal disorder resulting in accumulation of pristanic acid and 27-carbon bile acids such as trihydroxycholestanolic acid (THCA) and in fat soluble vitamin deficiency. Age of onset is variable with most reports describing neurological involvement in adults (sensorimotor neuropathy, cerebellar ataxia, seizures) and one report describing coagulopathy in a neonate. This is the first report of AMACR deficiency presenting with mild liver dysfunction and gallstones.

Methods: The index case is an 8 year old boy who is the third child of consanguineous Arab parents. He was referred with persisting transaminaemia following laparoscopic cholecystectomy for gallstones. Liver biopsy findings on light microscopy showed minimal fibrosis and occasional necrotic hepatocytes. In light of mild developmental delay further metabolic investigations were performed including very long chain fatty acid (VLCFA) determinations. Plasma pristanate was markedly elevated but VLCFA concentrations were essentially normal. The 2 older sisters (11 and 13 years), the oldest with gallstones also, both had mild transaminaemia and markedly elevated pristanate.

Results: Urine bile acid analysis by GCMS for the index case revealed the presence of trihydroxycholestanolic acid (THCA) in keeping with clinical suspicion of AMACR deficiency. Subsequent sequence analysis of the AMCAR identified a c.877T>C (p.Cys293Arg) mutation in all 3 children. This previously unreported mutation affects a highly conserved region and is predicted to be pathogenic. Subsequent staining of liver tissue with anti-AMACR antibody further confirmed deficiency of AMACR expression in the index case when compared to controls. All children are treated with ursodeoxycholic acid and fat soluble vitamin supplementation and remain well at the last follow up. The role and benefit of a low phytanic acid diet has yet to be explored in these cases.

Conclusion: This case report is the first to identify children presenting with AMACR deficiency manifest as mild liver dysfunction with gallstones. A novel pathogenic mutation has been identified in this family. We have illustrated that immunohistochemical interrogation of liver tissue can aid in early diagnosis whilst awaiting further molecular diagnostic tests. To consider peroxisomal disorders in children with unexplained liver disease is important even when neurologic findings are minimal.

Disclosure of Interest: None Declared
STUDY OF ACUTE LIVER FAILURE IN NEWBORNS AND YOUNG CHILDREN WITH AN UNDERLYING INHERITED METABOLIC DISEASE
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Objectives and Study: To study the demographic, clinical and laboratory findings, diagnoses and outcome of children under 5 years who were admitted with acute liver failure (ALF) secondary to an underlying inherited metabolic disease (IMD). ALF was defined as a prothrombin time (PT) > 15 seconds and/or an International normalised ratio (INR) > 1.5 and not corrected by vitamin K, in the presence of hepatic encephalopathy (HE), or a PT > 20 seconds and/or an INR > 2.0 in the absence of HE.

Methods: A retrospective case note review of children who were admitted between January 2001 to 2012 to King’s College Hospital with ALF and a multi-centre review of their long term outcome.

Results: A total of 127 children were identified from the database. 36 children (28%; 17 boys; median presenting age 6 weeks, range 1 day-41 months) had an underlying IMD including galactosemia in 17, mitochondrial cytopathy in 7, ornithine transcarbamylase (OTC) deficiency in 4, tyrosinemia type 1 in 4, Niemann-Pick C (NPC) in 3 and congenital disorder of glycosylation type 1 in 1. The remaining aetiologies were: indeterminate in 40 (32%), infectious in 15 (12%), neonatal hemochromatosis in 11 (9%), hemophagocytic syndrome in 8 (6%), drug toxicity in 5 (4%) and other in 10 (8%). Of the 36 children with an IMD consanguinity was present in 16 (44%), developmental delay in 3 (8%), jaundice at presentation in 28 (78%), hepatomegaly in 27 (75%) and HE in 8 (22%). The median peak INR was 4.8 (range, 1.8-15), aspartate transaminase 334umol/L (range, 39-15791) and bilirubin 227umol/L (range, 13-692). Liver biopsy was done in 9 children (25%), neuroimaging in 10 children (28%), bone marrow aspiration in 7 (19%) and muscle biopsy in 5 (14%). 29/36 children with an IMD survived (81%). 4 children with mitochondrial cytopathy (including 1 after transplantation during the postoperative period) and 3 with NPC died. 4 children (1 OTC deficiency; 3 mitochondrial cytopathy) underwent liver transplantation. Follow up data was available for 23 children (mean follow up period, 4 years 3 months) in whom 13 (57%) were identified as having evidence of developmental delay.

Conclusion: IMD is a common cause of ALF in children. Indeterminate cases may include undiagnosed metabolic disease. Survival of children with IMD-related ALF is good, however, long term developmental outcome is less favourable.

Disclosure of Interest: None Declared
GLYCOGENIC HEPATOPATHY – AN AVOIDABLE COMPLICATION OF INSULIN DEPENDENT DIABETES MELLITUS OR A CONSEQUENCE OF MITOCHONDRIAL DYSFUNCTION?

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Objectives and Study: Mauriac disease, the association of growth failure, massive hepatomegaly and Cushingoid features in children with poorly controlled type 1 diabetes should be obsolete with modern insulin regimes. Over the last 10 years more than 30 children have presented to our paediatric liver centre with the syndrome however. Though the condition is closely associated with a high HbA1C, the aetiology is not fully understood.

Methods: diagnosed with glycogenic hepatopathy, the hepatic manifestation of Mauriac syndrome, were prospectively identified. Clinical, histological and biochemical data were reviewed. SPSS 17.0 was used for statistical analysis.

Results: Thirty one children (16 boys) with a median age of 15.1 years (IQR14, 16) presented within the study period. Median age of diagnosis of diabetes was 10 years (11, 16). Median units of insulin/kg/day was 1.33 with a median HbA1C of 11% (9.9, 12.4%). Growth was impaired: median height z-score was -1.01 (-1.73, 0.4) and weight was -0.11(-0.8, 0.17). Hepatomegaly was universal with splenomegaly in 5. Transaminases were abnormal in the majority with a median AST of 76IU/l (44, 187), ALT of 76IU/l (69, 177) and GGT of 71IU/l (47, 114). Though no child was ketoacidotic at time of measurement, lactate was abnormal in 16. Liver biopsy was undertaken in 19 (61%). All demonstrated enlarged hepatocytes with clear cytoplasm with glyogenated nuclei in 17 of 19. Steatosis (mostly macrovesicular) was also present in the majority. Interestingly, inflammation was present in 8 (42%); this was mainly periportal. Fibrosis was seen in 14 (73%) and was mild in the majority of cases though 2 children had bridging fibrosis. Steatosis, inflammation and fibrosis have not been well described previously in this condition. Megamitochondria were seen in 7 biopsies. One boy with a high serum lactate was found to have mitochondrial depletion of 29% of normal in liver biopsy. It is not clear whether this depletion was a primary or secondary phenomenon. The presence of megamitochondria correlated with AST (p=0.026) and presence of fibrosis on biopsy. At follow-up to 6.5 years following presentation, 17 children had normal or improved transaminases, in 13 there was no change.

Conclusion: Despite modern insulin regimens and monitoring in children with type 1 diabetes, Mauriac syndrome still exists. Although previous reports have not found inflammation or fibrosis in liver tissue, we have found both in significant amounts. The association of megamitochondria and high lactate levels in children with the condition may suggest a possible mechanism for pathophysiology of the condition.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Liver copper concentration is regarded to be a very sensitive and specific diagnostic test in Wilson disease (WD). Concentrations above 250 µg/g dry weight have very high Positive Predictive Value in adults, whereas concentrations below 50 µg/g dry weight practically exclude diagnosis of WD. However there is very limited data concerning liver copper content validation as diagnostic test in children with increased ALT and no features of liver insufficiency WD. The aim of the study was to validate the test in a cohort of children with WD.

METHODS: 74 patients with WD diagnosed according to Ferenci score were the study group. 211 patients with liver diseases other than WD and no persistent hyperbilirubinaemia were the control group. They all have liver biopsy performed with liver copper measurement in specimen. Sensitivity and specificity were assessed for cut-off value of 250 µg/g dry weight and discriminant ability and optimal cut-off point were established with ROC curve analysis.

RESULTS: Liver copper concentrations were 882; 626; 1124 [median, Q1, Q3] µg/g dry weight and 29; 18; 72 in study and control group respectively. For cut off point of 250 µg/g dry weight the sensitivity was 0.96 (0.88; 0.99 [95% CI]) - 3 out of 74 patients had liver copper under 250, and the specificity was 0.98 (0.95; 0.99) - 4 out of 211 patients had liver copper over 250. Area under ROC curve was 0.996. The optimal cut off point for our groups was 304 with sensitivity 0.96 (0.89; 0.99) and specificity 0.99 (0.97; 0.99).

CONCLUSION: Liver copper concentration has very high discriminant ability in differential diagnosis of children in presymptomatic WD, however optimal cut off point (304) should be slightly higher.

DISCLOSURE OF INTEREST: None Declared
HEPATOLOGY

PO-H-0346

COMPARISON OF HEPATIC AND URINARY COPPER LEVELS IN PATIENTS WITH WILSON’S DISEASE AND OTHER CHRONIC LIVER DISEASES WITH OR WITHOUT CHOLESTASIS

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Objectives and Study: Liver and urine copper levels may overlap in patients with Wilson’s disease (WD) and other chronic liver diseases with bile stasis. We aimed to compare copper parameters in pediatric patients with WD against a control population of patients with liver disease other than WD.

Methods: 41 children with chronic liver disease (21 cholestatic, 20 non-cholestatic, aged 132.3±50.1 months) and 35 children with WD that confirmed by ATP7B genotype (122.4±45.3 months) were included. Patients were included in non-WD chronic liver disease group when Ferenci diagnostic scores were between 0-1.

Results: Mean serum direct bilirubin levels were 13.4±8.7 mg/dl and 0.66±0.72 mg/dl in cholestatic and non-cholestatic liver disease groups, respectively. When WD and chronic liver disease patients were compared, liver copper levels were found to be significantly higher in WD group (655.5±785.4 versus 177.6±343.8 µg/g/dry weight (p=0.001). In Non-WD group liver copper levels were significantly higher in cholestatic group than non-cholestatic group (264.9±463 versus 94.4±133.8 (p<0.05). In Non-WD group liver copper levels were lower than 50 µg/g in 19 patients (46.3%), between 50-250 µg in 12 patients (29.2%), and higher than 250 µg in 10 patients (24.5%). 6 out of 10 pts with high liver copper had cholestasis. In WD patients liver copper levels were lower than 100 µg/g in 3 (%8.5), between 100-250 µg in 9 (25.7%), and higher than 250 µg/g in 23 (66%) patients. When WD and cholestatic + non cholestatic chronic liver disease patients were compared, 24 h urine copper levels were found to be significantly higher in WD group 970.9±1569.1 versus 91.5±138.4, p=0.0001. In non-WD group 24 h urine copper levels were significantly higher in cholestatic group than non-cholestatic group (136.2±150.7 versus 48.8±133.3 (p=0.012). In 41 non-WD chronic liver disease patients a positive correlation was detected between direct bilirubin and liver copper levels (p=0.017 r=0.417). In 35 WD pts a positive correlation was detected between direct bilirubin and 24h urine copper level (p=0.008 r=0.439). A ROC analysis of liver copper at the cutoff value of 98 showed a sensitivity of 91%, specificity of 65.4%, area under the curve = 0.838. The 24 h urinary copper diagnostic cutoff value was found to be 67.5 (sensitivity 85%, specificity 71%, area under the curve = 0.843.

Conclusion: In non-WD chronic liver diseases, liver copper accumulation increased in parallel with cholestasis. In our study, 24 h urinary copper excretion and liver copper level were highly informative when 67.5 µg/24h and 98 µg/g/dry weight were considered as upper limit of normal respectively.

Disclosure of Interest: None Declared
Objectives and Study: Wilson's disease (WD) is a genetic disorder characterized by copper accumulation mainly in the liver. The treatment is based on chelators, and/or zinc. Efficacy of monotherapy with zinc has been questioned by Weiss et al. (1). Aim: to evaluate reasons for treatment changes in WD patients diagnosed in childhood.

Methods: 44 patients with WD, referred to our Department of Pediatrics (1984-2012), were analyzed. 42 had hepatic presentation and 2 were recruited for family screening. For each patient, the type of treatment carried out was classified in: D-penicillamine; zinc salts; combination of D-penicillamine and zinc. Reasons for therapy changes were: treatment failure, adverse events, patient demand (not linked to adverse events) and maintenance regimen. We excluded from our analysis, discontinuation of treatment linked to shift to maintenance therapy. We calculated the duration of each block of treatment until a change of medication or until the end of the follow-up period. We analyzed events of treatment changes using Kaplan-Meier estimation.

Results: 44 (31 males, median age at diagnosis = 5.9 years, range = 1-16.9) of the 48 evaluated patients, were selected for treatment analysis. Changes in medical treatment were common events resulting in a total of 79 treatment blocks (32 penicillamine therapy, 35 zinc therapy and 12 combination therapy). Of these, 76 (31 penicillamine therapy, 34 zinc therapy and 11 combination therapy) were suitable for analysis. A change in medication due to treatment failure or adverse events, not linked to the transition to maintenance therapy, was observed in 4 of 34 zinc blocks (12%), 13 of 31 penicillamine blocks (42%) and 4 of 11 combination blocks (36%). Discontinuation due to adverse events was most common in patients receiving penicillamine with 6 (5 penicillamine, 1 combination) of 42 block treatments stopped for this reason. A change in medication due to treatment failure was observed in 16 blocks of 76 (21%): 8 of 31 penicillamine treatments (26%), in 4 of 34 zinc blocks (12%) and 4 of 11 combination blocks (36%). This reached statistical significance comparing zinc versus combination therapy, but not zinc with penicillamine. Among treatment failure blocks, noncompliance to therapy was pointed out in 1 of 8 penicillamine treatments (12%), 2 of 4 zinc (12%) and 4 of 4 combination treatments (100%).

Conclusion: Therapy discontinuation for treatment failure and/or adverse events was more common on penicillamine than on zinc. Differently from Weiss data (1), our study confirmed that zinc monotherapy is effective in controlling liver disease in patients with WD, diagnosed and treated since childhood.


Disclosure of Interest: None Declared
HEPATIC STEATOSIS AND THYROID FUNCTION TESTS IN OVERWEIGHT AND OBESE CHILDREN AND ADOLESCENTS
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Objectives and Study: The association between abnormal thyroid function and nonalcoholic fatty liver disease (NAFLD) is biologically plausible given the common clinical and biochemical features of visceral obesity, insulin resistance, hypertension, hypertriglyceridemia, and lipid peroxidation observed in both NAFLD and hypothyroidism. To our knowledge, none of the previous studies have investigated the relationship between hepatic steatosis and thyroid function in childhood. Therefore, the aim of our study was to explore in a population of 402 overweight and obese children with no clinical, autoantibody, and ultrasonographic evidence of thyroid disease, the association between thyroid function tests [thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3)] and hepatic steatosis as well as metabolic syndrome (MetS) and its parameters.

Methods: Hepatic steatosis was diagnosed by ultrasound after exclusion of infectious and metabolic disorders. Fasting serum samples were taken for determination of thyroid function (TSH, FT4, FT3), along with alanine aminotransferase (ALT), lipid profile, glucose, insulin, and insulin resistance (IR).

Results: Eighty-eight children (21.9%) had TSH above the normal range (> 4.0 mIU/L). FT3 and FT4 were within the reference intervals in all subjects. Elevated TSH was associated with an increased odds of having hepatic steatosis [OR 2.10 (95% CI, 1.22-3.60)], hepatic steatosis with elevated ALT [2.42 (95% CI, 1.29-4.51)], hypertriglyceridemia, elevated total cholesterol, and IR as well as MetS (considered as a single clinical entity), after adjustment for age, gender, pubertal status, and body mass index (BMI)-SD score (or waist circumference), as well as FT3 and FT4. No association was found between FT4 and hepatic steatosis, as well as MetS and its parameters after controlling for age, gender, pubertal status, and BMI-SDS (or waist circumference).

Conclusion: In overweight/obese children, elevated TSH concentration is a significant predictor of hepatic steatosis, and lipid and glucose dysmetabolism, independently of the degree of total and visceral obesity. Nonetheless, our data are associations and do not prove causality. The possibility that thyroid hormones and NAFLD share common genetic or environmental influences accounting for the observed association cannot be discounted. It is also possible that hepatic steatosis affects thyroid function rather than the other way around. A longitudinal study with a cohort of children with and without hepatic steatosis at baseline would help clarify this.

Disclosure of Interest: None Declared
DOES VITAMIN-E IMPROVE THE OUTCOMES OF PEDIATRIC NAFLD? SYSTEMATIC REVIEW & META-ANALYSIS
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Objectives and Study: To complete a systematic review of the literature, and perform a meta-analysis to determine the efficacy of adjuvant vitamin E on the outcome of non-alcoholic fatty liver disease (NAFLD) in children

Methods: Systematic review and meta-analysis of randomized trials published between January 1969 and September 2012 that examined the role adjuvant vitamin E given at any dose or duration, alone or in combination with other interventions on the outcome of pediatric NAFLD (younger than 18 years). The outcomes are ALT normalization & histology improvement. Studies identified through MEDLINE, PUBMED, EMBASE & Cochrane CENTRAL Register Controlled Trials & Cochrane database of systematic reviews & extracted by 2 independent reviewers.

Results: Four randomized control trials (RCT) & one quasi-randomized study were found in pediatrics involving total number of 270 participants. There was no statistical significant difference in the effect of adjuvant vitamin E on normalizing serum ALT (RR= 0.95) (CI =0.75-1.21), P = 0.32 for heterogeneity, $I^2 = 15\%$. Sensitivity analysis showed that using higher dose of vitamin E, longer duration of therapy or adding vitamin C to vitamin E did not change the effect on the outcome. Only two studies looked to the histological changes as an outcome, they used different definitions for histology improvement. When we pooled the data from these two studies for meta-analysis looking for the proportion of participants with histology improvement, we observed a substantial heterogeneity between the two studies; therefore, it was not appropriate to combine their results statistically.

Conclusion: Our meta-analysis did not find a significant effect of adjuvant vitamin E alone or in combination with vitamin C over placebo in normalizing serum ALT. Data on the long term effect of adjuvant vitamin E on histology improvement in NAFLD patients are still lacking, further larger & well-designed RCTs are still needed in children to answer this question. Life style interventions (diet & exercise changes) are, so far, the only proven therapeutic intervention for NAFLD in children.

Disclosure of Interest: None Declared
HEMEOXYGENASE-1 GENE PROMOTER POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY TO NON-ALCOHOLIC FATTY LIVER DISEASE IN CHILDREN AND ADOLESCENTS

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Objectives and Study: Oxidative stress is increased in nonalcoholic fatty liver disease (NAFLD). Heme oxygenase (HO) is important in the defense against oxidative stress. This study aimed to assess the association of the length of (GT) n repeats in HO-1 gene promoter with NAFLD among obese children.

Methods: A total of 101 obese children aged 6-17 years were recruited. We measured anthropometric and serum biochemical variables. We screened the allelic frequencies of (GT) n repeats in the HO-1 gene promoter in these obese children. The (GT) n repeats of the HO-1 gene was amplified by PCR. The PCR products were analyzed with an automated DNA sequencer. NAFLD was determined through liver ultrasonography. We assessed the effects of the length of (GT) n repeats in HO-1 gene promoter on pediatric NAFLD.

Results: Of 101 obese subjects, 25 (24.8 %) had NAFLD. There were no significant differences between patients with and without NAFLD with regard to sex, body mass index (BMI), blood pressures, serum cholesterol, triglycerides and 2-hour plasma glucose level. The GT repeat numbers ranged from 16 to 37, and (GT) 23 and (GT) 30 are the two most common alleles in our study population. Because the distribution of numbers of (GT) n repeats was bimodal, we divided the alleles into 2 subclasses: class S included shorter (< 27) repeats, and class L included longer (≧27) repeats. The proportion of L allele frequency was significantly higher in patients with NAFLD (66.0 %) than in those without NAFLD (50.0 %) (P=0.04). The alanine aminotransferase (ALT) level was higher in patients carrying L alleles (L/L and L/S) than patients with S alleles (S/S) [46.2±49.3 IU/L versus 30.2±20.1 IU/L]. With regard to the genotypic distribution, the odds ratio (OR) of NAFLD was 8.00 (95% CI 1.01-63.19, P=0.04) in patients carrying L alleles (L/L and L/S).

Conclusion: In this hospital-based study, the obese children with larger GT repeats were susceptibility to have NAFLD.

Disclosure of Interest: None Declared
DOES THROMBIN GENERATION TEST PROVIDE ANY ADDITIONAL INFORMATION IN CHILDREN WITH LIVER DISEASE?
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Objectives and Study: There is now evidence that the balance between pro- and anticoagulant factors is maintained also in liver disease and that individual screening coagulation tests are insufficient to predict the risk of bleeding or thrombosis (1).

The objective was to evaluate if the thrombin generation tests provide any additional information, compared to routine coagulation tests, in children with liver disease.

Methods: 82 pediatric patients with liver disease were enrolled at our tertiary referral center for pediatric hepatology; 71 with standard risk of bleeding and 11 with increased risk of bleeding. Increased bleeding risk was defined by at least one of following; INR >1.4, APTT >44 sec., fibrinogen <1.5g/L or overt bleeding. Platelet-poor plasma was analyzed with the fluorogenic Calibrated Automated Thrombogram (CAT) to test thrombin generation incl. endogenous thrombin potential. Further, routine coagulation tests (incl. INR, APTT, fibrinogen) and specific levels of pro- and anticoagulant factors were analyzed. 34 age-matched healthy children served as controls.

Results: The 71 liver patients with standard risk of bleeding had an endogenous thrombin potential similar to normal controls. Among the eleven patients with an increased bleeding risk there were reduced levels of procoagulant factors (II, VII, IX, X and for adolescents also V and fibrinogen) and concomitant lower levels of anticoagulant factors such as antithrombin and protein C. These patients had a reduced endogenous thrombin potential, compared to standard risk patients, and coherent with their results of the routine coagulation tests.

Conclusion: Thrombin generation tests with this commercially available method on platelet-poor plasma provide similar information as routine coagulation tests in children with liver disease, with and without increased bleeding risk. Measurement of thrombin generation with current assay does not provide additional information regarding the hemostatic function in children with liver disease.


Disclosure of Interest: None Declared
Objectives and Study: Obesity, insulin resistance and dyslipidemia are the most significant risk factors of non-alcoholic fatty liver disease (NAFLD), but the role of adipokines in the patomechanism of this disease is not clear. Therefore, the aim of the study was to evaluate the serum concentration of novel adipokines in obese children with NAFLD.

Methods: Forty five obese (BMI>95pc) children, age range 7-17, mean 13 years, were admitted to our Department with suspected liver disease (hepatomegaly, and/or ultrasonographic liver brightness and/or increased ALT activity). Viral hepatitis (HBV, HCV), autoimmune and metabolic liver diseases (Wilson’s disease, alpha 1 antitrypsin deficiency, cystic fibrosis) were excluded. Fasting serum levels of chemerin, omentin, vaspin were determined (ELISA, BioVendor). The degree of liver steatosis in ultrasound (USG) was graded according to Saverymuttu et al. Advanced liver steatosis was defined as a score >1. 1HMR spectroscopy was performed with 1.5T scanner and with PRESS sequency; total lipid concentration was assessed in relative units in comparison to unsuppressed water signal. ROC analysis was used to calculate the power of the assays to detect fatty liver or advanced steatosis.

Results: Fatty liver was confirmed in 39 children by USG and in 33 patients by 1HMR (19 of them had also an increased ALT activity /NAFLD/). Chemerin level was higher (p>0.001) and vaspin level was lower (p=0.019) in children with NAFLD compared to control group (n=30). Significant positive correlations were found between the total liver lipids in 1HMR and chemerin (r=0.33; p=0.02) and vaspin (r=0.4; p=0.006). The ability of serum chemerin (cut-off=192.3ng/ml, Se=72%, Sp=58%) to differentiate children with fatty liver in 1HMR from those without steatosis was significant (AUC=0.7, p=0.05). Chemerin > 228.9ng/ml had a specificity of 100% and a sensitivity of 58% (AUC=0.8, p=0.026) in predicting advanced liver steatosis. Omentin and vaspin did not allow a useful prediction.

Conclusion: Chemerin seems to be the most suitable non-invasive biomarker in predicting both advanced liver steatosis in children with NAFLD and fatty liver in obese children.

Disclosure of Interest: None Declared
HEPATOLOGY

PO-H-0353

GAMMA-GLUTAMYLTRANSFERASE AS A POTENTIAL BIOMARKER OF THE CARDIOVASCULAR RISK IN CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Objectives and Study: Non-alcoholic fatty liver disease (NAFLD) is regarded as a specific feature of the metabolic syndrome which is characterized by the increased risk of early development of the cardiovascular diseases. The results of studies in adults suggested that gamma-glutamyltransferase (GGT) may be identified as the independent biomarker of the increased cardiovascular risk. Therefore, the aim of the study was to evaluate the GGT serum activity in children with NAFLD.

Methods: Sixty two obese (BMI>95pc) children, age range 7-17, mean 12 years, were admitted to our Department with suspected liver disease (hepatomegaly and/or ultrasonographic liver brightness and/or increased ALT activity). Viral hepatitis (HBV, HCV), autoimmune and metabolic liver diseases (Wilson’s disease, alpha 1 antitrypsin deficiency, cystic fibrosis) were excluded. The degree of liver steatosis in ultrasound (USG) was graded according to Saverymuttu et al. Advanced liver steatosis was defined as a score >2. 1HMR spectroscopy was performed with 1.5T scanner and with PRESS sequency; total lipid concentration was assessed in relative units in comparison to unsuppressed water signal. ROC analysis was used to calculate the power of GGT to detect fatty liver or advanced steatosis.

Results: Fatty liver was confirmed in 49 children by USG (26 of them had also an increased ALT activity /NAFLD/). We found significant correlation between GGT and ALT level (r=0.62; p>0.0001), hsCRP concentration (r=0.57; p>0.0001), the degree of liver steatosis in USG (r=0.4; p=0.001) and total amount of lipids in 1HMR spectroscopy (r=0.43; p=0.0008) and negative correlation of GGT with adiponectin (r=-0.35; p=0.02). The ability of serum GGT activity (cut-off=19IU/l, Se=92%, Sp=69%, PPV=86%, NPV=82%) to differentiate children with NAFLD from those without steatosis was significant (AUC=0.87, p=0.0002). GGT > 27IU/l had a sensitivity of 76% and specificity of 68% (AUC=0.74; p=0.035, PPV=32%, NPV=90%) in predicting advanced liver steatosis.

Conclusion: The higher level of GGT in children with NAFLD compared to obese patients without liver pathology and the correlation of this enzyme with other biomarkers of cardiovascular risk (hsCRP, adiponectin) may suggest the higher risk of cardiovascular diseases in NAFLD children.

Disclosure of Interest: None Declared
THE RELATIONSHIPS BETWEEN BIRTH WEIGHT AND OBESITY, NON-ALCOHOLIC LIVER DISEASE AMONG 6-15 YEARS CHILDREN

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Objectives and Study: To evaluate the effect of birth weight on obesity, non-alcoholic liver disease in low birth weight (LBW) and high birth weight (HBW) children compared with normal birth weight (NBW) children of Shanghai China. This study follows a representative sample (n=3008) of children age 6-15 years old from different suburban and urban districts in Shanghai China.

Methods:
Physical examination (height, weight, waist circumference) and ultrasonic testing of liver were carried out by trained physicians. To determine the risk factor of developing general obesity and non-alcoholic liver disease. LBW and HBW children were tested with general and central obesity respectively.

Results: Among 6-15 years female children, the risk of being non-alcoholic liver disease for high birth weight group were 2.6 times as much as that of normal birth weight group (OR=2.6, 95%CI: 1.06-6.38, P=0.037). Among the male and female participants, the risk of being general obesity for high birth weight group were 1.36 times as much as that of normal birth weight group respectively (OR=1.36, 95%CI: 1.03-1.8, P=0.0171).

Conclusion: Children's birth weight has a strong influence both on general obesity and non-alcoholic liver disease. High birth weight is a strong risk factor for childhood general obesity. Among female children, high birth weight was significantly associated with non-alcoholic liver disease.

References:

**Disclosure of Interest:** None Declared
VITAMIN D DEFICIENCY IS COMMON IN OBESE CHILDREN WITH BIOPSY-PROVEN NASH: A PROSPECTIVE OBSERVATIONAL STUDY
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Objectives and Study: Pediatric obesity has now become an epidemic phenomenon ("obesity epidemic"). Severe comorbidities are seen even in children, such as non alcoholic fatty liver disease (NAFLD) and steatohepatitis (NASH). Vitamin D (VD) deficiency has been shown to be frequent in obese adults and children, even if the bio-molecular mechanism of this association is not yet clear. It has been hypothesized that VD deficiency can exacerbate liver disease through the activation of a pro-inflammatory environment in animal models. We looked at VD levels in a selected group of obese children with Insuline Resistance (IR), affected by biopsy proven NASH.

Methods: From January to March 2012, 17 obese children (10 males, mean age 13±2.5 years) with IR and NASH were enrolled in this prospective study. They all had a normal calcium intake in the diet. No child had renal disease. All patients were tested for 25-hydroxy-vitamin D [25(OH)D] serum level. All children also underwent DEXA scan.

Results: At enrollment mean BMI was 31±5 kg/m², mean Insuline serum level was 18.7±2.6 and 101.7±19.1 UI/ml at time 0 and after 120 minutes at Oral Glucose Tolerance Test, respectively. Not all children had impaired liver function tests (mean AST level 32±15 UI/ml, and ALT level 41±27 UI/ml). All children had normal calcium serum levels (above 9 mg/dl). VD levels were impaired and considered suboptimal in 11/17 (65%) children (mean 25(OH)D: 19.5±5.6 ng/ml). The Bone Mineral Density of all patients was in the normal range.

Conclusion: This is, at our knowledge, the first observational prospective study evaluating VD levels in obese children with IR and biopsy proven NASH. These preliminary data confirm that suboptimal VD levels are common in obese children with comorbidities. Lower serum levels of VD may be involved in the pathophysiology of NASH. Further larger studies, even prospective interventional trials assessing NASH before and after VD supplementation, are required to confirm these data.

Disclosure of Interest: None Declared
Objective and Study: Liver biopsy is the gold standard to evaluate liver fibrosis. However, this procedure has some limitations and risks. Transient Elastography (TE) is an alternative technique to determine liver stiffness non-invasively, quickly, easily and reliably. Reference values for the pediatric population have mostly been obtained using a probe for adults. Very recently, one single paper published data with a pediatric probe in German children.

Objective: To establish reference values of transient elastography using the pediatric probe on healthy children in our population.

Methods: After informed consent from parents was obtained, measurements were performed in healthy children admitted for minor surgical procedures, meeting following inclusion criteria: no previous history of gastrointestinal pathology and with a recent blood tests showing normal liver function. Subjects were classified into three age groups: Group 1 (0-3 years old), Group 2 (4-8 years old) and Group 3 (9-15 years old). FS measures liver stiffness, through mechanical vibration pulse and ultrasonic waves. The probe is applied in the midaxillary line, between the ribs and on the hepatic silhouette. Depending on chest circumference (CC), two types of pediatric probe were used: S1 for CC < 45 cm, and S2 for CC 45-75 cm. For a valid FS, a minimum of ten valid determinations must be obtained, with a success rate of over 60%. Two values have to be taken into account: the ratio between the number of valid measurements and the total number of measurements, i.e. the success rate, and the stiffness or the median of all valid determinations expressed in kiloPascal (kPa).

Results: We were able to perform the test in all cases, in 1.2 - 6.3 minutes time, and a success rate of 91-100%. Group 1 (n = 6) average is 3.17 kPa (range 2.8-5.1 and standard deviation (SD) ± 1.17), for Group 2 (n = 4) average is 2.75 kPa (range 2.7-3.8 and SD ± 0.50) and for Group 3 (n = 7) average is 3.86 kPa (range 2.7-6.3 and SD ± 1.35). A comparison of the means of the three groups by ANOVA displays p=0.302 which implies that there is no statistically significant differences among the three groups.

Conclusion: TE has proved to be a rapid and well tolerated test in all age groups. The normal range of liver stiffness that has been obtained in our population ranges is 2.7 - 6.3 kPa. We intend to expand the sample size to strengthen our results. This is mandatory to further correlate the values of TE with the histology in patients with liver dysfunction of different etiologies, and to establish the cutoff points for the different stages of fibrosis.

Disclosure of Interest: None Declared
LIVER STIFFNESS MEASUREMENT USING SUPersonic SHEar IMAGING: FEASIBILITY AND COMPARISON WITH LIVER BIoPsy IN THE ASSESSMENT OF LIVER FIBROSIS IN CHILDREN

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1 pediatric radiology, 2 Hopital Bicêtre, Assistance Publique Hopitaux de Paris, 3 Inserm, 4 pediatric hepatology, Hopital Bicêtre, Assistance Publique Hopitaux de Paris, Le Kremlin Bicêtre, France

Objectives and Study: Supersonic Shear Wave Elastography (SSWE) is a new non-invasive method to measure liver stiffness (LS). This ultrasound elastography technique is based on the direct measurement of the shear-wave velocity which is directly related to LS. The aim of this study is to evaluate the feasibility of SSWE in children, and to measure its diagnostic accuracy in the assessment of liver fibrosis by using liver biopsy as the reference standard.

Methods: We prospectively included forty-five children who underwent liver biopsy. Fibrosis was staged according to the METAVIR scoring system. The diagnostic accuracy of SSWE was evaluated using the Area Under the ROC (AUROC) for significant (≥F2) or advanced fibrosis (≥F3). The results of a previous feasibility study in 44 healthy children were considered as F0 for fibrosis to calculate the AUROC for moderate fibrosis (F1-F2).

Results: Forty-five children were included. Forty-eight couple liver biopsy/elastometry were studied. Median age was 2 years (1 month to 17 years). Twenty-one had a liver transplantation, 11 biliary atresia, and 13 others. Measurement of liver stiffness was feasible in all patients. Median time between liver biopsy and elastometry was 2 days (from 0 to 90 days). The METAVIR score was F0 in 4 cases, F1 in 21, F2 in 9, F3 in 7, and F4 in 7. The diagnostic performance for the prediction of moderate (F0 vs F1-F2), significant (≥F2) or advanced fibrosis (≥F3) are given in table 1. The correlation between elastometry by SSWE and fibrosis score was lower in liver graft recipients at the acute phase (0.47) compared to other patients (0.70 to 0.87). Twelve patients had discordance between liver stiffness and fibrosis score. Venous congestion and/or cholestasis were present in 7.

<table>
<thead>
<tr>
<th>METAVIR Threshold</th>
<th>F0 vs F1-F2 (31 patients)</th>
<th>≤ F2 (25 patients)</th>
<th>≤ F3 (16 patients)</th>
<th>≤ F4 (9 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUROC (IC)</td>
<td>0.95 (0.89-1)</td>
<td>0.94 (0.87-1)</td>
<td>0.93 (0.85-1)</td>
<td>0.96 (0.9-1)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>90%</td>
<td>87%</td>
<td>78.6%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Specificity</td>
<td>95.7%</td>
<td>92%</td>
<td>97.1%</td>
<td>95.1%</td>
</tr>
<tr>
<td>Well classified</td>
<td>92.3%</td>
<td>89.6%</td>
<td>91.7%</td>
<td>93.8%</td>
</tr>
</tbody>
</table>

Conclusion: Liver stiffness measurement by SSWE is feasible in children. Diagnostic accuracy for liver fibrosis seems to be good even for minimal or mild fibrosis. Further studies are necessary to evaluate the accuracy of this technique in homogeneous groups of pathology and to understand its pitfalls.

Disclosure of Interest: S. Franchi-Abella Consultant for: supersonic imagine, France, L. Corno: None Declared, B. Ducot: None Declared, E. Gonzales: None Declared, M. Fabre: None Declared, D. PARIENTE: None Declared
LIVER STIFFNESS MEASUREMENT USING SUPersonic SHEar-WAVE ELASTOGRAPHY: FEASIBILITY STUDY IN HEALTHY CHILDREN

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1pediatric radiology, 2Hopital Bicêtre, Assistance Publique Hopitaux de Paris, 3Inserm, 4pediatric hepatology, Hopital Bicêtre, Assistance Publique Hopitaux de Paris, Le Kremlin Bicetre, France

Objectives and Study: Supersonic ShearWave Elastography™ (SSWE) is an innovative technique for the assessment of tissue elasticity based on the combination of a radiation force induced in tissue by an ultrasonic beam and an ultrafast imaging technique capturing in real time the propagation of the resulting shear waves. The purpose of this study is to evaluate the feasibility in children, to determine potential factors which may influence the measurement, and to define the normal SSWE values in normal pediatric liver.

Methods: Liver stiffness measurements were performed in 51 healthy children aged 0 to 18 years classified as: preterm and term newborns, less than 1 year, 1-5 years, 5-10 years and more than 10 years old. Two probes (high and low frequency), two measurement locations (epigastric and intercostal) and two kinds of respiration (Apnea and free respiration) were tested.

Results: Measurements were technically possible in each child. The mean elasticity value was 6.58 +/- 1.46 kPa. Elasticity values were statistically different according to the probe: 5.96 +/- 1.31 kPa and 6.94 +/- 1.42 with the high frequency and low frequency probes respectively (p = 0.006). There was no influence of gender, age, measurement location or respiratory condition.

Conclusion: SSWE is a new non-invasive method that is integrated in an ultrasound scanner. This technique is fast and easily feasible in children. The probe must be adapted to the morphotype of the child as in B mode. The average values are statistically significantly higher with the low frequency probe relative to the high-frequency probe, with a difference of less than 1 kPa that may not be significant in clinical practice.

Disclosure of Interest: S. Franchi-Abella Consultant for: supersonic imagine, France, L. Corno: None Declared, L. Corno: None Declared, B. Ducot: None Declared, E. Gonzales: None Declared, D. PARIENTE: None Declared
Objectives and Study: Hepatic haemangioendothelioma (HHE) are rare vascular tumours. Treatment can be conservative (corticosteroids, diuretics) or surgical/radiological (hepatic artery ligation (HAL)/embolisation, resection or liver transplantation). The rarity of the condition and lack of randomised controlled trials makes therapeutic decisions particularly challenging. Propranolol has been used in the treatment of cutaneous and solid organ haemangiomas or haemangioendotheliomas. Our aim was to assess the efficacy and safety of Propranolol in the treatment of HHE.

Methods: 42 patients were referred with HHE between May 1998 and September 2012. Our initial protocol was to use corticosteroids and/or diuretics and/or surgical/radiological intervention. Since April 2008, Propranolol was added to the protocol. Patients were categorised depending on whether they received Propranolol (Group 1) or not (Group 2). Patients were followed up with serial ultrasound scans. The starting dose of Propranolol used was 0.5mg/kg in 2 divided doses titrating up to a maximum dose of 2mg/kg in 2 divided doses.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>16</td>
<td>26</td>
</tr>
<tr>
<td>Presentation</td>
<td></td>
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<tr>
<td>Symptomatic/Incident</td>
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<td>8/9/9</td>
</tr>
<tr>
<td>Antenatal</td>
<td></td>
<td></td>
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<tr>
<td>Severity</td>
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<tr>
<td>PICU Admission</td>
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<td>4</td>
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<tr>
<td>Haematological</td>
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<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Treatment</td>
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<tr>
<td>Steroids/Diuretics</td>
<td>8/7</td>
<td>6/7</td>
</tr>
<tr>
<td>Treatment</td>
<td>0 (0/0)</td>
<td>14 (0/10)</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>Surgical (ligation/hepatectomy)</td>
<td>2 (2/0)*</td>
<td>10 (8/2)</td>
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<tr>
<td>No Treatment</td>
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<table>
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<tr>
<th>Radiological</th>
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<tr>
<td>Diffuse Lesion</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Improvement (mean time in months)</td>
<td>3.9</td>
<td>6.8</td>
</tr>
</tbody>
</table>

* Both these babies received propranolol after HAL. The first baby was listed for liver transplantation after he had developed ischaemic hepatitis following HAL. While he was on the waiting list, Propranolol was started 4 months after ligation. The second baby had a primary HAL as she was clinically unstable. Due to the diffuse nature of the tumour, it was assumed that ligation might not be as effective and listing for liver transplantation was considered. However, she was started on Propranolol a week after the ligation. Both the babies responded to Propranolol and recovered completely and did not require liver transplantation.

Propranolol was very well tolerated. Only one patient discontinued treatment because of wheezing. Two children became hypotensive and one child became hypoglycaemic. All three continued Propranolol after a dose reduction and subsequently tolerated titration to maximal dose.

**Conclusion:** Propranolol is a safe and effective treatment modality with or without steroids/diuretics for HHE and may obviate the use of surgical or radiological interventions.

**Disclosure of Interest:** None Declared
HEPATOLOGY

PO-H-0360

LIVER DISEASE IN INFLAMMATORY BOWEL DISEASE
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Objectives and Study: To describe the features of liver disease in patients with inflammatory bowel disease (IBD).

Methods: Retrospective review of patients with IBD referred to our Paediatric Liver Centre, between September 2004 and 2009, because of abnormal liver function tests (LFTs).

Results: 43 patients were identified (31M: 12F). Median age at IBD diagnosis was 10.9 yrs (2-15); 27 had ulcerative colitis, 13 indeterminate colitis, 2 Crohn's disease and 1 indeterminate colitis and coeliac disease. LFTs were abnormal at IBD diagnosis in 17, while became abnormal 20 mths (1-81) after diagnosis in 26. Median time for referral to our centre was 9 mths (0-117) after IBD diagnosis.

At presentation blood tests were: AST 69 IU/l (range 15-1245), ALT 15 IU/l (range 13-251), GGT 206 IU/l (range 6-498) and INR 1.07 (range 0.86-2.23). Total bilirubin was >20 µmol/l in 8. IgG was increased in 21. 6 patients were positive for antinuclear antibody, 5 for anti-smooth muscle antibody and 2 for both. No one was anti LKM-1 positive. 26 were ANCA positive.

Of 41 who underwent biliary imaging (MRCP/ERCP), 31 had cholangiopathy 28 of whom had bile duct damage (BDD) on liver histology; of these 18 who also had interface hepatitis (IFH) and/or positive auto antibodies were diagnosed as autoimmune sclerosing cholangitis (ASC), whilst 10 with no IFH and/or positive autoantibodies as sclerosing cholangitis (SC). Two with cholangiopathy on MRCP and no BDD on histology, but IFH and/or positive autoantibodies were diagnosed as ASC. 26 were ANCA positive.

Conclusion: The high incidence of cholangiopathy in children with IBD and abnormal LFTs in our study highlights the need for prompt referral to a specialised paediatric liver centre for diagnosis and appropriate management.

Disclosure of Interest: None Declared
Objectives and Study: Phototherapy (PT) is the standard treatment for neonatal jaundice. Exchange transfusion (ET) has been the “rescue treatment” for severe hyperbilirubinemia which is either acute or not rapidly responsive to PT. Studies to improve ET efficacy and minimize its risks have been hampered by the relative low application rate of ET and by the lack of an in vivo model system. An appropriate animal model for ET should resemble the human situation as much as possible, and rapidly and safely reduce unconjugated bilirubin (UCB) and free bilirubin (Bf) levels. Aim: To develop an animal model for ET during unconjugated hyperbilirubinemia.

Methods: We established a rat model for ET in hyperbilirubinemic Gunn rats (n=30, body weight 269-330g). Gunn rats have a genetic incapacity to conjugate UCB, resulting in a lifelong unconjugated hyperbilirubinemia. Under general anesthesia, the right jugular vein was cannulated for the alternate extraction of native blood and the infusion of fresh whole rat Wistar donor blood (1 ml per cycle in 1 min). ET was performed at a rate of 1 ml/min, for 20 minutes, after which the anesthesia was stopped. Blood was collected before the ET (T0), and at 1, 3, 6, and 24 hours after finishing the ET. After 48 hours, all animals were exsanguinated. Plasma UCB and Bf levels were analyzed.

Results: We performed ET in 30 Gunn rats with 100% survival. The recovery after ET was rapid, illustrated by maintenance of body weight during the 48 h after ET (at T48, 100 ± 3 % compared to T0, NS). ET rapidly decreased plasma UCB concentrations (from 14.9 mg/dL at T0, to 8.3 mg/dL at T1; -44%, p<0.05), and plasma Bf concentrations (from 13.8 to 2.1 µg/dL; -85%, p<0.05). During the subsequent time points, plasma UCB and Bf levels returned to pre-ET values, conform physiological expectations for Gunn rats. At T48 plasma UCB and Bf levels were back to T0 values.

Conclusion: We successfully developed the first animal model for exchange transfusion during unconjugated hyperbilirubinemia. We expect that this Gunn rat-ET model will be very valuable to evaluate the effect of modulating ET procedures and techniques, and to compare its efficacy in combination with other treatments to prevent brain damage during acute severe hyperbilirubinemia.

Disclosure of Interest: None Declared
OPTIMIZING THE ACUTE TREATMENT OF SEVERE UNCONJUGATED HYPERBILIRUBINEMIA: EXCHANGE TRANSFUSION, PHOTOTHERAPY, ALBUMIN ADMINISTRATION, OR A COMBINATION THEREOF?

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Objectives and Study: Neonatal unconjugated hyperbilirubinemia carries the risk of neurotoxicity. Only free bilirubin (Bf), the fraction of unconjugated bilirubin (UCB) not bound to albumin, can induce neurotoxicity after translocation across the blood-brain barrier. Acute treatment of severe unconjugated hyperbilirubinemia can involve phototherapy (PT), albumin (Alb) administration and exchange transfusion (ET). Based on its invasiveness and related risks, ET is considered as a “rescue treatment”. It has remained unclear whether ET is more effective than the combination of PT plus albumin administration, mostly due to limitations to study this in acutely hyperbilirubinemic infants. We addressed this comparison in a recently developed Gunn rat-ET model. Aim: To determine the most effective treatment (combination) of ET, PT and Alb with respect to reducing plasma UCB and Bf concentrations within 2 hours in Gunn rats.

Methods: Gunn rats (10-12 weeks of age, bodyweight: 254-335 g) were randomized to receive either PT (n=7), PT+Alb (n=7), ET (n=7), ET+PT (n=7), ET+PT +Alb (n=7) or no treatment (controls, n=3). ET was performed via the right jugular vein, at a rate of 1 ml/min, for 20 minutes (1 ml per cycle in 1 min). Albumin i.p. injections (2.5 g/kg) were given immediately after the ET or just before starting PT. PT was started immediately after ET and for the PT-only groups at T0. Blood was collected before starting PT or ET (T0) and at 1, 3, 6, and 24 hours after ET. For the PT-only groups the same time points were used. After 48 hours, all animals were exsanguinated. Plasma UCB and Bf concentrations were analyzed.

Results: PT and PT+Alb did not decrease UCB concentrations within 2 h, in contrast to Bf concentrations (PT: -51%; p<0.001, PT+Alb: -64%; p<0.001). Yet, ET was profoundly more effective in decreasing both plasma UCB (-58%, p<0.01) and Bf (-85%, p<0.05) than either PT or PT+Alb. Combining ET with either PT or with PT+Alb did not further significantly decrease plasma UCB or Bf concentrations within 2 h.

Conclusion: We successfully applied a novel Gunn rat-ET model to compare acute treatments for severe hyperbilirubinemia. Our data indicate that ET is most effective in decreasing UCB and Bf within 2 hours of treatment, and that combining ET with either PT or PT+Alb does not further potentiate this rapid hypobilirubinemic effect.

Disclosure of Interest: None Declared
TARGETING THE ENHANCER OF ZESTE HOMOLOGUE 2 (EZH2) IN HEPATOBLASTOMA

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Objectives and Study: Hepatoblastoma (HB) is the most common malignant live tumour in children. Although the treatment of HB has been improved, it is still lack of treatment strategies for fatal outcomes of fast development and recurrence. Here, we would like to investigate the effects of targeting EZH2, the catalytic subunit of Polycomb repressive complex 2, in the tumorigenesis of HB.

Methods: Western-blot analysis and immunostaining analysis were used to determine the amount of EZH2 expression in HB and their adjacent controls. Lentivirus-mediated RNA interference (RNAi) was employed to knock-down EZH2 in two HB cells, HepG2 and Huh6, to study the roles of EZH2 in tumorigenesis.

Results: In this study, we demonstrated that EZH2 was highly expressed in 5 HB tumour tissues, including subtypes of 4 immature embryonal tumours and 1 small cell undifferentiated type tumour. In 2 fetal pattern tumours, another type of HB, we did not found significant increased of EZH2 expression compared to their matched controls. Inhibition of EZH2 by RNAi could suppress proliferation of both HepG2 and Huh6 significantly in vitro. After depletion of EZH2, those cells were arrested at G1/S point, which indicated that G1 phase increased and S period reduced. Further analysis the p27 protein, an important inhibitor of G1/S, was increased significantly in response to down-regulation of EZH2.

Conclusion: These findings established a role of EZH2 in hepatoblastoma tumorigenesis and identify EZH2 as a potential therapeutic target especially in immature subtypes.

Disclosure of Interest: None Declared
INCIDENCE OF GALLSTONES AND INTESTINAL FAILURE ASSOCIATED LIVER DISEASE IN CHILDREN ON LONG-TERM PARENTERAL NUTRITION AT HOME
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Objectives and Study: Children with severe long-term intestinal failure (IF) dependent on parenteral nutrition (PN) for >27 days may present with intestinal failure associated liver disease (IFALD), cholestasis and gallstones. The aetiology of cholestatic liver disease is multifactorial with risk factors such as prematurity, sepsis, surgical diagnosis and intravenous lipid emulsions. Our aim was to determine the incidence of IFALD, sludge and gallstones and their complications in children with severe IF long-term/home PN.

Methods: A retrospective study was performed in a tertiary paediatric centre. Liver function tests and abdominal imaging were reviewed in 75 patients (53% male) aged birth-17 years treated with PN for a median of 5 years. Any abnormality affecting the hepatobiliary system and complications were included and factors that might predispose to IFALD/ gallstones were documented.

Results: 393 abdominal ultrasounds were performed in 75 patients. Underlying diagnoses were short bowel syndrome in 21(28%), small intestinal enteropathy in 36(48%) and motility disorder in 18(24%). 28 (37%) children had IFALD. 58 (77%) patients had abnormal abdominal imaging (213/393 or 54%), in 90 scans (23%) with multiple abnormalities in 19 (23%). 19 (25%) patients had gallstones, 8 (11%) biliary debris and 5 (7%) both. 4 (5%) patients underwent a cholecystectomy as a result. In 11 (15%) the gallstones/biliary debris remained, in 8 (10%) resolved and in 6 children biliary debris formed to gallstones in follow up scan and in other 3 children gallstones lead to biliary duct dilatation. Hepatomegaly was present in 22 (29%), splenomegaly in 5 (7%) and hepatosplenomegaly in 17 (23%) patients. 2 (2%) patients had focal liver lesions on ultrasound. 87 scans were performed with contemporaneous IFALD, in the majority with 74 (18%) type I, 9 (2%) type II and 4 (1%) with type III. 58/213 abnormal ultrasounds were performed in children with contemporaneous IFALD compared to 29/180 normal, p=0.001. The presence of IFALD, especially type I was significantly associated with an abnormal scan (p=0.02), biliary debris (p<0.001) and splenomegaly also with type II (p=0.001 and 0.04).

Conclusion: Hepatobiliary pathology is common in children on long term PN th gallstones in 25% of cases. Cholecystectomy may be needed. The incidence of IFALD and gallstones in PN patients in our study is comparable with current literature. Imaging plays a key role in the management of these patients. Abdominal ultrasound is an appropriate investigation since there were no instances where pathology was missed on ultrasound and subsequently identified on other cross-sectional imaging.

Disclosure of Interest: None Declared
A DIAGNOSTIC SCORING SYSTEM FOR AUTOIMMUNE ACUTE LIVER FAILURE IN CHILDREN

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Objectives and Study: Autoimmune hepatitis (AIH) is considered an underdiagnosed cause of acute liver failure (ALF) both in adults and children. If steroids are initiated promptly, patients with autoimmune acute liver failure (AI-ALF) may survive without transplantation (OLT). There are no reported series of children with AI-ALF. We aimed to report our experience and propose a scoring system for diagnosing AI-ALF in this setting.

Methods: We retrospectively reviewed all cases of ALF referred to our Hospital in the last 16 years. ALF was defined by high transaminases, INR ≥ 2.0 regardless of encephalopathy, no previously recognised chronic liver disease. AI-ALF was diagnosed in the presence of positive autoantibodies (ANA, SMA, LKM, LC1) and a compatible histology. Features of children with AI-ALF were compared to non AI-ALF patients and a diagnostic score was built on the basis of statistically significant differences between the two groups.

Results: We identified 46 children with ALF; 10/46 (21.7%, M/F=6/4, median age of 6.4 years, range 1.3-15.1, Group 1), had AI-ALF (AIH1=4; AIH2=6); 36/46 (78.3%, M/F=20/16, median age 2.4 years, range 0.2-13.7, Group 2), had ALF due to acetaminophen overdose (6), metabolic disorders (3), Wilson’s disease (3), mushroom poisoning (3), viral infection (1) and indeterminate (20). Histological evaluation was carried out in 93% of patients. In Group 1 median age at diagnosis was greater (6.4 y vs 2.4 y in Group 2, p<0.05), alanine aminotrasferase (ALT) was lower (1020 U/L vs 3229 U/L, p<0.05), IgG was greater (1845 mg/dl vs 971 mg/dl, p<0.001). Based on these results we defined a scoring system including autoantibody positivity, ALT levels, Immunoglobulin levels and age at onset to diagnose children with AI-ALF (range -2 to +6). The optimal cutoff point on the ROC curve was 3 (sensibility 100%, specificity 97.2%, area under the curve 0.994).

Conclusion: In our experience AI-ALF accounts for 22% of all paediatric cases of ALF. A simple diagnostic score may be utilized to identify children with such aetiology, allow prompt treatment and probably avoid OLT in a proportion of cases.

Disclosure of Interest: None Declared
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SERUM CREATININ AND THE PRESENCE OF ENCEPHALOPATHY AT PRESENTATION MAY PREDICT MORTALITY IN CHILDREN WITH ACUTE LIVER FAILURE

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Objectives and Study: The aim of our study was to analyze the importance of certain prognosis factors in acute liver failure mortality in a pediatric population.

Methods: We performed a cross-sectional study on 38 consecutive patients diagnosed with acute liver failure in the 2nd Pediatrics Clinic, Cluj Napoca, Romania, between January 2008 and October 2012. The inclusion criteria were: age between 0 and 18 years, no previous cause of encephalopathy, acute hepatic decompensation (acute-on-chronic liver failure cases were also included). Commonly available serum biomarkers were recorded at presentation: liver function tests (transaminases, total protein and albumin, coagulation parameters), glycemia, creatinin, sodium and potassium. We also assessed the presence and degree of hepatic encephalopathy using the West Haven criteria. PELD score was calculated in each patient. Overall survival at 45 days was assessed. Non-parametric statistic tests were used for data analysis.

Results: We included 38 children with a mean age of 7.43 years, 50% males. The most frequent etiology was mushroom poisoning (73.7% of cases); the other etiologies were acute viral hepatitis (8.7%), drug intoxication (8.7%) and acute-on-chronic liver disease - Wilson’s disease or biliary atresia (8.7%). Fifty percent of the patients died within the follow-up period. In univariate analysis, the following factors were found to positively or negatively correlate with short-term mortality: total bilirubin, transaminase levels, total protein and albumin, prothrombin time and INR, creatinin, sodium, PELD score and the presence of encephalopathy (p<0.05 in all cases). In multivariate analysis, however, only hepatic encephalopathy and serum creatinin were found to independently predict mortality (R²=0.78, p<0.001).

Conclusion: In our data set, high creatinin level and the presence of encephalopathy seemed to predict mortality in children with acute liver failure. Interestingly, PELD score was not found to independently predict death, maybe because of the heterogeneity of the sets, both in terms of etiology and age. However, both creatinin and encephalopathy are linked with the severity of liver disease in adults, so the correlation is not circumstantial. Creatinin measurement and assessment of encephalopathy are easy to perform in the ER, and should always be performed in children with acute liver failure.

Disclosure of Interest: None Declared
PEER TO PEER SUPPORT INTERVENTION FOR YOUNG PEOPLE WITH A CHRONIC LIVER CONDITION OUTSIDE A HOSPITAL SETTING
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Objectives and Study: Peer-based programmes have the potential to have a positive effect on many areas of a young person’s health and wellbeing including self-esteem, self-efficacy and expectations about individual control. Peer-based programmes innately recognise the unique skills and ability of young people to provide a constructive role in the solution to their own problems. Peer-based initiatives also recognise that once learned, peers can assist to develop these skills amongst other young people.1,2

Our pilot study aims to measure the impact and role of peer support in a four day adventure residential for young people with a liver condition.

Methods: 14 young people median age 14.5 years (12-17) (8 male, 6 female) with a liver condition (5 auto immune liver disease, 1 Alagille syndrome, 2 biliary atresia, 3 biliary atresia & transplant, 2 alpha 1, 1 no diagnosis) self-nominated to attend a four day residential with a range of activities - ice breakers, team building, down time, dormitory accommodation, 24 hour woodcraft survival and aerial ropes course. Parents were invited to complete a postal questionnaire post event. Final day written questionnaires were completed by participants.

Results: 14 families (10 mothers, 4 fathers) and all 14 participants completed questionnaires.

Parents reported the main reason for their child attending was to meet other young people with a liver condition.

<table>
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<tr>
<th>Parental reporting of their child’s self-confidence</th>
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<td>Self Confidence</td>
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<td>Post residential</td>
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<th>Parental reporting of their child’s self-esteem:</th>
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<td>Self Esteem</td>
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<tr>
<td>Post residential</td>
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All but 1 parent reported their child had gained a new, positive perspective on their liver condition post the residential. 62% of young people attended because they wanted to meet other patients. 85% rated their experience as 5/5, 15% rated it as 4/5. All reported the residential was worthwhile attending.
**Conclusion:** This project appears to have made an impact upon self confidence and esteem. The project has significant potential in empowering young people to develop peer to peer support skills and possibly enable greater compliance. There is a strong role for patient groups to empower young people to take control of their health and achieve life goals outside of the hospital setting. This should be encouraged actively by professionals.

**References:**

**Disclosure of Interest:** None Declared
Objectives and Study: Liver failure in infancy is rare but carries a significant mortality. The clinical presentation and results of initial investigations may help direct clinicians to the possible aetiology and guide treatment decisions. These infants require early referral to a paediatric liver centre were liver transplantation can be considered. This study highlights the aetiologies, associated features, helpful investigations and outcome of young infants presenting with liver failure.

Methods: All infants presenting within 90 days from birth with a hepatic-based coagulopathy (INR ≥2) or encephalopathy were included in a retrospective case note review over a 19 year period (1993 - 2012).

Results: 81 infants (M=51) presented with liver failure; aetiologies included metabolic disease 30, (galactosaemia 11, tyrosinaemia 3, mitochondrial cytopathy 11, transaldolase deficiency 1, inborn error of bile salt metabolism 2, long chain 3-hydroxyacyl-CoA dehydrogenase deficiency 1, probable cholestatic liver disease 1), neonatal haemochromatosis (NH)7, infection 13, (Herpes simplex virus (HSV) 9, congenital CMV infection 2, enterovirus 1, E.Coli 1), infiltrative 6 (haemophagocytic lymphohistiocytosis 5, acute lymphoblastic leukaemia 1), hypoxic/ischaemic 15, hypopituitarism 3, and unknown 6.

Infants with metabolic disease were mainly jaundiced at presentation (77%, median bilirubin 207(16-767umol/L)) with mild transaminitis (Median ALT 85(16-1996 IU/L)). They had associated raised lactate (median 4(1.4-22 mmol/L)) however patients with mitochondrial cytopathy had markedly raised lactate (median 6.2(3-22 mmol/L)). Infants with infectious aetiology were mostly term (median gestation 39 weeks) but with low birth weight (median 2.7 kilograms). They had marked transaminitis (median ALT 895 (111-2726 IU/L)) and coagulopathy (median INR 6 (2.6-20)) at presentation.

Infants with infiltrative disease mainly developed jaundice (83%), acidosis (83%), with moderate transaminitis (median ALT 562(36-1592 IU/L)) and a significantly raised lactate (median 10.6(6.9-12.6 mmol/L)). They also had the poorest outcome with 100% mortality. Infants with hypoxic insult had associated renal impairment (73%), acidosis (60%) and a high lactate (median 4.3(1.3-16 mmol/L)). Only five patients were transplanted (2 NH, 2 HSV and 1 mitochondrial) three of whom died post transplant. The overall survival rate was 59%.

Conclusion: Aetiology of liver failure was established in 93% of infants. Careful attention to history, presenting symptoms and associated biochemical abnormalities may help guide in determining the aetiology of liver failure and therefore treatment decisions and prognosis.

Disclosure of Interest: None Declared
ORAL AND DENTAL HEALTH IN CHILDREN WITH CHRONIC LIVER DISEASE

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Objectives and Study: With the increasing survival rate of children with end-stage liver disease after liver transplantation, contributing factors for the morbidity and mortality must be improved prior to transplantation. Therefore, we aimed to analyze the oral and dental health status of children with chronic liver disease (CLD) in order to reflect the importance of dental care in these patients.

Methods: 31 children with CLD (patient group), 17 children with chronic renal failure (CRF) that did not require dialysis (patient control group) and 35 healthy children (control group) comprised the study group. The parents were interviewed about various oral health-related factors (questionnaire) and then children were participated in a clinical dental examination. The caries experience of the children was recorded according to the criteria of WHO and dental plaque (PI) and gingival indexes (GI) were assessed. Salivary parameters including salivary flow rate (SFR), buffer capacity (BC) and salivary mutants streptococci (SMC) and lactobacilli colonization (LC) were investigated. Mandibular bone mass was assessed by antegonial index (AI) in panoramic radiographs. The decayed, missing and filled teeth (DMFT) index was calculated.

Results: The results are shown in Table 1. The prevalence of dental caries was found significantly higher in patients with CLD than CRF (p<0.05, OR: 7.91, 95% CI: 1.1-67.9). Enamel hypoplasia was more common in patients with CLD than healthy controls (p<0.05, OR: 2.65, 95% CI: 0.8-8.2). Percentage of high BC was more common in patients with CRF than patients with CLD and healthy controls (p<0.05). Other parameters were not significant difference among the groups.

DMFT index in patients with CLD were not associated or correlated with any factors including PELD score, Child-Pugh score, presence of ascites, portal hypertension, malnutrition, cholestasis and anemia and etiology (metabolik vs. others).

Table 1: Oral and dental parameters of the groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CLD (n=31)</th>
<th>CRF (n=17)</th>
<th>Control group (n=35)</th>
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<tbody>
<tr>
<td>Questionnaire score</td>
<td>7.5 ± 1.4</td>
<td>7.5 ± 1.1</td>
<td>7.4 ± 1</td>
</tr>
<tr>
<td>Presence of caries, n (%)</td>
<td>29 (93.5)%</td>
<td>11 (64.7)%</td>
<td></td>
</tr>
<tr>
<td>Enamel hypoplasia, n (%)</td>
<td>17 (54.8)%</td>
<td>7 (41.1)%</td>
<td>11 (31.4)%</td>
</tr>
<tr>
<td>SFR, mean ± SD ml/min.</td>
<td>0.39 ± 0.1</td>
<td>0.4 ± 0.11</td>
<td>0.38 ± 0.09</td>
</tr>
<tr>
<td>BC, high, medium, low %</td>
<td>45.2%, 38.7, 16.1</td>
<td>70.6, 29.4, 0</td>
<td>45.7%, 41.1, 14.2</td>
</tr>
<tr>
<td>SMC and LC, &gt;10° col. n (%)</td>
<td>23 (74.1), 22 (70.9)</td>
<td>8 (47), 9 (52.9)</td>
<td>18 (51.4), 18 (51.4)</td>
</tr>
<tr>
<td>DMFT index, mean ± SD</td>
<td>0.11 ± 0.09</td>
<td>0.20 ± 0.1</td>
<td>0.15 ± 0.08</td>
</tr>
<tr>
<td>AI</td>
<td>2.8 ± 0.87</td>
<td>3.04 ± 0.80</td>
<td>2.5 ± 0.77</td>
</tr>
</tbody>
</table>

p<0.05
**Conclusion:** Although DMFT index was similar among the groups, our investigation has shown that patients with CLD were increased risk of caries and enamel hypoplasia. Their susceptibility to caries may be associated with lower BC compared to patients CRF, but no difference was found in other factors.

**Disclosure of Interest:** None Declared