EXCLUSIVE ENTERAL NUTRITION IN PAEDIATRIC CROHN’S DISEASE: A MULTI-SITE AUDIT

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Objectives and Study: The British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) guidance (October 2008) advocates the use of Exclusive Enteral Nutrition (EEN) as an alternative first line agent to oral corticosteroids for induction of remission in paediatric Crohn’s disease. Medium/long term use of corticosteroids is known to cause significant adverse effects. EEN is not known to produce any harmful consequences but can sometimes be difficult to tolerate. The aim of the audit was to assess whether EEN was being offered at two neighbouring district general hospitals (DGHs) in accordance with BSPGHAN standards and whether EEN courses were producing a remission rate similar to that in the literature.

Methods: All patients on the Crohn’s Disease Register at two neighbouring DGHs were included. Data was collected from medical and dietetic records. Data was analysed using excel sheet.

Results: 95% of children had tried a course of EEN either at diagnosis or after relapsing. 95% children tolerated a full course of EEN. In accordance with guidance, 83% EEN courses lasted 6–8 weeks. Remission was achieved in 78% overall, which was consistent with the literature. 71% of those patients who achieved complete remission with EEN had a relapse, however, time until relapse was highly variable (<2 months to >3 years). Of the patients who relapsed, 60% chose not to retry EEN. The length of period for food reintroduction was much more variable compared to the literature. Average number of dietetic consultations for induction of remission and food reintroduction were also variable across sites.

Conclusion: In accordance with guidance, EEN was widely used in both the DGH settings. It was tolerated well and proved to be an effective treatment achieving complete remission in 78% of patients. Our findings support the use of EEN as a first line treatment for paediatric Crohn’s disease, with clear benefits over the use of oral corticosteroids. It should, therefore, be considered as primary treatment in all paediatric Crohn’s disease patients. There needs to be a consensus guideline for food reintroduction following 6–8 weeks of exclusive EEN. There is also a need for more collaborative research and regular local and national audits into the care of paediatric Crohn’s disease patients.

References:
The British Society of Paediatric Gastroenterology, Hepatology and Nutrition (2008) Guidelines for the Management of Inflammatory Bowel Disease (IBD) in Children in the United Kingdom

Disclosure of Interest: None declared.

NUTRITIONAL MANAGEMENT OF INFANTS WITH CHOLESTASIS IN A TERTIARY PAEDIATRIC LIVER UNIT

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Objectives and Study: Cholestatic infants benefit from feeds rich in medium chain triglycerides (MCT). In our centre infants presenting with conjugated hyperbilirubinaemia commence on a lactose free, MCT containing feed (Pregestimil, Mead Johnson). Upon exclusion of galactosaemia if the infant continues to be cholestatic feeds may be changed to a whole protein, MCT rich (75%) feed (Caprilon, SHS International). In the older infant with fluid/electrolyte problems, feeds may be changed to a low sodium feed, containing MCT (32%) and branched chain amino acids (32%) (Generaid Plus, SHS International). Nasogastric (NG) feeds may also be indicated. Our aim is to report on the use of specialist infant formulas and the nutritional management of infants with cholestasis in a tertiary paediatric liver unit.

Methods: Dietetic records of 40 infants (27 male) between 2007–2009 were retrospectively reviewed. Parameters assessed were age, final diagnosis, feed choice and dilution, mode of feeding, anthropometry (weight z score), liver function tests (serum bilirubin, serum GGT) and serum sodium.

Results: 90% of infants had tried a course of EEN either at diagnosis or after relapsing. 95% children tolerated a full course of EEN. In accordance with guidance, 83% EEN courses lasted 6–8 weeks. Remission was achieved in 78% overall, which was consistent with the literature. 71% of those patients who achieved complete remission with EEN had a relapse, however, time until relapse was highly variable (<2 months to >3 years). Of the patients who relapsed, 60% chose not to retry EEN. The length of period for food reintroduction was much more variable compared to the literature. Average number of dietetic consultations for induction of remission and food reintroduction were also variable across sites.

Conclusion: In accordance with guidance, EEN was widely used in both the DGH settings. It was tolerated well and proved to be an effective treatment achieving complete remission in 78% of patients. Our findings support the use of EEN as a first line treatment for paediatric Crohn’s disease, with clear benefits over the use of oral corticosteroids. It should, therefore, be considered as primary treatment in all paediatric Crohn’s disease patients. There needs to be a consensus guideline for food reintroduction following 6–8 weeks of exclusive EEN. There is also a need for more collaborative research and regular local and national audits into the care of paediatric Crohn’s disease patients.

References:
The British Society of Paediatric Gastroenterology, Hepatology and Nutrition (2008) Guidelines for the Management of Inflammatory Bowel Disease (IBD) in Children in the United Kingdom

Disclosure of Interest: None declared.
weight z score $-2.27$ (range $-4.51$ to $-0.13$), bilirubin 120\text{mmol/L} (range 31–312), GGT 314\text{IU/L} (range 22–2604). Patients continued on Caprilon for a median time of 13 weeks (range 2–50 weeks). Feeds were concentrated for 75% of patients due to suboptimal weight gain. At time of change from Caprilon median weight was 5.79 kg (range 2.96–9.51 kg), median weight z score $-2$ (range $-4.34$ to +1.7). Feeds were changed to standard/high energy formula if the cholestasis had resolved or to Generaid Plus for infants with fluid/electrolyte problems.

Nine infants were changed to Generaid Plus at median parameters of: age 30 weeks (range 27–47), bilirubin 175\text{mmol/L} (range 49–534); GGT 468\text{IU/L} (42–1993), serum sodium 136\text{mmol/L} (range 134–149), weight 5.98 kg (range 4.9 kg–8.3 kg) and weight z score of $-2.04$ (range $-0.38$ to $-4.34$). Ten infants (25%) required NG tube feeding due to inadequate oral intake. Of these 7 patients were tube fed at home which was well tolerated. At time of NG tube placement patients had a median weight of 4.96 kg (range 4.89–5.31 kg) and median weight z score of $-3.09$ (range $-2.21$ to $-3.85$).

**Conclusion:** In our experience we have used higher concentration MCT feeds and only 25% required NG tube feeding.

**Disclosure of Interest:** None declared.

**AHP - 003**

**THE USE OF PARTIALLY HYDROLYSED GUAR GUM IN CHILDREN WITH SHORT BOWEL SYNDROME:**

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**Objectives and Study:** Nutritional management of infants and children with Short Bowel Syndrome (SBS) is a challenge. Clinical studies of adult patients suffering diarrhoea from a range of causes have shown that supplementing enteral feeds with Partially Hydrolysed Guar Gum (PHGG) can reduce mean frequency of diarrhoea and improve tolerance to enteral feeds. The authors are not aware of any clinical studies published in paediatric patients. Our aim is to describe our experiences with a series of paediatric patients with SBS where nutritional intake was supplemented with PHGG.

**Methods:** Retrospective data was collected on eight patients with SBS (aetiology: Necrotising Enterocolitis (3), Gastroschisis (2), Jejunal Atresia (2), Ileal Atresia (1)), four of whom had PHGG supplementation. The sample and the control group were matched on gut length and the presence of a colon. Data was collected at baseline and at the next full nutritional review. Parameters assessed were age, diagnosis, gut length, nutrition, PHGG supplementation, data collection time line and bowel motion frequency.

**Results:** At baseline median age of sample group was 3 years and 7 months (range 9–85 months); control group 3 years and 8 months (range 27–136 months). Median remaining gut length in the sample group: 40 cm (range 40–70 cm) and in the control group: 50 cm (range 50–65 cm). In sample group 3 patients had colon present, 1 had descending colon. The same distribution was seen in the control group. PHGG was introduced between five months and 6 years post surgery. Median time of data collection from baseline to next nutritional review was 5 months (range 0.5–7 months) for the sample group and 7 months (range 3–8 months) for the control group. Median stool motion frequency in the sample group at baseline was 10 per day (range 8–10) and following PHGG supplementation was 3.5 per day (range 2–4). In the control group median stool motion frequency was 4 per day (range 2–9) and at next nutritional review 4 per day (range 2–4). Nutritional intake at baseline was as follows: Sample group: 100% enteral feeds (2); parenteral nutrition (46% of energy intake) with enteral feeds and solids (1); solids only (1). Control group: 100% enteral feeds (1); enteral feeds and solids (2); solids only (1). Following PHGG supplementation we observed one patient stopping parenteral nutrition and tolerating a full oral diet. This patient had a descending colon only. In the control group one patient was commenced on parenteral nutrition due to poor growth. No changes were observed in nutritional intake of all other patients.

**Conclusion:** Our cases suggest a positive effect on stool motion frequency of adding PHGG to enteral feeds and solids in infants and children with SBS.

**Disclosure of Interest:** None declared.

**AHP - 004**

**GASTROSTOMY REVIEW 2006–2009**

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**Objectives and Study:** Increasing numbers of patients require gastrostomy insertions for feeding. There has been recent key developments in operative techniques which include percutaneous endoscopic placement to one stage button insertion, inserted laparoscopically which has decreased length of stay of patients in hospital. It is imperative we audit care and reduce incidence of complications as parents are being discharged quicker into the community. To review numbers of patients referred for gastrostomy insertions and to identify reasons for referrals and monitor complications.

**Methods:** A post operative gastrostomy proforma was developed by the multidisciplinary team. The proforma included information related to diagnosis, demographics, operative procedure, device used, complications and pre and post operative follow up care provided.

The information was collated by nutritional care nurses in hospital. A homecare nurse who worked with the team was instructed to visit family pre and post operatively at home and use proforma to feed back any concerns.

The information was then put onto an excel spreadsheet by the enteral coordinator. The data was collated and analysed at
weekly meetings to ensure data was complete and that complications and trends were identified quickly.

**Results:** 330 patients were referred for gastrostomy insertions using the following techniques:
- Percutaneous insertion (n = 175)
- Open procedure (n = 37)
- Laparoscopic placement (n = 117)
- Gastropexy placement (n = 1)

Main diagnostic categories of children requiring feeding were cerebral palsy, global developmental delay, epilepsy, Crohn’s disease and propionic academia.

Mean age in 2008 was 4 years and in 2009 was 5 years with range of under 1 s to 16 years.

Main complications included:
- Leakage (n = 36)
- Infection (n = 23)
- Sore/red/discomfort/pain (n = 13)
- Granulation tissue (n = 19)
- Misplacement (n = 5)
- Defective device/wear and tear (n = 3)
- Team not informed of admission (n = 3)

Home care nurse discussed with team individual patient issues and treatments were implemented using skin care gastrostomy protocols.

**Conclusion:** Weekly reviews and audit has helped us to recognise trends/patterns in data. It has also provided us with accurate information related to work load activity, identifying complications early and rectifying them as soon as possible. It has also been instrumental in identifying staffing levels required in nutritional care to support the service. The data has provided a forum with surgeons to discuss types of devices used, minimisation of complications and issues related to specific operative procedures.

**Disclosure of Interest:** None declared.

**AHP - 005**

**USING PLAY SPECIALIST THERAPY TO REDUCE THE USE OF SEDATION FOR ANORECTAL MANOMETRY TESTS**


**Objectives and Study:** Anorectal manometry tests are increasingly used to evaluate children with chronic constipation and/or faecal incontinence. The procedure can be frightening for the child causing them stress and anxiety and reducing their ability to cooperate. For this reason, sedation is frequently used prior to the procedure. However, this impacts on their ability to practice tensing and relaxing their rectal muscles and limits their capacity to see the effect these exercises have on controlling their bowels. There have been studies, which show that children who are well prepared for medical interventions have less anxiety and greater cooperation (Ellerton and Merriam, 1994; Felder-Puig, 2003). We demonstrate how a hospital play specialist can reduce the need for sedation in anorectal manometry tests.

**Methods:** A 12 month study was conducted involving 80 patients aged 5−16 years old undergoing anorectal manometry. In the first 6 months of the study anorectal manometry procedures were performed without the intervention of a play specialist. The following 6 months all the children admitted for anorectal manometry tests were introduced to the hospital play specialist prior to their procedure. The play specialist had developed a manometry preparation book with photographs. This along with dolls and real medical equipment was used to prepare the children for the procedure. The child’s anxiety levels and their ability to cope with the procedure were assessed and the play specialist advised the gastroenterology team whether the child required sedation. The play specialist then accompanied the child to provide distraction techniques during the test.

**Results:** In the first 6 month period 40 children underwent anorectal manometry, 28 of them (70%) needed sedation. The following 6 month period a further 40 children were admitted for anorectal manometry. 5 of them required sedation (12.5%). The test was abandoned on 2 of these children as the sedation was unsuccessful.

**Conclusion:** The results of our study demonstrate that since the intervention of a play specialist there has been an 82% reduction in the use of sedation for anorectal manometry tests. Play and distraction techniques can be effective in reducing the anxiety associated with the procedure. Avoiding the use of sedation improves biofeedback therapy in children with faecal incontinence. Not having to use sedation means children can be discharged sooner and procedures are carried out quicker, allowing for more tests to be done on a theatre list. We recommend play specialist therapy as an alternative means of preparing children for anorectal manometry tests instead of sedation.

**References:**

**Disclosure of Interest:** None declared.

**AHP - 006**

**CARTOON EDUCATIONAL PRESENTATION PREPARES CHILDREN FOR ENDOSCOPY**

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**Objectives and Study:** Children are fearful of upper endoscopy and colonoscopy. Conventional methods of preparation, including discussion with the procedure nurse, anaesthetist and physician just prior to the endoscopy do not allay anxiety and leave many questions unanswered.
We have recently introduced a 10-minute feature cartoon (www.kavor.org.il) which explains the build-up to the procedure in a child-friendly manner. The cartoon’s efficacy was compared to conventional preparation.

**Methods:** During the weeks prior to the introduction of the cartoon, children aged 10–16 were asked to fill out a questionnaire including questions on the knowledge, preparation and details of the procedure about to be performed. This group was compared to a group of children who viewed the cartoon to prepare for the procedure.

**Results:** There were 10 children in each group. Prior to the introduction of the cartoon presentation half of the children were satisfied with the preparation they received and this improved after the introduction of the cartoon. Reduction in anxiety was also noted after the introduction of the cartoon. The cartoon reduced explanation time for the endoscopy staff.

**Conclusion:** A computer-based cartoon presentation is preferred by children, is more informative and helpful and may save time for the endoscopy staff.

**Disclosure of Interest:** None declared.

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**PA-G-019**

**REFLUX ESOPHAGITIS PREVALENCE AND EVOLUTION IN H. PYLORI-POSITIVE VS. -NEGATIVE CHILDREN**


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**Objectives and Study:** There are many controversies regarding the development/worsening of reflux esophagitis (RE) after H. pylori (HP) eradication. Only few data exists in pediatric patients. The aim of the study was to assess a possible protective role of H. pylori infection for RE development/evolution.

**Methods:** We included in a prospective study 103 dyspeptic children (43 males, age range 5–18 years) admitted in our department between 2005 and 2009. They were previously diagnosed for RE (Savary-Miller endoscopic criteria) and also checked for the presence of HP infection (rapid urease test and/or histology). All RE patients received therapy with omeprazole (b.i.d., 3 months), those HP positive also receiving clarithromycin and amoxicillin (b.i.d., in addition to the first week of omeprazole therapy). The patients having only HP infection received a triple therapy (omeprazole, clarithromycin and amoxicillin, b.i.d., 1 week). Most of the patients (n = 75, 26 males, age range 5–18 years) completed the study and were re-evaluated after 3 months for RE and HP status according to the initial diagnostic protocol. Regarding the RE assessment, we considered a better endoscopic grade or endoscopic healing as favourable evolution and the same/worse endoscopic grade as unfavourable evolution, respectively.

**Results:** At the initial diagnostic work-up HP infection was present in 55/103 (53.39%) patients, of which 34 had also RE. In 48/103 H. pylori negative patients RE was present in 38/48 cases. There was no significant difference (P > 0.05) in RE prevalence between HP positive vs. – negative patients. The study was completed by 54 patients initially diagnosed with RE and 21 initially HP positive patients without RE. Among the RE patients who completed the study, 26/54 (48.14%) were initially HP positive. The eradication rate was 61.53% (16/26 patients). According to HP status the RE patients were assessed in three groups, as follows: Group A (persistent positive, n = 10, 8 males, age range 8.5–17 years), Group B (initially positive, n = 16, 6 males, age range 10–15 years) and Group C (initially negative, n = 28, 4 males, age range 5–18 years). Regarding the RE status after 3 months of omeprazole therapy, a favourable endoscopic evolution was present in: 8/10 patients from group A, 8/16 patients from Group B and 18/28 patients in Group C, respectively. There were no statistical differences between RE favourable evolution in the above mentioned groups (P > 0.05). In the initial HP positive cases without RE the eradication rate was 61.9% (13/21 patients). None of them developed endoscopic findings of RE at re-evaluation.

**Conclusion:** RE prevalence/evolution in dyspeptic children is not related to HP status.

**Disclosure of Interest:** None declared.

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**PA-G-020**

**HYPNOTHERAPY FOR CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN OR IRRITABLE BOWEL SYNDROME: LONG TERM FOLLOW-UP**

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**Objectives and Study:** Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) in childhood are among the most common reasons for consultation in paediatrics with reported prevalences of 1 to 19%. Treatment usually consists of education, reassurance and dietary advice as extra fibres. Nevertheless, a significant proportion continues to experience symptoms and for long, efficient therapies for this group of patients have been lacking. In 2007 we showed that gut-directed hypnotherapy (HT) is highly effective in the treatment of paediatric patients with FAP and IBS. At one year follow-up 85% of the patients were in clinical remission compared to 25% in the group who received standard medical treatment (SMT). Aim of this study was to investigate and compare the long term effects of hypnotherapy and standard medical treatment in children with FAP or IBS.

**Methods:** All 52 participants of our previous trial were invited to fill out a standardized abdominal pain diary, on which pain frequency and intensity were scored, as well as associated symptoms like flatus, loss of appetite and nausea. Furthermore, the Children’s Somatisation Inventory and a
questionnaire regarding doctor’s visits and school/ work absenteeism in the past 12 months were filled out. Clinical remission was defined as >80% improvement in pain scores compared to baseline scores.

**Results:** Two patients of the SMT group were lost to follow-up and one refused to participate. In the HT group all patients participated in this follow-up study, resulting in 20 SMT patients and 25 HT patients. After a mean duration of 4.8 years follow-up (3.4–6.7), hypnotherapy was still highly superior to conventional therapy with 68% versus 20% of the patients in remission after treatment. Pain intensity and pain frequency scores at follow-up were 2.8 and 2.3 resp. in the HT group compared to 7.3 and 7.1 in the SMT group ($P < 0.01$). Also the associated symptom score was significantly lower in the HT group (1.3 vs 2.6; $P < 0.01$), but somatisation scores were comparable between groups (18.3 vs 22.7; $P = 0.37$). Furthermore, no difference was found in the number of doctors visits, the use of medication, and missed days of school or work between the two treatment groups.

**Conclusion:** The effects of gut-directed hypnotherapy are long lasting in children with FAP or IBS with two thirds still in remission 5 years after treatment.

**Reference:**

**Disclosure of Interest:** None declared.

**PA-G-021**

RECTAL PROLAPSE IN CHILDREN: AETIOLOGY AND TREATMENT


**Objectives and Study:** Rectal prolapse is considered as a self-limited condition; however it can cause substantial distress to children. It is mainly attributed to chronic constipation, acute diarrhoea, and cystic fibrosis. We identified a substantial number of children not matching the major reported aetiologies. We describe our experience of patients presented with rectal prolapse to establish the associated conditions.

**Methods:** A retrospective analysis of all children referred with rectal prolapse to our tertiary hospital from 2000–2007 was performed by systematic review of outpatient summary letters and records on the hospital information system.

**Results:** 100 patients were identified with rectal prolapse, with median age being 4 years (range 1–17). 64% of patients were male and 36% female. Constipation was the most common association (50%). Other associations include chronic diarrhoea (10%); enterobius vermicularis infestation (4%); food allergy (4%); colonic polyp (3%); anorectal anomaly (3%); ulcerative colitis (2%); mucosal prolapse syndrome (2%); cystic fibrosis (2%); coeliac disease (1%); Hirschsprung’s disease (1%). In 18% no obvious underlying cause was found. Investigations included sweat test (57%), colonoscopy with biopsy (15%), coeliac screening (8%), examination under anaesthesia (7%), and rectal biopsy (5%). Of the cohort 62% were treated with laxatives, 19% required surgical intervention (15% sclerotherapy, 2% rectal mucosal resection, 2% both) and 27% were given toileting advice.

**Conclusion:** In 40% of patients, a diagnosis different from chronic constipation or diarrhoea was identified and resulted in a focussed therapy. Worm infestations, food allergy, polyps, anatomical conditions and coeliac disease have been identified in addition to cystic fibrosis. In 19% children surgical intervention was needed. We will discuss an algorithm for diagnostic and therapeutic management.

**Disclosure of Interest:** None declared.

**PA-G-022**

ESOPHAGEAL IMPEDANCE IN CHILDREN: SYMPTOM-BASED RESULTS

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**Objectives and Study:** To correlate the data from esophageal impedance (MII-pH) with symptoms.

**Methods:** MII-pH tracings (Sandhill Scientific) from 225 children referred for suspected gastro-esophageal reflux (GER) disease were analysed. Automatic and manual reading were performed. Only tracings with symptoms were included. Symptoms were considered associated if within a 2-minute a GER episode. Different age groups (1–6, 6–12, >12 months) and symptoms were analysed.

**Results:** In 126 patients (median age 9, range 1–176 months) ≥1 symptom was associated with reflux. Out of 2172 events recorded, 1136 (52%) were associated with reflux (45% acid, AR, 51% weakly acid, WAR, and 3% alkaline reflux, AlkR). There was significant ($P < 0.001$) more frequent association between symptoms and WAR in the first 6 months of life and with AR in the other ages. Crying was slightly (50% vs 44%, $P = NS$) more associated with GER in children than in infants and cough was significantly ($P < 0.05$) more associated with GER in infants. In infants $<6$ months of age, WAR was significantly ($P < 0.0001$) more associated with crying, coughing and vomiting than AR. Only for cough in 6–12 months old infants and for cough and vomiting in children, symptoms were significantly ($P < 0.01$) more associated with AR than with WAR. Symptoms were associated with proximal reflux and with meal in 70% and 6% of GER related episodes, respectively. The symptom index (SI) and
symptom association probability (SAP) were positive for all GER episodes in 104 (83%) and 58 (46%) patients and for AR in 51 (49%) and 27 (47%). For crying, cough and vomiting the positive SI was determined, in 1–6 months infants, more by WAR than AR whereas in children more by AR than WAR in all symptoms except crying. For crying, the SAP was positive in 25% of the patients (similar AR and WAR). For cough, SAP was positive in nearly 1/3rd with predominance of WAR in 1–6 months old infants and WAR). For vomiting the positive SI was determined, in 1–6 months infants and of AR in 6–12 months old infants. No patient and no symptom had a positive SAP for AlkR.

Conclusion: MII-pH doubles the chance to find an association between symptoms and GER compared to the analysis of acid reflux. Cough was associated with GER more frequently than crying, especially in infants. Only in the first 6 months of life, symptoms are more frequently associated with weakly acid than acid GER.

Disclosure of Interest: None declared.

PA-G-023

GENETIC POLYMORPHISMS DETERMINING HOST RESPONSE OF CHILDREN INFECTED WITH HELICOBACTER PYLORI

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Objectives and Study: Peptic ulcer disease is the result of an imbalance between the aggressive and protective factors in all age groups. The role of both bacterial and host factors in the development of peptic ulcer disease in children is evaluated in this study.

Methods: Children undergoing endoscopical investigation in our pediatric endoscopy unit during a twelve months period were entered in the study. Children infected with HP constituted the study group whereas the noninfected ones were entered in the control group. Helicobacter pylori CagA status was analysed as the bacterial virulence factor in the study group, genetic polymorphisms of IL-1 beta (+3954), IL-10 (C-627A) and TNF alpha (G308A) were investigated by Polimerase Chain Reaction (PCR), Restriction Fragment Lenght Polymorphism (RFLP), Agarose Gel Electrophoresis. Biopsy samples were scored by Modified Sydney System for understanding the effect of both bacterial and host factors on histopathology.

Results: Fortysix children infected with Helicobacter pylori (Hp) and 103 uninfected children, (age range 3–18 years), who went under upper gastrointestinal (GI) endoscopy were selected. Hp colonisation was increased significantly by age (P < 0.05). Girls infected with Hp had higher rate of mononuclear infiltration than the infected boys (P = 0.004). Frequencies of gastric (P < 0.001) and duodenal (P = 0.02) lesions on endoscopy and mononuclear- polynuclear infiltration in stomach (P < 0.001) were statistically increased in Hp infected children. There were no significant correlations between cag A and histopathology, endoscopy and Modified Sydney Score. Genotype CA of IL-10 was found as a factor reducing mononuclear infiltration (P = 0.006, OR 12.5, 95 CI 2,06–76,1). There were no significant correlations between histopathology and host IL-1 beta and TNF alpha polymorphisms.

Conclusion: These findings suggest that host IL-10 CA genotype may act as a protective factor against mononuclear reaction caused by Hp.

Disclosure of Interest: Istanbul School of Medicine, Istanbul University, Turkey.

PA-G-024

IMPACT OF ANTISECRETORY TREATMENT ON ATYPICAL SYMPTOMS OF GASTROESOPHAGEAL REFLUX DISEASE

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Objectives and Study: Extraesophageal symptoms or atypical presentations have been ascribed to Gastroesophageal Reflux Disease (GERD) including hoarseness, cough, laryngitis, subglottic stenosis, and noncardiac chest pain, dental erosions, sinusitis, pharyngitis, and sleep apnea. The effect of antisecretory therapy on extraesophageal or atypical manifestations of GERD remains unclear.

Aim: To evaluate the effect of antisecretory treatment on atypical symptoms of GERD diagnosed by multichannel intraluminal impedance /pH-metry (MII/pH).

Methods: We recruited 78 consecutive children, from January 2008 to January 2009, with typical or atypical symptoms of GERD. All patients underwent MII/PH. Demographic data and symptoms were assessed using a validated questionnaire. Children with MII/PH positive for GERD were randomly treated with proton pump inhibitors (PPIs) or histamine H2-Receptor Antagonists (H2RAs), at the standard dose for a cycle of three months. All patients were recalled after one year from the end of the therapy to evaluate the long-term clinical outcome.

Results: Thirty-seven of 78 children had a pathologic MII/PH. Thirty-one (mean age ± SD: 40.6 ± 36.4 months; range: 1–181 months) out of 37 (83.8%) complained of atypical symptoms of GERD. Of the 31 children with atypical
symptoms of GERD, 16 (mean age ± SD: 46.4 ± 42.5 months) received PPIs (1.4 mg/Kg/die) and 15 (mean age ± SD: 44.5 ± 40.6 months) received H2RAs (at an average dose of 15 mg/Kg/die) for 12 weeks. Symptomatic scores at enrolment were not different in the two treatment groups. Fifteen of the 16 (93.8%) patients treated with PPIs had a complete resolution of symptoms; however, 5 (31.3%) of them needed a second cycle with the same drug for three months. One patient (0.62%) underwent Nissen fundoplication due to the persistence of symptoms.

Of the 15 patients treated with H2RAs, 4 (26.7%) had a complete resolution of symptoms, 1 (6.7%) needed another cycle with the same treatment and 10 (66.7%) changed from H2RAs to PPIs. Three of these ten patients (30%) obtained a partial resolution of symptoms, without a complete remission, which was obtained in the remaining patients (70%).

**Conclusion:** In children with atypical symptoms of GERD, the efficacy of PPIs is significantly ($P < 0.001$) superior than that of H2RAs, especially if patients are treated for a longer period of time.

**Disclosure of Interest:** None Declared.

**PA-G-025**

**CELIAC DISEASE SERUM DIRECTS ENZYMATIC DIGESTS OF GLIADIN AS WELL AS GLIADIN PEPTIDE 31–43 INTO LATE ENDOSONES OF ENTEROCYTES**

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**Objectives and Study:** Breastfeeding during gliadin introduction in the infant’s diet has a protective role in the pathogenesis of celiac disease (CD), which could be caused by anti-gliadin antibodies of breast milk. One precondition for oral tolerance seems to be the association of food antigen with HLA-DR molecules in late endosomes (LE) and their consecutive presentation at the basolateral membrane of enterocytes (Zimmer et al., Gastroenterology 118: 128, 2000). We have recently shown that toxic gliadin peptide 31–49 can be directed to LE of enterocytes by its conjugation with cholera toxin B (Zimmer et al., Gut in press).

We incubated duodenal biopsies of CD and control patients with PPIs and gliadin digests of gliadin as well as gliadin peptide 31–43 (GP). Serum of untreated CD and control patients as a source of antibodies were added; DMEM as cell culture medium was used as control. Staining of gliadin or GP and LE was achieved by anti-gliadin R5 and antibodies against the LE markers LAMP2/cathepsin-D, respectively. For evaluation we used immunofluorescence (IF)- and immunoelectron microscopy (IEM).

**Results:** Morphometrical analysis of IEM experiments showed that incubation with serum from CD patients increased the percentage of gliadin in LE from CD biopsies to 15% in comparison to 4% in control and CD biopsies without serum. Our IF results were confirmative, i.e. the median co-localization coefficient of GP and LAMP2 in Caco2 cells was 0.8 with CD serum, 0.43 with control serum and 0.48 with DMEM.

**Conclusion:** Our results indicate that serum of untreated CD patients is able to mediate the intracellular transport of toxic gliadin peptides to LE in enterocytes. We speculate that this effect is caused by gliadin-specific antibodies and is required for oral tolerance induction.

**References:** Zimmer et al., Gastroenterology 118: 128, 2000; Zimmer et al., Gut in press.

**Disclosure of Interest:** None declared.

**PA-G-026**

**STIMULATION OF IL-8 AND BETA-DEFENSIN-2 BY PATHOGEN-ASSOCIATED MOLECULAR PATTERNS OF SALMONELLA ENTERICA SEROVAR TYPHIMURIUM IN POLARISED HUMAN INTESTINAL EPITHELIAL CELLS**

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**Objectives and Study:** To investigate which pathogen-associated molecular patterns (PAMPs) of Salmonella enterica serovar Typhimurium (S. Typhimurium) stimulate epithelial IL-8 and βeta-defensin-2 (hBD-2) mRNA expression and protein secretion in human intestinal epithelial cells.

**Methods:** Polarised 14-day-old Caco-2 cells grown on transwells were stimulated with apical infection of S. Typhimurium strains for 2 hours (lipopolysaccharide [LPS, 10 μg/ml], flagellin [FlhC, 2 μg/ml] or S. Typhimurium SL1344 DNA [25 μg/ml]). Monolayers were also apically infected with S. Typhimurium strains with a multiplicity of infection (MOI) of 20:1 before infections were stopped with 1-hour gentamicin treatment (100 μg/ml). At 7 hours post infection IL-8 and hBD-2 mRNA expression were measured using quantitative real-time PCR; at 21 hours post infection basolateral and apical supernatants were respectively collected to measure protein levels of IL-8 and hBD-2 using ELISA. Statistical significance ($P < 0.05$) was tested using one-way ANOVA.

**Results:** Stimulation of Caco-2 cells with FlhC, or S. Typhimurium DNA induced mRNA expression of IL-8 ($62.4 \times 10^4$).
Objectives and Study: Necrotizing enterocolitis (NEC) is a devastating intestinal disease of premature infants. Epidermal growth factor (EGF) is a peptide with trophic, proliferating cell fraction and is not usually expressed by resting cells (G0). Ki-67 is a specific marker of actively growing cells, and hBD-2 (11.5 \times 10^6 \text{ copies of mRNA transcripts/mug total RNA}) was induced in NEC rats, but not in the EGF or DF rats. Autophagy was induced in IEC-6 cells and stimulation with FliC induces the highest level of IL-8 and hBD-2 gene expression among the PAMPs. S. Typhimurium SL1344, DeltaSspaS, and DeltaSfliM induced IL-8 mRNA levels (93.2 \times 10^6, 45.5 \times 10^6, 20.3 \times 10^6 \text{ copies of mRNA transcripts/mug total RNA, respectively}), whilst only S. Typhimurium SL1344 and DeltaSspaS, but not S. Typhimurium DeltaSfliM, induced hBD-2 mRNA levels (62.2 \times 10^6, 38.0 \times 10^6 \text{ copies of mRNA transcripts/mug total RNA, respectively}). S. Typhimurium SL1344 and DeltaSspaS, but not S. Typhimurium DeltaSfliM, induced basolateral secretion of IL-8 (SL1344: 98.0 \pm 10.4 \text{ pg/ml}, DeltaSspaS: 75.5 \pm 19.7 \text{ pg/ml}, P < 0.05; DeltaSfliM: 43.5 \pm 9.4 \text{ pg/ml}, P > 0.05; vs non-infected controls: 51.4 \pm 17.9 \text{ pg/ml}) and apical secretion of hBD-2 (SL1344: 12.1 \pm 2.7 \text{ pg/ml}, DeltaSspaS: 10.4 \pm 2.7 \text{ pg/ml}, P < 0.05; DeltaSfliM: 4.4 \pm 0.2 \text{ pg/ml, P > 0.05; vs non-infected controls: 4.6 \pm 0.8 \text{ pg/ml}}).

Conclusion: FliC is the principle S. Typhimurium PAMP that elicits IL-8 and hBD-2 gene transcription and protein secretion. However, exposure to S. Typhimurium DNA triggers IL-8/hBD-2 mRNA expression and infection with a FliC-deficient mutant strain S. Typhimurium DeltaSfliM stimulates IL-8 mRNA expression, indicating that additional PAMPs may play a role in eliciting epithelial pro-inflammatory responses.

Disclosure of Interest: None declared.

PA-G-028

POST-NATAL GUT IS ABLE TO GENERATE NEW NEURONS: A NOVEL FINDING IN A RAT MODEL OF INTESTINAL RESECTION

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Objectives and Study: Proliferation of new neurons in mammals is observed in fetal life whereas it is restricted to few brain regions in adulthood. Extensive resection of small bowel results in substantial gut structure remodelling. However, post-surgery adaptive modifications of small intestinal mucosa are well known, but there are few data on nervous plexuses. We investigated intestinal neuronal modifications in a rat model of extensive gut resection.

Methods: Growing 210 to 270 grams Sprague-Dawley female rats (n = 32) were divided in: 2-day (n = 6), 7-day (n = 5), 15-day (n = 11) post resection groups, which had 75% of the jejunooileum removed, and the sham-resected control group (n = 10). Neuronal proliferation was studied by Ki-67 antigen, a protein expressed in nuclei during all active phases of the cell cycle (G1, S, G2 and M phases) and in chromosomes during mitosis, but not expressed in resting cells (G0). Ki-67 is a specific marker of actively proliferating cell fraction and is not usually expressed by serum-free conditions with/without EGF (10 nM). Expression and localization of ATG5, Beclin-1, and LC3II in the intestinal epithelium were evaluated in both in vivo and in vitro models. Transmission electron microscopy was used to visualize morphological changes between the groups. The presence of Beclin-1 and LC3II was also evaluated by fluorescent microscopy in intestinal samples obtained from NEC patients and appropriate controls.

Results: In the ileum of NEC rats, Beclin-1 and LC3II protein levels were significantly increased. EGF treatment of NEC reduced expression of Beclin-1 and LC3II. Beclin-1 and LC3II were localized to the epithelium of ileal crypts. Typical signs of autophagy were observed in the epithelium of NEC rats, but not in the EGF or DF rats. Autophagy was induced in IEC-6 cells and supplementation of EGF inhibited autophagy induction. Strong signal for Beclin1 and LC3II was detected in samples of small intestine from patients with NEC compared to no staining in controls.

Conclusion: These results indicate activation of autophagy in the ileum of NEC rats. EGF treatment reduces and normalizes intestinal autophagy in both in vivo and in vitro conditions. This is a novel mechanism of EGF-mediated protection against intestinal epithelial injury. Most importantly, activation of autophagy was also observed in the intestinal epithelium of NEC patients. Supported by the NIH Grant HD-39657 (to B.D.).

Disclosure of Interest: None declared.
neurons. Neurofilament NF11 staining was used on parallel
cuts of tissue layers to confirm that the Ki-67-positive cells
were neurons. Ileal myenteric neurons were investigated at
different times of harvest: 2, 7 and 15 days.

**Results:** As expected, Ki-67 positive ileal myenteric neurons
were not found in controls, indicating resting cells. However,
al 6 samples of intestine at 2 days showed ileal myenteric
ganglia (1 ganglion each 4–5 ganglia) containing scattered
Ki-67 positive cells (1–3 cells each ganglion). As judged by
the typical Ki-67 nuclear staining, the positive cells were in
active phases of the cell cycle that lead to mitosis. The
neuronal nature of the cells was confirmed by neurofilament-
positivity on an adjacent section. The novel neurogenesis
was observed in the samples collected at 2 days. At 7 and
15 days post-resection, Ki-67 positive neurons were no
longer detected, indicating that neurogenesis was already
completed.

**Conclusion:** Proliferating neuronal cells were detected in
ileal myenteric plexuses 2 days after extensive gut resection,
suggesting that intestinal neurogenesis does exist in adults
as an adaptive response. Adult neuronal proliferation is
observed early after bowel resection, before adaptive muco-
sal hyperplasia becomes evident and it could be a driver
of intestinal structural adaptation. This data open novel
perspectives to the use of neuronal trophic factors and stem
cells in the management of intestinal adaptation after exten-
sive resection.

**Disclosure of Interest:** None declared.

**PA-G-029**

**ELECTROPHYSIOLOGICAL STUDIES AS THERAPEUTIC ENDPOINT MEASURES IN CF**


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**Objectives and Study:** A wide range of clinical trial end-
points is needed to adequately evaluate proposed therapeutic
agents in cystic fibrosis (CF). Although Nasal Potential
Difference (NPD) measurements may be of benefit; the
inability to perform this test on young children may limit
its utility. Aims: To evaluate the potential usefulness of
electrophysiological studies, ex vivo, on rectal biopsy
samples as a surrogate marker for measurement of CFTR
function. These results were compared to NPD results from
the same subject.

**Methods:** Intestinal Current Measurement (ICM) and NPD
were performed on healthy controls (routine colonoscopy)
and CF patients (sigmoidoscopy). Median values comprising
the ICM (carbachol, histamine, and forskolin responses) and
NPD (basal and chloride transport responses) tests were
determined. For each response, the Wilcoxon rank sum test
was applied to determine the ability of each measure to
distinguish between CF and healthy controls.

**Results:** ICM measurements demonstrated a median (inter-
quartile range) carbachol response in healthy control subjects
(n = 29 subjects; 40 analyzable biopsies) of 11.1 (7.9, 20.75)
μA/cm², histamine response of 8.7 (5.0, 12.9) μA/cm², and
a forskolin response of 3.9 (2.3, 7.4) μA/cm². These
responses were inverted in CF subjects (n = 8, 10 analyzable
biopsies) with a mean carbachol response of −2.5 (−4.8,
−1.6) μA/cm², histamine of −1.0 (−1.6, 0) μA/cm², and no
forskolin response. Each of the ICM measurements effec-
tively distinguished between CF and controls (P < 0.0001).
NPD measurements demonstrated a median basal PD
response in healthy control subjects (n = 7) of −12.0 mV
(13.5, −8.0) and a chloride transport response of 14.0 mV
(12.20.5). In CF subjects (n = 8), the median values were
−49.0 mV (−51.5, −42.5) and −2.0 mV (−3.0, 0), respect-
ively. Similar to ICM, each of the NPD measurements
distinguished between healthy controls and CF (P < 0.0005).

**Conclusion:** ICM is equivalent to NPD in the ability to
distinguish CF patients from healthy controls. Rectal biopsy
studies, like NPD, allow measurement of CFTR mediated
chloride transport which has the potential for use as a
therapeutic endpoint for studies in CF patients. This is of
particular importance in evaluating young children who are
less likely to tolerate NPD.

**Disclosure of Interest:** None Declared.

**PA-G-030**

**INTESTINAL OXIDATIVE STRESS IS A PATHWAY OF INTESTINAL DYSFUNCTION IN HIV-INFECTED CHILDREN**

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**Objectives and Study:** Intestinal dysfunction, consisting in
nutrient malabsorption and intestinal inflammation, is
frequently observed in untreated HIV-infected children, and is,
at least in part, reversed after the onset of antiretroviral
therapy. HIV could play a direct enteropathogenic role since
its Tat protein inhibits cell proliferation, impairs sodium-D-
glucose symporter and induces cytotoxic damage and oxi-
dative stress (OS) in Caco-2 cells. Aim of this study was to
analyse the presence of intestinal and systemic OS and their
determinants in HIV-infected children.

**Methods:** Intestinal redox status was evaluated by 8-hydrox-
xydeoxygenosine (8-OHdG), an established biomarker of
OS, in rectal dialysis of HIV-infected children and healthy
controls. Systemic OS was assessed in urine and serum
samples.
Results: Twenty-six HIV-infected children (10 males; mean age 11.4 ± 4.3 years) and 9 healthy controls (7 males; mean age 8.5 ± 6.4 years) were enrolled. Eleven HIV-infected children had a viral load >40 copies/ml and 15 had undetectable HIV RNA (<40 copies/ml). Intestinal 8-OHdG was significantly higher in HIV-infected children (7.39 ± 1.27 ng/ml) compared to controls (4.42 ± 1.06 ng/ml; P = 0.03). Furthermore, intestinal 8-OHdG was higher in children with HIV RNA >40 copies/ml (7.75 ± 1.16 ng/ml) compared to patients with undetectable HIV RNA (5.74 ± 1.34 ng/ml; P = 0.07) and controls (4.42 ± 1.06 ng/ml; P = 0.04). A linear correlation was found between viral load and intestinal 8-OHdG concentration (r = 0.43; P = 0.05), while OS did not correlate with the number of CD4 positive lymphocytes. Systemic OS did not significantly differ between HIV-infected children and controls, and it did not correlate with viral load.

Conclusion: Intestinal but not systemic OS is increased in children with HIV infection and correlates with HIV viral load, suggesting that HIV-associated intestinal dysfunction is related to an impairment of redox status induced by Tat protein.

Disclosure of Interest: None declared.

PA-G-043

HEIGHT AND WEIGHT AT DIAGNOSIS IN PEDIATRIC CROHN’S DISEASE PATIENTS IN EUROPE

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Objectives and Study: To compare growth parameters in newly diagnosed pediatric Crohn’s disease (CD) patients in four regions of Europe.

Methods: The EUROKIDS registry is a web-based registry of newly diagnosed pediatric IBD patients that was initiated in 2004. Thirty-five centres in 18 countries were divided into four regions: Northern Europe (Denmark, Norway, Sweden), Western Europe (Belgium, France, Germany, The Netherlands, United Kingdom), Southern Europe (Greece, Israel, Italy, Portugal) and Eastern Europe (Croatia, Czech Republic, Hungary, Latvia, Poland, Slovenia). CD patients were included when a complete diagnostic work-up according to the Porto-criteria was done and data on height, weight and onset of symptoms were available. The WHO Growth Reference and Growth Standard were used to determine height for age (HFA) and body mass index (BMI) for age SD-scores.

Results: From May 2004 until May 2009, 1008 CD patients (597 M), who met our inclusion criteria, have been registered. Mean age at diagnosis was 12.6 yr (range 1.2 – 17.9 yr), with a mean delay in diagnosis of 0.69 yr (±0.9 SD). This delay was significantly shorter in Southern Europe compared to the rest of Europe. The majority of patients (62%) had disease involvement of both the small bowel and colon, 11% had isolated small bowel disease and 27% had isolated colonic disease. Mean SD-scores for HFA and BMI were −0.11 (± 1.2 SD) and −0.74 (± 1.3 SD). There was only a significant difference in the percentage of patients with HFA ≤−2 SD between Western and Northern Europe (P = 0.01). The percentage of patients with BMI ≤−2 SD was significantly lower in Southern Europe compared to the rest of Europe. In addition, there was a significant difference between Western and Eastern Europe (P = 0.028). Children with disease involvement of the ileum had significantly lower SD-scores for HFA and BMI. Furthermore, those children who were registered as having delay in growth or pubertal development (n = 237), had a significantly longer diagnostic delay, and lower SD-scores for HFA and BMI.

Table: Growth retardation at diagnosis of pediatric CD patients

<table>
<thead>
<tr>
<th></th>
<th>Northern Europe (n = 151)</th>
<th>Western Europe (n = 411)</th>
<th>Southern Europe (n = 152)</th>
<th>Eastern Europe (n = 294)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFA ≤−2 SD n (%)</td>
<td>3 (2)</td>
<td>33 (8)</td>
<td>7 (5)</td>
<td>17 (6)</td>
<td>0.048</td>
</tr>
<tr>
<td>BMI ≤−2 SD n (%)</td>
<td>26 (17)</td>
<td>63 (15)</td>
<td>12 (8)</td>
<td>64 (22)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Pearson Chi Square.

Conclusion: There are significant differences in height and weight of newly diagnosed pediatric CD patients between regions in Europe. Disease involvement of the ileum is related to lower SD-scores for HFA and BMI, while patients who are registered as having growth failure at diagnosis have a longer diagnostic delay. Additional risk factors will be further analyzed.

Disclosure of Interest: None declared.

PA-G-044

IMMUNE MODULATION BY POLYUNSATURATED FATTY ACIDS

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Objectives and Study: In recent decades there has been a dramatic increase in the prevalence of atopic disease, which is characterized by a bias in favour of a Th2-cytokine profile. Since sensitization may occur at an early age, early exposure to factors that favor this bias might predispose individuals to develop atopic responses. The increase in atopic disease coincides with changes in the intake of polyunsaturated fatty acids (PUFAs), which makes these compounds very interesting candidates for dietary intervention studies. Polyunsaturated fatty acids (PUFAs) are precursor-molecules for eicosanoids such as leukotriens, prostaglandins and...
resolvins. Furthermore, PUFAs can alter immune cell function via various mechanisms, including modulation of receptor functions and activation of transcription factors.

**Methods:** The effects of different dietary fatty acids (FA) (saturated and omega-3/omega-6 poly-unsaturated) were investigated in two mouse models: (1) the vaccination model, in which the Delayed Type Hypersensitivity (DTH) response and other immune parameters were studied in C57BL/6 mice, and (2) the ovalbumine (OVA)-induced model for experimental allergic asthma in BALB/c mice. 3 wk-old mice were put on different diets two weeks before vaccination (model 1) or sensitization (model 2) until the end of the experiment.

**Results:** In model 1, the DTH-response was most profound in mice fed the diet with the highest omega-3 PUFA content. In model 2, mice fed this diet had a less severe acute allergic skin response (ASR). In addition, the most severe ASR was observed in mice fed a saturated FA diet.

**Conclusion:** Results obtained from model 1 indicate that a high omega-3 PUFA diet contributes to an increased Th1-response to vaccination. Additionally, results from model 2 suggest that this diet lessens the Th2-response. Furthermore, results obtained from the latter model indicate a diet with high levels of saturated FA may contribute to an increased severity of allergic symptoms. 

**Disclosure of Interest:** None declared.

**PA-G-045**

**CHARACTERISTICS OF INNATE AND ADAPTIVE IMMUNITY IN THE PERIPHERAL BLOOD OF PEDIATRIC PATIENTS WITH CROHN DISEASE AFTER INFLIXIMAB THERAPY**

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**Objectives and Study:** Infliximab (IFX) is indicated for medically refractory luminal and fistulizing Crohn disease (CD). However, the mechanism of IFX action is not fully understood. The dysfunction of innate and adaptive immunity in CD could be modulated by IFX therapy. To our knowledge, there is no extensive pediatric study in this issue. The objective of our study was to investigate the systemic effect of IFX treatment on the members of innate and adaptive immunity in pediatric CD patients.

**Methods:** 12 children (6 girls, median [interquartile range], 14 years [11–16]) with conventional therapy refractory CD were enrolled. Induction therapy with 5 mg/kg IFX at weeks 0 (baseline), 2 and 6 weeks were administered. 15 children (9 girls, 12 years [8–16]) served as controls. Peripheral blood was taken as a part of routine investigations, and mononuclear cells were separated for flow cytometry. We investigated the prevalences of the members of adaptive immunity, including naïve and effector, Th1 and Th2 committed, and IL-17R and IL-23R expressing lymphocytes, along with that of FoxP3 regulatory T cells (Tregs). The prevalence of the members of innate immunity, such as natural killer (NK) and NKT cells, and expression of TLR-2 and TLR-4 on myeloid and plasmacytoid dendritic cells (DCs) and macrophages was also determined.

**Results:** The members of adaptive immunity did not change at the baseline compared to controls. However, the prevalence of effector CD4+ lymphocytes, that of Th1 CD4+ lymphocytes was increased after 6 weeks of IFX therapy compared to baseline and to controls. Interestingly, FoxP3 labeled Treg cells increased during IFX therapy (median, control, 1.25, 0. week, 1.31, 6. weeks, 1.96, P < 0.01). The prevalence of IL-17R+ and IL-23R+ lymphocytes along with NK and NKT cells was comparable. The higher expression of TLR-2 and TLR-4 on DCs compared to controls decreased with 6 weeks of IFX therapy (P < 0.01). The prevalence of DCs particularly plasmacytoid DCs increased, while that of macrophages decreased with 6 weeks of IFX therapy compared to baseline.

**Conclusion:** Our results suggest that IFX therapy has a systemic impact on the members of adaptive and innate immunity. However, we observed deficiencies only of innate immunity at the baseline and it is disappeared with IFX therapy. Further studies will be required to analyze these cells in the intestinal mucosa of pediatric patients with CD.

**Disclosure of Interest:** None declared.

**PA-G-046**

**ANALYSIS OF THE PROTECTION AGAINST NOROVIRUS INFECTIONS ELICITED BY BREAST MILK**

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**Objectives and Study:** Noroviruses (NoVs) are a leading cause of gastroenteritis worldwide. The inability to replicate NoVs in cell cultures has prevented investigation into their pathogenicity and immune response. Noroviruses recognize human histo-blood group antigens (HBGAs) in a diverse, strain-specific manner. Certain constituents of these HBGAs may confer susceptibility or resistance to specific NoVs. Human milk is rich in oligosaccharides that are either in free forms or as glycoconjugates. The role of these milk components in its innate immunity is being recognized. Our aim was to assess the implication of specific and non-specific immune effectors in breast milk in the protection against NoVs infections.

**Methods:** Colostrum, transitional, mature breast milk and serum samples from 111 mothers were analysed by ELISA for antibodies to NoVs, and for their blocking activity on the binding to saliva from a secretor (FUT2+) individual of breast milk and on the α1,3 fucosyltransferase-2 (FUT2) blood group system. A novel global blocking assay was developed based on a novel blocking peptide from the ABO blood group system. NoV infections in this issue.

**Results:** In model 1, the DTH-response was most profound in mice fed the diet with the highest omega-3 PUFA content. In model 2, mice fed this diet had a less severe acute allergic skin response (ASR). In addition, the most severe ASR was observed in mice fed a saturated FA diet.

**Conclusion:** Results obtained from model 1 indicate that a high omega-3 PUFA diet contributes to an increased Th1-response to vaccination. Additionally, results from model 2 suggest that this diet lessens the Th2-response. Furthermore, results obtained from the latter model indicate a diet with high levels of saturated FA may contribute to an increased severity of allergic symptoms.

**Disclosure of Interest:** None declared.
Disclosure of Interest:

Explain these findings.

Investigation of the HBGA phenotype and the oligosaccharides content of breast milk are required to find out an explanation to these findings. The blocking assays showed a significant inhibition by 94/105 colostrum, 93/102 transitional and 80/85 mature milk samples.

Conclusion: Most of the serum and breast milk samples exhibit a blocking effect on the binding of NoV VLPs to saliva. No correlation exists neither between this activity and the concentrations of anti-NoV antibodies detected nor with saliva. No correlation exists neither between this activity and the concentrations of anti-NoV antibodies detected nor with the anti-NoV IgA titers in serum and breast milk. Further investigation of the HBGA phenotype and the oligosaccharides content of breast milk are required to find out an explanation to these findings.

Disclosure of Interest: None declared.

PA-G-047

MORE ACCURATE LOCALIZATION OF INFLAMMATORY LESIONS BY 18-FLUORODEOXY-GLUCOSE POSITRON EMISSION PHOTOGRAPHY (18FDG-PET) AS COMPARED TO HYDRO-MAGNETIC RESONANCE IMAGING (MRI) IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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Objectives and Study: MRI techniques are increasingly replacing small bowel barium follow-through and conventional enteroclysis in the diagnosis of IBD. While hydro-MRI avoids radiation exposure and intubation of the duodenum, its sensitivity in detecting inflammatory changes in the gut may be lower. 18FDG-PET is a radionuclide scan with a low radiation exposure and high sensitivity for inflammation. The results of MRI and PET exams in paediatric IBD are compared to histology as gold standard.

Methods: 14 paediatric patients (9 boys) between 8 and 17 years of age with newly diagnosed IBD (11 Crohn’s disease, 3 ulcerative colitis) underwent hydro-MRI of the abdomen following bowel distension with oral contrast, administration of IV contrast and reduction of peristalsis with butylscopolamine. 3 patients had an additional 18FDG-PET scan and 11 an integrated 18FDG-PET/CT exam. Each abnormality observed within the GI tract was assigned to 1 of the following 7 segments: stomach and duodenum, jejunum, ileum, ascending colon, transverse colon, descending colon, or rectosigmoid. Segments with abnormalities suggesting IBD were classified as diseased. All patients had upper and lower endoscopy done. In total biopsies from 75 GI segments were available for histological diagnosis. A comparison was drawn between the results of imaging and pathologic studies.

Results: MRI correctly identified the disease status of 21 out of 75 segments. The radionuclide scans correctly identified the disease status of 47 out of 75 segments (with PET scan in 10 out of 17 and combined PET/CT scan in 37 out of 58). Mild to moderate disease activity in the upper GI tract remained unrecognized by MRI and was only detected in two cases detected by PET or PET/CT. Jejunal disease activity shown in 3 patients by radionuclide scan could only be detected in 1 patient by MRI. Compared to histology all imaging procedures had a low sensitivity (MRI 28%, PET and PET/CT 65%), but a high specificity (MRI 93%, PET and PET/CT 79%) and a high positive predictive value (MRI and PET 95%, PET and PET/CT 90%) for the detection of local disease activity.

Conclusion: 18FDG-PET is more sensitive than hydro-MRI for the detection of localized disease in paediatric IBD. While MRI shows bowel wall thickening, luminal narrowing, or enhanced contrast uptake as signs of progressed IBD, the PET scan identifies the metabolic increase of early inflammatory lesions. Larger comparative trials are necessary to prove the additional benefit of the more accurate localization of inflammatory lesions by 18FDG-PET in view of the additional radiation exposure.

Disclosure of Interest: None declared.

PA-G-048

POLYUNSATURATED FATTY ACIDS ALTER THE PHENOTYPE OF HUMAN MAST CELLS IN VITRO

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Objectives and Study: The increased n-6:n-3 fatty acid ratio in Western diets may contribute to the rapid increase in prevalence of allergic diseases. Key effector cells in allergy are mast cells (MC).

Methods: The effect of different fatty acids on MC activation was studied. Therefore separate long chain n-6 (arachidonic acid, AA) and n-3 (eicosapentaenoic acid, EPA and docosahexaenoic acid, DHA) polyunsaturated fatty acid (PUFA) incorporation was investigated in human MC lines (LAD2, HMC-1). Next to degranulation and mediator secretion (release of PGD2 and cytokines such as TNF-alpha, IL-4 and IL-13), generation of reactive oxygen species (ROS) and phosphorylation of mitogen-activated protein kinases (MAPK) was examined.

Results: Incubation of MC with AA, EPA or DHA for 24 hours increased PUFA content of the cellular membrane. Incubation with PUFA did not reduce IgE-mediated degranulation by LAD2 cells. However, mediator release of ionomycin/PMA stimulated HMC-1 cells was differentially regulated. IL-13 (P < 0.01 for all PUFA) and IL-4 (P < 0.05 for EPA and DHA) secretion were inhibited, whereas AA
enhanced TNF-alpha release ($P < 0.05$). The effect of DHA on IL-13 release was most pronounced and associated with a reduction in ROS generation ($P < 0.01$). AA incubation increased PGD$_2$ secretion, whereas n-3 PUFA reduced PGD$_2$. Cyclooxygenase (COX) inhibitors showed that the reduction in IL-13 secretion by PUFA was independent of COX. Preliminary results demonstrated that the ionomycin/PMA-induced phosphorylation of MAPK was inhibited by n-3 PUFA.

**Conclusion:** Long chain PUFA differentially alter mast cell activation which may affect the development of allergic diseases.

**Disclosure of Interest:** This study was financed by the Nutricia Research Foundation.

B. Schouten, M. Balvers, J. Garssen, Danone Research, employee.

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**PA-G-049**

**CYTOPROTECTIVE EFFECT OF ALPHA-MELANOCYTE STIMULATING HORMONE AND MET-ENKEPHALIN ON MURINE MODEL OF INFLAMMATORY BOWEL DISEASE**

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**Objectives and Study:** Met-enkephalin (MET) and alpha-melanocyte stimulating hormone (alpha-MSH) are endogenous opioid peptides with cytokine properties. The therapeutic potential of alpha-MSH on inflammatory bowel disease (IBD) has been demonstrated in a few studies, but the efficacy of MET and the alpha-MSH+MET mixture on colonic lesions has not yet been tested.

**Methods:** Colitis was induced in male Wistar rats by intracolonic administration of 2,4,6-trinitrobenzene sulphonic acid (TNBS). The peptides were given i.p. 1 h before the TNBS dissolved in 40% ethanol enema. Controls received physiological saline i.p. Five progressive doses of alpha-MSH (0.25–4 mg/kg) and MET (0.625–10 mg/kg); and two doses of alpha-MSH + MET mixtures (1 mg/kg + 2.5 mg/kg and 1 mg/kg + 5 mg/kg) were tested. Animals were sacrificed after 72 h and area of mucosal lesions involving the distal 10 cm of colon was assessed in mm$^2$ by means of image analysis software. Statistical analysis was performed with the ANOVA and subsequent post hoc analysis with Tukey HSD.

**Results:** The results of measurements implicate a dose-related modulatory effect of peptides on the tissue lesions provoked by TNBS, with a U-shaped dose-response curve. The area of colonic damage was significantly reduced following pretreatment with a single dose of 1 mg/kg alpha-MSH, as compared to control animals ($P = 0.022$). Other doses of alpha-MSH or any dose of MET did not have significant effects. Best cytoprotection was achieved by the mixture 1 mg/kg alpha-MSH + 5 mg/kg MET ($P = 0.005$; vs. control).

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**Conclusion:** The TNBS colitis is a simple, highly reproducible and robust model suitable for screening of cytoprotective agents. This study confirms the pharmacologically relevant cytoprotection of alpha-MSH on TNBS colitis in rats. The protective effect of the alpha-MSH+MET mixture was even stronger, indicating that the peptides have additive effects. These results are in line with others showing that the alpha-MSH+MET mixture is effective in controlling inflammatory and immune-mediated disorders (i.e. asthma, multiple sclerosis). So far, neither peptide exhibited toxicity or side effects when given in pharmacological doses. Therefore, the combination of alpha-MSH and MET could be further investigated in experimental protocols for IBD.

**Disclosure of Interest:** None declared.

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**PA-G-050**

**PREDICTORS OF POOR OUTCOME IN PEDIATRIC CROHN’S DISEASE**


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**Objectives and Study:** In pediatric Crohn’s disease (CD), early intensive therapy should be preferably considered in patients with poor outcome (PO). The aim of the study was to identify predictors of PO at diagnosis of PO of CD in a pediatric population-based population and to assess the relevance of predictors that have been proposed in adults (1,2).

**Methods:** Among 537 paediatric CD patients ≤ 17 years at diagnosis prospectively enrolled in the cohort between 1988 and 2004, 297 (55%) who had a follow-up ≥ 5 years were included in this retrospective analysis. Clinical and demographic factors associated with the development of PO within 5 years after the diagnosis were studied. Three definitions of PO based on events that happened during the first 5 years of the disease were evaluated: (a) St Antoine Hospital (France) definition including at least one of the following criteria: >2 steroid courses or dependency, further hospitalization for flare-up or complications, presence of disabling chronic symptoms, need for immunosuppressive therapy and intestinal resection or perianal surgery; (b) Liège Hospital (Belgium) definition including at least one of the following criteria: complex perianal disease, colonic resection, >1 small-bowel resection or definite stoma; (c) a new definition that we propose including nutritional impairment defined by a BMI or weight or height < -2 Zscore and at least 1 intestinal resection or 2 perianal surgeries.

**Results:** According to definition (a), the rate of PO was 76%. Independent predictors at diagnosis were L2L3 (Montreal classification) (OR: 3.74 [1.71–8.22]) and nutritional impairment (OR: 2.47 [1.26–4.85]). According to definition...
(b), the rate of PO was 34% and the only predictive factor was B2B3 behaviour at diagnosis (OR: 3.26 [1.77–6.02]). According to definition (c), the rate of PO was 15% and predictors were B2B3 behaviour (OR: 3.42 [1.17–9.95]), nutritional impairment at diagnosis (OR: 5.35 [1.89–15.16]), and age between 14 and 17 years at diagnosis (OR: 4.07 [1.44–11.49]).

**Conclusion:** Using a new discriminant definition, 15% of children developed PO within 5 years after diagnosis. Nutritional impairment and stricturing or penetrating behaviour at diagnosis were predictors of PO as well as age between 14 and 17 years at diagnosis. If validated, these predictors may be useful to select patients in whom early intensive therapy should be considered.

**References:**

**Disclosure of Interest:** None declared.

**PA-G-051**

**LEAN BODY MASS, PHYSICAL ACTIVITY AND ENERGY EXPENDITURE IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE COMPARED TO HEALTHY CONTROLS**

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**Objectives and Study:** Physical activity of paediatric patients with inflammatory bowel disease (IBD) may be impaired compared to healthy children. To test this hypothesis in patients’ daily life, the SenseWearPro2 bracelet was applied in IBD patients and controls.

**Methods:** Forty-one IBD patients (27 Crohn’s disease, 26 boys) and an equal number of healthy controls matched for age and sex participated. The following items were assessed and expressed as age- and sex-related standard deviation scores (SDS): height, weight, body-mass-index (BMI) and lean body mass as phase angle α determined by Bioelectrical Impedance Analysis (BIA). Grip force was measured with a standard dynamometer at the non-dominant arm. SenseWearPro2 bracelets were applied for 3 consecutive days to measure total energy expenditure (TEE) expressed as Metabolic Equivalent of Task (MET = kcal/hour/kg body weight), the duration of physical activity and the number of steps. Caloric TEE (calTEE) and caloric active energy expenditure (calAE) were calculated by the manufacturer’s software. Student’s t-test or Mann-Whitney-U-test was performed.

**Results:** Patients had a mean age of 15.0 ± 2.9 years (range 7.8–19.3) and disease duration of 3.5 ± 2.7 years (0.2–12.6). According to the Paediatric Crohn’s Disease Activity Index (PCDAI) and Paediatric Ulcerative Colitis Activity Index (PUCAI), 32 patients were in remission, 7 (3 CD) had mild and 2 (0 CD) moderate disease activity. Compared to controls, patients showed lower SDS for height (<0.49 ± 0.94 versus 0.17 ± 0.88, P = 0.002), weight and phase angle α (table), but no differences in BMI and grip force. Data recorded by SenseWearPro2 (table) showed for patients a trend to lower TEE, a shorter duration of physical activity (–19%) and less number of steps (–16%). The calculated daily calTEE and calAE were significantly decreased in patients, but these findings may be explained by the lower body weight and shorter duration of physical activity compared to controls.

**Table:** Differences between patients and controls in weight, phase angle α and SenseWear-Data

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
<th>P-level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight SDS</td>
<td>-0.70 ± 0.93</td>
<td>-0.09 ± 0.86</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Phase angle α SDS</td>
<td>-0.71 ± 0.93</td>
<td>0.10 ± 0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TEE [kcal/h/kg]</td>
<td>1.65 ± 0.18</td>
<td>1.74 ± 0.22</td>
<td>&lt;0.008</td>
</tr>
<tr>
<td>Physical activity: duration [h/day]</td>
<td>2.25 ± 1.04</td>
<td>2.77 ± 1.35</td>
<td>&lt;0.046</td>
</tr>
<tr>
<td>Daily number of steps</td>
<td>9506 ± 3083</td>
<td>11252 ± 3378</td>
<td>&lt;0.017</td>
</tr>
</tbody>
</table>

**Conclusion:** Lean body mass and physical activity were reduced in paediatric IBD patients compared to healthy age- and sex-matched controls, despite a well controlled disease activity. Since both factors have a negative long-term impact on bone quality and quality of life, potential interventions for improvement should be explored.

**Disclosure of Interest:** None declared.

**PA-H-032**

**RELAPSING FEATURES OF BILE SALt EXPORT PUMP (BSEP) DEFICIENCY IN TWO PATIENTS SUCCESSFULLY TRANSPLANTED FOR PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS TYPE 2 (PFIC2)**


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**Objectives and Study:** PFIC2 is caused by mutations of ABCB11 gene encoding for BSEP. Liver transplantation (OLTx) is traditionally thought of as curative for severe forms of PFIC2. Recently, four patients successfully transplanted for PFIC2 redeveloped features of BSEP deficiency in presence of serum anti-BSEP antibodies.

**Methods:** We report two more patients with post-OLTx features of BSEP deficiency.
Results: PFIC2 was diagnosed in a girl and a boy with normal GGT PFIC, on absence of canalaricular BSEP immunodetection and on mutation analysis of ABCB11. Biliary bile acid concentration was very low in the girl (0.1 mmol/L). LT was performed at age 9 and 2.8 years, respectively, without major complications. Cholestasis with normal GGT activity redeveloped 15 years after LT in the lady at age 26, during pregnancy, and 4.8 years after LT in the boy, during immunosuppression reduction. Liver biopsy showed in both canalaricular cholestasis, giant hepatocytes, slight lobular fibrosis, without evidence of rejection. In the lady, canalaricular BSEP immunostaining was negative and cholestasis progressed, being resistant to any increase of immunosuppression. She was listed for a second LT, but, while waiting, she developed melanoma and atrial fibrillation, and suddenly died of cardiac arrest. Her newborn girl have developed an hepatocellular cholestasis with normal GGT activity, spontaneously disappearing at 4 months. In the boy, canalaricular BSEP immunostaining was faint, and increase of immunosuppression caused resolution of cholestasis. Ten years post-LT cholestasis didn’t recur, liver tests are normal, but histology shows persistence of giant hepatocytes and lobular fibrosis, and an atrial fibrillation of unknown cause developed. Immunofluorescence staining of normal human liver sections with patient’s sera, collected at time of post-LT acute cholestasis, using an antihuman IgG antibody to detect serum antibodies, showed reactivity to a canalaricular epitope.

Conclusion: These data suggest that alloimmune-mediated BSEP dysfunction may occur after LT in PFIC2 patients naive for BSEP. Alloantibodies generated against BSEP of donor liver may inhibit BSEP function and lead to a PFIC2-like phenotype. This new disorder may be treatable or resistant to increase of immunosuppression, and may be associated with extrahepatic features and/or offspring transient neonatal cholestasis of possible immune mediated mechanisms.

Disclosure of Interest: None declared.

PA-H-033

MANAGEMENT OF HEPATOPULMONARY SYNDROME IN CHILDREN. A SINGLE CENTRE REPORT

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Objectives and Study: Hepatopulmonary syndrome (HPS) is a vascular disorder of the lungs characterised by portal hypertension, intrapulmonary right-to-left shunting, and arterial hypoxaemia. Liver transplantation (OLT) cures HPS but, due to the risk of severe hypoxaemia at operation, the outcome has been described as poorer than the average. We aimed to calculate the proportion of children diagnosed over the last 10 years and to review the management and outcome of HPS at our institution.

Methods: We interrogated our database for patients with HPS and we collected the following data: demographic features, degree of intrapulmonary shunting, gas exchanges, response to oxygen and inhaled nitric oxide (iNO), perioperative complications, outcome. The diagnosis of HPS was established if a patient had reduced pulse oximetry and confirmed right-to-left shunting documented by contrast enhanced echocardiogram (CEE) or pulmonary scintigraphy, and exclusion of other causes of hypoxaemia.

Results: 14 out of 371 (3.7%) children, 4 males, had HPS, median age at diagnosis 6.1 years (0.6–12.5) median age at OLT 6.4 years (0.7–13.4). None died before OLT. The underlying liver disease was biliary atresia (8), hepatoportal sclerosis (2), portal vein thrombosis (2), PFIC1 (1), Abernethy sdr (1). The median time of diagnosis from the onset of liver disease was 4.9 years (0.3–9.3). The median time on the waiting list was 3.9 months. At the time of diagnosis the median oxygen saturation was 82% (76–94), PaO2 levels 47.5 mmHg (37–70). 13 patients were diagnosed by CEE and all but one child received oxygen supplementation before transplant. There was a significant correlation between PaO2 at diagnosis and time to resolution of HPS (r = −0.6, P = 0.019). At the time of OLT the median oxygen saturation was 80%; after transplant 8 patients who were poor responders to oxygen received inhaled nitric oxide with a statistically significant increase in PaO2/FiO2 ratio (P = 0.01). There was no perioperative mortality nor major complications. All but one continued oxygen supplementation after OLT for a median of 54 days (range 12–210). The 1 year survival was 100%.

Conclusion: In our experience the overall outcome of patients with HPS is excellent, with no mortality and weaning from oxygen supply in a few months. A timely diagnosis and rapid listing is advocated, but also in children coming to OLT with severe hypoxaemia it is possible to carry out the procedure successfully. Patients with severe right to left shunting may benefit from perioperative administration of inhaled nitric oxide. Such management allows an excellent survival rate.

Disclosure of Interest: None declared.
with non-alcoholic fatty liver disease (NAFLD), and correlated results to clinical, metabolic, and histologic findings.

Methods: A total of 24 children (17 boys, 7 girls; mean age, 12.4 ± 0.57 years), undergoing hepatic biopsy for suspected NAFLD were included in the study. Clinical and laboratory data including body mass index (BMI), BMI– standard deviation score, waist circumference, and lipid profile, aminotransferases, gamma-glutamyltransferase, glucose, insulin, and insulin resistance as homeostasis model assessment of insulin resistance were collected. Hepatic fat morphology and severity were recorded in each biopsy specimen. The NAFLD activity score (NAS) and the stage of fibrosis were also assessed. Hepatic fat fraction (HFF) by MRI was obtained 1 to 7 days before liver biopsy using a modification of the Dixon method. Correlation coefficients and linear regression analyses were used to compare HFF to histological, clinical and metabolic data. The degree of steatosis, as determined by the pathologist, was used as a continuous variable in the regression models.

Results: In these patients, the degree of steatosis, mainly macrovesicular, ranged from 10 to 95% (mean ± SD, 39 ± 28; median, 40). HFF ranged from 5 to 44% (mean ± SD, 19 ± 15; median, 13.5). According to the histological grade of steatosis, the mean HFF was 8.8 ± 3.6 % for mild, 22 ± 8.5 % for moderate, and 39.7 ± 5 % for severe fatty liver infiltration. The differences were statistically significant between mild and moderate steatosis (P < 0.001), and moderate and severe steatosis (P < 0.001). HFF was highly correlated with histological steatosis (r = 0.868, P < 0.0001). With a cutoff of 5%, HFF had a sensitivity of 95.8% for the diagnosis of histological steatosis ≥ 10%. Among clinical and laboratory data, HFF was significantly associated with waist circumference (r = 0.462, P < 0.05), and insulin resistance (r = 0.495, P < 0.05). Moreover, HFF was associated with necroinflammation (P < 0.05), and NAS (P < 0.0001) scores, but not with fibrosis stage.

Conclusion: MRI is an accurate methodology for quantitative assessment of fat accumulation in pediatric NAFLD. Increasing HFF is associated with higher necroinflammation and NAS score.

Disclosure of Interest: None declared.

PA-H-035

INTESTINAL ABSORPTION IN CHILDREN AFTER INTESTINAL TRANSPLANTATION

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Objectives and Study: Irreversible intestinal failure (IF) requires intestinal transplantation (ITx) for restoring an intestinal function allowing parenteral nutrition (PN) weaning and growth. Very few study involved the functional capacity of intestinal allograft. This one analysed intestinal absorption rate of pediatric patients after ITx at the time of PN weaning.

Methods: 18 children aged 1.5 to 10 years received ITx, with liver in 2 cases and/or colon in 14 cases using tacrolimus, steroids and IL-2 blockers as induction treatment. Small bowel graft was always put as an ileostomy. PN was slowly tapered as enteral tube (nasogastric or gastrostomy) feeding (ETF) progressed according to digestive tolerance (stool output) and body weight gain. ETF was based on semi-elemental diet containing 50% energy as lipid with 50% medium chain triglycerides. A few days after PN weaning, intestinal absorption assessment was performed by using 3 days stool balance analysis. Fat, nitrogen, and total energy content were determined by the method of van de Kamer, elemental nitrogen analysis, and bomb calorimetry, respectively. Results were analysed according to the resting energy expenditure (REE) calculated from Schofield formula.

Results: All children were weaned from PN while on full ETF after 31 to 83 days post Tx (median: 44). Mean daily stool output at time of analysis was 11.37 ml/day (range: 314–2025 ml/day). Median intakes were: energy 108 kcal/kg/day (range: 79–162 kcal/kg/day), lipid 37.5 kcal/kg/day (range: 20–57.5 kcal/kg/day) and nitrogen 18.0 kcal/kg/day (range: 12.7–27.0 kcal/kg/day). The median absorption rates were 85% (range: 75–95%) for energy, 79% (range: 54.5–92.5%) for lipid and 75% (range: 61.5–88%) for nitrogen. The ratios of ingested energy/REE and absorbed energy/REE were 2.1 (range: 1.73–3.06) and 1.84 (range: 1.47–2.92, respectively).

Conclusion: These results show that PN weaning with appropriate weight gain may be achieved within 1 to 3 months after ITx. The ratios ingested energy/REE and absorbed energy/REE indicate a suboptimal graft absorption rates requiring to provide energy intake ≥ 2xREE. Energy and nitrogen supplies must be progressively increased and adapted according to the digestive tolerance and to the body weight gain.

Disclosure of Interest: None declared.

PA-H-036

THE INFLAMMATORY BOWEL DISEASE (IBD) ASSOCIATED TO AUTOIMMUNE SCLerosing CHOLANGITIS (ASC) IN CHILDREN: CLINICAL, ENDOSCOPIC AND HISTOLOGICAL FEATURES IN A COHORT OF 49 PATIENTS

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Objectives and Study: The inflammatory bowel disease associated to autoimmune sclerosing cholangitis (ASC-IBD) has been recently recognized as a distinct entity in adult patients. Compared to ulcerative colitis, several unique
features had been highlighted such as younger age, prevalence of male sex, dominant picture of pancolitis with ileitis in up to 50% of cases, lower histologic activity especially in the rectum and increased risk of colorectal dysplasia and cancer. Data regarding pediatric patients are very scanty.

**Methods:** Medical records of all children with ASC-IBD evaluated in the participating centres between 1980 and 2006 were reviewed. Patients who did not undergo diagnostic colonoscopy with biopsies were excluded.

**Results:** 86 children with autoimmune biliary disease were identified: 53 had also a diagnosis of IBD (61.5%). Medical records allowed a detailed review in 49: 36 children had ASC, 6 small-duct sclerosing cholangitis and in 7 cholangiography was not performed. 29 were males (M:F 1.45:1) and median age at diagnosis of IBD was 9.6 years. 80% of patients presented with symptoms of bowel disease and abnormal GGT and/or aminotransferase activity. Most frequent symptom of IBD was muco-hematic diarrhea (44%), but 15% of patients were asymptomatic. Laboratory features included hypergammaglobulinemia in 33 patients (67%) and autoantibodies not typical of IBD (ANA, SMA, LC-1) in 38 (77%) with ANCA detectable in 41 (53%). Endoscopic features included pancolitis in 70% and ileitis in 56%. Rectal sparing was recorded in only 16% of biopsies and in most cases also macroscopic examination of the rectum was abnormal. Histological features were more consistent with those of ulcerative colitis, but in 13 cases (26%) a massive eosinophilic infiltration was present in all explored segments. After a median follow-up of 6.7 years only a case of low grade dysplasia was recorded. 65% of patients were either always asymptomatic or never relapsed but most of them received immunosuppressive treatment for concomitant liver disease.

**Conclusion:** IBD-ASC phenotype in children is mostly characterised by a mild clinical course and asymptomatic patients are common. Pancolitis and ileitis are prominent endoscopic features. Eosinophilic inflammation is a peculiar histological picture. Dysplasia is an exceptional finding in childhood.

**Disclosure of Interest:** None declared.

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**PA-H-052**

**LOW PRE-TREATMENT NUMBERS OF CD4+/PD-1+ LYMPHOCYTES AND LOW HCV-SPECIFIC IL-10 PRODUCTION DURING THERAPY WITH PEGYLATED-INTERFERON+RIBAVIRIN PREDICT RESPONSE IN CHILDREN WITH CHRONIC HEPATITIS C**

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**Objectives and Study:** Chronic hepatitis C (CHC) in children progresses slowly with potential acceleration in adulthood. Pegylated-interferon (Peg-IFN)/ribavirin treatment prevents disease progression. Control of viral replication depends on efficient immune reactivity. Immune cells expressing programmed death 1 (PD1) receptor are exhausted and have limited anti-viral function. Low frequency of CD127+cells is linked to viral persistence. Limited data are available on PD1 and CD127 lymphocyte expression in predicting therapy response.

**Aim:** To investigate whether CD4+/PD1+ and CD4+/CD127+cell numbers, and HCV-specific immune responses, are affected by Peg-IFN/ribavirin and predict therapy outcome in perinatally acquired CHC.

**Methods:** Patients: Twenty-one children (11 males, median age 13 years) treated with Peg-IFN/ribavirin were divided into 3 groups according to response to therapy: 13 responders (R), 4 non-responders (NR) and 4 relapsers (Rel). CD4+/PD1+ and CD4+/CD127+cell numbers were determined by flowcytometry on PBMC at baseline (W0), week 12 (W12), W24, end-of therapy (EOT) and 6-month follow-up (FU). PBMC IFN-gamma and IL-10 production after exposure to HCV antigens (core, NS3, NS4 and NS5) was evaluated by intracellular cytokine staining.

**Results:** At W0 number of CD4+/PD1+cells was lower in R than NR and Rel (4.7 ± 0.7 vs. 6.8 ± 1.6 vs. 8.2 ± 1.8%, P = 0.04), while there was no difference in CD4+/CD127+cell number among groups. At W0 number of HCV antigen-induced IFN-gamma-producing cells was similar in R, Rel and NR, while that of IL-10-producing cells was lower in R than Rel and NR (core-CD4+/IL-10+: 2.1 ± 0.3% vs 3.7 ± 0.9% vs 4.2 ± 1.7%, P = 0.04). Similar results were obtained for NS3-CD4+/IL-10+cell numbers. In R, a decrease in numbers of IFN-gamma- and IL-10-producing cells, and of CD4+/PD1+cells was observed at W12, W24, EOT and FU, when HCV-RNA was undetectable [core-CD4+/IL-10+: 2.1 ± 0.3% (W0) vs. 1.2 ± 0.3% (W12), P = 0.03]. Similar results were obtained for NS3- and NS4-CD4+/IL-10+cells. Core-CD4+/IFN-gamma+cells decreased in Rel, at W12 (2.0 ± 0.5%, P = 0.04), W24 (1.8 ± 0.5%, P = 0.03) and EOT (1.6 ± 0.4%, P = 0.03) when compared to W0 (3.0 ± 0.3%), returning to W0 levels at FU when HCV-RNA was detectable; while HCV-specific IL-10 production and number of CD4+/PD1+cells were similar during therapy and FU. In NR, HCV-specific IFN-gamma and IL-10 production and number of CD4/PD1+cells were similar during therapy and FU.

**Conclusion:** Low pre-treatment CD4+/PD1+cell number and low HCV-specific IL-10 production during treatment are associated with successful response to antiviral therapy and may predict outcome.

**Disclosure of Interest:** None declared for all authors.

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**PA-H-053**

**ISOLATED SMALL BOWEL TRANSPLANTATION-SURVIVAL RATES ARE COMPARABLE TO HOME PARENTERAL NUTRITION**

Disclosure of Interest: None declared.

PA-H-054

ADULT HUMAN LIVER STEM CELLS ARE RESISTANT TO HEPATITIS B VIRUS INFECTION IN VITRO

IN VITRO RESISTANT TO HEPATITIS B VIRUS INFECTION ADULT HUMAN LIVER STEM CELLS ARE PA-H-054

Objectives and Study: To assess whether mesenchymal stem cells derived from adult human livers are infectable by HBV in vitro.

Methods: Adult Human Liver Stem Cells (AHLSC) were cultured as previously described (1). AHLSC were also studied after hepaticogenic differentiation. Primary liver cells (PLC; >95% hepatocytes) were obtained from adult liver digestion by collagenase P. A HBV-infected human hepatoma cell line (HepAD38) was used for the production of infective virions. AHLSC were incubated for 72 h with HBV (100 gen.equiv/cell), then washed and cultured in normal conditions. Total viral DNA, HBsAg and HBeAg were dosed in supernatant using qPCR and ELISA. The presence of intracellular HBV DNA and covalently closed circular DNA (cccDNA) was evaluated with PCR and real time PCR. Intracellular viral RNA (precore mRNA and pregemomic RNA) was dosed by real time RT-PCR. Expression of HBsAg and HBeAg was investigated by immunofluorescence and confocal microscopy.

The study was supported by the ESPGHAN Charlotte Anderson Young Investigator Travel Award 2009 and by the Fonds National de la Recherche Scientifique Belge.

Results: After incubation of AHLSC with HBV and subsequent extensive washing, both HBsAg and HBeAg were absent from culture supernatant. HBsAg became then detectable from day 3 to day 10 post-infection, while HBeAg was always negative. On the contrary, HBeAg was detectable in PLC culture from day 7 to day 15 post-infection. Immunostaining for both HBsAg and HBeAg was negative at fluorescence and confocal microscopy. Analysis of AHLSC culture supernatant by qPCR revealed the presence of HBV DNA from day 3 up to day 35 post-infection. Real time PCR performed on digested AHLSC intracellular DNA (Plasmid-Safe DNase) revealed the presence of cccDNA from 4 days up to 28 days post-infection. A very small amount of viral RNA was found in AHLSC 4–14 days post-infection (0.01% of RNA found in HepAD38 cells) by real time RT-PCR. Incubation of in vitro differentiated AHLSC with HBV led to a significant increase of precore mRNA levels (3.3 times higher, P < 0.05) and cccDNA levels (2.7 times higher, P < 0.05) compared to undifferentiated cells.

Conclusion: AHLSC can take up HBV in vitro. Viral entry is proved by the presence of cccDNA inside the cells at different times post-infection. Nevertheless, the absence of HBeAg in culture supernatant and the extremely low levels of viral RNA suggest that AHLSC are not permissive for HBV replication. The significant increase of cccDNA and viral RNA levels detected in differentiated AHLSC supports the hypothesis that undifferentiated mesenchymal stem cells lack of the intracellular machinery necessary to replicate HBV.
Disclosure of Interest: None declared.

PA-H-055

PRESENCE OF OESOPHAGEAL VARICES IN CHILDREN WITH INTESTINAL FAILURE ASSOCIATED LIVER DISEASE
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Objectives and Study: Children with splenomegaly and portal hypertension due to primary liver disease demonstrate presence of gastro-oesophageal varices (GOV) on oesophago-gastroduodenoscopy (OGD). Intestinal failure – associated liver disease (IFALD) is a secondary liver disease developing in 40% to 60% of infants requiring long term parenteral nutrition for irreversible intestinal failure. A proportion of these children develop life threatening complications of cirrhosis and portal hypertension. Assessment of portal hypertension is important to determine the type of intestinal transplantation (ITx) offered as a life saving option. Intestinal transplant is the only life saving option for these children. During small bowel transplant assessment within our programme, we observed absence of GOV despite advanced hepatic fibrosis and splenomegaly.

Aim: To evaluate the incidence of GOV in children with IFALD referred for small bowel transplant assessment.

Methods: Medical records of 82 patients who underwent assessment for small bowel transplant (SBtx) over the last 5 yrs (Sept 04 to Dec 09) were reviewed. Data detailing spleen size, splenomegaly, liver biopsy with staging of hepatic fibrosis and presence of GOV on oesophago-gastroduodenoscopy (OGD) was recorded.

Results: 82 children with median age of 1 yr (range 0.4 yr to 20.6 yr) were assessed. 71(86%) of these children had splenomegaly on ultrasound scan (USS) and evidence of IFALD. Twenty-two children had advanced liver disease (bilirubin >300 μmol/l, coagulopathy) and obvious evidence of portal hypertension (stomal bleeding, ascites etc) thus obviating the need for further invasive procedures. Thirty-four children underwent OGD and liver biopsy (fifteen children did not have simultaneous liver biopsy and OGD and were excluded from the study). Thirty-three children had presence of fibrosis on liver biopsy. Mild to moderate fibrosis was noted in 21 (64%) and only 2 children (9%) had oesophageal varices (grade 1). Moderate to severe fibrosis was noted in 12 (36%) children and only 3 (21%) children had GOV.

Conclusion: Presence of GOV in children with IFALD, splenomegaly is common and GOV are infrequent even in children with moderate to severe fibrosis.

In conclusion, better methods for assessment of portal hypertension are needed to make a decision about the type of ITx offered to children with advanced IFALD.

Disclosure of Interest: None declared.

PA-H-056

ADULT HUMAN HEPATOCYTES INDUCE INTERLEUKIN-10 PRODUCING ALLOGENEIC DENDRITIC CELLS WITH TOLEROGENTIC PROPERTIES
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Objectives and Study: One of the major limitations of liver cell transplantation is the fading of the metabolic effect that could be related to cell graft rejection. To further determine the involvement of the immune response in this loss of effect, we investigated the immunogenic properties of isolated human mature liver cells (hLC) and compared it to those of adult derived human liver progenitor cells, an alternative cell candidate for LCT (1).

Methods: The constitutive expression of cell surface markers was analyzed on isolated liver cells by flow cytometry at the basal state or after pre-incubation with pro-inflammatory cytokines. Human liver cells were co-cultured with allogeneic human adult peripheral blood mononuclear cells (PBMC) using transwells or not. The proliferation and the activation of PBMC were evaluated by the tritiated thymidine incorporation method and flow cytometry respectively. The cytokine levels were also evaluated in the culture supernatants by ELISA or by flow cytometry following intracellular staining. After 48 hours of co-culture with allogeneic hLC, dendritic cells were harvested and co-cultured with allogeneic naive CD4 T lymphocytes. We used tritiated thymidine incorporation to compare the proliferation of naive CD4 T lymphocytes induced by mDC previously co-cultured with hLC and mDC cultured in medium alone.

Results: Both hLCs and progenitor cells expressed major histocompatibility complex (MHC) class I and FAS but did not express human leukocyte antigen (HLA)-DR, FAS-ligand and co-stimulatory molecules CD80 and CD40. In a model of coculture with allogeneic hLC, dendritic cells were harvested and co-cultured with allogeneic naive CD4 T lymphocytes. We used tritiated thymidine incorporation to compare the proliferation of naive CD4 T lymphocytes induced by mDC previously co-cultured with hLC and mDC cultured in medium alone.

Conclusion: In children with IFALD, splenomegaly is common and GOV are infrequent even in children with moderate to severe fibrosis.
Conclusion: Our results suggest that both hLC and progenitor cells present low immunogenic phenotype in vitro. We further demonstrated that allogeneic hLC but not undifferentiated or differentiated progenitor cells, promote a cell contact-dependent production of IL-10 by circulating mDC which consequently present tolerogenic properties.

Reference:

Disclosure of Interest: None declared.

PA-H-057

EFFECT OF H1N1 VACCINATION ON PATIENTS WITH JUVENILE AUTOIMMUNE LIVER DISEASE (AILD)

Objectives and Study: After reports on flare-up of AILD after vaccination (1) we wanted to investigate if the adjuvanted H1N1 vaccin might constitute a risk of inducing relapse in patients with juvenile AILD.

Methods: 26 patients (20 girls, mean age 15.7 yrs, median 15 yrs, 4–21 yrs) participated. 19 (16 girls) had a primary AILD and 7 (4 girls) had primary sclerosing cholangitis. 24 of them received 1 dose (0.25–0.50 ml, according to age) of “Pandemrix” (Glaxo-Smith-Kline, Rixensart, Belgium) split virion, inactivated, adjuvanted influenza vaccin. Further 2 children presented with confirmed primary H1N1 infection. One week after the vaccination liver function tests (LFT = serum aminotransferases and GGT) were checked. Elevated LFT led to repeated check-ups. In the 2 patients with influenza LFT were checked on repeated occasions.

Results: Before vaccination 12 of the 26 children were in total and 8 in subtotal (LFT <3 times upper normal level) biochemical remission. No clinical symptoms other than the usual fever and/or local reaction were observed after vaccination. The two children with influenza had mild clinical course. 4 of the 26 vaccinated children increased their LFT after the vaccination more than 50 %. 2 of them had moderate (60 and 70 % higher than their baseline values) and two had severe (800% and 1700%) elevation of LFT 1 week after the vaccination. The 2 patients with the severe response remained clinically healthy and their synthetic function remained intact. In one of them LFT returned to baseline within a few weeks, the other has a sustained relapse. All patients with flare-up had circulating autoantibodies and/or elevated serum IgG levels but so had also many non-responders.

1 of the 2 patients with clinically overt influenza developed a moderate (70%) elevation of LFT during her illness. We did not follow similarly the LFT of children with non-autoimmune liver disease. But occasionally we found 2 of them with moderate post-vaccinatory response.

Conclusion: We conclude that 1) H1N1 vaccination might induce a flare-up of AILD; 2) the level of this might be considerable and there might be risk for decompensation; 3) there might be a striking discrepancy between symptoms and LFT levels; 4) the risk of flare-up is not exclusive for patients with AILD; 5) usual immunological markers are unreliable predictors of the risk for flare-up; 6) only systematic post-vaccinatory follow-up of LFT can trace the patients at risk; 7) this surveillance after vaccination is probably necessary for all children with chronic liver disease; 8) it remains unclear whether the response is due to the attenuated virus or to the adjuvant.

Reference:

Disclosure of Interest: None declared.

PA-H-058

LOW FREQUENCY OF ABCB4 MUTATION IN CHILDREN WITH CLINICAL SUSPICION OF MDR3 DEFICIENCY
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Objectives and Study: ABCB4 encodes multidrug resistance protein 3 (MDR3), a canalicular floppase for phosphatidylcholine. ABCB4 mutation in either the homozygous or heterozygous state is linked with a form of progressive familial intrahepatic cholestasis and with several adult liver disorders. We have investigated ABCB4 mutation and canalicular expression of MDR3 in a cohort of children with cholestatic liver disease suggestive of MDR3 deficiency.

Methods: 37 subjects with suspected MDR3 deficiency (8 of them with cholestatic conditions such as biliary atresia or alpha 1-antitrypsin deficiency, but with unusual clinical features) were investigated by sequencing of ABCB4 and multiplex ligation-dependent probe amplification (MLPA) analysis. The expression of MDR3, MRP2 and BSEP was assessed by immunohistochemistry in liver biopsy specimens (n = 23).

Results: Mutations in ABCB4 were detected only in 10 of 37 subjects, despite extensive analysis by sequencing and MLPA. None presented microdeletions or duplications of exons. Sequence analysis identified 14 different mutations, of which 10 were missense mutations. Four patients were compound heterozygotes. A single heterozygous mutation was found in 6 patients. On immunohistochemical analysis, all liver biopsy specimens showed normal staining for MRP2 and BSEP. 3 of 10 children with mutations in ABCB4 lacked MDR3 expression (one was compound heterozygote and the other two were single heterozygotes). Faint MDR3 expression was found in 3 children carrying a single mutation. In one patient who required liver transplantation, canalicular
MDR3 expression was absent, but no mutations in ABCB4 were found. Notably, heterozygous missense mutations in ABCB4 were identified in three children affected of different cholestatic conditions who exhibited an atypical course. The mutation P352L was found in a child with biliary atresia. The previously reported mutations S320F and T175A were present in a proband with lithiasis and in a proband with PiSZ. The mutation P352L was found in a child with biliary atresia. The aim of the study was to evaluate the prognostic value of histopathological findings with special care to severity of liver fibrosis at the moment of operation.

Methods: We performed analysis of 152 wedge liver biopsies taken at the time of HPE. Patients were divided into prognostic groups 3 months after HPE: group 1 - bilirubin level <2 mg% (n = 70), group 2 - bilirubin level >2 mg% (n = 82) and 5 years after HPE: group A - patients with native liver, bilirubin level <6 mg% (n = 60); group B - death, liver transplantation or bilirubin >6 mg% (n = 92).

Severity of fibrosis (Ichak scale) was separately analysed as a risk factor of survival with native liver (SNL) and development of portal hypertension (PH). The statistical analysis was based on Chi2, Fisher, logistic regression and log-rank test for Kaplan Meier survival curves.

Results: There was no difference in histopathological parameters between prognostic groups 3 months and 5 years after HPE. The following parameters were evaluated (p value for differences in groups 1 and 2/A and B): fibrosis (P = 0.86/0.58); zone 3: P = 0.77/0.23), focal necrosis (P = 0.23/0.67), microabscessus (P = 0.98/0.23), ballooning of hepatocytes (P = 0.08/0.06). Stage of liver fibrosis was not a risk factor of PH development in multifactorial regression analysis (P = 0.45). The actuarial 5/10-year SNL was not dependent on severity of liver fibrosis (log-rank test P = 0.84).

Conclusion: The severity of histopathological changes in liver biopsy at the moment of Kasai procedure has no prognostic value in children with biliary atresia.

Disclosure of Interest: None declared.

PA-H-060

LIVER DISEASE IN MITOCHONDRIAL FATTY ACID OXIDATION DEFECTS


Objectives and Study: Mitochondrial fatty acid oxidation defects (FAOD) are a group of severe inherited metabolic diseases which threaten the vital prognosis whereas their treatment is effective and easy to perform. Fatty acid oxidation is the essential metabolic pathway that provides the energy requirement in almost all organs during period of catabolic stress and, in heart and muscle at all time. Signs of FAOD are due to the lack of energy supply as well as the toxicity of metabolites that accumulate secondary to the enzymatic block. Although identified since the 1980s, their description remains still incomplete and we sought to specify hepatic semiology.

Methods: Through a French retrospective multicentric study, we analysed 158 children aged less than 6 years affected with a FAOD confirmed by enzymatic study and/or molecular analysis. The hepatic involvement was defined by various combinations of hepatomegaly, raised blood transaminases or GGT levels, hepatic insufficiency with a prothrombin time less than 30% or INR >2, hepatic steatosis (liver hyperechogenicity and/or histological microvacuolar steatosis), and Reye syndrome (coma and one of the following criterion such as steatosis or raised blood transaminases or hyperammoniemia).

Results: Hepatic involvement was found in 89% of patients, whatever is the causing defect. Hepatomegaly (92%), increased blood ALAT levels (82%), and steatosis (88%) are the most frequently observed symptoms. Reye syndrome (49%), increased GGT (37%), and liver failure (27%) were
other main signs. In the newborn period and in infancy, hepatomegaly and steatosis are almost constant signs, whereas Reye syndrome is frequent in childhood. Extra hepatic symptoms (neurological, muscular, cardiac, hemodynamic involvements, hypoketic hypoglycemia) are often in the foreground while hepatopathy can progressively worsen in the following hours. Isolated hepatic manifestations are exceptional (n=2).

Conclusion: Unexplained failures of organs which need strong energy requirements, such as myocardium, skeletal muscle or central nervous system, associated with the presence of hepatic symptoms at any age are noticeable criteria to suggest a FAOD and should prompt to look for steatosis which is characteristic.

Disclosure of Interest: None declared.

PA-N-061

A SEVERE FORM OF ABETALIPOPROTEINEMIA CAUSED BY NEW SPLICING MUTATIONS OF MTP

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Objectives and Study: Abetalipoproteinemia is a rare autosomal recessive disease characterized by very low levels of plasma cholesterol and triglyceride levels, and by the absence of lipoproteins containing apolipoprotein B. It is caused by a deficiency of microsomal triglyceride transfer protein (MTP).

Methods: We reported 2 children with a severe form of abetalipoproteinemia. The diagnosis was performed on endoscopic and biochemical findings. Combining genomic and complementary DNA analysis, we determined MTP mutations. We studied the functional consequences of these mutations on the triglyceride transfer function using duodenal biopsies and on the subcellular localization of MTP, transfecting wild-type and mutant cDNA, with a fluorescent tag, in HepG2 and HeLa cells.

Results: Abetalipoproteinemia was diagnosed in a 13-month-old boy, and then in his 6-year-old sister, born from caucasian non-consanguineous parents. He had a failure to thrive, associated with an enteropathy and a steatohepatitis (ALT = 60 UI/l and hyperechogenic liver). Endoscopy found white duodenal villi, corresponding to large fat inclusions as confirmed by histology. Plasma total cholesterol levels were 0.77 and 0.58 mmol/l, and plasma triglyceride levels were 0.07 and 0.05 mmol/l, respectively for both children, with vitamin E deficiency (0.41 and 0.16 mg/l). Their parents had normal lipid profiles. These children were compound heterozygotes with 2 new mutations of MTP, 619 G>T and c.1237→A>G. cDNA analysis revealed a deletion of exon 6 and 10, respectively. The deletion of exon 6 induced a shift in the open reading frame leading to a premature stop codon at position 234, without translated protein. The second mutation induced a frank deletion of exon 10. It did not affect protein translation nor its endoplasmic reticulum localization but MTP lost its triglyceride transfer function.

Conclusion: These splicing mutations of MTP, with deletion of exon 6 or 10, resulted in a severe form of abetalipoproteinemia. Amino-acids 413→448 are not involved in MTP localization but MTP lost its triglyceride transfer function.

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PA-N-062

A PROTOTYPE OF INFANT FORMULA SPECIALLY DESIGNED FOR CHILDREN UNDER 3 YEARS OF AGE WITH CHRONIC RENAL FAILURE: IMPACT ON METABOLIC CONTROL AND BODY COMPOSITION OF PATIENTS

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Objectives and Study: Background: Adequate nutritional support helps to achieve good metabolic control and optimum nutritional status in infants and children with chronic renal failure (CRF).

Aim: To evaluate the changes in metabolic control and body composition in children with CRF younger than 3 years of age, fed with an infant formula specially designed for this situation, and compare them with those fed with a standard infant formula.

Methods: Prospective, randomized study. Children were assigned to group A (study), fed with the special formula, or group B (controls), fed with a standard formula (making the necessary adjustments to guarantee metabolic control). Energy and protein recommended intakes were similar in both groups. BUN/creatinine ratio (BUN/cr), serum triacylglycerides (TAG), potassium and parathyroid hormone (PTH) levels were measured. Anthropometric measurements were expressed as z-scores. Body composition was assessed by bioimpedance analysis (BIA). Monitoring was made along 12 months.

Results: Thirty-four children assessed. Group A, n=17, mean age 1.18±0.93 years, glomerular filtration rate (GFR) 41±30.5 ml/min/1.73m2. Group B, n=17, mean age 1.03±0.83 years, GFR 45±27 ml/min/1.73m2. Group A showed greater improvement in weight and height z-scores. Deltaz-score for height was 1±3.39 in group A and 0.21±3.88 in group B. BIA body cell mass (BCM),
expressed as % lean body mass, showed more significant improvement in group A (initial BCM 41.68±4.1%, final BCM 44.6±3.8%, P<0.02) than in group B (initial BCM 41.42±4.6%, final BCM 42.7±3.8%, P<0.05). BUN/cr in group A tended to decrease (initial 33±34, final 28.3±21), while it increased in group B (initial 32±42, final 46.5±34, P=0.05). There was significant correlation between BUN/cr ratio and the intake of non-protein kilocalories per gram of nitrogen, and significant negative correlation between BUN/cr ratio and TAG levels. Potassium levels remained high in group B, and significantly decreased in group A (initial 4.6±0.7 mEq/L, final 4.1±0.3 mEq/L, P=0.02). PTH levels increased in group B (initial 71±101 pg/ml, final 81±78 pg/ml) and decreased in group A (initial 94.5±81 pg/ml, final 67.9±52 pg/ml), although differences observed were not significant.

**Conclusion:** 1. Although macronutrient recommended intake was similar with both formulas, the use of the special prototype determined a better linear growth and body composition.

2. The main goals achieved with the use of an infant formula specially designed for children with CRF were the decrease in BUN/cr ratio and better control of serum potassium levels.

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R. Chifre and M Rivero, Grupo Ordesa, Employees.
(TINE) were performed at 4 and 5½ years, respectively. Neurological condition was summarized as a clinical classification, a neurological optimality NOS, and fluency scores.

**Results:** No significant differences were observed amongst intervention groups for the rates of minor neurological dysfunction (MND) ($P=0.212$; $P=0.175$), NOS ($P=0.683$; $P=0.872$) or fluency scores ($P=0.173$) neither at 4 nor at 5½ years of age. However, logistic regression analyses showed an increasing risk of MND at 5½ years of age with increasing arachidonic acid (AA) levels in maternal plasma PLs at 20 and 30th weeks of pregnancy (IC 95% for Exp B: 1.249–3.711, $P=0.002$ and 1.444–3.899; $P=0.001$ respectively) and at delivery (1.137–2.739; $P=0.01$). In addition, a significant association between the occurrence of optimality (NOS = 63) at 5½ and levels of DHA in cord plasma PLs (Exp B IC 95%: 1.040–1.891; $P=0.027$) and DHA levels in maternal erythrocytes at delivery (Exp B IC 95%: 1.142–2.542; $P=0.009$ for phosphatidylethanolamine PLs and 1.235–3.586: $P=0.006$ for phosphatidylcholine PLs) was observed. Furthermore, an increasing risk of being classified as non-fluent (fluency score <15) at 4 with increasing AA/DHA quotient in maternal plasma PLs at delivery (Exp B IC 95%: 1.028–13.230; $P=0.045$) was observed.

**Conclusion:** This study shows neither beneficial nor harmful effects of maternal DHA and/or 5-MTHF supplementation during pregnancy on long term neurodevelopment of their offspring. But higher DHA levels in maternal and fetal blood and lower AA levels in maternal plasma during the course of pregnancy seem to be related to a better neurological outcome in the children at 4 and 5½ years of age.

**Disclosure of Interest:** *This work is a part of the 6th EU Framework Program EARNEST Project Contract n° 007036.*

**PA-N-065**

**SOLID INTRODUCTION AND GROWTH IN THE FIRST TWO YEARS OF LIFE IN FORMULA-FED CHILDREN**

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**Objectives and Study:** A potentially negative effect of early solid introduction could be more rapid weight gain in infancy which is associated with later obesity. We tested the hypothesis that the timing of solid introduction has no influence on growth during the first two years of life.

**Methods:** The study is based on a double blinded, randomized controlled trial comparing two groups of children fed cow’s milk formula with either higher or lower protein content. Eligible for study participation were apparently healthy, singleton, term infants. Children were recruited in five countries (Belgium, Germany, Italy, Poland, Spain). Repeated standardized anthropometric measurements were taken. The week of solid introduction was assessed by questionnaire and prospective three day weighed food records at monthly intervals. Linear regression analysis was applied to test the effects of feeding on z-scores at 24 months. Multilevel growth models were used to construct longitudinal models of anthropometric z-scores trajectories of each child over the first 2 years of life.

**Results:** Of originally 1090 formula-fed children included in the study 687 (63%) completed the study until 24 months of age. In 682 children all anthropometric measurements and in 671 also the week of solid introduction were available. The median age at solid introduction was 19 (25.−75. perc. 17–21) weeks. Almost a quarter of the children received solids before 17 weeks and 60% between 17 and 23 weeks of age. The timing of solid introduction was significantly associated with country of study center, gender, parental nationality, marital status, and maternal smoking behaviour. Those children becoming slimmer between baseline and 3 months of age were fed solids earlier. Solid introduction did not predict anthropometric measures at 24 months of age, growth trajectories however, differed significantly between the children: those children introduce to solids in the first 12 weeks catched up growth between 3 and 6 months whereas those introduced to solids >23 weeks of age grew slower and stayed on lower trajectories.

**Conclusion:** Solid introduction did not influence the weight or length at 24 months. However, the growth pattern differed significantly by the timing of solid introduction with a catch-up growth in those introduced to solids in the first 12 weeks.

**Disclosure of Interest:** None declared.

**PA-N-066**

**HYPERANDROGENISM, ENERGY METABOLISM AND INSULIN SENSITIVITY IN CHILDREN WITH 21-HYDROXILASE DEFICIENCY**

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**Objectives and Study:** Background: 21-hydroxylase deficiency causes an increase in the production of androgens. Patients can present hyperandrogenism during infancy.

**Aim:** To assess testosterone levels in children with 21-hydroxylase deficiency and their relation with energy metabolism, body composition and metabolic impairment.

**Methods:** Children with 21-hydroxylase deficiency were assessed and compared with healthy controls, matched by age and gender. Body composition was estimated using skinfold-thickness equations and bioimpedance analysis. Fat body mass (FBM) and lean body mass (LBM) were expressed as percentage normal level (%N). Resting energy expenditure (REE) was assessed by indirect calorimetry. Testosterone and basal insulin (radioimmunoassay) and glucose levels were determined. Glucose overload test was performed in the group of patients.
Results: Sixty-six children assessed. Thirty-two healthy controls (15 male, mean age 10.43 ± 2.6 years) and 34 patients (18 males, mean age 11.2 ± 4.6 years). Testosterone levels varied widely (mean 1766 ± 2555 ng/dl). Basal insulin was higher in patients, without significant differences. Testosterone levels neither correlated with insulin nor with HOMA. Glucose overload tests were normal. REE per kilogram of LBM (REE/LBM) was significantly lower in patients than in controls (35 ± 6.5 vs 40.7 ± 7.5 Kcal/Kg). REE showed negative correlation with testosterone levels. Patients showed higher FBM (186 ± 73 %N vs 125.7 ± 26 %N, P = 0.008) and LBM (116 ± 8.5 %N vs 99.7 ± 10.7 %N, NS). Significant correlation was noted between basal insulin and FBM, between HOMA and FBM and between testosterone and LBM, but not between testosterone and an FBM.

Conclusion: 1. Testosterone levels were related to LBM, but not to FBM.
2. REE was lower in patients than in controls and showed negative correlation with testosterone.
3. Insulin levels and HOMA were slightly increased and related to FBM and were not related to testosterone.

Disclosure of Interest: None declared.

PA-N-068

ASSESSMENT OF A BODY COMPOSITION INDEX BASED ON ARM MUSCLE AND ARM FAT AREA IN NORMAL WEIGHTED AND UNDERNOURISHED CHILDREN: COMPARISON TO DUAL-ENERGY X-RAY ABSORPTIOMÉTRY

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Objectives and Study: Upper arm areas can estimate nutritional status and body composition. Two indexes have been successively developed to calculate those upper arm areas, - Upper arm Muscle Area and Upper arm Fat Area (UMA/ UFA) by Jelliffe (1969) and Upper arm Muscle area Estimate and Upper arm Fat area Estimate (UME/UF E) by Rolland-Cachera (1997)-. The aim of the study is to compare those two indexes together and to DEXA in order to assess the pertinence of Cachera’s index in comparison with Jelliffe’s index to estimate the total body composition in a population of children undernourished.

Methods: The arm circumference (C) and the triceps skinfold thickness (TS) were measured for 71 children aged 4 to 8 years old: 51 children well-nourished and 20 undernourished (ratio weight/height <85%). The total upper arm area TUA is equal to C2/4π. The upper arm muscle areas -UMA = (C−(TS × π))2/(4 π) and UME = TUA-C × (TS/2)- were compared one with the other, and also to lean body mass (LBM) measured by DEXA. The arm fat areas were also studied -UFA = TUA-U MA and UFE = C × (TS/2)- and compared to the results of fat mass (FM) obtained by DEXA.

Results: Arm fat areas, UFA as UFE, have a good total fat mass predictive value (r = 0.86 for well-nourished and r = 0.59 for undernourished), but total lean body mass is lower correlated to arm muscle areas (for well-nourished, r = 0.21 with UME and r = 0.23 with UMA; for undernourished, r = 0.41 with UMA as UME). If we use one or the other index, LBM and FM percent calculated from arm areas are as well correlated to total %LBM and %FM obtained by DEXA, (r = 0.73 for well-nourished et r = 0.61 for undernourished). However the %LBM and %FM calculated with arm areas don’t allow an estimation of the total body

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composition estimation: the difference between those two methods is too important for both groups.

**Conclusion:** Both indexes have the same level of correlation with total body composition for well-nourished and undernourished children. However, fat mass has higher predictive value than lean body mass. Those results together with the superiority of UME/UFE index over the UMA/UFA one for normal weighted and obese children, already described by Rolland-Cachera, enable us to conclude that for arm area’s calculation for children using RC indicator is preferable to the Jelliffe one.

**Disclosure of Interest:** None declared.

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**PA-N-069**

**SUPPLEMENTATION OF THE MATERNAL DIET WITH ALPHA-LINOLENIC ACID (ALA) MODIFIES THE DEVELOPMENT OF THE ENTERIC NERVOUS SYSTEM WITH FUNCTIONAL CONSEQUENCES ON INTESTINAL PERMEABILITY IN NEWBORN PIGLETS**

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**Objectives and Study:** The enteric nervous system (ENS) participates in the regulation of various mucosal functions such as intestinal motility and secretion but also permeability. The ENS shares embryologic similarities with the CNS whose perinatal development is known to be modulated by n-3 polyunsaturated fatty acids (PUFA). We hypothesized that n-3PUFA in the maternal diet modify the development of the ENS, by analogy with the CNS, and have consequences on the regulation of jejunal permeability of newborn piglets.

**Methods:** The intestinal permeability was measured on 28 day-old piglets nursed by sows who had been fed either a lard-based diet (LAR, ALA = 3.5% of total fatty acid) or a linseed oil based-diet (LSO, ALA = 28.3%) during gestation and lactation. Basal jejunal permeability to FITC-dextran 4000 (FD4) was evaluated in Ussing chambers. Different cytokines mRNA in the tissue.

**Results:** Basal jejunal permeability to FD4 was higher in LSO compared to LAR piglets (229 ± 1.2% for LAR vs 266 ± 0.9% for LSO, P < 0.05) and the mRNA relative expression of ChAT was greater in the LSO group compared with the LAR group (1.9 ± 0.6 vs 1.1 ± 0.6, P < 0.05). Despite the increase in permeability the cytokine profiles (IL-1β, IL10, TGF-β) did not differ between the two groups.

**Conclusion:** In conclusion, supplementation of the maternal diet with ALA modified the development of the ENS and the nervous regulation of jejunal permeability, with the induction of a cholinergic tonus. The consequences of such differences on the maturation of the gut immune system of newborn warrant further investigations.

**Disclosure of Interest:** None declared.

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**PD-G-082**

**TARGETING OF GLIADIN PEPTIDE ALPHA 31–49 TO LATE ENDOSEOMES OF ENTEROCYTES OF INFANTILE MICE BY CONJUGATION TO CHOLERA TOXIN B SUBUNIT (CTB)**

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**Objectives and Study:** The physiological response to food antigens and commensal flora is a state of specific immunological unresponsiveness - known as oral tolerance. Coeliac disease (CD) - a multisystemic autoimmune inflammation of the small intestine - is a result of a breakdown in oral tolerance to wheat gluten and related cereals in HLA-DQ2/8 positive individuals. However, the molecular mechanisms relevant to the induction of oral tolerance towards toxic small intestinal enterocytes remain poorly understood. The translocation of luminal antigen to LAMP- and HLA-DR-positive late endosomes of small intestinal enterocytes is thought to be a decisive mechanism for the induction of oral tolerance (1).

**Methods:** After intraoperative application of gliadin peptides in defined segments of the jejunum of gliadin-naive 10-day-old mice we compared the subcellular localization of both toxic and non-toxic gliadin peptides in the enterocytes. Using an immunogold technique on thin frozen sections of small bowel biopsy tissue we focussed on the question whether gliadin peptides segregate along the endocytotic pathway. In addition we tried to modulate the sorting of the toxic peptide M1 (α31–49) towards late endosomes based on the model of the non-toxic peptide M3 (α229–246) by conjugation to cholera toxin B subunit (CTB). The labelling densities of gliadin peptides in endosomes of enterocytes were quantified morphometrically.

**Results:** Unlike the control peptide of gliadin M3 the toxic gliadin peptide M1 (α31–49) fails to reach late endosomes and thereby escapes antigen presentation by HLA-DR...
molecules at the basolateral membrane. Strikingly, M1 being linked to cholera toxin B subunit can be rerouted to late endosomes.

**Conclusion:** The separate pathway of gliadin peptide M1 and its absence in late endosomes seems to be a crucial process and could explain the peptide’s toxicity (2,3) and its failure to induce T lymphocytes. The presentation of gliadin peptides by HLA-DR molecules via late endosomes of enterocytes might be essential in the induction of tolerance towards gliadin. Hence, the successful sorting of M1 in late endosomes by conjugation to CTB could be a potentially promising both preventive and therapeutic approach in the treatment of coeliac disease.

**References:**

**Disclosure of Interest:** None declared.

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**PD-G-083**

**EVALUATION OF THE QUALITY OF GUIDELINES FOR ACUTE GASTROENTERITIS IN CHILDREN, WITH THE AGREE INSTRUMENT**

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**Objectives and Study:** The number of available Clinical Practice Guidelines (CPGs) is rapidly growing and several studies suggested that many are of poor quality.

Main study aim was to assess the quality of CPGs using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument, a validated international tool.

**Methods:** CPGs were identified by searching Medline and Embase. CPG databases and relevant web-sites of agencies and professional organizations that produce and/or endorse guidelines. Included in the study were CPGs in English that addressed the management of AGE in children.

**Intervention:** Retrieved CPGs were evaluated with the AGREE instrument for quality assessment by six independent reviewers. AGREE consists of 6 domains for a total of 23 items and the cut-off for good quality is >50%.

**Results:** Nine CPGs were identified. Main quality domains of most recent CPGs are reported in table. Principal AGREE domains and relative CPGs scores are reported in table. Four were evidence-based (EB) and two of these included tables of evidence. Eight CPGs (88%) scored <50% for ‘applicability’, 7 (77%) for ‘stakeholder involvement’ and 6 (66%) for ‘editorial independence’. Compared with non-EB-CPGs, EB-CPGs had higher quality scores for all AGREE domains, with a significantly better score for ‘rigor of development’ (P < 0.001), ‘stakeholder involvement’ and ‘clarity of presentation’ (P < 0.01), and for applicability (P < 0.05). Over time, the quality of guidelines tended to improve. Inter-reviewer agreement was substantial-to-excellent.

**Conclusion:** The overall quality of CPGs on AGE management in children is fair. Aims, target population, synthesis of evidence, formulation of recommendations and clarity of presentation are points of strength. Weak issues are cost/efficacy analysis and applicability, including identification of organizational barriers and adherence parameters.

**Disclosure of Interest:** None declared.

**Table: AGREE domains scores (%) of most recent CPGs for AGE**

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<th>Stakeholder involvement</th>
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<th>Clarity and presentation</th>
<th>Applicability</th>
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**PD-G-084**

**GLIADIN DIRECTLY ELICITS A TH1 IMMUNE RESPONSE IN DECIDUA FROM CELIAC PREGNANT WOMEN**

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Objective and Study: The association between maternal celiac disease (CD) and the increased risk of adverse pregnancy-related events has been epidemiologically established; however the pathogenic mechanisms of this phenomenon remain poorly understood. A Th2 phenotype of the decidual immune response is necessary for the maintenance of pregnancy. Aim of this paper is to assess if gliadin triggers a direct Th1 immune response in the decidua of celiac women.

Methods: Decidual samples were obtained from five treated celiac women upon elective cesarean section and incubated in vitro with a peptic tryptic digest of gliadin (GLY 200 μg/ml) for 24 hours. As negative control, deciduas were obtained from healthy women matched for age and parity.

Results: The exposure to GLY increased the density of CD3+ (40 ± 9 vs 9 ± 6 stained cells / mm², P < 0.01) and CD25+ (46 ± 7 vs 10 ± 5 stained cells / mm², P < 0.01) T cells within the decidua and the expression of FAS on the membrane of decidual cells (220 ± 47 vs 6 ± 5 positive cells / mm², P < 0.01) respect to celiac decidua exposed to culture medium alone. We also observed higher interferon-γ level in the culture medium of decidua exposed to GLY (604 ± 84 pg/ml vs 134 ± 45 pg/ml, P < 0.01). GLY did not exert any of these effects on decidua from healthy donors.

Conclusion: Gliadin directly elicits a Th1 immune response in celiac decidua, deranging the placental environment and affecting its capability to maintain a proper pregnancy. These finding suggest novel mechanisms for CD-associated adverse pregnancy events.

Disclosure of Interest: None declared.

PD-G-085

ABNORMAL GASTROINTESTINAL PATHOLOGY IN CHILDREN WITH AUTISTIC SPECTRUM DISORDER: A SYSTEMATIC REVIEW

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Objectives and Study: The significance of the association between many gastrointestinal pathologies and autism is yet to be discovered. The aim of this paper is to review available evidence that documented any link between autism and gastrointestinal pathology in children.

Methods: The following sources were searched: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1980–August week 2 2009), EMBASE (1980–August Week 2 2009), Pubmed (last 180 days), Web of Science, and Scopus, using these terms: “autism” or “autistic spectrum disorder” AND “intestinal” or “gastrointestinal” or “colitis”. In addition, relevant studies were identified through browsing the reference lists of the included articles for relevant citations. Cohort studies/case series reporting gastrointestinal pathological examination findings in autistic children <18 years old were included. Only studies written in English were included.

Results: Only 8 studies have looked into the histopathological features of gastrointestinal tract in children with autism. The majority of these trials did not include comparison/control groups. Apart from intestinal lymphonodular hyperplasia, the majority of these findings were not reproducible.

Conclusion: Gastrointestinal Pathological findings in children with autism have been inconsistent. The current available evidence does not support a link between gastrointestinal pathology and child autism. The significance of intestinal lymphonodular hyperplasia in these children is unknown. Large properly conducted prospective controlled trials are needed.

Disclosure of Interest: None.

PD-G-086

ACID INHIBITORS AND RISK OF INFECTIONS IN INFANTS

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Objectives and Study: To assess the prevalence of infections in infants treated with acid inhibitors for suspect or proven gastroesophageal reflux disease (GERD).

Methods: All infants who started treatment with H2RA or PPI were recruited. Age, dose and duration of treatment, number and kind of infection, and use of probiotic were recorded during follow-up visits and analysed according to different age groups. Patients with a follow-up less than 2 months or with incomplete data, known immune defect, malformations, neurological disorders, previous recurrent respiratory infections were excluded. Number and kind of infections were compared with retrospective data of age-matched healthy controls.

Results: The data of 146 infants and 41 controls were analysed. Compared to controls infants treated with acid inhibitors showed a significant (P < 0.001) increased number of infections up to 9 months of age (17 vs. 2 in 1–3 months of age, 32 vs. 4 in 4–6 months of age, 49 vs. 5 in 7–9 months of age, 6 vs. 3 in 10–12 months of age). Only 4 cases of pneumonia were reported (3 with PPI and 1 with H2RA). Urinary infections occurred in 7 infants (1 control and 6 with PPI). Infants with PPI showed a significant (P < 0.05) higher number of infections compared to infants with H2RA. The median of follow-up was 4 months (range 2–12 mo) every 2 months till the end of treatment. Lactobacillus reuteri (DSM 17938, 108 cfu, 5 drops per day, BioGaia AB Sweden) was used in unslected 16 patients who showed a significant (P < 0.01) reduced number (n = 3) of infections compared to the group with acid inhibitors without probiotic.
Conclusion: Infants treated with acid inhibitors (PPI more than H2RA) are at risk population for gastrointestinal and respiratory infections especially in the first months of age. Our preliminary results showed a possible protective effect of the use of a probiotic (L. reuteri) in addition to PPI in these patients.

Disclosure of Interest: None declared.

PD-G-087

GLIADIN PEPTIDES CAN ALTER ACTIN CYTOSKELETON OF DENDRITIC CELLS
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Objectives and Study: Gliadin peptides can induce several non-immunological effects on different cell lines not only from celiac disease (CD) patients. The gliadin peptide P31–43 can alter actin cytoskeleton in Caco-2-cells (Barone et al, 2007). Since dendritic cells (DC) play a crucial role in the immune response triggered by gliadin in CD patients, we aimed to investigate the direct effect of some gliadin peptides on DC. In particular actin cytoskeleton rearrangements and surface profile markers were assessed after treatment with gliadin peptides.

Methods: DC from 10 controls and 10 CD patients, 5 in the active and 5 in the remission phase of the disease, were generated from peripheral blood monocytes. Phalloidin staining after cells adhering on fibronectin was used to evaluate actin cytoskeleton at confocal microscopy. Cytofluorimetric analysis was used to assess the degree of maturation of DC.

Results: The effect on actin cytoskeleton of a 3 hours treatment with peptic-tryptic digest of gliadin (PTG), the toxic peptide P31–43 and the immunogenic peptide P56–68 was assessed. PTG induced a marked rearrangement of actin cytoskeleton in DC from controls inducing an elongation of dendrites, but only a milder effect on cells from CD patients whose shape was already elongated compared to controls (36.8 ± 8.9% of cells with more than 3 small and/or 1 long dendrite in controls vs 72.5 ± 8.7% in CD-patients, \( P = 0.00065 \)). Gliadin peptide P31–43 favoured an elongated morphology of DC, but only in controls (from 36.8 ± 8.9% elongated cells to 49.3 ± 8% in the presence of P31–43, \( P = 0.049 \)), while the peptide P56–68 had only a mild not statistically significant effect on controls DC cytoskeleton. After FACS analysis we observed that both gliadin peptides P31–43 and P56–68 induced an increase in the percentage of CD83 positive cells (\( P < 0.05 \)), indicating an induction of maturation. Furthermore the immunogenic peptide P56–68 could induce an increase in the mean fluorescence intensity (MFI) of HLA-DR in dendritic cells from both groups (\( P < 0.05 \)).

Conclusion: Gliadin can induce a marked alteration of actin cytoskeleton of DC from control subjects, but does have only a marginal effect on CD patients cells, whose shape is constitutively altered probably on a genetic basis. Gliadin peptides may also induce the maturation of dendritic cells indicating a further role of gliadin in the immune deregulation that characterizes the pathogenesis of celiac disease.


Disclosure of Interest: None declared.

PD-G-088

BIFIDOBACTERIUM BIFIDUM REDUCES INTESTINAL APOPTOSIS IN IN VIVO AND IN VITRO MODELS OF NECROTIZING ENTEROCOLITIS
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Objectives and Study: Necrotizing enterocolitis (NEC) is the most common intestinal disease of premature babies. Although end-stage NEC is characterized histopathologically as extensive necrosis, apoptosis may account for the initial loss of epithelium prior to full development of disease. Recently, we showed that oral administration of Bifidobacterium bifidum OLB6378 reduces the incidence of NEC in the rat model. However, little is known about the mechanism(s) of probiotic-mediated protection against NEC.

The aim of this study was to evaluate the effect of B. bifidum treatment on apoptosis using a rat model of NEC and IEC-6 cells.

Methods: Premature rats were divided into the following groups: hand-fed with formula (NEC), or hand-fed with formula supplemented with 5 x 10⁶ CFU B. bifidum OLB6378 per day. Both groups were exposed to asphyxia/cold stress to develop NEC. Pro-apoptotic and anti-apoptotic markers were evaluated in the terminal ileum. Apoptosis was induced in IEC-6 cells by incubating with TNF-α and IFN-γ for 4hrs. Cells were pre-treated for 15 min with 1 x 10⁵ CFU of B. bifidum. Flow cytometry (annexin-labeled) and caspase-3 staining were used to quantify apoptotic cells.

Results: B. bifidum significantly decreased apoptosis in both in vivo and in vitro models of NEC. Pro-apoptotic markers Bax and Cleaved Caspase-3 were decreased in animals receiving B. bifidum treatment compared to NEC animals. Anti-apoptotic Bcl-w was increased in treated animals compared to NEC rats. The Bax/Bcl-w ratio indicates that cell survival is favored in animals receiving a B. bifidum supplemented diet. In IEC-6 cells, apoptosis was significantly decreased after B. bifidum pre-treatment.

Conclusion: The ability of B. bifidum OLB6378 to down-regulate apoptosis both in the rat NEC model and the IEC-6 cell line suggests a molecular mechanism by which probiotics reduce intestinal injury and preserve intestinal integrity.
Supported by the NIH Grant HD-39657 (to B.D.) and a gift from Meiji Dairies Corporation.

Disclosure of Interest: None declared.

PD-G-089

EARLY INTRODUCTION OF GLUTEN IS ASSOCIATED WITH FUNCTIONAL CONSTITUTION IN CHILDHOOD: THE GENERATION R STUDY

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Objectives and Study: Food allergy and celiac disease may lead to childhood constipation. Early introduction of food allergens and gluten in the first year of life has been suggested to play a role in these food intolerances but it is unclear whether this also holds true for development of childhood constipation. The aim of this study was to assess the association between the timing of introduction of food allergens and gluten early in life and functional constipation in childhood.

Methods: This study was embedded in the Generation R study, a population-based prospective cohort study from foetal life until young adulthood. Children were excluded in these analyses in case of twinborn, siblings within the cohort, presence of a congenital heart condition, anemia in the past year or growth retardation. Subsequently, data on stool pattern was available in 4651 children. Functional constipation at 24 months of age was defined according to the Rome II criteria.

Results: At the age of 24 months, 12% of the children had functional constipation. After adjustment for birth weight, gestational age, gender, mother’s educational background and ethnicity, functional constipation was more prevalent in children who received gluten before or equal to the age of 6 months (OR: 1.36; 95%CI: 1.11 – 1.67). No significant association was found between timing of introduction of cow’s milk, hen’s egg, soy, peanuts and tree nuts with functional constipation. After adjustment for birth weight, gestational age, gender, mother’s educational background and ethnicity, functional constipation was more prevalent in children who received gluten before or equal to the age of 6 months (OR: 1.36; 95%CI: 1.11 – 1.67). No significant association was found between timing of introduction of cow’s milk, hen’s egg, soy, peanuts and tree nuts with functional constipation.

Conclusion: These results suggest that early gluten introduction in the first year of life may provide a trigger for functional constipation in childhood.

Disclosure of Interest: None declared.

PD-G-090

GLIADIN PEPTIDE P31–43 INDUCES TRANS-PRESENTATION OF IL15/IL15R-ALPHA COMPLEX


Objectives and Study: We previously observed that Peptic Tryptic digest of A-gliadin (PTG) and gliadin peptide P31–43 can interfere with maturation of endocytic vesicles from early to late endosomes both in CaCo2 cells and in biopsies from CD patients. As a consequence tyrosine kinase receptors, such as EGFR (Epidermal Growth Factor Receptor), stays longer activated leading to actin modifications and cell proliferation. On the other side gliaind and peptide P31–43 can induces in mucosa from CD the increase of a key mediator of innate immunity: IL15. Recently has been shown that the complex IL15/IL15R-Alph can be presented on the cell surface, and that this trans-presented form of IL15 is responsible for most of IL15 activity including induction of proliferation of several cell types and the homeostasis of innate effectors. Aim of our work is to understand the molecular mechanisms of gliadin mediated IL15 increase.

Methods: Protein levels and distribution was analyzed by Facs, Elisa and immunofluorescence in CaCo2 cells. WB and trasfection were used to test IL15 R alpha siRNA. BrdU (Bromodeoxiuridine) incorporation consented the analysis of cell proliferation.

Results: After three hours treatment with P31–43, IL15 and IL15R-Alphas proteins were found increased only on CaCo2 cells’ surface and not in the medium or in the intracellular compartment. The presence of IL15 on the cells surface is reduced by acid wash and by silencing the mRNA of IL15R-Alpha with a specific IL15 R Alfa siRNA, showing that IL15 is linked to its receptor. Markers of recycling vesicles, such as transferrin and Lamp2, were increased too, on the cells surface, implying that a P31–43-mediated interference with IL15/IL15R -Alpha vesicular trafficking can be the reason of the complex increase on the cell surface. SiRNA for IL15 R-Alpha can prevent P31–43 and PTG induced increase of proliferation in CaCo2 cells and in the enterocytes of biopsies from CD patients.

Conclusion: Gliadin peptide P31–43 induces trans-presentation of IL15/IL15R-Alpha complex on the surface of Caco2 cells interfering with its vesicular trafficking. The complex so presented functions as a growth factor both in CaCo2 cells and in the enterocytes of biopsies from CD patients.

Disclosure of Interest: None declared.

PD-G-091

POTENTIAL CELIAC PATIENTS: A MODEL OF CD PATHOGENESIS


Objectives and Study: The pathway of gluten-induced immunoresponse in Celiac Disease (CD) has not been yet...
new understanding could help to elucidate the mechanism through which CD manifests in so many different ways: from classical malabsorption to very light or complete absence of symptoms associated to moderate damage of intestinal mucosa (Marsh 1) or even normal mucosa (Marsh 0). Potential celiac cases produce Anti-Transglutaminase Antibodies, but have no (classified as M0) or minimal (classified as M1) small intestinal mucosa damage. The aim of the study is to explore in a sizeable cohort of potential CD cases, the presence of genetic and expression factors that may differentiate potential CD cases from full blown CD patients.

**Methods:** The study includes 643 CD cases, 83 potential CD patients and 711 controls, all from the same region of Southern Italy. They were genotyped for eight of the most CD-associated SNPs by Taqman technology (Applied Biosystems); HLA typing was performed by Eu-Gen risk kit (EUROSPITAL). The expression of three genes of 4q27 locus (IL2, IL21, KIAA1109) was studied by real-time PCR. For this purpose intestinal biopsy samples of 17 full CD patients, 15 potential CD (M0 and M1), 14 healthy controls and 8 CD patients on a gluten-free diet were obtained.

**Results:** Potential CD cases less frequently belong to the high HLA risk classes, more frequently they show very low or moderate HLA-related risk. Candidate Gene SNPs typing shows that the genotype of the REL gene SNP (rs842647) can differentiate Controls from Potential CD patients and Celiac from M1 Potential cases. Expression studies show that IL21 is suppressed in potential Celiac cases compared with Controls and Celiac patients too; IL2 is over-expressed in M0 Potential but not in M1; KIAA1109 gene shows an expression similar to that of IL2, so both can well differentiate M0 from M1 Potential Celiac cases.

**Conclusion:** Potential celiac cases are a living model of the gradual expression of the phenotype of CD. They have a minor HLA related risk and a different polymorphism in the NF-kb related gene c-REL. Expression data allow to differentiate full blown CD from Potential: IL21 is fully suppressed in potential. Within the same cohort of potential cases they IL2 and KIAA1109 distinguish between infiltrated M1 (similar to full blown celiacs) and completely normal patients M0. Natural immunity, as well as adaptive one, is indeed involved in the gluten-induced pathogenesis of CD. Potential celiac cases, being somewhat the ‘intermediate’ phenotype of CD, give a significant contribution to the understanding of the mechanism of disease.

**Disclosure of Interest:** None declared.

**PD-G-092**

**USE OF RAPAMYCIN (SIROLIMUS) AS RESCUE TREATMENT IN REFRACTORY PAEDIATRIC INFLAMMATORY BOWEL DISEASE**

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**Objectives and Study:** To study the indications, side effects and outcome of the usage of Rapamycin, a novel immuno-suppressive agent, which inhibits proliferation of antigen-activated T-lymphocytes, in children with refractory IBD.

**Methods:** Review of case records of 14 patients (9 male), median age 11 years 5 month (4.3 to 16.8) who received Rapamycin between 2006 and 2009.

**Results:** Indications for Rapamycin: Ulcerative colitis (n = 6), Indeterminate colitis (2), Autoimmune enteropathy (4), IPEX (1) and Crohn’s disease (1). Median age at introduction of Rapamycin was 9.8 years (range 1.3–15.2) Main indication was non-response to intense standard treatment regimes(5-Aminosalicylates, corticosteroids, thiopurines, Ciclosporin and monoclonal antibodies). Rapamycin was not used on its own, it was used in combinations with 5-Aminosalicylates (10/14), thiopurines (11/14), Prednisolone (14/14) and Infliximab (12/14) in 9/10 patients, with additional Basliximab (8/14) in 5/10 patients, and with additional MMF (7/14) in 3/10 patients. Adalimumab (7/14), Ciclosporin (3/14), Tacrolimus (2/14) and Methotrexate (2/14) were given in further combinations. Rapamycin was added at a daily dose of between 1.0 mg to 5 mg, median 2 mg. Median duration of follow-up was 32 months (range 4–41). In ulcerative colitis: 3/5 patients went into remission, 1/5 improved and 1/5 did not respond. In indeterminate colitis: both patients did not respond. In autoimmune enteropathy: 2/4 patients went into remission, 2/2 did not respond. In IPEX-Syndrome: no response, patient received bone marrow transplantation. In Crohn’s disease: patient went into clinical remission. No side effects were recorded other than worsening diarrhoea and PR bleeding in one patient after only 5 days on Rapamycin, probably more due to the underlying disease rather then the medication.

**Conclusion:** Rapamycin appears effective in rescuing over 50% of patients with IBD refractory to conventional intensive treatment regimes.

**Disclosure of Interest:** None declared.
in children are lacking. Therefore, we studied five potential serum fibrosis markers to assess the liver fibrosis parallel to biopsy in children with NAFLD.

**Methods:** We determined fasting serum level of hyaluronic acid (HA) (Corgenix), laminin (Takara), YKL-40 (Quidel) and cytokeratin-18: M30 and M65 (Peviva AB) in 52 children (age range 4–19, mean 12 years, 80% of them were overweight or obese) with biopsy-verified NAFLD. Viral hepatitis (HBV, HCV), autoimmune and metabolic liver diseases (Wilson’s disease, alpha 1 antitrypsin deficiency, cystic fibrosis) were excluded. Fibrosis stage was assessed in a blinded fashion by single pathologist according to Kleiner. Receiver operating characteristics (ROC) analysis was used to calculate the power of the assays to detect liver fibrosis (AccuROC, Canada).

**Results:** Liver fibrosis was diagnosed in 19 children (37%). The levels of HA, CK18 M30 and M65 were significantly higher in children with diagnosed fibrosis compared to children with simple steatosis (P = 0.04; 0.05; 0.03 respectively). The ability of serum HA (cut-off 19.1ng/ml, Se = 84%, Sp = 55%, PPV = 52%, NPV = 86%), CK18 M30 (cut-off 2100 u/l, Se = 79%, Sp = 60%, PPV = 56%, NPV = 82%) and CK18 M65 (cut-off 1690 u/l, Se = 84%, Sp = 53%, PPV = 53%, NPV = 84%) to differentiate children with fibrosis from those with simple steatosis was significant (AUC = 0.672, 0.666, 0.689 respectively). Laminin and YKL-40 did not allow a useful prediction.

**Conclusion:** Cytokeratin-18 and hyaluronic acid seem to be the most suitable serum markers predicting liver fibrosis in children with NAFLD. Application of these markers may identify patients at risk of disease progression.

**Disclosure of Interest:** None declared.

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**PD-H-105**

**OUTCOME OF BILIARY ATRESIA PATIENTS WITH 20 YEARS NATIVE LIVER SURVIVAL**

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**Objectives and Study:** Surgical treatment of biliary atresia (BA) through the Kasai portoenterostomy has markedly improved short-term outcome. Despite the success, most BA patients still require a liver transplantation during their life. Relatively little is known about long-term transplant-free survival of BA. We have assessed the outcome of all BA patients surviving 20 years with native liver using a national database.

**Methods:** All 106 patients born between 1977 and 1988 who underwent surgical correction for BA in The Netherlands were included. Clinical characteristics, liver biochemistry and ultrasonography parameters of patients alive with native liver were collected at the age of 20 years.

**Results:** Twenty six percent of the patients (28/106) were alive with native liver at the age of 20 years (at 10 years; 41%). Twenty year transplant-free survival of type I/II BA was 39% and of type III 25% (P = 0.09). In the 1977–1982 cohort only 20% (10/50) reached a 20 year survival with native liver. This percentage increased to 32% (18/56) of patients born in 1983–1988 (P = 0.03). Long-term transplant-free survival was not associated with an early (<60 days) Kasai procedure. After 20 years, normal serum bilirubin levels were found in 54% of transplant-free patients (15/28). Clinical or ultrasonographic signs of cirrhosis were absent in 21% (6/28) of these patients after 20 years follow-up.

**Conclusion:** More than 25% of BA patients survive at least 20 years with native liver in The Netherlands. Survival has increased during the last decades. Interestingly, one fifth of the long-term transplant-free survivors are symptom-free and do not have clinical or radiological signs of cirrhosis or portal hypertension.

**Disclosure of Interest:** None declared.

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**PD-H-106**

**RE-EVALUATION OF THE DIAGNOSTIC CRITERIA FOR WILSON’S DISEASE IN CHILDREN WITH MILD LIVER DISEASE**

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**Objectives and Study:** Wilson’s disease (WD) is a challenging diagnosis, especially in children. Early diagnosis is desirable in order to avoid disease progression. Aim of our study was to re-evaluate the conventional diagnostic criteria and Ferenci’s diagnostic score (1) in WD children with mild liver disease.

**Methods:** We retrospectively evaluated 43 consecutive children with WD (28 boys, age range: 1.1–20.9 years) and 58 age- and sex-matched patients with liver disease other than WD. Both groups were symptom-free with hypertransaminasemia as prevalent sign of liver disease. In all WD patients diagnosis was confirmed by molecular analysis and/ or liver copper content.

**Results:** ROC analysis for ceruloplasmin at cut-off of <20 mg/dl showed sensitivity of 95.4% (95% CIs, 84.5–99.4%) and specificity of 84.4% (95% CIs, 72.5–92.6%). Optimal basal urinary copper diagnostic cut-off was found to be >40 mcg/24 h (sensitivity of 78% [95% CIs, 62.4–89.4%] and specificity of 87.9% [95% CI, 76.7–95%]). Urinary copper after penicillamine challenge had 15.4% sensitivity only. Liver copper >250 mcg/g dry weight had 96.7% sensitivity [95% CIs, 82.8–99.9%] and 95.8% specificity [95% CIs, 78.9–99.9%]. Ferenci’s diagnostic score showed 93% positive and 91.6% negative predictive value, respectively.
Table: Diagnostic accuracy of conventional diagnostic criteria for WD at different thresholds

<table>
<thead>
<tr>
<th>Test</th>
<th>Cut-off</th>
<th>Sensitivity (95%CIs)</th>
<th>Specificity (95%CIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceruloplasmin</td>
<td>&lt;10 mg/dl</td>
<td>65.9% (50–79.5%)</td>
<td>96.5% (88–99%)</td>
</tr>
<tr>
<td>Ceruloplasmin</td>
<td>&lt;20 mg/dl</td>
<td>95.4% (84–99%)</td>
<td>84.4% (72–93%)</td>
</tr>
<tr>
<td>Basal 24 h urinary</td>
<td>&gt;100 mcg/24 h</td>
<td>63.4% (47–78%)</td>
<td>96.5% (91–99.9%)</td>
</tr>
<tr>
<td>Basal 24 h urinary</td>
<td>&gt;40 mcg/24 h</td>
<td>78% (62.4–89.4%)</td>
<td>97.9% (76.7–95%)</td>
</tr>
<tr>
<td>24 h urinary copper PCT</td>
<td>&gt;1575 mcg/24 h</td>
<td>15.4% (4.3–34.8%)</td>
<td>96.5% (88.1–99.6%)</td>
</tr>
</tbody>
</table>

Conclusion: Urinary copper excretion is suggestive of WD when above 40 mcg/24 h, rather than 100 mcg/24 h, as suggested by recent AASLD guidelines (2). Instead, penicillamine challenge test should not be performed in asymptomatic patients. Ferenci’s diagnostic score shows good diagnostic accuracy. Diagnosis of WD requires multiple tests and high index of suspicion.

References:

Disclosure of Interest: None declared.

PD-H-107

EFFECTS OF A NEW SYMBIOTIC FORMULATION CONTAINING LACTOBACILLUS PARACASEI B21060 IN A MODEL OF INSULIN RESISTANCE AND NONALCOHOLIC STEATOHEPATITIS IN YOUNG RATS

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Objectives and Study: Nonalcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease in the pediatric population. Insulin resistance (IR) appears to be critical in its pathogenesis and also present in lean, non-diabetic patients. Few possible therapeutic approaches have been proposed to limit different steps of NAFLD development or progression to steatohepatitis. Experimental studies support the pathogenic role of an altered intestinal permeability and/or an increased LPS-containing microbiota for fatty liver and IR development. Thus an emerging potential therapeutic utility of probiotics has been addressed also considering the limited side effects.

We evaluated the therapeutic effects of a symbiotic formulation composed by a mixture of Lactobacillus paracasei B21060 and two prebiotics, arabinogalactan and fructooligosaccharides (FLORTEC®), in an experimental model of NAFLD induced in young rat. For this purpose we chose a high fat diet (HFD), rich in unsaturated and saturated fats.

Methods: Just after weaning, male Sprague-Dawley rats were divided into three groups as following: 1) a control group receiving the standard diet (STD; 10.5% fat, 16.4% proteins, and 73.1% carbohydrates; 4.06 kcal/g); 2) a HFD fed group (HFD; 58.0% fat, 16.4% protein, and 25.5% carbohydrates; 5.6 kcal/g); and 3) HFD fed animals treated by gavage with FLORTEC® (FLO; 2.5x108 bacteria/kg/die) for 5 weeks.

Results: In the early state of pathology, body weight gain, caloric intake, fat mass, triglycerides and liver weight did not vary among groups. However, HFD showed a marked increase in serum amino transferases and in fasting serum glucose level that were significantly reduced by FLO treatment. HFD-induced glucose tolerance impairment was significantly improved by symbiotic formulation. IR occurred in HFD was associated to a strong increase in tumor necrosis factor (TNF)-alpha, interleukin (IL)-6, SOCS-3 and in phosphorylation of insulin receptor substrate (IRS)-1Ser307. HFD also decreased adiponectin mRNA and peroxisome proliferator-activated receptor (PPAR)-alpha expression in adipose tissue and in liver, respectively. FLO reduced TNF-alpha and IL-6 hepatic levels and restored adiponectin and PPAR-alpha expression. Moreover, FLO prevented the HFD-induced toll-like receptor 4 overexpression in liver.

Conclusion: The efficacy of FLORTEC® on limiting molecular events underlying the onset of insulin resistance and nonalcoholic steatohepatitis suggest its potential clinical relevance.

References:

Disclosure of Interest: No conflict of interest.

PD-H-108

PSYCHOMOTOR EVALUATION OF PEDIATRIC LIVER TRANSPLANT RECIPIENTS AND PARENTAL ASSESSMENT BEFORE AND AFTER TRANSPLANTATION

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Objectives and Study: Increasing evidence points to pre- and post- transplant psychomotor deficits in pediatric liver transplant (LT) recipients. Parental involvement and family dynamics are important for psychomotor development, and
both are challenged in the families of children with life-threatening disease. The aims of our study were: 1) to assess children and parents individually, 2) to assess the parent-child relationship 3) to look for correlations between parental functioning and patient outcome, all before and after LT.

Methods: Patients, parents and the child-parent pair were assessed using age-appropriate scales before transplant, 1 year- and 2-years- following transplant. Written and spoken French or German was required to participate. The study was approved by the institutional ethics committee.

Results: Subjects: 21/80 consecutive patients followed at our institution for LT participated in the study over 2 yrs. 57% of families were Swiss. Actuarial patient survival was 90% overall. Indications for LT were similar to those reported previously. 4 patients were not evaluated pre LT. 19 mothers and 16 fathers were evaluated pre-LT, while only 8 fathers were seen post-LT. Development quotient (DQ): No subjects scored in the ‘very good’ range. There was an increasing proportion of children with deficits from LT to 2 yrs: 17.6% vs 28.6%. Subjects 0–2 yrs were more likely to have normal DQ at transplant (66.7% vs 50% for older children). Abnormal development was more prevalent 2 yrs post-LT among patients transplanted in the older age group (P = 0.02). Mother-child relationship was measured as normal in 59% of families pre-LT, increasing to 67% at 2 yrs. The trend was more favourable in families where the child was transplanted as an infant (P = 0.014 at 12 months post LT, P = 0.022 at 24 months post LT). Protective factors for normal DQ: a) higher maternal score pre-LT (P = 0.03), b) diagnosis of biliary atresia at all time points, and c) German or French mother tongue pre-LT. Parents: Mothers’ performance score improved from a mean of 59% pre-LT to 71% post-LT. Positive predictors of normal functioning included siblings, a diagnosis of biliary atresia. Employment was predictive of better adaptation at 2 yrs. Fathers scored higher than mothers for performance at all time points, although this finding did not reach significance.

Conclusion: In this small, but representative cohort, we show that there is a trend toward increasing psychomotor impairment post LT, confirming the findings of others. The novel findings include: parental education has unpredictable effects on DQ peri-transplant, maternal functioning is more severely affected than paternal, and employment and siblings aid in the recovery of maternal functioning.

Disclosure of Interest: None declared.

Objectives and Study: Adherence is a common and concerning problem for adolescents with liver disease. It has been reported that 76% fail to take post liver-transplant (LT) medications, with poor adherence being attributed as the cause of graft loss in 12%. Adherence is a complex, multi-factorial issue and psychosocial factors e.g. co-morbid mood disorders and poor understanding of condition have been highlighted as important in maintaining non-adherence in the general population, yet little is known about their role in adolescents with chronic liver disease (CLD) and LT. We recently have set up a specialist clinical psychology service for teenagers and young adults with liver disease and the aim of this study was to investigate the incidence of co-morbid mood disorders and poor understanding of condition in non-adherent adolescents and young adults with CLD and LT.

Methods: Twenty-five patients (15 female) with median age of 17.3 yrs (range 12–27) were referred for a psychological assessment because of non-adherence over a 1 year study period. They were assessed for the presence of co-morbid mood disorders ie anxiety disorders (eg panic disorder, generalised anxiety disorder, obsessive compulsive disorder and phobias), depressive disorders and suicidal ideation. The UK Mental Capacity Act (2005) guidelines were used to assess whether patients had enough understanding to make an informed decision about whether to take their medication.

Results: Twelve patients were diagnosed with liver disease during infancy, the others at a median age of 11.4 yrs (range 6.6–14.9). Fourteen were transplanted at median age of 11.3 yrs (range 0.5–18.9); 7 required re-transplantation. The table shows the incidence of co-morbid mood disorders in the study population, CLD group and LT group. In the LT group depression was more common in re-transplanted. Only 1 patient in the CLD and none in LT group were considered to have enough understanding to make an informed decision about whether to take their medications.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Overall n=25</th>
<th>CLD n=11</th>
<th>LT n=14</th>
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<tbody>
<tr>
<td>Anxiety</td>
<td>60%</td>
<td>73%</td>
<td>50%</td>
</tr>
<tr>
<td>Depression</td>
<td>52%</td>
<td>64%</td>
<td>43%</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>36%</td>
<td>36%</td>
<td>35%</td>
</tr>
</tbody>
</table>

Conclusion: A significant proportion of patients with CLD and LT; non-adherent to medications, experience psychological difficulties. Furthermore, in all but 1 of this sample, understanding of condition and the need to take medications was absent. Whilst further research is needed to investigate these initial results in more depth, there is a clear need to improve understanding in young people concerning their liver disease and the need for medications. Secondly, there is a role for improving detection of psychological problems in young people with liver disease. Whether addressing these two issues could improve adherence in this population needs to be investigated.

Disclosure of Interest: None declared.
THE ASSESSMENT OF LIPID PROFILE AND OXIDATIVE STRESS IN PAEDIATRIC AND ADULT LIVER TRANSPLANT RECIPIENTS

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Objectives and Study: High total cholesterol, triglyceride, low-density lipoprotein cholesterol, and low-density cholesterol concentration are well-known risk factors for atherosclerosis and cardiovascular events both in the general population and after transplantation. According to our previous study (Transplant Proc 2007, 39: 1523–1525) lipids disturbances due to recently used immunosuppressant regimen are less common than seen before.

Objective: To assess the cardiovascular risk factors in pediatric and adults patients 1–5 years after liver transplantation.

Methods: The study group consisted of 67 children (48 girls and 19 boys) aged 10.4 ± 4.9 years and 44 adults (17 woman and 27 man) aged 46.5 ± 7.6 y after liver transplantation with good liver function. In all patients lipid parameters and lipid peroxides were measured on fastum before.

Results: Few children presented with abnormal lipid profile: hypertriglyceridemia (>150 mg/dl) was present in 9/67 pts, hypercholesterolemia (>200 mg/dl) in 19/67, low HDL-C (<45 mg/dl) in 13/67. Abnormal lipid parameters were present in a significant but a small number of adults: hypertriglyceridemia in 12/44, hypercholesterolemia in 14/44, low HDL-C in 22/44. There were no differences in serum total cholesterol-TC (180.6 ± 49.4 mg/dl vs. 167.7 ± mg/dl), TG (88.4 ± 54.80 vs. 81.1 ± 42.4 mg/dl), LDL-C (110.8 ± vs. 104.9 ± 24.5 mg/dl), HDL-C (53.2 ± 10.1 vs. 46.8 ± 11.0 mg/dl), Apo A1 (1.4 ± 0.24 vs 1.3 ± 0.33 g/l), Apo B (1.1 ± 1.73 vs. 0.8 ± 0.20 g/l), LCAT (151.1 ± 64.3 vs. 129.2 ± 21. nmol/ml/h), glutathione (745.2 ± 88.9 vs. 729.8 ± 121.0 µmol/ml) and GPx (33.8 ± 5.8 vs. 31.5 ± 4.36 U/gHb) activity between transplanted children and a control group of 67 healthy children (mean values with SD).

Conclusion: Lipid disturbances are not very common in children and adult liver transplant recipients. Pediatric population of liver transplant recipients does not present with increased risk of disturbed lipid metabolism and increased oxidative stress.


Disclosure of Interest: None declared.
**Objectives and Study:** Paediatric chronic HCV (CH-C) infection is a mild disease with potentially severe acceleration in adulthood. Successful antiviral therapy with pegylated interferon-alpha (Peg-IFN)+ribavirin achieves sustained virological response (SVR = negative HCV RNA 6 months after therapy) in 50–60%, preventing disease progression. Treatment side effects may lead to dose reduction and affect response. Higher haemoglobin (Hb) decrease at therapy week-12 (TW12) is associated with SVR in adults. Little is known about the influence of side effects on therapy response in children.

**Aim:** To investigate whether side effects during antiviral therapy with Peg-IFN+ribavirin affect response in perinatally acquired CH-C.

**Methods:** Patients: 21 children (11 males, median age 13 yrs) treated with Peg-IFN/ribavirin were divided according to SVR: 13 responders (R), 4 non-responders (NR) and 4 relapsers (Rel).

**Methods:** Baseline biochemical (ALT, AST, GGT), haematological (Hb, neutrophil (neu) and platelet count), virological and histological indices were recorded. Presence of flu-like, thyroid, neuropsychiatric, skin/hair, gastrointestinal and joint symptoms was assessed prospectively. Changes in haematological/biochemical parameters at TW4, 8, 12 and 24 were compared to baseline and all side effects to therapy response. Dose reductions of Peg-IFN and ribavirin were recorded.

**Results:** Genotype 1 was more frequent in NR and Rel than R (75%, 75% vs. 40%, \( P = 0.02 \)). Histological and biochemical indices were similar in the three groups except for GGT that was significantly higher in NR than in Rel and R (65 vs. 29 and 14 IU/l, \( P = 0.02 \)). NR were older than Rel and R (14.5 vs. 13 and 10.5 yrs, \( P = 0.05 \)). Frequency of haematological side effects was similar in all groups, but the drop in Hb levels and neu count was greater in R than Rel and NR at TW12 (Hb: 1.7 vs. 1.3 and 0.9 g/dl, \( P = 0.04 \) and neu: 1.3 vs. 1.1 and 0.9x10^9 cells/ml, \( P = 0.03 \)). Neuropsychiatric symptoms were more frequent in NR and Rel than in R (75%, 75% vs. 38%, \( P = 0.02 \)). There was no difference in dose reductions among groups.

**Conclusion:** Response to Peg-IFN+ribavirin in children with CH-C is associated with younger age, non-genotype 1, low baseline GGT, sharper decrease of Hb levels and neu count during the first 12 weeks of therapy and lower frequency of neuropsychiatric side effects. Whether this is due to non-adherence or different drug bioavailability in NR needs to be investigated.

**Disclosure of Interest:** None declared to all authors.

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**PD-H-113**

**INTRA-HEPATIC IRON DEPOSITION CORRELATES WITH NONALCOHOLIC STEATOHEPATITIS IN CHILDREN**

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**Objectives and Study:** Nonalcoholic steatohepatitis (NASH) develops from simple fatty liver through multifactorial molecular pathways, with a central role for insulin resistance, oxidative stress and cytokines imbalance. It is well known that intra-hepatic iron accumulation may act as oxidative stress enhancing factor, promote fibrosis through hepatocellular necrosis and inflammation with activation of Kupffer cells. However, the real role of iron overload in the pathogenesis of NASH is still controversial in adults and certainly not well known in children. The aim of this study was to investigate the hepatic levels of iron in paediatric patients with NASH.

**Methods:** Sixty-six consecutive children with nonalcoholic fatty liver disease (NAFLD) mean age of 11.41 ± 3.07 yrs (25 female and 41 male), were investigated. The examination programme included medical history, clinical and biochemical investigation, and histological evaluation. Hepatic iron deposition was detected by Perls’ acid ferrocyanide staining and scored according to Scheuer from grade 1 to grade 4 (grade 1 minimal deposition, grade 4 massive deposits and grade 2 and 3 intermediate amounts).

**Results:** We found that 36.4% of children with NAFLD had NASH (NAFLD activity score ≥5), and 22.7% displayed hepatic iron overload. Interestingly, we observed that, despite the deposition of iron does not exceed grade 2, it affects both hepatocytes and Kupffer cells. We used Pearson’s coefficient of correlation and linear regression analysis to assess the association between iron accumulation and NAFLD activity score. At the regression analysis iron accumulation explained 29% of the variance in the NAFLD activity score (\( P < 0.001 \)).

**Conclusion:** Our findings demonstrate that, iron accumulation strongly correlate with NASH in children reinforcing the hypothesis that elevated levels of hepatic iron may act as co-factor to the progression from simple fatty liver to NASH.

**Disclosure of Interest:** None declared.

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**PD-H-114**

**CHARACTERIZATION AND EVALUATION OF STEMNESS POTENTIAL OF MESENCHYMAL CELLS ISOLATED FROM NORMAL ADULT RAT LIVER**

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**Objectives and Study:** Development of liver cell-based therapies is hampered by the increasing significant shortage limiting the availability of mature hepatocytes. Search of alternative cell sources is currently evaluated. Stem/progenitor cells have been isolated from different tissue sources and studied for their potential to be differentiated into highly...
functional liver cells. In this context, we previously characterized human adult derived liver mesenchymal stem cells (hADLSC) both in vitro and in vivo. However, preclinical studies are mandatory to carry out the potential of such cells to restore liver diseases. The aim of this study was to evaluate the presence of homologous cells in adult rat liver. Isolation and characterization of such cells are very useful to assay the in vivo efficacy of liver mesenchymal stem cells in a syngeneic animal models of liver metabolic diseases.

**Methods:** Collagenase-isolated rat liver cell suspensions were cultured in hepatocyte specific medium for 15 days and then switched to DMEM medium. Using different techniques, cells were characterized from passage 2 to 8.

**Results:** As demonstrated in hADLSC, mesenchymal stem cell markers profile has been confirmed in rADLSC. Analysis of hepatic markers profile revealed that rADLSC expressed hepatic markers such as UDP-glucuronosyltransferase 1A1, glucose-6-phosphatase (G6P) and MRP2 mRNA. In contrary to hADLSC, rat isolated cells expressed cytokeratin (CK) 8, CK18 mRNA but not albumin, TAT, TDO, HNF4. Furthermore, rADLSCs expressed biliary markers like CK19. rADLSCs were able to store glycogen and present active G6P enzyme.

In vitro differentiation experiment confirmed limited differentiated potential of rADLSCs since these cells were not able to differentiate into adipocytic/osteocytic lineages. At passage 4, expression of TDO and Albumin was upregulated in rADLSCs submitted to hepatogenic differentiation protocol whereas expression of CK18 and CK19 was downregulated. Functional metabolic tests are currently ongoing.

**Conclusion:** According to our data and despite the same culture process, several differences concerning hepatic markers and hepatogenic potential were observed between human and rat cells. Next step of our study is to investigate the efficacy of these in vivo in a metabolic animal model.

**Disclosure of Interest:** None declared.

**PD-N-093**

NEONATAL DIETARY N-3 LONG-CHAIN POLYUNSATURATED FATTY ACIDS PREVENT EXCESSIVE FAT DEPOSITION IN ADULT MALE MICE IN AN EXPERIMENTAL MODEL OF NUTRITIONAL PROGRAMMING


**Objectives and Study:** The prevalence of childhood obesity has increased rapidly over the past decades and has a strong link to adult obesity, which is associated with several morbidities. The trajectory of obesity appears to start at a preschool age suggesting that early critical periods of development play an important role. The nutritional environment during fetal and neonatal life is thought to influence development of metabolic homeostasis thereby affecting susceptibility to metabolic disease. Proliferation and differentiation of preadipocytes, for instance, are directly affected by dietary fatty acids. The objective of the present study was to investigate whether fat quality during early neonatal life has sustained effects on adult metabolic profile and body composition in a new model of nutritional programming in mice.

**Methods:** Male offspring of healthy, normal weight C57Bl/6j dams were subjected to an early diet containing 21 En% fat, consisting either of 100% vegetable oils (CTRL) or 80% vegetable oils and 20% tuna fish oil (n-3 LCP) from postnatal day (PN) 2 to 42. Subsequently, mice of both experimental groups were switched to a moderate Western style diet (WSD) until dissection on PN 98. Body composition was measured by dual x-ray absorptiometry at PN 42, 70 and 98. After dissection, plasma lipid profile, glucose, insulin and adipokines were measured. Weight of white adipose tissue depots and epididymal adipocyte size were also determined at PN 98.

**Results:** Dietary n-3 LCPs directly affected body composition as shown by a lower fat mass on PN 42 in n-3 LCP fed mice compared to CTRL fed mice (4.3 ± 0.64 g versus 3.5 ± 0.50 g, respectively; \(P < 0.01\)). Additionally, during WSD challenge from PN 42 to 98, beneficial effects of neonatal n-3 LCPs on fat accumulation persisted and the difference in body fat mass even increased between n-3 LCP and CTRL fed mice (8.4 ± 1.1 g versus 6.1 ± 1.4 g, respectively; \(P < 0.001\)). Moreover, mice fed n-3 LCP during neonatal development had a healthier plasma lipid profile, healthier plasma glucose homeostasis and less hypertrrophic adipocytes in the epididymal fat depot at PN 98 compared to CTRL fed mice.

**Conclusion:** This study has shown for the first time that fatty acid composition of neonatal nutrition plays an important role in the development of body composition and metabolic homeostasis. This might be mediated by lasting effects of dietary fatty acids on development and function of white adipose tissue during neonatal life. Moreover, neonatal n-3 LCPs may protect against excessive fat deposition in a moderate obesogenic environment during adolescence and adulthood.

**Disclosure of Interest:** None declared.

**PD-N-094**

INFLUENCE OF MATERNAL BMI AND GESTATIONAL DIABETES ON MTOR AND PPARG GENE EXPRESSION IN THE TERM PLACENTA

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www.jpgn.org
**Objectives and Study:** It is now well established that changes in the maternal diet at defined stages of pregnancy can affect offspring’s risk of later metabolic disease (1). Such alterations of fetal growth can be due to substantial modifications of materno-fetal energy partitioning regulated in part by the maternal nutrient target of rapamycin (mTOR) and the peroxisome-proliferator activated receptor (PPAR-gamma). However, the influence of maternal body mass index (BMI) and/or insulin sensitivity on the regulation of placental energy metabolism has yet to be established. This is clearly important as it will improve our understanding of the potential effect of maternal obesity and gestational diabetes on pregnancy outcomes.

**Methods:** Placental samples were collected from healthy pregnant women participating in the PREOBRE Project directed by the University of Granada (Spain). The subjects were recruited at 20 weeks of gestation and divided into four groups according to their BMI and glucose tolerance. Mothers were either classified as lean (pre-pregnancy BMI <25 kg/m²; normal glucose tolerance; n = 56), overweight (pre-pregnancy BMI 25 kg/m² < BMI <30 kg/m²; normal glucose tolerance; n = 23), obese (pre-pregnancy BMI ≥30 kg/m²; normal glucose tolerance; n = 12) or gestational diabetic (pre-pregnancy BMI <25 kg/m²; glucose intolerant; n = 17). At delivery, placenta from each individual was sampled in order to analyse mTOR and PPAR-gamma gene expression by real-time RT-PCR.

**Results:** The mRNA abundance for mTOR in placenta of lean mothers was respectively two and three times lower than in the placenta of overweight (but not obese) (P < 0.05) and gestational diabetic mothers (P < 0.001). Interestingly, diabetic mothers overexpressed mTOR when compared to overweight (P < 0.05) and obese (P < 0.005). In addition, the placenta of overweight, obese and gestational diabetic mother overexpressed the gene encoding for PPAR-gamma compared to lean women (P < 0.05).

**Conclusion:** We have shown that both being overweight and glucose intolerance during pregnancy alters placental energy metabolism pathways. Overexpression of mTOR and PPAR-gamma within the placenta could promote nutrient uptake thereby altering fetal growth and body composition. This may also contribute to local chronic pro-inflammatory states within the placenta or fetus and further suggests that mTOR and PPARG are key gene targets for fetal programming.

**Reference:**

**Disclosure of Interest:** None declared.

**PD-N-095**

**METABOLIC SYNDROME IN AN OBESE PEDIATRIC POPULATION**

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**Objectives and Study:** Apply the International Diabetes Federation (IDF) consensus definition of the MS in children and adolescents to a pediatric obese population.

**Methods:** Prospective study of overweight children and adolescents followed in the PGHNU from 1/2/99 to 31/12/09. The pediatric IDF2005 consensus definition of the MS in children and adolescents was used. The waist circumference (WC) used was >90th percentile for age and gender. The insulin resistance index was calculated thought the HOMA-IR. In a stepwise multivariate logistic regression, using as dependent variable the MS, and as independent variables gender, body mass index (BMI), HDL, high blood pressure (BP) in father and mother, diabetes in father and mother, dyslipidemia in father and mother, obesity in father and mother.

It was considered high risk for CVD, WC ≥80 cm for female and ≥84 cm for male, and it was considered very high risk of CVD, WC ≥88 cm for the female and WC ≥102 cm for the male.

**Results:** Number of patients 865, 53.5% females. Mean age at first attend 9.44 ± 3.45 years and mean BMI 26.43 ± 4.31 kg/m². About 1st degree familiar antecedents, 31% presented HBP, 9.6% type 2 Diabetes mellitus, 41% dyslipidemia and 55.3% obesity. A total of 14.0% patients (n = 848) had raised systolic blood pressure (BP) and 4.4% raised diastolic BP (>95 for age and sex) in the first appointment. Acantose nigricans (AN) observed in 38.5% (n = 848), striae in 17.3%. Presented values of WC of high risk of CVD 59.4% of the cases and 25.9% had values of WC of very high risk of CVD (n = 845).

At the first blood sample, 15.4% (n = 747) patients had high cholesterol (>200 mg/dl), 41.5% (n = 727) had low HDL, 8.8% (n = 713) had high triglycerides (>150 mg/dl) and 5.8% (n = 723) had increase fasting blood glucose (>100 mg/dl). Elevated HOMA-IR (>2.0) in 50.7% (n = 560). The presence of striae (P = 0.001) and AN (P = 0.04) were significantly associated to insulin resistance by HOMA-IR.

A total of 54 (13.0%) patients had criteria for MS, 49 (49/398 = 12.3%) in the age between 10–16 years and 5 (5/17 = 29.4%) in the >16 years (P = 0.056), 25 males and 29 females (P = 0.469). MS is associated with adult definition of high risk for CVD (P = 0.003).

In MVA, for each increase in one BMI unit the risk of MS increases 1.16 times (P = 0.001), diabetes and HBP in the father are correlated with MS P = 0.025 and P = 0.027, respectively. Higher HDL was associated with protective effect for MS (odds 0.90, P = 0.001).

**Conclusion:** The pediatric MS by IDF was significantly associated to adult definition of high risk for CVD. In this overweight population this IDF’s pediatric MS definition proves to be suitable.

**Disclosure of Interest:** None declared.
PD-N-096

EFFECTS OF A NEW PREBIOTIC MIXTURE ON FECAL GUT MICROBIOTA AND THE MUCOSAL IMMUNE SYSTEM IN HEALTHY INFANTS

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Objectives and Study: The intestinal microbiota play a crucial role in maturation of the mucosal immune system and the production of secretory immunoglobulin A (SIgA). Infant formula has been supplemented with a combination of neutral (scGOS/lcFOS) and acidic oligosaccharides (pAOS) and clinical effects on atopic dermatitis and febrile episodes have been reported. To further investigate mechanisms of action it was evaluated in this study whether this combination of oligosaccharides has an influence on the intestinal microbiota and the mucosal immune system.

Methods: In a randomised double-blind placebo controlled European multi-centre study, 1187 healthy term born infants were recruited to receive either a formula supplemented with a combination of neutral (scGOS/lcFOS) and acidic oligosaccharides (pAOS) a standard formula (control) or breast milk (reference). The analysis included faecal samples at 4 and 12 months (mo) of vaginally delivered infants, who received no antibiotics. Bifidobacteria were analysed by FISH, short chain fatty acids, pH and faecal SIgA, using standard laboratory techniques. Statistical analysis was performed by two sided Mann-Whitney U test.

Results: The analysis included stool samples of 114 infants: 42 of the prebiotic-(PG), 45 of the control-(CG) and 27 of the breastfed-group (BG). At 4 mo of age, the percentage of faecal bifidobacteria was higher in the PG vs CG (P < 0.01), while similar to the BG. At 12 mo of age, the percentage of bifidobacteria detected in the faecal samples of infants in the PG tended to be higher than those of infants in the CG (P = 0.08) and was comparable to the BG. At 4 mo of age, the proportion of acetate was higher in the PG vs the CG (P < 0.001), while the proportion of butyrate, propionate, and other SCFA were lower (P < 0.001; P < 0.01; P < 0.001). Infants in the PG had a lower faecal pH at 4 mo vs CG (P < 0.001). Similar results were observed at 12 mo of age (P < 0.001). No significant difference was found between PG and BG at 4 and 12 mo of age and. Faecal SIgA levels in the PG were higher vs the CG at 4 mo (1058 [179–7026]μg/g vs 470 [23–5862]μg/g; P < 0.01) and 12 mo (596 [25–2080]μg/g) vs 234 [22–2423]μg/g; P < 0.01) and similar to the BG at 4 mo (1393 [95–6974]μg/g) and 12 mo (328 [21–2168]μg/g).

Conclusion: These findings show that the supplementation of an infant formula with a prebiotic mixture of neutral (scGOS/lcFOS) and acidic oligosaccharides (pAOS) has effects on faecal bifidobacteria, metabolic activity of the intestinal microbiota and the mucosal immune system comparable to human milk.

Disclosure of Interest: The Study was sponsored by Danone.

PD-N-097

EXCESSIVE FAT DEPOSITION AND ADVERSE METABOLIC PROFILE IN ADULT MICE IS PREVENTED BY REDUCING DIETARY N-6 POLYUNSATURATED FATTY ACIDS DURING NEONATAL LIFE


Objectives and Study: Despite the exponential increase in obesity over the last decades, in particular in children and adolescents, no major increase in dietary fat and energy intake was found (1,2). Since dietary fatty acids have been shown to directly affect adipose tissue development, it is hypothesized that the reported shift towards increased n-6 and decreased n-3 FA intake could underlie the increasing prevalence of childhood obesity and development of metabolic disease (3). The objective of the present study was to investigate whether reducing n-6 PUFAs during early neonatal life has sustained effects on adult metabolic profile and body composition in a new model of nutritional programming in mice.

Methods: Male offspring of C57Bl/6j dams were subjected either a control diet (CTRL) or a low n-6 PUFA diet, in which linoleic acid (LA; C18:2 n-6) content was reduced by 50% (Low LA) from postnatal day (PN) 2 to 42. Subsequently, mice of both experimental groups were switched to a moderate Western style diet (WSD) until dissection on PN 98. Body composition was measured by dual x-ray absorptiometry at PN 42, 70 and 98. After dissection, plasma lipid profile, glucose, insulin and adipokines were measured.

Results: Fat accumulation during the WSD challenge was reduced by 27% in mice fed the Low LA diet compared to the CTRL diet (P < 0.001). Additionally, lowering LA intake during neonatal development resulted in a healthier plasma lipid profile with significantly reduced fasting triglyceride levels, improved insulin sensitivity measured by homeostasis model assessment of insulin resistance (HOMA-IR) and lower fasting resistin and leptin levels.

Conclusion: Reduction of n-6 PUFA intake during infancy and childhood may be sufficient to protect against excessive fat accumulation and an adverse metabolic profile induced by an unbalanced western style diet during adolescence and adulthood. This study has shown that fat quality of neonatal nutrition plays an important role in early development and could thus program adult body composition and metabolic homeostasis.

References:

PD-N-098

ANTIBIOTIC TREATMENT IMPROVES FAT ABSORPTION IN A MOUSE MODEL FOR CYSTIC FIBROSIS

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Objectives and Study: In cystic fibrosis (CF) patients, a certain degree of fat malabsorption usually remains, despite pancreatic enzyme replacement therapy. Non-pancreatic mechanisms are suggested to play a role in the remaining fat malabsorption, like small intestinal bacterial overgrowth (SIBO). We aimed to determine the contribution of SIBO to fat malabsorption under CF conditions.

Methods: Homozygous ΔF508 mice and wild type littermates received antibiotic (ciprofloxacin and metronidazol) or placebo treatment for three weeks. Before and after treatment, fat absorption was quantified by a 72 hours fat balance test. To compare the competence of fat digestion (lipolysis) and fatty acid uptake separately, we determined the plasma appearance of stable isotope-labeled fats ((tri-1,13C-tripalmitin) and fatty acid (1,13C-stearate), originating from intragastrically administered triglyceride (tri-1-13C-tripalmitin) and fatty acid (1-13C-stearate), respectively. At termination, bacterial load in the small intestine was quantified via qPCR. To evaluate the influence of antibiotics on secondary bile salt synthesis by intestinal bacteria, bile salt excretion in faeces was analyzed by gas chromatography. Values are in means ± SD.

Results: Bacterial load did not differ between ΔF508 and wild type mice and was not reduced in either genotype after antibiotic treatment. Antibiotic treatment decreased fat malabsorption in ΔF508 mice (from 10 ± 1% to 8 ± 1%; P < 0.01), especially the malabsorption of saturated fatty acids (from 15 ± 4% to 12 ± 3%, P < 0.01). Plasma concentrations of 13C-fats from 1-13C-tripalmitin and 1-13C-stearate were non-significantly higher in the antibiotic treated ΔF508 mice. Faecal bile salt excretion was reduced in the antibiotic treated ΔF508 mice compared to placebo, for primary (treated: 10.5 ± 5.3, placebo: 18.5 ± 2.5, P < 0.05) as well as secondary (treated: 0.4 ± 0.2, placebo: 7.0 ± 0.9, P < 0.01) bile salts (expressed as μmol per 100gram/body-weight/day).

Conclusion: Antibiotics decrease fat malabsorption in homozygous ΔF508 mice, although the mechanism does not seem to involve treatment of SIBO. Present data indicate that antibiotic treatment decreases fat malabsorption in CF mice by enhancing intestinal fatty acid uptake.

Disclosure of Interest: None declared.

PD-N-099

CAN ANTENATAL EDUCATION ALTER THE PREFERRED TIME OF WEANING?

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Objectives and Study: Postnatal nutrition and timely introduction of solids are important determinants of future health. Recent research in full term Irish infants identified that 70.5% were prematurely weaned. Our current study was therefore designed to identify whether a prenatal maternal educational intervention could alter the preferred time to wean.

Methods: An evaluative quantitative approach was utilized in this prospective intervention study. Firstly an antenatal questionnaire sought the participants’ opinions regarding appropriate time of weaning, information sources and demographics were recorded. Participants were randomized (single blinded) to group 1 (intervention) or 2 (control).

Group 1 was invited to attend and evaluate a weaning talk during their third trimester and complete a questionnaire on their planned time to wean.

Results: 154 consenting mothers were recruited. Pre-randomization they indicated intention to wean at 24.5 weeks, with 28% planning to wean outside ESPGHAN guidelines (17–25 wks). Their anticipated sources of weaning information included books (72.3%), Family (60.4%) and maternity hospital (37.1%). There were no differences between control and intervention group on opinions or demographics. 80 mothers were randomized to the intervention group and 45 (57%) attended the talk, with only 2% of attendees preferring to wean outside ESPGHAN guidelines post intervention and a paired samples t-test showed a change in preferred time of weaning (P = 0.003). Parents’ evaluation of the antenatal intervention talk was extremely positive for interest and relevance however 57.8% indicated a preference for its delivery postnatally.

Conclusion: Surprisingly 37% of all participants cited maternity hospitals as their intended source for information on weaning; however this is not usually addressed in most maternity education programs. Almost a third of mothers indicated an intention to wean at a time discordant with ESPGHAN guidelines. Following an antenatal weaning talk mothers preferred time of weaning was more closely aligned to the ESPGHAN guidelines, however a majority would have preferred its delivery postnatally. Analysis of third phase of this study at 7–9 months postnatally, will assess whether this alignment is sustained.

References:

Disclosure of Interest: None declared.

PD-N-100

FERMENTATION GENERATED HUMAN MILK OLIgosaccharides PROMOTE A THI RESPONSE IN A MURINE INFLUENZA VACCINATION MODEL

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Objectives and Study: The intestinal flora of breast-fed infants is dominated by Bifidobacteria, whereas the intestinal flora of bottle-fed infants consists of lower numbers of Bifidobacteria, but higher levels of Enterobacteria and other pathogenic germs. Oligosaccharides are a major constituent of human milk that demonstrated to promote the growth and activity of beneficial bacteria, mainly Bifidobacteria and Lactobacilli. However, the mechanism by which oligosaccharides exert their effects remains to be elucidated. To further study the mechanism by which oligosaccharides can modulate systemic immune responses, the present study examined by fermentation produced oligosaccharides that are identical to Human Milk Oligosaccharides (HMO) in a murine influenza vaccination model.

Methods: C57BL/6 mice received a control diet or a diet supplemented with different by fermentation generated HMO at a dietary dose of 1%. The mice were vaccinated twice with Influvac and the response was determined by the measurement of delayed type hypersensitivity (DTH) reaction in the ear pinnae. In addition, antigen-specific antibody and immunoglobulin-free light chain concentrations in serum, ex vivo induced splenic proliferation, the level of regulatory T cells and NK cells, and the functional activity of these NK cells were determined.

Results: The by fermentation generated HMO significantly enhanced the DTH responses. Supplementation with HMO reduced the level of regulatory T cells, whereas the percentage and activity of splenic NK cells increased. Furthermore, the level of antigen-specific IgG1 was significantly increased in mice fed with HMO. Interestingly, one HMO was able to significantly increase the serum concentration of free light chain, whereas others did not alter any differences. In addition, synergistic effects on the DTH response could be achieved by combination of these HMO with oligosaccharides from plant- and animal sources. No significant changes were detected on splenocyte proliferation.

Conclusion: These data suggest that HMO can stimulate the adaptive immune response into a Th1 direction, and therefore might provide an opportunity to inhibit infections and Th2-related immune disorders in humans.

Disclosure of Interest: None declared.

PD-N-101

TRIAL OF A MICRONUTRIENT RICH, LOW ENERGY DENSITY ENTERAL FEEDING FORMULA FOR GASTROSTOMY FEEDING DISABLED CHILDREN

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Objectives and Study: Gastrostomy feeding in the severely disabled child with oral-motor dysfunction improves overall weight gain but is often associated with excess deposition of body fat. Most proprietary feeds are not formulated to meet the nutritional needs of immobile children with severe motor deficits who have low energy expenditure. Our aim was assess the effect on weight, body composition and micronutrient status of disabled children fed a low-energy micronutrient replete enteral feed via gastrostomy.

Methods: We studied 14 children (7 boys, median decimal age 2.088 years) with severe Cerebral Palsy (GMFCS IV or V) who were gastrostomy fed. Subjects had all study assessments prior to commencing the low energy feed (baseline) and again after 6 months G-tube feeding of the low energy formula. Body composition and energy expenditure were measured using Doubly Labelled Water (DLW) O18 dilution. Anthropometry was used to measure growth, and micronutrient status was measured before commencing the low energy feed and was repeated 6 months later. The feed was given at energy levels no greater than 75% of the EAR for age and was adjusted where appropriate following the results of their energy expenditure dilution tests.

Results: The median percentage intake of the estimated average requirements (EAR) for energy (kilocalories) was 43% at the beginning of the study and 48.8% after 6 months on LEE. There was a significant increase in weight (p 0.012), mid upper arm circumference (p 0.043) and lower leg length (p 0.012) over the 6 months. Across the 6 month study there was no increase in triceps skinfold (p 0.123) or subscapular skinfold (p 0.4) thickness. This corresponds with the body composition results which showed no significant increase in fat mass index (p 0.345) or fat free mass index (p 0.249). Micronutrient levels remained within reference ranges with the exception of elevated chromium.

Conclusion: We have shown that severely disabled children who are fed a low energy, micronutrient complete, high fibre feed continue to grow at energy intakes below 75% of the
EAR. Weight gain was not associated with a disproportionate rise in fat mass or fat percentage. There was also continued significant MUAC and linear growth. The low-energy feed is particularly suited to this group of children with cerebral palsy as their low energy requirements can be delivered in a higher volume thus maintaining satiety while ensuring adequate growth and nutrition.

PB Sullivan, Danone, Scientific Advisory Board.
Conclusion: The delta weight gain between the 36th week and term appears to affect the development of fat mass at term corrected age. The clinical relevance of the accretion of fat mass during this “window period” needs to be further elucidated in terms of long term health consequences.

Disclosure of Interest: None declared.

PL-G-007

PEDIATRIC- AND ADULT-ONSET INFLAMMATORY BOWEL DISEASE: MORE SIMILARITIES THAN DIFFERENCES

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Objectives and Study: The few studies comparing pediatric- and adult-onset IBD have suggested a more “severe” phenotype and the need of a more aggressive therapy in early onset disease. Our aim was to compare IBD characteristics in a Canadian cohort of pediatric and adult-onset cases, using a cross-sectional prospective study (January 2006-September 2009).

Methods: Data for patients in the McGill IBD database were compared, using the Montreal classification for age, behavior and location.

Results: We analyzed the data sets for 270 pediatric- and 174 adult-onset IBD cases, with a mean follow-up of 5.8 and 9.8 y, respectively. CD predominated in both groups (87.8% in pediatric-, 59.8% in adult-onset IBD), but UC was more common among adults (36.8 vs 5.5%, P<0.0001). No difference was found in gender distribution between pediatric and adult age groups, for both CD (M: 56.5 vs 51%) and UC (M: 33.3 vs 56%). A positive family history (any member) was more often observed in pediatric-onset IBD cases (CD 32.1 vs 25%, UC 33.3 vs 25%), but the difference was not significant. There was no age related difference in the leading ethnicities, for both CD and UC. Pediatric-onset CD was more extensive (L3 ± L4: 49.8 ± 36.5%, L1 ± L4: 16.9 ± 31.7%, total L4: 64.6 vs 26.9%, P<0.0001). However, in multivariate regression, only L4 association remained significant for pediatric CD (OR: 3.4, 95%CI: 1.9–6.2, P<0.0001). Complicated behavior was less frequent in pediatric-onset CD (B2+B3: 19.8 vs 30.8%, P=0.028). However, this difference was not significant when adjusted for duration of follow-up (OR=0.85, P=0.57). Perianal disease did not differ by age group (pediatric-onset 18.6 vs 19.2%). Surgery was less frequent in pediatric CD (25.7 vs 37.5%, P<0.03), but this was not significant when adjusted for duration of follow-up (OR=1.08, P=0.78). By multivariate regression, the following associations were found for pediatric CD: smoking history (OR: 0.51, 95% CI: 0.3–0.7, P=0.001), extraintestinal manifestations (OR: 0.5, 95% CI: 0.3–0.9, P=0.02) and use of IMM (azathioprine/6-mercaptopurine and/or methotrexate) (OR: 1.99, 95% CI: 1.1–3.6, P=0.02). Contrary to most published data, pancolitis was commonly observed in adult-onset UC, as in pediatrics (65.6% vs 80% respectively, P=0.28).

Conclusion: In the Montreal region, CD has an overall predominance for both age groups. The only significant differences between pediatric and adult-onset CD observed were: less smoking and extraintestinal manifestations, more upper GI tract involvement and greater use of IMM. In UC, aside from the greater prevalence in adult-onset IBD, the other features are similar, including the high prevalence of pancolitis.

Disclosure of Interest: None declared.

PL-G-008

MOLECULAR ABNORMALITIES IN PAEDIATRIC BARRETT'S OESOPHAGUS: CAN WE TEST FOR POTENTIAL OF NEOPLASTIC PROGRESSION?

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Objectives and Study: Barrett’s oesophagus (BO) is a preneoplastic condition that predisposes to oesophageal adenocarcinoma (BA) and is a consequence of prolonged gastro-oesophageal reflux disease (GORD). The condition is mainly seen in adults and is thought to be a complex disease in which individual genetic predisposition interacts with environmental stimuli. The aim of our study was to investigate if genetic biomarkers of potential disease progression are the same in the rare situation of paediatric BO as described in the adults.

Methods: We performed Fluorescence In Situ Hybridisation (FISH) with probes from Abbott Vysis Corporation on 4 micron sections taken from 48 paraffin embedded sequential biopsies of ten cases of BO. The four probe sets were specific for HER2 at 17q12/17 centromere/4 centromere; p16 at 9p21/9 centromere; TP53 at 17p13/17 centromere/6 centromere and CCND1 at11q13/11 centromere. The probe sets were validated on 10 cases of adult Barrett’s adenocarcinoma.

Results: Out of the ten cases, six biopsies in five cases were informative. Two had gain of HER2 detected in one biopsy each (one also had gain of chromosome 17) and four separate cases showed p16 deletion in one biopsy of each (one also had gain of chromosome 9).

Conclusion: This work is evidence that the characteristic epithelial change in Barrett’s oesophagus is associated with genetic changes in children as well as adults. It confirms previous suggestions that early genetic events in BO are p16 deletion and gain of HER2 which have also been identified in adult patients with BA.
Absence of TP53 deletion and CCND1 amplification confirms that they are likely to be a later events than p16 deletion or HER2 gain in BO neoplasia.

Large cells = Nuclear truncation therefore 6 micron sections recommended.

50% of patients had at least one abnormal biopsy justifying FISH monitoring even at such an early stage.

The genetic markers informative in 50% of our cases were also identified in adult patients with Barrett’s adenocarcinoma. The importance of this study is that even at the paediatric level, Barrett’s oesophagus can show genetic changes associated with neoplastic progression.

Disclosure of Interest: None declared.

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**PL-G-009**

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<th>ATG16L1 AND IRGM CONTRIBUTE TO THE REGULATION OF IMMUNE RESPONSES</th>
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<tr>
<td>C. Strisciuglio 1, M.E. Wildenberg 2, A.C.W. Vos 2, A.P. Verhaar 2, G.R. van den Brink 2, D.W. Hommes 2</td>
</tr>
<tr>
<td>1Pediatrics, Policlinico Universita Federico II, Napoli, Italy, 2Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, Netherlands</td>
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Objectives and Study: Various polymorphisms in the autophagy related genes ATG16L1 and IRGM have been associated with the development of Crohn’s disease (CD). Autophagy is primarily known to be important in the survival of cells during starvation as well as the processing of intracellular bacteria. Although the link between decreased autophagy and an inflammatory disorder like IBD suggests a role for this process in the regulation of immune responses, no data has been available on this topic thus far. Therefore, this study focused on the effects of decreased ATG16L1 and IRGM expression on the immunogenicity of dendritic cells.

Methods: Monocytes obtained from healthy volunteers were cultured in the presence of GM-CSF and IL-4 to generate dendritic cells. Gene knockdown was achieved using siRNA technology. Dendritic cell phenotype was studied by flow cytometry, and functionality was tested in mixed lymphocyte reactions, an OVA processing assay and cytometric bead arrays.

Results: Knockdown efficiency achieved ranged from 25–85% in individual experiments. Interestingly, even the lower level knockdown resulted in a clear decrease in functional autophagy, indicating that relatively small changes in the levels of autophagy proteins (e.g., such as those caused by some point mutations) have a strong impact on the pathway as a whole. Decreased levels of autophagy did not decrease viability of dendritic cells under nutrient-rich conditions. Strikingly, ATG16L1 low and IRGM low dendritic cells induced significantly more T-cell proliferation in both an allogeneic mixed lymphocyte reaction and an antigen specific proliferation assay. This finding was consistent in both human and mouse cells, suggesting a conserved role for autophagy in the regulation of the immune reaction.

Flow cytometry showed ATG16L1 low and IRGM low dendritic cells to express levels of HLA-DR and co-stimulatory molecules comparable to that of control cells. Furthermore, decreased levels of autophagy did not result in an altered cytokine profile of these cells, indicating that mechanisms other than increased maturation underlie the increased immunoreactivity.

Conclusion: Even a partial decrease in autophagy results in an increased pro-inflammatory capacity in dendritic cells. This phenomenon may contribute to the increased immune activation seen in those CD patients carrying polymorphisms in these genes.

Disclosure of Interest: None declared.

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**PL-G-010**

<table>
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<th>HAEMATOPOEITIC STEM CELL TRANSPLANT FOR SEVERE INFLAMMATORY GUT DISORDERS WITH IMMUNE DYSREGULATION</th>
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<tr>
<td>1Paediatric Gastroenterology, Great Ormond Street Hospital For Children, 2Immunology/BMT, Great Ormond Street Hospital For Children, 3Gastroenterology, Great Ormond Street Hospital, 4Paediatric Gastroenterology, 5BMT, Great Ormond Street Hospital For Children, London, United Kingdom</td>
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Objectives and Study: Severe inflammatory gut disorders due to systemic immune dysregulation present a major challenge to clinicians. Some of these patients fail to respond to conventional therapies and many have a poor quality of life requiring long term parental nutrition and prolonged hospitalisation. Children with these disorders usually present early in life and in most cases have a significant family history of immune dysregulation indicating a possible genetic component to their disease. Haematopoietic Cell Transplant (HCT) could potentially offer a curative option for this group of patients. The aim of the Study is to determine if the natural history of severe inflammatory gut disorders can be altered by HCT.

Methods: We report six children with severe inflammatory gut disorders who were refractory to conventional immuno-suppressive therapies. The patients include two brothers with severe intractable ulcerating colitis of infancy, one of whom developed EBV driven LPD. The third patient had IPEX syndrome. The fourth patient had congenital pyloric stenosis, severe apoptotic inflammatory disorder. The fifth patient had autoimmune enteropathy with and a brother who died at 18 months with intestinal perforation and sepsis. The sixth patient presented with severe failure to thrive, recurrent frequent intestinal obstruction due to severe inflammatory stricturing disease and was fully TPN dependent. After evaluation by multidisciplinary teams all children underwent allogeneic HCT. Two children received matched family donors and four received matched unrelated donors. All patients were conditioned using reduced intensity conditioning. Median follow up post HCT is 4.5 years.
Results: Complete resolution of clinical symptoms was noted in five patients with significant improvement in the sixth. Five patients have managed to stop immunosuppressive therapy within one year following transplant and one patient is on a reducing dose of prednisolone. The latest patient was discharged home at the age of two years for the first time since birth. Complete mucosal healing was confirmed histologically in three patients and significant improvement was noted in one. The other two patients were not biopsied as they are clinically well.

Conclusion: Allogeneic HCT may be considered as a treatment option for children with severe inflammatory gut disorders that are refractory to conventional immunosuppressive therapy. A multidisciplinary approach is crucial for patient selection and management.

Disclosure of Interest: None declared.

PL-G-011

EXTENSIVE CASEIN HYDROLYSATES MAY PREVENT AUTOIMMUNE DIABETES BY AFFECTING INTESTINAL MICROBIOTA, BARRIER INTEGRITY AND IL-10 PRODUCTION

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Objectives and Study: Dietary and microbial factors are known to play a role in both experimental models of Type I Diabetes (T1D) and the onset of the disease. The beneficial effect of casein hydrolysates in diabetes prevention may not only comprise avoidance of cow’s milk protein but additional functionalities of the peptides. We set out to study the effect of hydrolysed casein (HC) and amino acid formulations on diabetes development in DP-BB rats with special reference to intestinal barrier function and flora composition.

Methods: Four groups of rats received either a diet with 20% HC (Nutramigen®), a diet with 20% regular HC (Pancase S), an Amino Acid PreMix® equivalent to 20% protein, or a standard diabetogenic lab chow. Intake started at weaning (d21) and lasted until the end of the experiment (d135). Development of diabetes was evaluated by clinical signs, weight loss, blood glucose levels, and degree of insulinitis upon termination. At intermediate time points blood (zonal, cytokines) and fecal samples (flora composition by qPCR) were collected. Intestinal permeability was measured (d65) by the Lactulose-Mannitol exclusion assay. Permeability of ileal specimens was also measured in vitro upon termination of the experiment by measuring transepithelial resistance in a snap-well model. Also in these specimens cytokine levels and Tight Junction protein expression were measured by qPCR analyses.

Results: Reduced incidence of diabetes development was observed in all groups receiving specific diets, with the most pronounced effects in the Nutramigen group (50% vs 85% in controls). Intestinal barrier integrity around the expected period of onset of diabetes was higher in animals receiving Nutramigen or Pancase S compared to controls. Supernatants from ileal tissues in the snap well assays showed higher IL-10 levels in the treatment groups with the highest level in the Nutramigen group. Qualitative flora changes, i.e., stable Lactobacilli levels especially in the Nutramigen group were associated with reduced diabetes development.

Conclusion: The experimental diets differentially reduced autoimmune diabetes development in DP-BB rats. Nutramigen significantly reduced T1D incidence with beneficial effects on intestinal barrier integrity, production of regulatory cytokines and intestinal flora composition. These observations support the beneficial effect of casein hydrolysates not only to be due to avoidance of diabetogenic proteins but with complementary effects of functional peptides on mechanisms underlying T1D pathogenesis.

Disclosure of Interest: EAF van Tol, Mead Johnson Nutrition, employee.
L. Harthoorn, Mead Johnson Nutrition, employee.

PL-G-012

AUTOIMMUNE ENTEROPATHIES- A CLINICAL AND MOLECULAR CHARACTERISATION


Objectives and Study: The pathophysiology of early onset forms of autoimmune enteropathy (AIE) remains largely unknown. With the recent discovery of disease-causing mutations in the FOXP3 gene a first step in unraveling its causes was made.

Aim: To analyze the molecular basis of neonatal or early postnatal AIE based on clinical, genetic and functional immunological data.

Methods: Data of a single center series of 11 children with AIE starting within the first 4 months of life were collected and analyzed. All patients had a complete gastroenterological and immunological work-up. Function of regulatory T cells were analyzed using a co-culture system after isolating CD4+CD25+ from CD4+CD25- cells. FOXP3 staining was analyzed by FACS and genetic analyses of FOXP3 and IL2RA were performed using standard protocols.

Results: AIE was severe and life threatening requiring total parenteral nutrition in all patients. Associated extra-intestinal autoimmunity was seen in all children. 9 of eleven patients showed a defective function of regulatory T cells. In these 9 patients FOXP3 protein expression was reduced or absent, with an abnormal (cytoplasmic) retention in one patient. However, only 7 of these 9 patients had a mutation in FOXP3 gene, no mutation in IL2RA was observed in all 11 children.

Conclusion: A dysfunction of regulatory T cells plays a key role in the development of early-onset AIE with FOXP3 as
Disclosure of Interest: grant support of PHRC and INSERM.

PL-H-037

ANTENATAL TREATMENT OF PERINATAL HEMOCROMATOsis WITH HIGH-DOSE INTRAVENOUS IMMUNOGLOBULIN: THE FRENCH COHORT


Objectives and Study: Perinatal hemochromatosis (PH) is a rare gestational disease resulting in fetal liver cirrhosis and extrahepatic iron overload sparing the reticuloendothelial system. An alloimmune etiology has been recently strengthened by the effectiveness of the prevention of recurrences of fetal disease using transfusions of high-dose intravenous immunoglobulin (IVIG) during pregnancy. This study summarizes the French experience with the use of IVIG during pregnancies of mothers at risk for the recurrence of PH.

Methods: From 2004 to 2008, this multicentric prospective study included 8 pregnant women, who had at least one previous gestational history of fetal or neonatal death related to PH, registered on the French Alloimmunisation National Network. Diagnosis of PH of the index cases was confirmed by a National Experts Committee. During pregnancy women received IVIG at 1 g/kg body weight weekly from the 16th gestation’s week (WG) until birth. Data from treated pregnancies were compared with previous untreated ones, which were used as historical controls.

Results: All 8 neonates born to women treated with IVIG survived in spite of mild liver disease in 5. An antioxidant treatment was provided in 3 neonates. An analysis comparing outcomes of treated (n=8) and untreated (n=9) gestations showed a significant improvement of survival of neonates with gestational therapy (survival 8/8 vs 0/9; P < 0.001). Side effects of IVIG were present in 5 cases leading to one premature stop.

Conclusion: Antenatal treatment with IVIG in women at risk for PH recurrence 1) improves the survival outcome of pregnancies 2) has to be considered to any woman with a complicated pregnancy of certified PH.

Disclosure of Interest: None declared.

PL-H-038

DIAGNOSTIC VALUE OF MARKERS OF OPERATIONAL IMMUNE TOLERANCE AFTER PEDIATRIC LIVER TRANSPLANTATION

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Objectives and Study: 20–50 % of patients after pediatric liver transplantation are believed to develop operational immune tolerance allowing them to get rid of lifelong immunosuppression with known side-effects such as arterial hypertension, renal insufficiency, cardiovascular disease and infections (1). Thus, a prospective differentiation between patients developing immune tolerance from those requiring ongoing immunosuppression would be of great clinical advantage. So far markers of immune tolerance have been investigated only retrospectively in successfully weaned patients, based either on analysis of T-cell subpopulations (gammadelta-T-cells and regulatory T-cells [Treg]) or gene expression profiles.

Methods: 60 children aged 11–268 months (median 99) were investigated 1–180 months (median 41) after liver transplantation under standard immunosuppression with known side-effects such as arterial hypertension, renal insufficiency, cardiovascular disease and infections (1). Thus, a prospective differentiation between patients developing immune tolerance from those requiring ongoing immunosuppression would be of great clinical advantage. So far markers of immune tolerance have been investigated only retrospectively in successfully weaned patients, based either on analysis of T-cell subpopulations (gammadelta-T-cells and regulatory T-cells [Treg]) or gene expression profiles.

Results: A delta1/delta2-gammadelta-T-cell-Ratio >1,5 proposed to be associated with operational tolerance was found in 15/60 patients. 45/60 patients with a Treg-percentage ≥2,3% were identified (2). Out of the 15 patients with high delta1/delta2-ratio, two developed a rejection under therapy (13,3%), while 12 out of the remaining 45 (26,6%) developed rejection (P=0,298). The analysis of Tregs showed 12 rejections in the group of 45 patients with Treg ≥2,3% (26,6%) and 2 rejections in the remaining group <2,3% (13,3%, P=0,298). The parameters delta1/delta2-ratio and Tregs were not significantly correlated (P=0,675, Pearson Product Moment Correlation).

The subgroup combining a delta1/delta2-ratio >1,5 with higher Tregs consisted of 11 patients, with one history of
rejection (9%). In contrast, the subgroup with delta1/delta2-ratio <1.5 and Treg <2.3% consisting of 12 patients showed 2 rejections (16.6%, P = 0.61).

**Conclusion:** The prospective analysis of T-cell-subpopulations under immunosuppression alone is not a safe predictor of immune tolerance, since 9–13% of the positively tested patients still developed rejections under therapy. It is not clear whether additional markers such as FoxP3-expression or specific gene expression profiles have a positive effect on diagnostic accuracy. It also remains to be elucidated whether weaning itself can modify the T-cell subpopulation pattern.

**References:**

**Disclosure of Interest:** None declared.

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**PL-H-039**

NON-INVASIVE BIOMARKERS AND PAEDIATRIC NAFLD: NEW METHODS TO PREDICT DISEASE AND STRATIFY SEVERITY

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**Objectives and Study:** Estimated to occur in 10% of children, the spectrum of non-alcoholic fatty liver disease (NAFLD) ranges from simple steatosis to inflammation and fibrosis (non-alcoholic steatohepatitis). Progression of disease to cirrhosis and hepatocellular carcinoma is dependent on necroinflammatory severity and fibrogenesis. There is a real need for non-invasive methods of screening, of stratifying disease severity and of following disease progression / response to treatment. The aim of this study was to evaluate a combination of serum biomarkers as measures of disease activity and severity in children with NAFLD.

**Methods:** Forty-five paediatric patients who were biopsy proven to have NAFLD (in whom other causes of known liver disease were excluded) were enrolled in the study. Anthropometric, biochemical and radiological data were collected and serum was stored at −80°C. CK18 M30 fragments, hyaluronic acid, leptin and adiponectin were measured in serum using specific ELISAs and high sensitivity C-reactive protein (hsCRP) with an automated colorimetric assay. Liver biopsies were scored by a single pathologist according to the NASH activity score (NAS). Data was analysed using SPSS v17.0.

**Results:** Median age was 12.7 years (IQR 9.8–14.2), 55% (25 children) were male. Median BMI z-score was 1.66 (1.22–2.07). At presentation, insulin resistance was found in 66%. CK18 M30 levels were significantly higher in patients with NAFLD as compared to age matched healthy controls, median; 288 IU/L (202–494) versus 172 IU/L (146–205) respectively (P < 0.001). CK18 M30 levels could also distinguish between significant steatohepatitis (NAS≥5), median; 347 IU/L (IQR 258 – 509) and simple steatosis (NAS<3), median; 191 IU/L (IQR 167 – 197), (P = 0.006). Significant fibrosis (≥F2) could be differentiated from no / minimal fibrosis (<F2) using CK18 M30, median; 393 IU/l (225–533) vs. 243 IU/l (190–317), (P = 0.03). Leptin was useful in distinguishing fibrosis grade <F2 from ≥F2 (21.9 ng/ml (16.6 – 83.6) versus 55.9 ng/ml (32.6–77) (P = 0.03). Though neither adiponectin nor hsCRP reached statistical significance in predicting NASH versus NAFLD, the leptin / adiponectin ratio demonstrated significance on predicting fibrosis form no fibrosis (P = 0.048). Hyaluronic acid was not able to discriminate simple steatosis from NASH nor fibrosis (≥F2) from no fibrosis (<F2).

**Conclusion:** This study combines the use of markers for different processes in the development of NASH. Serum biomarkers, especially CK18 M30 fragments, are of potential use in stratifying disease severity and thus in longitudinal monitoring of disease progression in paediatric NAFLD.

**Disclosure of Interest:** None declared.

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**PL-H-040**

ROLE OF ABCB4 GENE IN PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS TYPE 3 (PFIC-3): FINAL REPORT OF AN ITALIAN MULTICENTER STUDY


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**Objectives and Study:** To define the frequency of ABCB4 mutations among children with PFIC-3 and to characterize the genotypes with respect to severity of symptoms, response to ursodeoxycholic acid (UDCA) therapy and outcome of the disease.

**Methods:** Data were collected in a multicenter study carried out within the Italian Society for Paediatric Gastroenterology, Hepatology and Nutrition. Molecular analysis of ABCB4 was performed in 133 children with PFIC and high serum GT activity. ABCB4 mutations were classified as “disease causing mutations” (DCMs) or “benign substitutions” according to the prediction algorithm PolyPhen (http://genetics.bwh.harvard.edu/pph).

Liver histopathology of patients who were found to carry ABCB4 mutations and had undergone liver biopsy (n = 14)
was reassessed by a single pathologist and immunohistochemistry performed using antibodies against ABCB4 and Cytokeratin 19.

**Results:** Thirty-one mutations were identified in 28 patients from 22 families, including 20 DCMs that should result in substantial impairment of floppase activity. Twenty patients carried 2 mutated alleles and 8 only 1. At presentation (age: 1–204 months), 20 patients were symptomatic; serum bile acids concentrations were increased in all except one asymptomatic patient, with higher levels in those with DCMs on both alleles (109.6 ± 39.9 μM/L) compared to those with two “benign substitutions” or a single mutated allele (56.8 ± 87.1 μM/L) (P = 0.0035). Cirrhosis was present in 15 patients: all, except one, carried two mutated alleles (with exclusively DCMs in 11). Of the 10 patients with absent or faint canalicular expression of ABCB4 protein, 8 carried exclusively DCMs. All patients were treated with UDCA; a complete biochemical response occurred in patients carrying a single mutated allele or two mutated alleles with “benign substitutions”.

Five out of 6 patients with a particularly rapid evolution toward liver failure before adolescence had two mutated alleles with DCMs. The other 22 patients, 9 with cirrhosis, are alive with native liver after a mean follow-up of 72 months (range 3–349).

**Conclusion:** A variety of clinical features is associated with defined ABCB4 genotypes in children with PFIC-3. DCMs on both alleles are associated with reduced expression of ABCB4 protein, lack of response to UDCA and rapid evolution to end stage liver disease. However ABCB4 mutations accounts for a low percentage of cases (21%) suggesting a genetic heterogeneity of PFIC-3 disease.

**Disclosure of Interest:** None declared.

**PL-H-041**

**ENDOTHELIAL DYSFUNCTION IN PEDIATRIC NONALCOHOLIC FATTY LIVER DISEASE**

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**Objectives and Study:** Nonalcoholic fatty liver disease (NAFLD) is consistently associated with features of the metabolic syndrome, a condition carrying a high risk of cardiovascular events. In a preliminary study [1] we showed that carotid artery intima-media thickness (IMT) was highest in obese children with fatty liver than obese children without liver involvement or normal weight subjects. These results needed to be confirmed and expanded, and it was with this aim that we measured the vasodilatory response of the brachial artery to ischemia (a test of endothelial response) as well as carotid IMT in a large number of obese children with and without NAFLD, and lean subjects.

**Methods:** We compared flow-mediated dilation (FMD), carotid IMT, lipid profile, glucose, insulin, and insulin resistance (as homeostasis model assessment of insulin resistance, HOMA-IR) in 80 obese children with NAFLD (mean age ± SD, 11.4 ± 3.1 years), 110 obese children without liver involvement (mean age ± SD, 10.5 ± 2.9 years), and 130 control subjects (mean age ± SD, 11.5 ± 3.3 years). The diagnosis of NAFLD was based on ultrasound scan and increased alanine aminotransferase (ALT), after exclusion of infectious and metabolic disorders.

**Results:** Children with NAFLD had significantly reduced FMD (mean ± SD, 8.5 ± 8.0) and significantly enhanced carotid IMT (mean ± SD, 0.55 ± 0.1) than obese children without liver involvement (11.6 ± 11.2 and 0.51 ± 0.09), and control children (13.9 ± 13.2 and 0.42 ± 0.05). Compared to obese subjects without hepatic steatosis, those with NAFLD had higher waist circumference, arterial blood pressure, triglycerides, insulin and HOMA-IR. Within the entire group of obese children, linear regression analysis showed that both FMD and carotid IMT were correlated with waist circumference, BMI-SD score, triglycerides, insulin and HOMA-IR, and ALT levels, after adjustment for age and gender. FMD and carotid IMT were also modeled as categorical variables and obese subjects were stratified into two groups according to the median values to perform multivariate logistic regression analysis. The risk of a low percent FMD and a high IMT was associated with the number of features of metabolic syndrome as well as to the presence of NAFLD.

**Conclusion:** This study, which is the first to report FMD in children with NAFLD, suggests that the presence of liver disease entailes more severe anatomic and functional changes in the arterial wall, and its presence may help identify individuals with increased cardiometabolic risk.

**Reference:**


**Disclosure of Interest:** None declared.

**PL-H-042**

**BILE SALT MOLECULAR CHANGES CONTRIBUTING TO LIVER DISEASE IN DF508 AND G551D CYSTIC FIBROSIS (CF) MOUSE MODELS**


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**Objectives and Study:** The pathophysiology of hepatobiliary disease in CF is not understood. Moreover, CF liver disease is more severe in patients with df508 mutations than in those with mild variants such as G551D. We showed in a DF508 mouse model (Freudenberg et al. 2008. Am J Physiol...
Gastrointest Liver Physiol 294;1411–20) that bile acid malabsorption leads to a more hydrophobic bile acid profile as well as inducing enterohepatic cycling of bilirubin, both of which render bile cytotoxic to cholangiocytes and gallbladder bile lithogenic. Here we analysed biochemical and genetic changes in bile acid synthesis and the secretion of common biliary lipids and bile salt species in dF508 and G551D mouse models compared with wild type (WT) mice.

Methods: Fecal bile acid excretion was quantified by a validated enzymatic method. Expression of the bile acid synthetic enzymes CYP7a1, CYP8b1, CYP27a1 and CYP7b1 was investigated by real time (RT)–PCR. Biliary lipid secretions of individual bile salts in hepatic bile were determined by standard methods.

Results: Compared with WT, fecal bile acid excretion was significantly elevated in all CF mice of both sexes. In both mutant models, the bile acid profile was altered by a highly significant increase in hydrophobic taurocholic acid with reciprocally decreased tauromuricholates. In dF508 mice, hepa-
tic secretion rates of bile salts and cholesterol, and cholesterol were increased significantly, but in G551D only cholesterol secretion was so affected. Consonant with these findings, CYP7a1 and CYP7b1, involved in cholic acid synthesis, were significantly elevated in dF508 but not in G551D mice. The enzymes involved in chenodeoxycholate and murichol-
olate synthesis were unchanged in either species.

Conclusion: In both CF mouse models, bile acid malabsorption leads to important changes in biliary lipid composition and bile acid profiles. As a consequence, biliary cholesterol lithogenicity is increased, with a more hydrophilic bile acid profile in CF mice. In the more severe dF508 mutation, the upregulation of the classic pathway of bile acid synthesis (CYP7a1 and CYP8b1) suggests a strong FXR-mediated mechanism due to deficiency of bile acid returning in the enterohepatic circulation. On the basis of these studies, we believe that pharmacologic intervention to correct bile acid malabsorption in CF may prevent liver disease and gallstones.

Disclosure of Interest: None declared.

PL-N-076
SUBOPTIMAL VITAMIN K STATUS DESPITE SUPPLEMENTATION IN CHILDREN AND YOUNG ADULTS WITH CYSTIC FIBROSIS

Objectives and Study: Vitamin K deficiency is common in unsupplemented patients with cystic fibrosis (CF) and pancreatic insufficiency (PI) and current recommendations support routine vitamin K supplementation. For children and adolescents with CF and PI, although the current minimum and maximum recommended supplemental dose of vitamin K ranges from 300–500 ug/d respectively, its efficacy to normalize vitamin K status remains unclear. This study examined the impact of vitamin K supplementation on vitamin K status in children and young adults with CF and PI and compared their vitamin K status to healthy subjects.

Methods: In 8- to 25-yr old subjects with CF and PI (n = 97), vitamin K supplemental intake, dietary intake by 3-day food records, serum undercarboxylated osteocalcin as % total osteocalcin (%ucOC) and proteins induced by vitamin K absence-factor II (PIVKA-II; n = 60) were assessed. %ucOC was compared to a reference group of 140 healthy subjects, ages 6- to 21-yrs. Vitamin K status was defined as sufficient (<20% ucOC), insufficient (20–50% ucOC), and deficient (>50% ucOC) and as deficient by PIVKA-II >2 ng/mL. Subjects with CF and PI were divided into three vitamin K supplementation groups; <150 ug/d (low); 150–999 ug/d (mid); and ≥1000 ug/d (high) corresponding to vitamin K from multivitamins/no supplement, CF-specific vitamin preparations, and mephyton (5000 ug/dose twice a week), respectively.

Results: For subjects with CF and PI, %ucOC was 33.7 ± 17.9%. PIVKA-II was 4.5 ± 6.5 ug/L and median intake of vitamin K was 62 ug/day from diet and 300 ug/day from supplement. %ucOC was negatively correlated with age (r = -0.30, P = 0.003) and supplemental vitamin K intake (r = -0.42, P < 0.0001). In subjects with CF and PI, 27, 55 and 19% had %ucOC in the sufficient, insufficient and deficient range, respectively, while 50% had PIVKA-II levels in the deficient range. Subjects with CF and PI had higher %ucOC (poorer vitamin K status) in the low (44.9 ± 14.1) and mid (37.7 ± 15.7) but not high (21.9 ± 15.5) supplemental intake groups compared to healthy subjects (21.8 ± 8.8; both P < 0.05). Based upon PIVKA-II, 67, 58 and 29% of subjects in the low, mid and high supplemental intake groups, respectively, were vitamin K deficient.

Conclusion: In children and young adults with CF and PI, vitamin K status is often suboptimal despite routine supplementation with CF-specific preparations. Only those taking high-dose vitamin K achieved a vitamin K status similar to healthy controls. Supported by Cystic Fibrosis Foundation (STALL100A0), Yale and Tufts University School of Medicine Labs, and CTRC (UL1RR024134) and Nutrition Center at CHOP.

Disclosure of Interest: None declared.

PL-N-077
THE EFFECT OF ENTERAL SUPPLEMENTATION OF NEUTRAL AND ACIDIC OLIGOSACCHARIDES ON INTESTINAL PERMEABILITY IN PRETERM INFANTS
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Objectives and Study: Preterm infants have an impaired gut barrier function. The lower endogenous infection rate in
preterm infants receiving neutral and acidic oligosaccharides, as previously found, may originate from improved gut barrier function. We hypothesise that enteral supplementation of a prebiotic mixture consisting of neutral oligosaccharides (short chain galacto-oligosaccharides (SCGOS)/long chain fructo-oligosaccharides (LCFOS)) and acidic oligosaccharides (AOS) may improve gut barrier function, as reflected by decreased intestinal permeability.

Aims: To determine the effects of enteral supplementation of SCGOS/LCFOS/AOS on intestinal permeability, as measured by the sugar absorption test, in the first week of life in preterm infants. Furthermore, to determine host- and treatment-related factors associated with intestinal permeability.

Methods: In a randomised controlled trial, preterm infants with a gestational age <32 weeks and/or birth weight <1500 g received enteral supplementation of SCGOS/LCFOS/AOS or placebo (maltodextrin) between days 3–30 of life. Intestinal permeability, reflected by the urinary lactulose/mannitol (L/M) ratio after oral ingestion of lactulose and mannitol, was measured at 3 time points: before the start of the study (t = 0), at day 4 (t = 1) and day 7 (t = 2) of life. Data were analysed by generalised estimating equations. SPSS 15.0 was used for data analysis. A p value of <0.05 was considered significant.

Results: In total, 113 infants were included. Baseline patient characteristics and nutritional characteristics were not different between the SCGOS/LCFOS/AOS (n = 55) and the placebo group (n = 58). In both groups, the L/M ratio decreased from t = 0 to t = 2 (P < 0.001). Enteral supplementation of SCGOS/LCFOS/AOS had no effect on the decrease of the L/M ratio between t = 0 and t = 2. Low birth weight increased the L/M ratio (P = 0.002). Exclusive breast milk feeding during the first week of life decreased the L/M ratio (P < 0.001).

Conclusion: Enteral supplementation of a prebiotic mixture, consisting of SCGOS/LCFOS/AOS, does not enhance the postnatal decrease in intestinal permeability in preterm infants in the first week of life. The lower endogenous infection rate in preterm infants receiving SCGOS/LCFOS/AOS, as observed previously, cannot be explained by improved gut barrier function, as reflected by intestinal permeability in the first week of life. A beneficial effect of SCGOS/LCFOS/AOS may involve other aspects of gut barrier function, for example modulation of the intestinal microbiota or the intestinal inflammatory response.

Disclosure of Interest: None declared.

PL-N-079

THE EFFECT OF DAYCARE ATTENDANCE ON INFANT AND TODDLER’S GROWTH

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Objectives and Study: Many Israeli infants attend daycare centers from a very young age. This may be associated with recurrent infections, nutritional changes and significant stress in infants and toddlers due to the separation from their parents and the need for integration with peers. We hypothesized that growth may be negatively affected in children attending daycare centers. We therefore studied

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the association between daycare attendance and changes in the height, weight and weight/height ratio over a 6 months period.

Methods: Data was retrieved from 3 maternal and child health care centers in the Haifa area representing an average socioeconomic status. Parents were asked to fill a short questionnaire regarding the infant, the daycare and some demographic data.

Results: One hundred and seventy infants participated in the study. The research group consisted of 85 infants that started daycare center prior to the age of 18 months, while the control group consisted of 85 infants that started daycare after this age. The main findings of the study showed that the research group had significantly shorter stature 3 months after the enrollment to the daycare compared to the control group (mean height percentiles of 56.9 versus 66.3, respectively, \( P = 0.024 \)). This trend was even worse after 6 months (mean height percentiles of 52.3 versus 63.7, \( P = 0.022 \)). Later age of enrollment to the daycare center was significantly associated (\( P = 0.009 \)) with height percentile deceleration. We did not find significant effects of daycare attendance on weight or weight/height ratio.

Conclusion: The mechanism for this observation is possibly stress related growth hormone suppression. Our findings reinforce the importance of monitoring infant/toddler weight and height growth velocities, especially when he/she is introduced to daycare attendance.

Disclosure of Interest: None declared.

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**PL-N-081**

**MATERNAL DIETARY COUNSELLING INITIATED IN EARLY PREGNANCY MODIFIES CORD BLOOD FATTY ACIDS**

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Objectives and Study: Fetal life and early infancy are considered critical periods, when nutritional environment can carry a lasting effect on later health. The aim of this study was to explore the effect of early maternal dietary counselling on infant serum fatty acid composition since polyunsaturated fatty acids (FAs) are considered immunomodulatory.

Methods: At the first trimester of pregnancy, 90 women were randomised to receive either intensive dietary counselling by a nutritionist or as controls. All women also attended municipal well-women clinics. Intensive dietary counselling aimed to modify dietary intake to conform with current recommendations, assessing adherence to a Mediterranean diet including fish and olive oil.

Methods: The study population consisted of 156 children (71 girls), whose BMI z-score was 4.5 ± 1.4 and their mean age was 8.2 ± 2.7 years. They all underwent ultrasonography to measure the intima-media thickness (IMT) of carotids and to study the morphology of the liver. Their serum glucose, insulin, HOMA index, lipids, TNFalpha; were measured as well. For those who gave their consent (70 pts), 6-keto PGF1alpha was also evaluated.

Results: According to IMT measurement, patients were divided in Group A (0.6–0.7 mm) with a BMI z-score of 4.6 ± 1.4 and Group B (0.4–0.5 mm) with a BMI z-score of 4.1 ± 0.9 (\( P = 0.2 \)). Liver steatosis was present in 23/76 pts of Group A (30.2\%) and in 11/80 pts of Group B (13.7\%). Serum Glucose (mg/dl) and fasting Insulin levels (\( \mu \)U/ml) were respectively 89.3 ± 6.6\( \mu \)U/ml and 14.6 ± 7.7\( \mu \)U/ml in Group A and 88.0 ± 8.5\( \mu \)U/ml and 11.0 ± 5.8\( \mu \)U/ml in Group B (\( P = 0.001 \)). Data of pts are reported in the table:

Conclusion: Increased carotid IMT was documented in 76/156 children (48.7\%) and fatty liver in 34/156 (21.8\%). Fasting insulin levels, HOMA index, triglyceride levels and 6-Keto-PGF1alpha were significantly different between Group A and Group B. These data might suggest that higher insulin resistance and triglyceride levels, together with low levels of 6-keto PGF1alpha could be considered risk factors for early vascular damage and hepatic steatosis in obese children.

Disclosure of Interest: None declared.
recommendations, emphasis put on the quality and quantity of fat. Intakes of nutrients were calculated from 3-day food records at the third trimester of pregnancy. Infant’s cord blood samples were collected and analysed for serum phospholipid, cholesterol ester and triacylglycerol fatty acids by gas chromatography.

**Results:** Dietary counselling resulted in higher intakes of polyunsaturated FAs [mean 6.1 (SD 1.5)%] and lower intakes of saturated FAs [10.7 (2.5)%] as a proportion of energy intake in the intervention group compared to the control group [4.9 (1.5)% and 13.1 (3.3)% respectively, \( P < 0.001 \)]. The serum triacylglycerol n-3 FAs were higher [mean difference 1.46 (95% CI 0.44–2.48)% of total FAs, \( P = 0.006 \)] and the sum of polyunsaturated FAs tended to be higher [1.81 (–0.15–3.78)%] than those of control group [4.9 (1.5)% and 13.1 (3.3)% respectively, \( P = 0.069 \)] in the cord blood of infants whose mothers received vs. not received dietary counselling. Again, the sum of saturated FAs [–1.31 (–2.59–0.04)%, \( P = 0.043 \)] and the ratio of \( \Sigma n-6 \) to \( \Sigma n-3 \) [–0.50 (–0.95–0.06)%, \( P = 0.029 \)] was significantly lower. No modifications of phospholipid or cholesterol ester FAs were detected.

**Conclusion:** Maternal dietary counselling resulted in increased intakes of unsaturated FAs and was reflected as a favorable lipid profile in cord blood. Particularly the increase in n-3 FAs may carry potential anti-inflammatory and beneficial health effects during the important period of rapid maturation and development.

**Disclosure of Interest:** None declared.

**PO-AHP-121**

**GENERATIONAL CHANGES IN THE GROWTH OF CHILDREN FROM MARIBOR AND SLOVENIA**

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**Objectives and Study:** Among the numerous factors which influence child’s growth and development are also factors of changeable socio-economical environment and life style (1). Our aim was to evaluate these changes and contribute to preventative measures and evaluation of child’s growth in paediatric practice. Therefore, we decided to estimated the state of body growth in two generations of Maribor’s children at five and six years of age of both gender and find out secular changes and to define standards.

**Methods:** We used Cameron’s measurement and statistical method (2,3). Representative sample (gender and age) of 1461 children from Maribor in the year 1996 and sample of 608 Maribor’s children, measured in 1966, 28 body features were studied and compared in each population unit. In the second part of this paper we present a part of the anthropometric measurement study carried out for standardization of the DENVER II developmental screening test. There were 1596 healthy Slovene children between zero and six and half years of age included into observation. Children come from Maribor, Koper, Velenje and Ljubljana.

**Results:** Changing trends show increased tendency towards decrease or increase of the most body measurements. In everyday practice most often are used these measurements: body mass, head circumference, body length in babies and body height in pre-school children. Our measurements have proved, with \( p \)-value = 0.001 that measurements of children in 1966, also shown in diagrams, are significantly different from measurements in 1996.

**Conclusion:** Diagrams were made for following body measures: body mass, body height, head circumference, upper arm circumference, tugh circumference and body mass index. Comparative analysis with Euro-Growth study showed that our results correspond with European standards (4,5). Therefore, our results are suggested to be applied in everyday paediatric practice.

**References:**

**Disclosure of Interest:** None declared.

**PO-AHP-122**

**A PILOT PROJECT TO EVALUATE AN INTENSIVE DESENSITISATION, ORAL TOLERANCE THERAPY AND HUNGER PROVOCATION PROGRAMME FOR CHILDREN WHO HAVE HAD PROLONGED TUBE FEEDS**

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**Objectives and Study:** Three children on prolonged PEG feeding supplementary to oral feeding participated in a pilot project that compared an intensive multi-disciplinary feeding programme with a traditional feeding multi-disciplinary programme for long term tube feeders.

**Methods:** Two children underwent a daily one week long intensive group feeding therapy programme, whilst the third
The two children who participated in the intensive programme demonstrated a significant increase in oral intake with a maintained reduction in daily tube feeds. Child 1 had a weight increase as follows; beginning of intervention = 12.5 (0.4th-2nd) to week end 12.8 (0.4th - 2nd); Child 2 had a slight weight loss as follows; beginning of intervention = 11.8 (0.4th) to week end 11.6 (0.4th.). Child 3, who carried on with the traditional Feeding Clinic approach had comparison results as follows; beginning 11.4 (75th) to week end 11.4 (75th). At the first post follow up, a month after completion of the programme, child 1 had completed a staged discontinuation of tube feeds, child 2 had maintained tube feeds at a reduced level as per their intervention week. No weight loss was reported with any of the children. The children maintained oral motor skills as assessed using the Paediatric Oral Motor Skills Package, (POSP; 1996) and significantly increased the number of spoonfuls taken orally. Parental language style and children’s verbal responses were also analysed and significant differences in these areas were noted, with parents using a less directive and more facilitative style, with children becoming more actively involved in the social aspect of the mealtime.

Conclusion: Qualitative results from parent participants suggest an intensive programme has longer term maintenance effects for both the child and parents. This programme should be replicated on a larger scale and its success compared with a more Traditional Feeding Clinic approach for reduction in tube feeds, maintenance of progress and quality of life outcomes.

Disclosure of Interest: None declared.

PO-AHP-123

SAFETY AND EFFICACY OF HEPARON JUNIOR IN INFANTS WITH CHOLESTATIC LIVER DISEASE

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Objectives and Study: Children with cholestasis benefit from feeds that are rich in medium chain triglycerides (MCTs), branched chain amino acids, and preferably low in sodium. Of the currently available specialist products Heparon Junior (SHS International) appears to have the optimal nutrient profile to meet the needs of these infants however there is no freely available published data on this product despite its use in continental Europe. The composition of Heparon Junior is high energy/high protein, nutritionally complete, with branched chain amino acids (30%), low sodium (0.56mmol/100mls), and high MCT (49%). Our aim is to evaluate the safety, tolerability, and efficacy of Heparon Junior in infants with cholestatic liver disease.

Methods: Seven (4 female) infants with cholestasis (median age 9 weeks (range 5–28 weeks)) were given Heparon Junior (minimum of 60% of energy intake) orally or via NG tube for a period of 24 weeks. Gastrointestinal symptoms (vomiting, diarrhoea, discomfort) were recorded daily by parents along with any additional observed adverse effects. Anthropometrics (calculated z scores for weight, length, body mass index (BMI) head circumference (HC), mid upper arm circumference (MUAC)), liver function tests (total bilirubin, GGT, AST, serum albumin and sodium) were assessed at baseline, 4, 12 and 24 weeks.

Results: The patients’ diagnoses were biliary atresia (4), idiopathic cholestasis (2) and alpha-1-anti-trypsin deficiency (1). Of these, 1 withdrew from study after 12 weeks as was no longer cholestatic, and 3 received liver transplants at weeks 18, 20 and 21 respectively. In these patients end data was analysed at 12 weeks rather than at 24 weeks. Median baseline serum markers were: total bilirubin 388mumol/L (range 12–164), GGT 832 (range 105–2080), AST 185 (range 61–294), albumin 39 (range 30–58). At completion median serum markers were: total bilirubin 62mumol/L (range 2–279), GGT 196 (range 15–381), AST 147 (range 61–306), albumin 35 (range 30–45). No adverse effects from Heparon Junior were reported to the investigators by parents or medical staff. No persistent gastrointestinal symptoms attributable to Heparon Junior occurred. Median z score change values from baseline to completion for anthropometrics were: weight 1.09 (range 0.53–2.66), length 0.47 (range 0.15–4.55), BMI 1.11 (range 0.15–1.62), HC 0.62 (range 0.40–2.15). MUAC z scores were calculated for 4/7 subjects (no WHO centile charts for infants <3 months) 1.10 (range 0–3.0).

Conclusion: These results show that Heparon Junior is safe, well tolerated and that cholestatic infants can show increased growth parameters when given Heparon Junior as their primary energy source.

Disclosure of Interest: M.Houchin, SHS International, Grant Research Support.

PO-AHP-124

THE USE OF FOOD AND SYMPTOM DIARIES WITHIN THE PAEDIATRIC GASTROENTEROLOGY SERVICE IN LEICESTER

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Objectives and Study: This study was undertaken to investigate the use of food and symptom diaries as a diagnostic tool within the Paediatric Gastroenterology Service.

Methods: 197 dietetic and medical records were reviewed over a 2 year period. Data collated included length of food and symptom diary, end diagnosis, if known, dietetic intervention, and medications prescribed.

Results: Symptomatology for all cases included loose stool/persistent diarrhoea/intermittent diarrhoea +/- abdominal
pain (non-inflammatory bowel/coeliac disease-related loose stool/diarrhoea). The majority (89%) of diaries issued were returned to the Dietitian. Most (72%) were kept for 10 days. Dietary manipulation resulted in 91%. Cow’s milk protein exclusion was the commonest simple exclusion with a high response rate of 88%. Simple wheat and egg intolerance were less frequent affecting only 5% and 1% retrospectively. Multiple food intolerance, fast transit and irritable bowel syndrome each accounted for about 10% of the sample. Constipation occurred in one third of the sample. From the information gathered at least 53% of all cases had subjective improvement of symptoms with some kind of dietary manipulation. 21% had healthy eating and appropriate fluid advice alone following the diary with good symptom resolution. Squash drinking syndrome numbers were sizeable yet other prominent diagnoses were less common.

**Conclusion:** Food and symptom diaries are a useful tool in paediatric gastroenterology to indicate a diagnosis. Dietary manipulation can help improve symptomatology in many instances where there is loose stool/persistent diarrhoea/intermittent diarrhoea +/- abdominal pain. Poor fluid and poor dietary fibre or excessive squash drinking were the causative factors in a significant number of cases. This data suggests a clear need for better nutrition education and support for parents and children.

**Disclosure of Interest:** None declared.

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**PO-AHP-125**

**AFLATOXIN LEVELS AND FUNGI IDENTIFICATION IN CERTAIN SYRIAN FOOD ITEMS**


**Objectives and Study:** It was aimed to evaluate aflatoxin levels in the most common foodstuffs at the local markets in Syria and to identify molds spread in these markets.

**Methods:** Different samples of foods were collected from the Syrian market and fungi were isolated and identified according to their morphology. In addition, the total aflatoxin levels of the samples were determined by using affinity chromatography at “The National Commission for Biotechnology”.

**Results:** In raw peanut sample, Aspergillus flavus had been identified and a level of 8.05 ± 4.95 ppb of aflatoxins was found. Raw grated and whole seed pistachios differ in aflatoxin levels from each other in according to the processes that applied on them. The maximum levels were found in the grated pistachios which reached 91.25 ± 26.25 ppb, while aflatoxin levels in the whole pistachios reached 26.5 ± 1.5 ppb. Raw walnut showed an aflatoxin level of 15 ± 3 ppb; on the other hand, raw corn and toasted corn occupied the levels ranges from 19.5 ± 12.5 ppb to 6.5 ± 1.2 ppb, respectively. As demonstrated above, all the samples exceeded the permitted levels according to international commissions with the exception of wheat flour sample, which breaks the role and appear to have normal levels of aflatoxin of 1.65 ± 1.65 ppb.

**Conclusion:** More education and observation on these toxins must be applied from the governmental authorities on the sellers, suppliers, farmers and even customers. Children’s foodstuffs should have less expiring dates than permitted to avoid aflatoxin building in these foods as less as possible. Finally, pediatricians and dietitians have an extremely important role in raising parents’ awareness about storing and handling kids’ food items. In addition, they should be informed about how to differentiate foods that have inappropriate smell to riddance it, even if it’s edible as the expiring date still valid.

**Reference:**


**Disclosure of Interest:** None declared.

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**PO-G-126**

**STUDY ON PHENOTYPE AND PARENTAL INFORMATION OF CHILDREN INVESTIGATED FOR COELIAC DISEASE AT ENDOSCOPY**

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**Objectives and Study:** Adequate parental information about disease and treatments is vital for provision of good care to children with chronic diseases. The aim of this study is to understand level of knowledge of Coeliac disease (CD) and
its treatments in parents whose children are being investigated for the condition.

Methods: Children and families presenting with suspected CD were recruited at the time of diagnostic endoscopy. Children were assessed for symptoms and examined which included growth measurement (height and weight). Parents were asked questions about CD prior to seeing a dietician. This study had ethical approval.

Results: 55 children (19 boys, 34.5%) and families were recruited in this study, with the majority of children (92.7%) referred by paediatric consultants. The median age at recruitment was 6.7 yrs (IQR 3.2 – 10.5 yrs). Children had a median height of $-0.7$ SDS (IQR = $-0.6$ - $-1.2$) and median weight of $-0.7$ SDS (IQR = 0.3 – $-1.3$). Commonest symptoms included abdominal pain (58.1%), distension (50.9%), failure to thrive (43.6%) and diarrhoea (38.2%). 9% were asymptomatic. 20 children (36.4%) had a positive family history. 43/55 (78.2%) were eventually diagnosed to have CD (48 had + serology) on duodenal biopsy. 36 Parents knew someone with CD (65.5%). Almost half of these were family members living within the same household (n = 17), 44 parents had looked up CD (80%) and accessed internet for information. 40 parents knew that CD affects the small intestine (72.7%) and 54 knew that a gluten free diet (GFD) is the standard treatment (98.2%); 52 parents knew that a GFD is for life (94.5%).

Nearly half of parents (44.6%) thought that maize contains gluten, whereas 98.2% identified that gluten is in wheat. Overall, only 38.2% parents correctly identified all gluten containing foods. Knowing someone with CD ($P = 0.02$), rather than higher level of parental education ($P = 0.08$), was predictive of better parental knowledge. Parents were also asked an open question to identify the most concerning factor about CD in their children. The two commonest worries were social implications of the diet (parties) (40%) and dietary restrictions for life (27.3%).

Conclusion: Parental knowledge about CD is generally good at the time of diagnosis of their children, with internet being the most common source of information. In addition, growth is reasonably preserved in this cohort. Despite this, one to one parental education about CD, particularly its treatment, needs to continue in the hospital focusing on information about gluten containing foods. This should also include recommendations regarding authentic websites about paediatric CD. This study from Wessex, UK is likely to be representative of practices in Europe.

Disclosure of Interest: None declared.

PO-G-127

NOVEL MUTATIONS UNDERLYING RARE FAMILIAL ENTEROPATHIES

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Objectives and Study: Microvillous Inclusion Disease (MVID) and Congenital Tufting Enteropathy (CTE) are congenital disorders of the intestinal epithelial cells that cause an intractable watery diarrhea with usual onset near birth. MVID is characterized by lack of microvilli on the surface of enterocytes with the occurrence of intracellular vacuolar structures containing microvilli. Whereas pathologic studies for CTE patients demonstrate villi with crowded epithelial cells forming tufts. MVID and CTE are very rare disorders and are inherited as autosomal recessive traits. Recently, mutations of MYO5B and EpCAM were identified as the underlying lesion resulting in MVID and CTE, respectively.

Methods: Four Saudi families were investigated, three with children affected by MVID and one with a child affected by CTE. Five patients and available unaffected individuals were subjected to genome-wide homozygosity scans using the Affymetrix 250K SNP array.

Results: Analysis with the copy number tool CNAG identified shared homozygous regions unique to the affected subjects. Of the three families with MVID, homozygosity was observed in two families at a locus on chromosome 18 which included MYO5B. Sequencing of MYO5B in individuals from these families identified two novel nonsense mutations in exons 24 and 36 (Q1047X and E1589X). In the other family homozygosity was absent at the MYO5B locus. However, a locus on chromosome 2 which included EpCAM was found to be homozygous in this family. Sequencing of EpCAM identified a 1 bp insertion (c.499insC) in exon 5 resulting in premature truncation of the mature protein. This was consistent with this family being classified as having CTE rather than MVID. The fourth family studied was referred with a diagnosis of CTE and was found to have the same 1 bp insertion consistent with a common founder.

Conclusion: The present study has identified novel nonsense mutations in MYO5B and EpCAM associated with autosomal recessive enteropathies in Saudi families. Our findings expand the limited spectrum of MYO5B and EpCAM mutations associated with gastrointestinal genetic disorders and provide an opportunity to investigate phenotype/ genotype correlations.

Disclosure of Interest: None declared.

PO-G-128

SEROPREVALENCE OF ANTI-TTG IGA ANTIBODIES IN BELGIAN CHILDREN AND ADOLESCENTS

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Objectives and Study: Coeliac Disease (CD) is an immune-mediated enteropathy caused by a permanent sensitivity for
Disclosure of Interest: None declared.

**PO-G-129**

PREVALENCE COELIAC DISEASE IN BOSNIAN PRESCHOOL CHILDREN

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Objectives and Study: Coeliac disease appears to be polyfactorial, both in that more than one genetic factor can cause the disease. Unfavourable events associated with coeliac disease may be prevented by a gluten free diet. The aim of this study was to investigate the clinical polymorphisms and distribution of diseases in a small cohort of Bosnian celiac disease kids patients.

Methods: Serological blood tests are the first-line investigation required to make a diagnosis of coeliac disease. The diagnosis of celiac disease was based on small-bowel biopsy showing severe villous atrophy with crypt hyperplasia.

Results: IgA deficiency is present in 2.5 % of kids patients with coeliac disease, and in turn, this condition features a tenfold increased risk of coeliac disease. The prevalence of clinically diagnosed disease is 0.12% children in Bosnia and Herzegovina.

Conclusion: Coeliac disease is caused by a reaction to gliadin, a prolamin (gluten protein) found in wheat, and similar proteins found in the crops. A simple rapid test performed in primary care at the preschool check-up identified most undiagnosed cases of coeliac disease in the community.

References:


Disclosure of Interest: No disclosure.

**PO-G-130**

DISTINGUISHING CELIAC DISEASE FROM OTHER CAUSES OF CHRONIC ENTEROPATHY IN CHILDREN UNDER TWO YEARS OF AGE: THE ROLE OF ANTIBODIES ANTI-DEAMIDATED GLIADIN PEPTIDES

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Objectives and Study: Discriminating between coeliac disease (CD) and other enteropathies in children aged less than 2 years may represent a clinical challenge since classical serum markers for CD, except anti-gliadin antibodies (AGA), are not uncommonly normal. The usefulness of a new class of antibodies, anti-deamidated gliadin peptides (aDGP), in the diagnostic approach to these patients has been assessed.

Methods: We investigated 40 children (median age: 16.8 months; age range: 4–24 months), with gastrointestinal symptoms suggesting CD (chronic diarrhoea, failure to thrive, vomiting) and high serum levels of conventional AGA, but normal values of serum IgA, anti-transglutaminase (anti-tTG), anti-endomysial antibodies (EMA) and no sensitization to the most common food antigens. All of them underwent measurement of serum levels of aDGP (IgA and IgG) and upper gastrointestinal endoscopy with duodenal
PO-G-131

“LATENT” COELIAC DISEASE IN CHILDHOOD: DOES IT REALLY EXIST? EXPLORING MORE DISTALLY BY MEANS OF ENTEROSCOPY. A CASE REPORT

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Objectives and Study: Coeliac disease (CD) is an immune-mediated disorder, whose defined triggers are gluten peptides from wheat and related cereals, characterized by chronic inflammation of the small intestinal mucosa that gradually leads to the development of villous atrophy. Some individuals with positive CD serology may exhibit a normal mucosa, i.e. Marsh 0, according to the Marsh-Oberhuber criteria, when duodenal biopsies are obtained by upper GI endoscopy. Such patients are commonly labelled as “latent” coeliacs, and many of them can later develop the typical lesions of CD. It is agreed that the histopathological pattern of CD is patchy and, thus, there is the risk of missed diagnoses, leading to the development of late complications. How to manage these patients? HLA testing, serological and endoscopic re-evaluation, gluten free diet trial in symptomatic patients, should provide further information; otherwise, controversies remain.

We report the case of a 4-year-old boy with iron deficiency anaemia who was referred to our Unit because he was positive for CD immunological markers (anti-endomysial and anti-transglutaminase antibodies). Therefore, he underwent upper GI endoscopy but, despite multiple duodenal biopsies, the histological findings were not consistent with CD (Marsh 0); furthermore, parents refused to keep him on a gluten free diet only based on serological assessment. In order to obtain more tissue samples along the small bowel we performed single-balloon enteroscopy.

Methods: Upper GI endoscopy; single-balloon enteroscopy.

Results: Enteroscopy showed at the jejunum typical endoscopic (mosaic-patterned and nodular mucosa, scalloping of the folds) and histological features of CD (villous atrophy classified as Marsh 3c).

Conclusion: Our case of “latent” CD, with iron deficiency anaemia as the only sign of malabsorption, became “overt” CD when we went beyond conventional biopsies by means of enteroscopy. Does “latent” CD really exist? How useful is enteroscopy in this field? Further studies are needed to assess if enteroscopy can be of value in re-classifying CD and redirecting “latent” towards “overt” CD.

Disclosure of Interest: None declared.

PO-G-132

HANDGRIP STRENGTH AND ANTHROPOMETRIC MEASUREMENTS IN CHILDREN WITH CELIAC DISEASE. WHEN DO THEY RETURN TO NORMAL?

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Objectives and Study: Celiac disease is an autoimmune disease adversely effecting the nutritional status resulting in protein-calorie malnutrition (PCM). Implementation of gluten free diet (GFD) reverses the malnutrition and symptoms of the patients. Measurement of muscle strength could potentially show the earlier stages of PCM. The aim of this study was to assess the handgrip strength and anthropometric measurements of children with celiac disease and to compare with healthy children.

Methods: Anthropometric measurements (triceps skinfold thickness, height, weight, mid-arm circumference) were measured and mid-arm muscle circumference (MAMC) was calculated from these measurements. Handgrip strength was measured by hand dynamometry in children older than 5 years of age with celiac disease (both newly diagnosed and patients receiving gluten-free diet) between July 2009 and December 2009. Data about laboratory parameters (EMA and/or AGA IgG) and date of diagnosis were obtained in patient group. Healthy children without chronic illnesses were selected as control group and same measurements were performed.

Disclosure of Interest: None declared.
Results: 78 children were included in the study (44 celiac and 34 control). There were no differences between the gender distribution and the age of groups (11.5 ± 3.3 vs. 11.7 ± 2.8, respectively). Celiac group consisted of 7 newly diagnosed patients. Overall the median disease duration was 1.6 yrs (0 to 11.1 yrs). At the time of study, 19 of the 44 patients had negative EMAs, thus were in good adherence to diet. Celiac patients had significantly lower triceps skinfold thickness (9.2 ± 3.1 mm to 13.6 ± 6.4 mm, \( P < 0.001 \)), weight (33.5 ± 11.3 kg to 45.1 ± 24.8 kg, \( P = 0.014 \)), mid-arm circumference (18.8 ± 3.4 cm to 21.4 ± 3.6 mm, \( P = 0.002 \)), MAMC (15.9 ± 2.8 to 17.1 ± 2.1, \( P = 0.05 \)) and there was a trend for handgrip strength to be lower with respect to healthy children (12.3 ± 5.9 kg to 15.2 ± 5.6 kg, \( P = 0.06 \)). When we looked at the disease duration, children at the time of diagnosis had the lowest measurements amongst all groups. Children receiving GFD for more than 2 years had similar measurements to healthy children. Patients had significantly lower values for all the measurements in the first 2 years of GFD including handgrip strength. Patients with EMA negativity had a tendency to be more strengthier and to have more subscapular skinfold thickness even when newly diagnosed patients were excluded from analysis.

Conclusion: This study shows that children with celiac disease gain their strength and muscle and fat mass within the first 2 years of GFD. Thereafter their body muscle and fat mass and handgrip strength seems to be similar to healthy children. Whether diet adherence might accelerate this catch-up needs further investigation.

Disclosure of Interest: None declared.

PO-G-133

QUALITY OF LIFE AND GLUTEN FREE DIET COMPLIANCE AT CELIAC DISEASE ROMANIAN CHILDREN
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Objectives and Study: The aim of the study was to assess differences in quality of life at children with celiac disease (CD) according to the clinical presentation at diagnosis compared to a control lot and to determine the compliance to gluten-free diet.

Methods: The study developed between January 2008 - November 2009 and included 2 lots of children. The first lot was composed of 30 celiac patients, divided in 3 subgroups: 8 patients with classical forms of CD, 18 with atypical forms and 4 cases with silent CD. For every CD patient, we selected a subject matched for age and sex, included in control lot. We prospectively evaluated the newly diagnosed CD patients and the healthy controls using parents-administered questionnaires: The Family Quality of Life Questionnaire 2000 at diagnosis and at 3, 6 and 12 months of treatment.

Results: The questionnaires included 10 questions with multiple choice answer, each answer being quoted with a score. At diagnosis, patients with classical symptoms exhibited a significantly more pronounced alteration of all items of the questionnaires than atypical and silent cases (\( P < 0.001 \)). We also obtained a significant difference comparing the classical CD patients baseline scores with the control lot (\( P < 0.0001 \)). We did not obtained significant differences comparing silent CD patients baseline scores with the control lot (\( P > 0.05 \)). We also assessed the compliance to gluten free diet. The respond to diet was appreciated by clinical, biological, immunological and histological criteria. At 28 patients improving of clinical symptoms appeared from the first months of gluten free diet. In evolution, 19 patients were totally adherents to gluten free diet on long term. In 9 cases, children were consuming involuntary trace amount of gluten. In 2 cases with silent CD the parents refused from the start the diet for their children. Treatment produced a substantial and rapid (3 months) improvement of scores in classical and atypical patients. Both subgroups attained comparable final scores with the control lot. There were no differences comparing strictly adherents with partially complaints (\( P > 0.05 \)).

Conclusion: Atypical/silent CD patients had a significantly better baseline quality of life than those with classical symptoms. Treatment induced a rapid and significant improvement in symptomatic cases. All subgroups had similar one year scores, comparable to healthy controls. Incomplet awarness of untreated celiac disease risks was the base of noncompliance in those 2 silent cases that refused to follow the diet.

Disclosure of Interest: None declared.

PO-G-134

CLINICAL, MORPHOLOGICAL AND IMMUNE-GENETICAL CORRELATIONS IN ROMANIAN CELIAC DISEASE CHILDREN
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Objectives and Study: The aims were to perform a screening study on a pediatric group that associates certain risk factors for celiac disease (CD) and to assess the correlations between different forms of celiac disease, immunological, morphological parameters and haplotypes.

Methods: The study developed between January 2008 - November 2009. The serological tests used for screening included IgA anti-tissue transglutaminase (IgA tTG) and anti-endomysial antibodies (EMA). In case of positive result for at least one test, we performed intestinal biopsy. Interpretation was done according to Marsh criteria. The study included 2 groups. The first lot was made of 30 celiac patients diagnosed with CD during screening. The second lot was composed by 30 control subjects matched for age and
sex. We assessed the HLA DQ2 and DQ8 using PCR technique to all celiac patients and in control lot.

**Results:** From 30 celiac patients, 18 patients presented atypical forms of disease, 4 patients presented silent forms of disease, and only 8 associated the classical forms of disease. Alleles distribution in group of celiac patients was: 28 were positive for HLA DQ2 and from them 7 patients associated haplotype HLA DQ2 homozygous and 21 associated haplotype HLA DQ2 heterozygous. 2 cases presented HLA DQ8. In the control lot, 2 subjects from 30 associated haplotype HLA DQ2 heterozygous. The rest were negative for HLA DQ2 or DQ8. We tried to correlate the clinical forms of disease with IgA tTG antibodies serum level, severity of villous injury and haplotype. Bivariate and multivariate conditional logistic analyze were performed. We obtained a significant correlation between IgA tTG serum level and severity of villous injury ($r = 0.621092$). We also established a positive correlation only between subgroup Marsh IIIc and the severe classic form of celiac disease. The forms of disease and the haplotypes did not correlate.

**Conclusion:** The high frequency of CD (2.75%), diagnosed after screening in a selected group, corresponds with recent published data, being higher than the prevalence of the disease in general population. The polymorphism of CD presenting forms as well as the lack of concordance between clinical symptoms and the type of intestinal injury, make the intestinal biopsy the gold standard for diagnosis when the clinical suspicion of gluten intolerance exists. The HLA polymorphism seems to have no impact on clinical forms of disease. The presence of molecules DQ2 or DQ8 is mandatory, but not sufficient for development of celiac disease. Due to its high negative predictive value, the assessment of haplotype must be used in clinical practice only at uncertain cases.

**Disclosure of Interest:** None declared.

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**PO-G-135**

**CELIAC DISEASE (CD) DIET DIFFICULTIES IN SYRIAN PATIENTS PRACTICES**

M. Bozo$^1$, M. Halaby$^2$, K. Tafish$^2$.

**Objectives and Study:** This is a Pilot study aiming to discover the difficulties and the facts of practicing gluten Free diet (GFD) among Syrian children with the celiac disease (CD).

**Methods:** Fifteen celiac children diagnosed by Intestinal Biopsy (IB) and anti–endomysial anti Bodies, under GFD from more than one year. GFD was evaluated for both difficulties during practicing their daily life; the data were collected by phone contacts.

**Results:** Total Number of patients is 15: 7 girls and 8 boys, aged from 4–12 years; the mean age is 8 years. 6 children (40% of the participants) described difficulties in the GFD, 5 children (33.4% of total children) broke their GFD, in the majority of cases the Violation happened out of home. 3 children (in total 20.4% of patients) were non-adherent to the GFD at school, 2 patients (13.36% from the whole group) in the company of relatives or friends. The apprehension of parents of the GFD was very good. 7 children (about 44.4% of the patients) found difficulties in the exclusion of bread from their diet; the others described different difficulties in different foods (in more than 13 food items).

5 children (represented by 33.4% of the participants) described psychological difficulties secondary to the GFD.

**Conclusion:** Many difficulties are described in the GFD in Syrian pediatric patients, the majority of surpasses presented out of home, some special foods were frequently violated, and some psychological difficulties presented.

**Disclosure of Interest:** None declared.

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**PO-G-136**

**INTERNALIZATION OF ALPHA GLIADIN PEPTIDE 31–43 BY CACO-2 CELLS DOES NOT REQUIRE A SURFACE RECEPTOR**

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**Objectives and Study:** Alpha gliadin peptide 31–43 (p31–43) is considered the main responsible of the innate immune response in celiac disease patients. Recent evidences indicated that p31–43 rapidly entered cells and interacted with the early endocytic vesicular compartment. However, the mechanism of p31–43 uptake is not completely understood. Our aim was to identify cell surface proteins involved in p31–43 internalization by Caco-2 cells.

**Methods:** We treated Caco-2 cells with p31–43, then we immunoprecipitated cell lysates with rabbit anti-p31–43 antibodies and analysed proteins by SDS-polyacrilamide gel electrophoresis.

**Results:** After treatment of Caco-2 cell lysates and, alternatively, Caco-2 living cells, with p31–43 and subsequent immunoprecipitation, we did not visualize on SDS-polyacrilamide gel electrophoresis any proteins that specifically interacted with p31–43. In addition, we incubated Caco-2 cells with p31–43 in the presence of a chemical cell-impermeable cross-linking agent. Also in this case, after immunoprecipitation, we could not identify any proteins able to interact with p31–43.

**Conclusion:** Although we explored many experimental conditions, we could not identify a possible receptor for p31–43 in Caco-2 cells. Since we evidenced that p31–43 was able to interact with a membrane-like environment in vitro (Vilasi S. et al. 2009), we hypothesize that membrane composition and organization, instead of specific proteins, may have a major role in p31–43 internalization by cells.
PO-G-137

ADDITIONAL CD SUSCEPTIBILITY VARIANTS IN THE HLA-B8-DR3-DQ2 CEH
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Objectives and Study: The major susceptibility locus in celiac disease CD is located within the MHC region on chromosome 6p21 and more than 90% of patients with CD express the HLA-DQ2 heterodimer. However, HLA-DQ2 is relatively common in the general population and is carried by approximately 30% of Caucasians. A considerable amount of evidence exists suggesting the presence of at least a second CD susceptibility locus within or close to the MHC. The identification of additional putative variants remains difficult due to the high degree of linkage disequilibrium in the region. Long genomic extensions in the MHC, termed “conserved extended haplotypes” (CEH) have been maintained unaltered during human evolution, and one such CEH, B8-DR3-DQ2, is strongly associated with CD. In order to find additional CD susceptibility loci in the MHC, we performed high resolution SNP genotyping of the MHC region in this CEH.

Methods: High resolution SNP scan was performed in a discovery sample set comprising 10 CD patients and 39 healthy blood donors of Caucasian origin who were homozygous for HLA-DR3-DQ2 and carried a single copy of the chromosome 6p21 haplotype. One sample was also added as a replication sample. Replication of the most significantly associated SNPs using Taqman technology was performed in an independent sample of 10 CD patients and 39 healthy blood donors. Genotyping of the most significantly associated SNPs using Taqman technology was performed in an independent sample of 525 CD patients and 563 controls of Caucasian origin, without HLA matching. Genotyping results were analyzed using PLINK v2.044 association analysis toolset. Fisher’s exact test was used for single marker allelic association analyses, and p-values below 10−3 were regarded significant.

Results: Two SNPs located on the telomeric end of the MHC, close to HLA-G and TRIM27, were significantly associated with CD and after replication in the larger, unselected sample set, showed modest association with the disease (p = 2x10−4; OR = 1.39 (1.17–1.66) and p = 6x10−10; OR = 3.21 (2.16–4.77), respectively). Neither of the SNPs was in LD with HLA-DR3-DQ2 or DR4-DQ8 haplotypes, and one of them remained significantly associated with disease risk after stratification for the major HLA class II determinants.

Conclusion: Further studies are necessary to confirm these results in different populations and to determine whether these SNPs are etiological polymorphisms. We are currently investigating the functional consequences of this polymorphism. Our results demonstrate that CEH conditioning is a powerful tool for the identification of minor risk variants in the MHC.

Disclosure of Interest: None declared.

PO-G-138

GLIADIN INDUCED APOPTOSIS IN T84 THREE DIMENSIONAL CELL MODEL
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Objectives and Study: Apart from HLA-DQ2, most of the genetic factors involved in celiac disease (CD) pathogenesis participate in the immune response and much less is known about secondary events that lead to intestinal tissue destruction and nutrient malabsorption. Dysregulation of apoptosis is one of the major characteristics of the mucosal damage observed in CD patients and it has been hypothesized that the increased apoptosis rate is a major factor responsible for villous atrophy in CD. Based on our previous data showing that genes for several apoptosis mechanisms are differentially expressed in celiac disease mucosa, the aim of this study was to investigate the contribution of gliadin to the induction of apoptosis in T84 intestinal cell line.

Methods: Undifferentiated and differentiated three-dimensional T84 cultures were studied. Human intestinal epithelial T84 cells were cultured in three-dimensional type I collagen gel. T84 cells were induced to differentiate by addition of 20 ng/ml human recombinant TGFβ1. T84 cells cultured within collagen gel supplemented with medium were used as undifferentiated model. After seven days PT(Pepsin-Trypsin)-gliadin was added to the culture in complete new medium at 500μg/ml and 250μg/ml concentrations, and equal concentrations of PT-BSA were used as control proteins. Apoptosis was measured using In situ Cell Death Detection Kit and the percentage of apoptotic nuclei was quantified under each condition. CASP3 expression was detected using immunofluorescence and results were expressed semiquantitatively, relative to the number of nuclei.

Results: The percentage of apoptotic nuclei was significantly higher in PT-gliadin incubated cultures, both in undifferentiated (>10% increase) and differentiated (aprox 5% increase). 0.5 μg/ml PT-gliadin induced strong CASP3
Disclosure of Interest: None declared.

PO-G-139

RELEVANCE OF THE MANUAL ORIENTATION OF THE ENDOSCOPIC BIOPSIES IN THE DIAGNOSIS OF GLUTEN-SENSITIVE ENTEROPATHY

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Objectives and Study: The method of choice for the histopathological diagnosis of gluten-sensitive enteropathy is the obtention of multiple duodenal endoscopic biopsies. It is important for the biopsies to be of good quality for its correct interpretation.

Objective: To compare the quality of duodenal biopsies with or without its manual orientation.

Methods: Endoscopic duodenal biopsies obtained from patients with suspected gluten-sensitive enteropathy were included. Both adult and pediatric patients were recruited; informed consent was obtained from all patients or their guardians. Antitransglutaminase antibodies and haplotypes HLA DQ2 and DQ8 were determined previously. At least four biopsies were obtained for all patients; half of them were manually orientated and stretched with the naked-eye over a vinyl surface with forceps before their inclusion in formalin (Group 1) and the rest were directly included in formalin (Group 2). All biopsies were reviewed blind by two pathologists and consensus was reached about their mucosal orientation and epithelium integrity.

Results: Results; Biopsies from 20 patients were included (mean age 31.05, 6 14.81, 13 women/7 men, 5 pediatric cases). AcTG were positive in 7 patients. HLADQ2 was present in 15 patients, HLA DQ8 in 3 patients, 2 patients presented both HLA types. One hundred and twelve biopsies were obtained (mean 5.6 per patient, 6 0.76). Two patients presented intraepithelial lymphocytosis compatible with Marsh 1, 7 patients presented a Marsh III lesion, 1 patient a non-specific chronic duodenitis and the rest were normal. Group 1 comprised by 59 biopsies (mean 2.95 per patient, 6 0.88) and there were 53 biopsies in group 2 (mean 2.65 per patient, 6 0.59). The pathologist considered the mucosa to be well-oriented in 84% (50/59) of biopsies of group 1 vs. 47% (25/53) in group 2 (P < 0.001). Twelve biopsies of group 1 and 13 biopsies of group 2 were demutated (P.N.S.). Only three patients of group 1 had one or no biopsy well oriented vs. 13 patients when biopsies of group 2 were considered (P=0.003).

Conclusion: Conclusions: Manual orientation of duodenal endoscopic biopsies at the moment of their obtention is useful to improve their quality without its manipulation affecting the integrity of the epithelium.

Disclosure of Interest: None declared.

PO-G-140

PROSPECTIVE STUDY ON THE INCIDENCE OF COELIAC DISEASE IN SPANISH CHILDREN (REPAC STUDY)

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Objectives and Study: Coeliac disease is an autoimmune chronic illness triggered by the ingestion of gluten in genetically predisposed people. Genetic predisposition is linked to HLA class II genes, although other non-HLA genes are also involved. Epidemiologic studies performed some decades ago estimated an incidence of 1:1000 live births, but prevalence evaluation in different European countries showed a higher frequency of coeliac disease affecting as much as 1:100 individuals. However, data about coeliac disease incidence (new cases diagnosed during a certain period) are scarce, and also the few prospective registries published so far detected incidence rates lower than 1:1000 live births. The aim of this study is to assess the incidence of new cases of coeliac disease in several geographical areas of Spain.

Methods: We conducted an observational, multicenter, prospective, nationwide registry (REPAC study) of new cases of coeliac disease in children less than 15 years of age diagnosed from 01–06–2006 until the 31–05–2007 in the participating hospitals. Catchment areas served by each hospital were clearly defined. Incidence data are expressed for each hospital and catchment area as the number of new cases:1000 live births, considering the number of live births in that area in 2006. Global incidence in all centers was estimated with the sum of the number of live births of all the areas included in the study.

Results: Data from 24 centers and their catchment areas were collected. 676 new cases of coeliac disease were registered for a population of 82,280 live births. Global estimated incidence was 8.21:1000 live births, ranging from 2.18:1000 to 14.54:1000 in different catchment areas. Estimated incidence represents the minimum range of incidence in that area as some new cases of coeliac disease could have been diagnosed in other centers.
Conclusion: This is the first prospective study of coeliac disease incidence in our country, which moreover considers many geographical areas located all over Spain. Global estimated incidence and incidence in each area are higher than those reported in other European regions using prospective registries, confirming CD is nowadays a prevalent disease and a real health and social problem in Spain.

Disclosure of Interest: None declared.

PO-G-141

STUDY OF CELIAC DISEASE IN WESTERN AUSTRALIAN CHILDREN AND ADOLESCENTS WITH TYPE I DIABETES MELLITUS

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Objectives and Study: The association between type I diabetes(DM I) and celiac disease (CD) is well established. Screening for CD is performed using measurements of IgA and IgA tissue transglutaminase antibodies (TTG). The diagnosis of CD is based on histological features of intestinal biopsy. To determine the prevalence of CD in Western Australian(WA)children with DM I. To study the demographic and biochemical features of diabetic children of WA with CD.

Methods: A retrospective study of children of WA who were diagnosed with DM I within the last 10 years (1999–2009). The details are obtained from departmental database and CD case notes. The age group of patients included in the study was 0–16 years. Newly diagnosed DM I cases in WA are generally referred to Princess Margaret Hospital which is the only tertiary pediatric hospital of WA. The new DM I cases undergo screening for CD at diagnosis of DM and two years later. The SAS9.1 method was applied to determine statistical figures.

Results: The number of children who were diagnosed with DM I within last 10 years was 1134 (females 531, 46.8% and male children 603, 53.2%). The prevalence of DM among the children of WA in the age group of 0–16 years was 2.4 per 1000 children. The number of children in the age group of 0–14 years who were diagnosed with both DM I and CD was 27(2.6%). Among children who were diagnosed with both DM I and CD, females accounted for 18.5% (22) and males accounted for 18.5% of the cases. The mean age at diagnosis of DM I in non-coeliac group was 9.2 years(SD4.2) and the mean age at diagnosis of DM in children with both DM and CD was 8.2 years(SD 3.9). Out of the 27 cases of CD, 20(74.1%) cases were diagnosed with both DM and CD at the same time. The rest of the 7(25.9%) CD cases were diagnosed with CD at least three months after being diagnosed with DM. The mean time period between the diagnosis of CD after being diagnosed with diabetes was 2.5 years(SD1.35). The mean HbA1C was 10.8(SD2.3) in non-coeliac group and 11.3(SD2.2) in celiac group.

Conclusion: There is an increase in prevalence of DM in children of WA as compared to reports of 0.59 per 1000 children, in 1988. The children with both DM and CD appear to be diagnosed with DM at a younger age compared to children with no CD. Among the CD cases, female children accounted for majority of the cases. The study supports the practice that diabetic children should be screened for CD regularly at every two years as majority of CD cases were diagnosed much later after the diagnosis of DM.

Disclosure of Interest: None declared.

PO-G-142

CELIAC DISEASE PREVALENCE IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES FROM SERBIA

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Objectives and Study: The association between celiac disease (CD) and type 1 diabetes mellitus (T1DM) is well known. Up to now, CD prevalence in children and adolescents with T1DM in Serbia has not been reported. The aim of this study was to determine CD prevalence and its clinical manifestations in our patients with T1DM.

Methods: One hundred twenty-one patients (70 girls, 51 boys, mean age 10.8 years) with T1DM (mean duration of diabetes 3.4 years) and 125 control group participants (75 girls, 50 boys, mean age 10.4 years) were tested for CD by tissue transglutaminase antibodies (tTG). In 7 serologically positive T1DM patients endoscopic small bowel biopsies were taken and examined histopathologically. In all patients with CD and T1DM age, duration of T1DM, height for age, body mass index, glycylated hemoglobin and clinical symptoms were noted.

Results: Nine patients with T1DM were positive on IgA tTG antibodies. In seven of them small bowel biopsy was performed, and all were proved to have CD by histopathology. The prevalence of biopsy-proven CD in children and adolescents with T1DM has been observed to be significantly higher in our study group when compared to controls (5.79% vs. 0.8%, P < 0.05).

Conclusion: The significantly higher prevalence of CD in children with type 1 diabetes, in accordance with the large data published in the literature, underlines the need of a regular screening of CD in patients with diabetes in order to promptly start a gluten-free diet when appropriate.

Disclosure of Interest: None declared.
PO-G-143

DIAGNOSTIC VALUE OF RAPID FINGER PRICK T-TG TEST IN DIAGNOSING COELIAC DISEASE IN HOSPITAL BASED DIAGNOSTIC CENTRE

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Objectives and Study: Current diagnostic criteria for coeliac disease (CD) are based on histological changes of small intestine, and serological markers, with antibodies against tissue transglutaminase (t-TG) being mostly used.

Rapid test for detecting antibodies against t-TG in whole blood samples has been developed recently, and has proved in many settings to be a reliable diagnostic tool in CD, especially when screening of larger population is considered.

Our aim was to determine the diagnostic value of rapid t-TG test in diagnosing new CD patients, as well as its value in detecting non-compliant patients on gluten free diet (GFD) in hospital based settings in NE Slovenia.

Methods: 310 consecutive children appointed to our hospital due to a suspected CD or seen in our celiac centre upon regular follow-up visits were included in the study. EU-tTG Quick test (Eurospital, Trieste, Italy) was used to detect t-TG antibodies from a sample of whole blood within 5 minutes and again in 10 minutes in all patients, simultaneously with t-TG ELISA test. Intestinal biopsy was confirmatory procedure in all newly diagnosed CD patients.

39 patients were considered as patients with newly diagnosed CD. 55 patients with proven CD who declared eating gluten free diet (GFD) upon regular follow-up visits were also included, as well as 4 patients that underwent gluten challenge for at least six months due to unclear initial diagnosis of CD.

Results: 33 newly discovered CD patients (84.6%) were tested positive for both t-TG ELISA and rapid t-TG test after five minutes. When the time of detection was increased to 10 minutes. The number of these patients (7.7%) were only t-TG ELISA positive.

32 patients on a GFD (58.2%) were tested t-TG ELISA positive, however only 6 of them (18.8%) were positive with rapid t-TG test after five minutes. This number has increased to 9 (28.1%) after 10 minutes.

3 out of 4 patients on a gluten challenge (75%) were tested positive for both t-TG ELISA and rapid t-TG test after five and 10 minutes.

3 control patients who were t-TG ELISA negative and also were negative genetically, were tested positive with rapid t-TG after five minutes (1.4%), this figure has increased up to 12 (3.8%) after 10 minutes.

Conclusion: Rapid t-TG test has proven to be a very useful test in detecting new CD patients in hospital settings, especially when the time of observation of the test is increased from five to 10 minutes. However its use in determining the compliance with a GFD in children was rather limited. The test has also proven to be useful in excluding CD.

We can therefore recommend the use of rapid t-TG test only for detecting new CD patients who need to undergo confirmatory intestinal biopsy, and not for the dietary monitoring upon follow-up visits.

Disclosure of Interest: None declared.

PO-G-144

DEAMIDATED GLIADIN ANTIBODY TESTS DIFFER IN CLINICAL PERFORMANCE

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Objectives and Study: Tissue transglutaminase antibodies (TTG) are considered the best serological marker for Coeliac disease (CD). Recently Deamidated gliadin (DGl) antibodies, specially IgG class, has been proposed as an extremely valuable marker as well, with the added value of not missing IgA deficient patients. Aim: To study the efficiency of Deamidated gliadin antibodies by different recently developed assays.

Methods: Phadia EliA (IgA and IgG) tests EliA Celikey® (TTG), EliA Gliadin and EliA GliadinDP (all 1:100 serum dilutions except for GliadinDP IgA (1:50) cut off values: negative <7U/ml, equivocal 7–10U/ml and positive >10U/ml.

IgA Endomysium Antibodies: In house method using Biosystems monkey esophagus coated Slides, sera dilution 1:5. Euroimmun Anti-Gliadin (GAF-3X) (IgA and IgG) (1:201 serum dilution), semiquanitative results, tests with <1 ratio are negative and with >1 ratio positive.

Inova QUANTA LiteTM Gliadin II (IgA and IgG)(1:101 serum dilution), test <20Units are negative.

300 sera were tested, 158 corresponding to active CD (ACD) cases with MARSH3 lesion, samples taken at the time of the small bowel biopsy and 142 to non CD patients with minor histological changes in the mucosa.

Results: 22/158 ACD sera were negative for EMA: 12 also negative for TTGIgA, 12 negative for DGl IgA (70% concordance) and 7 negative for DGl IgG, all of them being also negative for DGl IgA and all but 1 being negative for TTG IgA. 10 sera were negative in the Inova test for IgA and 7 for IgG, the same numbers were found for GAF-3x with a complete concordance between the 3 IgG DGl assays. In the whole group 8/158 were negative for DGl IgG in the Inova, 7/158 in the GAF-3X, 10/158 in the EliA GliadinDP IgG. 10/158 were negative in all 3 IgA DGl tests and 2 more were negative only in EliA GliadinDP IgA, thus sensitivity for IgA being lower than for IgG DGllassays.

9/141 nonCD were positive for EMA, all were TTG IgA positive and positive for IgG DGl both by Inova and GAF-3X, one being negative in the EliA GliadinDP IgG. IgG DGl was positive in respectively 7/141 (EliA GliadinDP IgA), 13/141 (Inova) and 17/141 (GAF-3X) specificity being respectively 95%, 90.8% and 87.2%. For IgG DGl specificity was 92
 %(EliA GliadinDP IgG), 88.6%(Inova) and 85.5%(GAF-3X) respectively.

**Conclusion:** Taking the histological lesion as the golden standard IgG DGl antibodies has the highest sensitivity of all tests i.e.93.7–95.5%. The highest specificity was observed for EliA GliadinDP IgA, i.e. 95%, higher than the other DGl assays (90.8% and 87.2%) and even higher than for IgATTG and EMA, both showing a specificity of 93.5%. The EliA GliadinDP IgG assay show the best efficiency by combining a high sensitivity and a high specificity, both over 90%.

**Disclosure of Interest:** M. Bolonio Grant/Research - Support from Phadia.

**PO-G-145**

**THE PREVALENCE OF CELIAC DISEASE IN CHILDREN WITH IRON DEFICIENCY ANEMIA**

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**Objectives and Study:** To determine the celiac disease (CD) prevalence in children with iron deficiency anemia (IDA) and to compare hematologic parameters between CD patients and other patients with IDA of obscure origin.

**Methods:** A total of 61 patients presenting with IDA, aged between 2–16 years, were included in this study. Hemoglobin (Hb), red cell indices (mean corpuscular volume-MCV, mean corpuscular hemoglobin-MCH, and mean corpuscular hemoglobin concentration MCHC), serum iron, iron saturation percentage and serum ferritin were determined. Venous blood samples for antigliadin antibody (AGA) and tissue transglutaminase antibody (tTG) were obtained from these patients. Upper gastrointestinal endoscopy (UGIE) was recommended to patients who had positive serology.

**Results:** Of 61 patients with ID, 13 (21.3 %) had positive serology for CD. The small intestine biopsy of the 13 patients showed villous atrophy (Marsh 3). The mean Hb level of the CD patients was significantly lower than other IDA of obscure origin patients (7.8 ± 2.6 vs 11.3 ± 0.9 g/dl, P < 0.05). There was a statistically significant negative correlation between antigliadin antibody/tissue transglutaminase antibody titers and Hb, red cell indices, serum iron, serum ferritin levels (P < 0.01).

**Conclusion:** Endoscopy and biopsies should be done as a routine investigation to every case with refractory IDA or IDA of obscure origin to exclude CD.

**Disclosure of Interest:** None declared.

**PO-G-146**

**SCREENING OF CELIAC DISEASE IN CHILDREN WITH ALOPECIA AREATA**

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**Objectives and Study:** Celiac disease (CD) is a lifelong gluten sensitive intestinal enteropathy with multifactorial etiology. Because CD is often atypical and silent on clinical grounds, many cases remain undiagnosed and CD may become apparent at any age. An association between alopecia areata and CD has recently been reported. Our aim in this study was to screening the CD in children with alopecia areata.

**Methods:** We investigated CD in 12 children with alopecia areata. Of subjects, 8 (66.7 %) were girls and 4 (33.3 %) were boys. Mean age was 8.88 ± 4.2 years (range, 3–17 years) in this study. Patients were tested for anti-tissue transglutaminase IgA. Parents of the children who had positive test result were informed about the disease, and a small intestinal biopsy was proposed. A pathologist blinded to the serology results examined all biopsy specimens according to the modified Marsh criteria.

**Results:** Of 12 children with alopecia, 5 (41.7 %) had positive anti-tissue transglutaminase IgA. Of children, 4 (80 %) were girls and one (20 %) were boys. None of the patients had chronic diarrhea abdominal pain and short stature. Biopsy of small intestinal mucosa was performed in all children. All of them had enteropathy of Type III-c according to Marsh’s criteria. We administered gluten free diet all patients.

**Conclusion:** Administration of a gluten-free diet to this patients resulted in complete hair growth. We suggest that children with alopecia areata should be screened for CD.

**Disclosure of Interest:** None declared.

**PO-G-147**

**IS THERE A DIAGNOSTIC TRANSGLUTAMINASE ANTIBODIES CUT-OFF IN A SELECTED PEDIATRIC POPULATION?**

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**Objectives and Study:** For Celiac Disease (CD) diagnosis the serological tests available for clinicians have reached a high diagnostic accuracy. As yet, small bowel biopsy remains the gold standard. Aim of our study was to evaluate a relationship among histological features and serological levels of anti-human tissue transglutaminase (tTG) antibodies, to identify a possible serological cut-off to be diagnostic among symptomatic pediatric patients.

**Methods:** 423 consecutive children (291 females) with clinical suspicion of CD were investigated for tTG IgA serum levels (ELISA, Quanta Lite h-tTG IgA–INOV A Diagnostics) and small bowel mucosal morphology (Marsh-Oberhuber classification). tTG IgA level was defined positive if >20 U. A total IgA deficiency was defined with values <0.06 g/L.
In Celiac Disease, Importance of Duodenal Bulb Biopsies

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Objectives and Study: Traditionally, for celiac disease, biopsies from the duodenal bulb have not been recommended on the assumption that the histology from this area may be difficult to interpret. The current guidelines recommend four biopsies to be taken from the distal duodenum for histological examination in celiac disease. The purpose of the study was to investigate the usefulness of duodenal bulb mucosal biopsies.

Methods: We studied all patients with a positive tissue transglutaminase antibody patient. Endoscopic biopsies were taken from the duodenal bulb and (or distal) part of the duodenum.

Results: Two hundred forty-nine patients were included, mean age 8.1 (± 4.7) years. 199 (80%) patients had abnormal distal duodenal biopsies, fifty-seven had Marsh type 1, one hundred twenty-one had Marsh type 2, and seventy-one had Marsh type 3 lesion. All but sixteen patients with abnormal distal duodenal biopsies also had abnormal bulb biopsies. Four (25%) patients had normal distal duodenal biopsies but abnormal bulb biopsies. Of these, one patient had Marsh type 2 and three had Marsh type 3 lesion. The distal duodenum was also grossly normal in these four patients. The histological diagnosis of celiac disease would not have been possible in these four cases with distal duodenal biopsies.

Conclusion: Biopsies taken from both sites can confirm histological diagnosis in all cases of celiac disease in clinical practice.

Disclosure of Interest: None declared.
sample size will be necessary to confirm the present data and to investigate the basis of this association.

**Disclosure of Interest:** None declared.

**PO-G-151**

**THE NATURAL HISTORY OF COELIAC DISEASE ANTIBODIES**

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**Objectives and Study:** The diagnosis coeliac disease (CD) is established by the golden standard of small bowel biopsies. Circulating CD antibodies at the time of diagnosis and their disappearance when following a proper gluten-free diet add extra weight to the diagnosis.

**Aim:** To evaluate the natural history of CD antibodies, anti-tissue transglutaminase (tTGA) and Endomysium (EmA), in children with CD while being on a gluten-free diet.

**Methods:** Multicenter study in 3 Dutch hospitals between January 2001 and December 2008. Inclusion criteria: 1) all patients younger than 19 years old newly diagnosed according to accepted ESPGHAN criteria and 2) having a TGA and/or EMA measurement around the moment of the diagnostic biopsies while consuming gluten; and 3) having at least 1 tTGA and/or 1 EmA measurements after starting a gluten-free diet.

In total, 8 different tTGA tests were used using as substrate guinea pig in one test (Sigma, in house assay) and human recombinant tTG (Varelisa®; Cellkey® and EliA ImmunoCap 250®; both from Phadia GmbH; Orgentec®; Diagnostica GmbH; Diarect®; AG; Roboscreen®; GmbH; Aesku-lisa® Diagnostics; Binding Site® Ltd). EmA was analyzed with standard indirect immunofluorescence tests. Statistical analyses were performed by using mixed model-repeated measurements and survival analysis.

**Results:** 130 children with CD were included (mean age 5.71 years (SD ± 4.23), male:female ratio 1:3). In total, 491 tTGA and 431 EmA determinations were performed. As expected during the gluten-free diet (tTGA and EmA decreased significantly in time ($P < 0.001$). The table shows the percentage of children becoming negative for tTGA and EmA in time while consuming a gluten-free diet.

<table>
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<tr>
<th>Time (months)</th>
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<td>tTGA**</td>
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<td>EmA</td>
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*Before starting the gluten-free diet; **The manufacturers recommended cut-off.

**Conclusion:** Doctors taking care of CD children should be aware that about 20–30% of patients will still have positive tTGA and EmA values after 18 months gluten-free diet. After 2 years, antibodies disappear in about 75–90% of the children, what is also the mean time needed for healing the small bowel mucosa in childhood CD.

**Disclosure of Interest:** None declared.

**PO-G-152**

**CHROMOSOMAL ABERRATIONS IN PERIPHERAL BLOOD LYMPHOCYTES IN PATIENTS WITH NEWLY DIAGNOSED CELIAC AND CROHN’S DISEASE**

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**Objectives and Study:** We have recently shown that paediatric patients with newly diagnosed celiac disease (CED) have an increased number of chromosomal aberrations in peripheral blood lymphocytes and that gluten-free diet has a significant lowering effect on their number (1,2). Chronic inflammation and the chromosomal instability have been both linked to an increased risk of malignancy (3), and chronic gastrointestinal diseases such as CED and Crohn’s disease (CD) have also been associated with the elevated malignancy risk (4,5). We have, therefore, decided to determine the number of chromosomal aberrations in peripheral blood lymphocytes in patients with newly diagnosed, untreated CD and CED.

**Methods:** In the 2.5 years period (06/2006 to 12/2008) we included 44 patients in the study; 19 patients with newly diagnosed CED (12/19 female, age range 1–16 y, mean 6.9 y); 13 patients with newly diagnosed CD before any treatment was started (9/13 female, age range 7–17 y, mean 12 y), and 12 healthy controls (8/12 female, age range 1–18 y, mean 8.5 y). CD and CED group did not differ compared to controls in regard to age and gender ($P = 0.5$, $P = 0.07$, $P = 0.8$, $P = 0.9$, respectively). Chromosome aberrations were analyzed in peripheral blood lymphocytes. For each subject 100 metaphases were analyzed for chromosome-type (breaks, gaps, exchange,acentric and dicentric fragments and ring chromosome) and chromatin-type aberrations (breaks, gaps, and chromatid exchange). A single cytogeneticist, who was blinded to the origin of the cells and was not involved in the treatment of the patients, performed the analyses.

**Results:** In comparison to healthy controls (mean 4 aberrations/100 metaphases), a significantly increased overall number of aberrations was found in, both, CED (mean 6.8 aberrations/100 metaphases) and in CD group (mean 6.2 aberrations/100 metaphases) ($P = 0.003$, $P = 0.04$, respectively). Increased number of aberrant cells was also found in CED (mean 6.4) and CD (mean 5.5) group compared to controls (mean 4) ($P = 0.002$, $P = 0.04$, respectively).
There was no statistically significant difference between CD and CED groups in regard to overall number of aberrations and aberrant cells ($P=0.47$, $P=0.27$, respectively).

**Conclusion:** Patients with active CED and newly diagnosed CD, before treatment was initiated, have significantly increased number of chromosomal aberrations in peripheral blood lymphocytes. This could be the link between the chronic inflammation and the increased risk for malignancy in both disorders.

**References:**

**Disclosure of Interest:** None declared.

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**PO-G-153**

**MUTATIONAL ANALYSIS OF SLC26A3 GENE AND CLINICAL CHARACTERISTICS IN KOREAN CHILDREN WITH CONGENITAL CHLORIDE DIARRHEA**


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**Objectives and Study:** Congenital chloride diarrhea (CLD) is an autosomal recessive disorder caused by mutations in the SLC26A3 gene encoding the chloride/bicarbonate exchanger in the intestinal epithelium. It is clinically presented by chloride losing diarrhea of prenatal onset leading to electrolyte imbalance or life-threatening dehydration. We analyzed the clinical characteristics and investigated the genetic background of Korean children with CLD for the first time in Asian population.

**Methods:** We retrospectively reviewed the characteristics of the 6 patients who were diagnosed with definite or presumptive CLD based on clinical diagnostic criteria. The gene analysis was performed in all patients by direct sequencing of the 20 exons and parts of exon-intron boundaries of SLC26A3 gene from genomic DNA.

**Results:** Total 6 patients (4 boys and 2 girls) were analyzed. All of them had a history of maternal polyhydramnios and represented high fecal chloride concentration (mean stool Cl$^{-}$ 146.5 mEq/L), hyponatremia (mean serum Na$^+$ 130 mEq/L), hypochloremia (mean serum Cl$^{-}$ 89.5 mEq/L) and metabolic alkalosis. The clinical features were variable in the field of initial presenting symptoms, age at diagnosis and clinical course during hospitalization. The mutations were identified in all patients and 4 novel mutations were found. They were 2 splice-site mutations (c.2063–1 G$>$ T in intron 18, c.1407+3 A$>$ C in intron 12) and 2 missense mutations (p.Pro131Leu in exon 5, p.Ser134Asn in exon 5). The most common mutation was c.2063–1G$>$T in intron 18 with an allele frequency of 70%. Two patients were homozygous for c.2063–1G$>$T and other four patients were compound heterozygous for c.2063–1G$>$T with c.1407+3 A$>$ C. p.Pro131Leu and p.Ser134Asn. There were no apparent differences in the clinical features or laboratory findings between c.2063–1G$>$T homozygotes and heterozygotes.

**Conclusion:** Since the clinical features are diverse, the analyzing of SLC26A3 gene is useful in the diagnosis of CLD. The c.2063–1G$>$T mutation screening may be used preferentially to confirm the CLD in Korean population who are clinically suspected of it.

**Disclosure of Interest:** None declared.

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**PO-G-154**

**CHANGES IN THE CLINICAL PRESENTATION OF CELIAC DISEASE AT ONE PEDIATRIC GASTROINTESTINAL UNIT OVER THE LAST DECADE**

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**Objectives and Study:** The presentation of Celiac Disease (CD) in children has changed in the last decades with a decrease in typical CD and an increase in atypical presentations. An older age at diagnosis has been observed. The aim of this study was to evaluate all cases of CD diagnosed at one Pediatric Gastrointestinal Unit (Ped GI) over the past decade. To assess changes in presentation and age at diagnosis. To study compliance with gluten free diet (GFD).

**Methods:** Medical records of all children diagnosed with CD and followed between January 1999 and August 2009 at our Ped GI unit were reviewed. Data collected included; age, sex, weight, height, reasons for investigation, serologic markers and hemoglobin level at diagnosis. The time that elapsed from diagnosis until serologic markers became negative was documented as well as, weight and height at follow-up visits. Histologic findings of the duodenal biopsy were recorded.

**Results:** 146 CD patients were diagnosed and followed at Kaplan’s Ped GI unit between 1999–2009. Ninety five were female (1:9:1). Thirty three were diagnosed between 1999–2004 (group I) and 113 between 2005–2009 (group II). Age at diagnosis 9 m-18y, mean 7.7 y. The mean age of the two groups was the same. In group I more children presented with classic CD (6/33, 18.2% vs 8/113, 7.1%, $P=0.08$) and with short stature (12/33, 36.4% vs 12/113, 10.6%, $P<0.005$). In group II more children presented with abdominal pain (44/113, 38.9% vs 6/33, 18.2%, $P<0.05$). The finding of subtotal villous atrophy on biopsy was significantly higher in group I (22/33, 69.7% vs 56/113, 49.5% $P<0.05$). 105 children were followed for at least 12 months on GFD, 83/105 (80%) adhered to GFD and became seronegative.

**Conclusion:** Over the past 5 years the number of CD cases at our Ped GI unit increased 3 fold, more children presented with abdominal pain and less with classic CD or short stature.
The finding of subtotal villous atrophy on biopsy has decreased. Compliance with GFD reached 80%.

Disclosure of Interest: None declared.

PO-G-155

FOOD-GRADE GLUTEN DEGRADING ENZYMES TO TREAT DIETARY TRANSGRESSIONS IN COELIAC ADOLESCENTS

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Objectives and Study: Enzymatic detoxification of gluten in the stomach may be helpful for coeliac disease (CD) patients who cannot follow a proper gluten-free diet. Some microbial enzymes commonly used as food supplements have shown significant gluten degrading activity in laboratory when used in combination1. The aim of this study was to investigate whether disease activity could be prevented or diminished in CD patients with lasting seropositivity by taking a cocktail of these enzymes in capsules at the time when meals with possible gluten are consumed.

Methods: We conducted a placebo-controlled, randomised, double-blind study. Inclusion criteria were age above 12 years and biopsy-proven CD with stably persisting seropositivity for transglutaminase antibodies (TG-Ab) on a self-reportedly fairly followed gluten exclusion diet for more than 1 year. The treatment schedule included placebo for the initial 4 weeks. Then subjects were randomised into enzyme (A) or placebo (B) groups for 12 weeks. After 12 weeks, group B received enzymes and group A continued with enzymes plus 2x500 mg per day gluten powder for another 12 weeks. Patients were instructed to not change their dietary habits. Disease activity was monitored by serum TG-Ab, small bowel biopsy and diet questionnaire. Primary endpoints were seronegativity or at least 50% decrease in serum TG-Ab levels.

Results: 35 CD patients (median age 17 years) were randomised, of them 26 completed all periods and 17 volunteered for biopsy before and after the treatment. Large changes (-60%+420%) in serum TG-Ab occurred in the first 4 weeks. In the subsequent periods, no significant differences were observed between placebo and treatment groups: 10.6% increase in median TG-Ab levels (range: -31+148%) with placebo versus 27.6% increase (range -38.7+198%) with enzymes. Only 3 treated patients achieved primary endpoints. Addition of 1 g/day gluten to the diet did not result in appreciable changes in antibodies in most subjects.

Conclusion: Notwithstanding our inability to demonstrate efficacy of food-grade enzymes for reversing disease activity in this cohort, such CD patients represent an important target for future non-dietary therapies. Two findings must be considered in the design of future therapeutic trials. First, the drug candidate should be able to protect against a daily consumption of more than 1 g gluten. Second, a subset of patients in such a study will likely feel adequately protected and will consequently increase gluten consumption.

Reference:

Disclosure of Interest: None declared.

PO-G-156

INTRACTABLE DIARRHEA WITH TUFTING ENTEROPATHY: CORRELATION BETWEEN HISTOLOGICAL LESIONS AND CLINICAL COURSE

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Objectives and Study: Tufting enteropathy is a congenital intestinal mucosa developmental disease characterized by severe intestinal insufficiency leading to dependence on parenteral nutrition and, in some cases, small bowel transplantation. In rare cases, a more favourable evolution has been reported. The aim of this study is to evaluate possible correlations between the intensity of the histological lesions in duodenal biopsies and the clinical outcome in children with tufting enteropathy treated in our institution.

Methods: Between 1993 and 2003, children were diagnosed with tufting enteropathy on the basis of the following criteria: 1) intractable diarrhea of neonatal onset with prolonged dependence on parenteral nutrition; 2) histological lesions of the intestinal mucosa: villous atrophy, epithelial dysplasia with enterocyte dedifferentiation and disorganization (“tufting”) of the surface epithelium, abnormal crypts. The histological lesions were semi-quantified and compared according to evolution over time and dependence on parenteral nutrition.

Results: Seven children, all from consanguineous parents, were followed for a median duration of 6.5 years. Three were definitively weaned from parenteral nutrition and experienced normal growth without nutritional assistance. These 3 children had severe diffuse histological lesions on initial biopsies. Although more focal, histological lesions were nevertheless always present at definitive parenteral nutrition weaning in 2 of these 3 patients.

Conclusion: Progressive suppression of parenteral nutrition is possible in some children with tufting enteropathy. In our experience, this favourable outcome could not be predicted from the intensity of the histological lesions. In the future, new biomarkers could best identify these lesions and their evolution.

 Disclosure of Interest: None declared.
PO-G-157

A NOVEL ALGORITHM FOR CHILDOOD CELIAC DISEASE SEROLOGICAL DIAGNOSIS BASED UPON INTESTINAL BIOPSIES

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Objectives and Study: There is a worldwide concomitant increase in both celiac disease (CD) diagnosis and the number of commercial assays for CD. There is a great need to select the best reliable serological assay for intestinal biopsy performance. The aim of the present study was to evaluate the performance and the diagnostic accuracy of 15 different assays for CD, in order to design the best case finding algorithm in an outpatient population setting.

Methods: 15 different assays were used to compare 55 blood samples of CD children (positive biopsy) to 52 samples from age and sex matched children with normal biopsy results; 7 ELISA assays for tissue transglutaminase antibodies (tTG), 4 ELISA assays for gliadin new-generation antibodies, 2 ELISA assays for combined gliadin and tTG antibodies, and 2 chemiluminescent immunoassays for tTG antibodies. Endomysial antibodies and total IgA were also measured. All patients were on gluten containing diet and the samples were drawn on the day of the biopsy. Scoring criteria were established for grading the assays performance and characteristics (analytical parameters, as well as statistical data -sensitivity, specificity, PPV, NPV, ROC analysis, participation in EQC).

Results: The combined IgA+IgG antibodies detecting assay against the gliadin- tTG complex exhibited the best sensitivity (100%). By adding 2 other ELISA assays with best specificities (detecting tTG-IgA or tTG-IgA+IgG antibodies), we were able to design a new cost effective algorithm for celiac detection with 100% sensitivity, 96.4% specificity and 93.5% accuracy.

Conclusion: The new generated IgG+IgA antibodies detecting assay against the new epitopes of the gliadin - tTG complex is the most effective first line diagnostic test for childhood CD. Adding 2 tTG-IgA+IgG diagnostic assays, in the second line, improves specificity. The better performance achieved with the cost-effective new algorithm represent a step forward in the debate of the need for intestinal biopsies performance for childhood CD diagnosis.

Disclosure of Interest: None declared.

PO-G-158

NOVEL SEROLOGIC MARKER FOR COELIC DISEASE - ANTIBODIES AGAINST DEAMIDATED GLIADIN

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Objectives and Study: Coeliac disease (CD) is an immune-mediated enteropathy cause by a permanent sensitivity to gluten in genetically susceptible individuals. It is recommended to perform serological test for CD in children with failure to thrive, persistent diarrhea or other persisting gastrointestinal symptoms and in asymptomatic children who have conditions associated with CD. There are different serological tests for detecting CD: anti-tissue transglutaminase IgA (tTG), anti-endomysium IgA (EMA), anti-gliadin IgA and IgG (AGA IgA and AGA IgG) antibodies. Measurement of anti-tTG IgA is recommended for initial testing for CD. Recently it was shown that antibodies recognizing partially deamidated gliadin have higher sensitivity and specificity for CD in comparison to antibodies recognizing native gliadin. The aim of the study was to assess the diagnostic performance of new ELISA test in which the antigen represents a repetitive motive of deamidated gliadin peptides (GAF-3X) and to compare it with anti-tTG test.

Methods: Study included 56 pediatric patients (F/M = 37/19; median age 11 years (range 7–15), for whom CD serology was requested. Anti-GAF-3X IgA and IgG together with anti-tTG IgA antibodies were measured in all sera using ELISA assays (Euroimmun, Lübeck, Germany). Manufacturer proposed cut off values were 20 RU/mL for anti-tTG and 25 RU/ml for GAF-3X IgA and IgG.

Results: Out of 56 patients 8 were positive for all 3 autoantibodies type, 1 for GAF-3X IgA and anti-tTG, 13 for anti-tTG and 1 for anti-GAF-3X IgA only. CD was biopsy confirmed in 14 patients of whom 7 were positive for all 3 autoantibodies type, 1 for anti-tTG and GAF-3X IgA and 2 for anti-tTG only. The residual 4 CD confirmed patients were on gluten free diet and 3 of them were seronegative while anti-tTG was positive in one.

With cut off values proposed by the manufacturer sensitivity and specificity was 100% and 73.8% for anti-tTG, 80.0% and 95.2% for anti-GAF-3X IgA and 70.0% and 97.6% for anti-GAF-3X IgG. According to ROC analysis, sensitivity and specificity for anti-tTG IgA was 100% and 95.2%, for anti-GAF-3X IgA 90.0% and 92.9%, and for anti-GAF-3X IgG 70.0% and 97.6% RU/mL, respectively. Optimal cut-off value for tTG-IgA was 48.6 RU/mL, and 22 RU/mL for both anti-GAF-3X IgA and anti-GAF-3X IgG.

The correlation between anti-tTG IgA and GAF-3X IgA or GAF-3X IgG was weak, but statistically significant (P < 0.001).

Conclusion: Determination of anti-GAF-3X along with anti-tTG with the use of appropriate cut off values can increase the overall sensitivity and specificity of CD screening panel. Anti-GAF-3X could be a better marker of dietary compliance than anti-tTG.

Disclosure of Interest: None declared.
PO-G-159

GLUTEN CONSUMPTION HABITS IN INFANTS OF THE REGIONAL COMMUNITY OF VALENCIA

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Objectives and Study: Coeliac disease (CD) is the most common food intolerance in Europe. Recent studies have shown that the timing of gluten introduction in relation to breast-feeding as well as the amount of gluten could be responsible for a higher incidence of the disease.

Aim: To develop and validate a frequency questionnaire (FFQ) to assess gluten consumption in children aged 6–36 months in Valencia (Spain).

Methods: Firstly, we prospectively collected information on the gluten-containing foods consumed by healthy children aged 3–36 months. All the products were then included in two different FFQs: one for infants aged 6–12 months and another for those aged 12–36 months old. To calculate the amount of gluten contained in these products we multiplied the content of vegetable proteins by 0.8 (Overbeek et al). The FFQs were validated by comparing the results obtained with a 7 days food registry.

Results: A total of 404 children participated in the study. No gluten consumption was referred below the age of 6 months (N = 80), and at the age of 9 months all had introduced gluten in their diet. In the 7–12 months age group (n = 111), the mean daily gluten intake was 2436 mg, and the most important gluten-containing food products consumed were bread, cereals, muffins and croissants. Mean daily gluten intake at 12–18 months was 5527 mg, 7139 mg at 18–24 months and 6997 mg at 24–36 months.

Conclusion: We have developed and validated two FFQs for infants aged 3–36 months, and this has allowed us to establish for the first time gluten consumption habits in Spanish infants.

Disclosure of Interest: None declared.

PO-G-160

EVALUATION OF PSYCHOLOGICAL IMPACT OF COELIAC DIAGNOSIS AND GLUTEN-FREE DIET DURING THE FOLLOW-UP IN SCHOOL CHILDREN DETECTED BY SALIVARY SCREENING

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Objectives and Study: Background: The usefulness of screening programs for coeliac disease (CD) is debated because of the low compliance to gluten-free diet (GFD) of adolescents and adults. Aim: Our aim was to evaluate the compliance to the GFD, the growth improvement, the psychological impact, and the well-being of a group of children with CD detected by a salivary screening test during the follow-up.

Methods: During the follow-up, a mean of 7.53 ± 0.82 months, 27 out of 34 asymptomatic CD screening detected children (mean age ± SD: 7.53 ± 0.82) were enrolled in follow-up program. During the follow-up, the CD diagnosis was confirmed by positive anti-tTG and anti-gliadin antibodies. The questionnaire was administered to parents asking information about alimentary family habits, incidence of seasonal infections and about GFD. We used 12 items divided in three sectors: “communication”, “having CD” and “diet”.

Results: All children showed a strict adherence to GFD and after at least 6–12 months tTGAb become negative. A weight and stature increase was also registered, reaching, after 12 months follow-up, a mean ± SD of 4.48 ± 2 Kg and 7.1 ± 1.22 cm, respectively. 4 children reached 24 months of follow-up with a mean ± SD weight and stature increase of 7.42 ± 6.76 Kg and 10.9 ± 0.98 cm respectively. It is worth noting that the weight increased of 1.9 ± 1 Kg and the height 3 ± 1.4 cm in only three months. Parents showed a great satisfaction for the screening and referred an increase of children’s appetite, an improvement of school and sport performances and a decrease of seasonal infections. Children’s answers showed a good facility of talking about CD and their diet. Nevertheless they complain about following GFD all life long.

Conclusion: Until now, the compliance to the GFD in screening detected CD patients has been optimal with a significant increase of the anthropometric parameters. The results of questionnaire prove a psychological impact of GFD comparable to that of Dutch symptomatic CD children. Parents demonstrated good skills facing CD problems and children exigencies organizing at least once a day gluten-free meals for all members of family. A longer follow-up might show if an early diagnosis in asymptomatic primary school-children will be followed by a long lasting compliance to a strict GFD.

Disclosure of Interest: None declared.

PO-G-161

COMBINATION OF MARSH IIIC MUCOSAL LESION ON THE FIRST SMALL BOWEL BIOPSY AND POSITIVE ANTIENDOMYSIUM ANTIBODIES IS SUFFICIENT FOR THE DIAGNOSIS OF COELIAC DISEASE IN PATIENTS YOUNGER THAN AGE 2 YEARS

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**Objectives and Study:** Diagnosis of celiac disease (CD), according to the revised criteria from 1990 (1), is based on small intestinal biopsy finding of the typical mucosal lesion and full clinical remission after gluten withdrawal. However, in children younger than two years, after initial biopsy, gluten challenge is still advisable, preceded and followed by the second and the third small bowel biopsy.

Aim of this study was to determine the predictive value of the combination of small intestinal biopsy finding and serologic markers for establishing the diagnosis of CD in children younger than two years at disease presentation.

**Methods:** One hundred children younger than two years who had the initial biopsy finding consistent with CD were included and prospectively followed since 1995. In 85 patients the “old” ESPGHAN criteria, based on three small bowel biopsies, were completed, confirming CD in 50/85 patients (69%) (group A). The other 35 patients (31%) (group B) either did not have CD or would eventually develop mucosal lesion (late relapsers). For a statistical analysis, chi square test, logistic regression and stepwise method were used.

**Results:** Groups A and B did not differ (P > 0.05) in clinical presentation in respect to: failure to thrive (96 vs 69%), diarrhea (81 vs 69%) and abdominal distension (73 vs 60%). However, the group A, at the time of the initial biopsy, had significantly more Marsh IIIc mucosal lesions (82 vs 25%, P < 0.01) and significantly more positive serological results: IgA antigliadin (AGA) (88 vs 24%, P < 0.01), IgG AGA (98 vs 59%, P < 0.01) and antienzymysium antibodies (EMA) (88 vs 17%). The best predictors for the final diagnosis of CD were Marsh IIIc (odds ratio 6.27, 95% confidence interval 1.51–25.98) on the initial small bowel biopsy and positive EMA (odds ratio 11.33, 95% confidence interval 2.74–46.85). Based on that, in 36/50 (72%) of our patients with proven CD (group A) the diagnosis could have been made after the first small bowel biopsy, while the rest should have completed the “old” criteria based on three biopsies.

**Conclusion:** In children younger than age two years, CD can be diagnosed after the first small bowel biopsy if there is a typical mucosal lesion of Marsh IIIc and positive EMA.

**Reference:**


**Disclosure of Interest:** None declared.

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**PO-G-162**

**QT PROLONGATION IN PAEDIATRIC COELIAC PATIENTS**


**Objectives and Study:** Several diseases may be associated with coeliac disease (CD) such as osteoporosis, dermatitis herpetiforme, chronic hepatitis, insulin-dependent diabetes and autoimmune thyroiditis. In adult patients idiopathic dilated cardiomyopathy myocarditis and prolonged QT interval have been described. However, up to now, no study has been performed in order to evaluate heart abnormalities after a gluten free diet(GFD). The aim of this study was to perform an electrocardiographic study in a series of CD children and adolescents at CD diagnosis on a gluten-containing diet.

**Methods:** We studied 60 CD children and adolescent (24 males, aged from 6–17 years), collected in the Paediatric Department of “Sapienza” University of Rome. Coeliac disease was diagnosed according to the North American Society for Pediatric Gastroenterology Hepatology and Nutrition criteria. Before the endoscopy, all patients underwent ECG.

All electrocardiograms were reviewed by the same observer and QT interval, as corrected for heart rate (QTc), was calculated according to Bazett’s formula and compared with the generally accepted upper normal limit for QTc (440 ms). No patient had a history of taking drugs known to induce QT prolongation. Patients with abnormalities were re-tested for ECG after 12 months of GFD.

**Results:** QTc interval was significantly more prolonged in 3 CD females out of 60 children (5%), showing normal electrolytes concentration. After 12 months of GFD, abnormal QTc interval was found normalized in all 3 patients. No other electrocardiographic abnormalities were found in children investigated.

**Conclusion:** Our results demonstrate that not only in adults but also in children a significant QTc prolongation could be found, and it reverses on a GFD. Although the QTc abnormality was mild, it should not be overlooked since the long QTc syndrome is associated with an increased risk of ventricular arrhythmias, syncope and sudden heart. This risk should be taken into account in subjects who undergo narcosis for endoscopy. The exact mechanism of QTc prolongation in CD patients is still unclear. Our study shows that electrolytes imbalance is not responsible of ECG abnormalities. A possible role might be played by nutritional deficiencies or autoimmune processes involved in CD.

**Disclosure of Interest:** None declared.

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**PO-G-163**

**ANTIBODIES AGAINST DEAMIDATED GLIADIN PEPTIDES OUTPERFORM ANTI-ENDOMYSIUM AND TISSUE TRANSGLUTAMINASE ANTIBODIES IN CHILDREN <2 YEARS**

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Objectives and Study: Immunoglobulin A (IgA) auto-antibodies against endomysium (EMA) and tissue transglutaminase (tTGA) are considered the most reliable serological tests to screen for celiac disease (CD). However, newly developed commercial ELISA tests using deamidated gliadin peptides (DGP) antigens may be of additional diagnostic value, especially in very young children, where EMA and tTGA have shown to be diagnostically less accurate. The aim of the present study was to determine the diagnostic accuracy of a new commercial ELISA kit (Bindazyme Human Anti-Gliadin EIA Kit IgG and IgA, The Binding Site, Birmingham, UK) and thereby determine whether antibodies against DGP (a-DGP) are useful in clinical practice, especially in young children.

Methods: The sera of 262 paediatric patients suspected of having CD were tested for EMA, tTGA and IgA and Immunoglobulin G (IgG) a-DGP. All patients had undergone a small intestinal biopsy to confirm or exclude CD. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using histology as the gold standard for CD. Additionally, these values were specifically calculated for children <2 years.

Results: One-hundred and forty-nine (56.9%) patients had a Marsh III lesion and where therefore diagnosed with CD. The sensitivity, specificity, PPV and NPV for IgA a-DGP were 72%, 92%, 92% and 71% respectively. For IgG a-DGP these values were 92%, 84%, 88% and 89% respectively. Sensitivity for EMA and tTGA were clearly better (98% and 97% respectively). However, specificities were disappointing, with values of 66% and 83% for EMA and tTGA respectively. The PPV and NPV for EMA was 79% and 96% and for tTGA 88% and 96%. However when the analysis was restricted to the 55 children <2 years, no misclassifications occurred when using IgG a-DGP; both sensitivity, specificity, PPV and NPV were 100%. Sensitivity for IgA a-DGP, EMA and tTGA was 85%, 95% and 98% respectively, with a specificity of 100%, 93% and 100%. The PPV was 100%, 97% and 100%, while the NPV was 71%, 88% and 94%.

Conclusion: In an overall analysis the antibody assay against deamidated gliadin did not outperform tTGA. However, when used in children <2 years IgG a-DGP had a 100% sensitivity and specificity for CD. In this specific age group IgG a-DGP seems to be preferred above tTGA.

Disclosure of Interest: None declared.

PO-G-165
TUFTING ENTEROPATHY: THE CLINICAL SPECTRUM
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Objectives and Study: Congenital Tufting Enteropathy (CTE) or intestinal epithelial cell dysplasia is a rare autosomal recessive diarrhoeal disorder. Most patients are dependent on parenteral nutrition (PN), but there are some variations in the clinical spectrum of presentation, associated morbidity, and long term outcome. The purpose of this study was to identify the magnitude of such variations, their significance and whether some patients can be weaned off PN in later life.

Methods: We retrospectively analyzed the data of 11 patients presenting with the histological appearance of epithelial cell tufting on intestinal biopsies between 1997 and 2008. We reviewed their demographics, clinical presentation, gastrointestinal areas affected histologically, weight gain, growth, need for PN, enteral feed tolerance, spectrum
of medical and surgical treatment, and associated morbidity and mortality.

**Results:** Eleven children (6 female) with CTE were identified and diagnosed at a median age of 4.5 years (range 8 weeks-18 years). The presenting features included diarrhoea (n = 10), vomiting (n = 8), and faltering weight gain (n = 7). Over the years of treatment and follow-up, most patients were gaining weight satisfactorily (n = 8), but the majority were not growing satisfactorily (n = 7). There was a proven delay in bone age in 6 out of 8 patients ranging from 10 months to 6 years delay with a median of 2 years in those who were affected. All teenagers had pubertal delay (n = 4). All patients were started on PN during infancy. Currently, three patients including one adult are still dependent on daily PN, two were weaned off PN and 6 patients are partially dependent on PN. Associated morbidity included GORD (n = 7), malrotation (n = 3), anti-cardiolipin thrombotic tendency (n = 2), gall stones (n = 2) and renal calculi (n = 1). In addition to the usual surgical interventions done for the above conditions, 2 patients had pyloromyotomy.

**Conclusion:** Although the current management practice for patients with CTE has helped with weight gain, it hasn’t improved their linear growth. There is a proven bone age delay and pubertal delay in those patients. Most patients could tolerate enteral feeding to a variable extent. Total enteral feeding is possible eventually in some children. We have identified a number of gastrointestinal and extra-gastrointestinal associations. Large studies (preferably multi-centre) are needed to verify the whole spectrum of associated morbidities. Well organised randomised controlled trials of measures to improve the height gain of children with CTE are recommended.

**Disclosure of Interest:** None declared.

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**PO-G-166**

**COAGULATION DISORDERS IN CHILDREN AND ADOLESCENTS WITH CELIAC DISEASE AT THE DIAGNOSIS**

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**Objectives and Study:** In western countries coeliac disease (CD) represents the most common malabsorptive disease. Among many others, one of the nutrients for which absorption can be impaired is vitamin K, which causes prolongation of the coagulation tests.

**Aim:** The aim of the present study was to evaluate the prevalence of coagulation disorders in a series of coeliac children and adolescents.

**Methods:** We carried out a cross-sectional analysis of data collected on 233 children and adolescents (85 males, age range: 11 months-19 years, median: 6.25 years) with CD diagnosed according to the NASPGHAN criteria, from February 2005 to November 2009. INR and PTT were collected before they underwent endoscopy and, when abnormal, repeated after intramuscular vitamin K administration. Prolonged INR was defined as >1.2, while prolonged PTT was defined as >35 seconds. Symptoms and BMI at the onset were registered; patients were classified according to the clinical form (typical, atypical and silent)

**Results:** Among 174 symptomatic patients the most frequent symptom was abdominal pain. 47.2% of patients showed a typical form of CD, 27.5% an atypical and 25.3% a silent form. 13 children (5.6%) reported prolonged INR. Among these, one female who didn’t improve INR after intramuscular vitamin K administration, showed factor VII deficiency. Moreover, three young babies (2 females, 1.5-2.8 years of age) with INR of 2.2, 1.32 and 1.27, complained worst clinical conditions (anorexia, abdominal distension and diarrhoea) and low BMI percentile (1st - 4th). In 16 children (7%) a prolonged PTT was found. Among these, a female showed the deficiency of XI factor, while another showed the presence of lupus anticoagulant antibodies.

**Conclusion:** The results of our study, performed in a large series of coeliac children and adolescents demonstrate a prevalence of prolonged INR and prolonged PTT of 5.6% and 7%, respectively. However, no patient showed any clinical signs of altered coagulation. Coagulation disorders should be related to malabsorption, as suggested by improvement after intramuscular vitamin K administration. This study suggests that there is need for coagulation disorders screening among patients with coeliac disease before performing the intestinal biopsies, in order to correct vitamin K impairment and exclude deficit of specific coagulation factors.

**Disclosure of Interest:** None declared.

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**PO-G-167**

**HOW MANY INTESTINAL BIOPSIES ARE NECESSARY TO CONFIRM THE DIAGNOSIS OF CELIAC DISEASE: THREE, TWO, ONE, . . OR NONE?**

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**Objectives and Study:** In 1969, ESPGAN strongly recommended three sequential biopsies for diagnosing celiac disease (CD) [1]. Twenty years later, ESPGHAN revised its former diagnostic criteria, maintaining the mandatory requirement of a first biopsy.[2]. The aim of our study is to evaluate if intestinal biopsy should be avoided in specific cases of children with classic CD clinical presentation, and in certain on-risk groups for CD, using in combination with positive determination of HLA DQ2/ DQ8, serologic CD markers, and good response (both clinical and serological) to gluten withdrawal.

**Methods:** Retrospective study, including 165 children and adolescents 3 (1–19) years old, 62% female, with intestinal
biopsy performed because CD suspect, and determinations of CD clinical manifestations, associated diseases, serologic CD markers, HLA DQ2/DQ8 and response to gluten withdrawal. The diagnostic rule to proof was: CD clinical manifestation or CD related diseases and positive EMA and/or tTGA and HLA DQ2 and/or DQ8, using the intestinal biopsy results as gold standard. Negative predictive value (NPV), sensitivity (Se), false negative (FN), positive predictive value (PPV), specificity (Sp) and false positive (FP) for clinical rule were estimated. All calculations were performed with SPSS 15.0 software statistical package.

Results: According to intestinal biopsy results 158 patients suffer CD and 7 not. Independently applying the clinical diagnostic rule 156 patients were CD classified and 9 not. The validity characteristics of the rule were:

NPV Se FN PPV Sp FP
78% 99% 1% 100% 100% 0%

Conclusion: Children showing classic CD clinical presentation should be confirmed without needing an intestinal biopsy. More extensive studies are necessary in larger paediatric and adult population in order to corroborate this conclusion and new revised diagnostic Criteria are needed based on new diagnostic approaches on genetic, immunology and gluten withdrawal response, enabling performing intestinal biopsies only in selected cases.

References:

Disclosure of Interest: None declared.

PO-G-168

INTESTINAL FATTY ACID-BINDING PROTEIN IN GLUTEN GENETICALLY PREDISPOSED SUBJECTS AND IN CHILDREN WITH SEVERE MALNUTRITION

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Objectives and Study: The intestinal fatty acid–binding protein (I-FABP) is strictly confined to the small intestine and it is involved in the triglycerides synthesis and secretion. The I-FABP’s normal serum concentration is lower than 200 pg/ml and it is due to the enterocytes' physiological turnover over. The elevated serum levels of I-FABP (>200 pg/ml) represent the consequence of a vascular or inflammatory acute episode, therefore I-FABP may be an early and sensitive plasma marker of intestinal injury. The aim of this study is to measure the I-FABP’s serum levels in healthy subjects, in celiacs, in severely malnourished children and in subjects genetically predisposed to gluten intolerance but without intestinal lesions or serological markers (anti-tissue transglutaminase or anti endomysium antibodies) typical of celiac disease (CD).

Methods: We enrolled 100 healthy subjects (median age 30y); 37 biopsy proven celiacs (median age 10y): 18/37 were symptomatic, 19/37 were asymptomatic; 16 severely malnourished children (median age 3y, W/H <70%) hospitalized at the “Divina Providencia” hospital in Luanda; 19 subjects genetically predisposed to gluten intolerance at risk of celiac disease (first degree relatives of celiac patients, median age 30y): 13/19 suffered from anaemia, explosive diarrhoea, pancytopenia, chronic fatigue, these subjects were tested before and after a year of a gluten free diet. The Elisa tests were performed following manufacturer’s instructions (HBT human I-FABP test). Our cut-off was previously calculated on 200 healthy subjects and expressed as the mean value plus 1 Standard Deviation (cut-off = 170 pg/ml).

Results: 5/100 healthy subjects were positive (specificity 95%). 24/37 celiacs were tested positive (sensitivity 70%): 16/24 were symptomatic and 8/24 were asymptomatic. In general, the I-FABP concentration of symptomatic celiacs and of asymptomatic celiacs were significantly different: 1145 pg/ml vs 342 pg/ml (P < 0.001). 13/16 severely malnourished children were tested positive with a mean I-FABP’s value of 562 pg/ml. 15/19 subjects genetically predisposed to the gluten intolerance were tested positive during the gluten containing diet and after a year of a gluten free diet 12/15 were tested negative and all the symptomatic subject dramatically improved.

Conclusion: The I-FABP is a useful marker to identify subjects (first degree relatives of celiac patients) with gluten dependent complaints in absence of the CD’s diagnostic criteria. In severely malnourished children the I-FABP high concentration indiate a mucosal lesion and this test might be useful for monitoring the nutritional rehabilitation in the future.

Disclosure of Interest: None declared.

PO-G-169

ENVIRONMENTAL FACTORS IN COELIAC DISEASE: A NATIONWIDE CASE-CONTROL STUDY (REPAC STUDY)

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Objectives and Study: Beside gluten intake, other environmental factors, insufficiently recognized, but probably acting at an early age, play a role in Coeliac disease (CD) development. The aim is to study the current presentation pattern of CD in our country together with environmental risk factors for CD development.
Methods: Prospective observational study and nationwide registry in Spain (REPAC), including all new CD cases in children (<15 years), from 06–2006 until the 05–2007. Participating centres have a well-established health area and population. Presentation patterns at diagnosis were recorded. Case/control 1:1 study with children paired for age and sex. Recorded data: nursery attendance, breast feeding, age at gluten introduction and infections 6 months prior to diagnosis. Paired analysis by univariate analysis of case/control pairs for each variable independently and by multivariate analysis (conditional logistic regression) for case/control 1:1.

Results: 39 hospitals included 993 new CD cases (60% women) and 744 paired controls. Mean age at diagnosis 3.7 years (DS 3.2), 39% younger than 2 yrs and 19% between 6–15 yrs. 7% were silent and 71% classic, 91% younger than 2 yrs, whereas paucisymptomatic and silent predominated in the 6–15 yrs group (respectively 46% and 25%) (P<0.0001). The most frequent symptom for <6 years was abdominal distension and for 6–15 yrs hyporexia, anorexia and ferropenia. The most frequent associated diseases were IgA deficiency (3%), diabetes type I (2.3%), thyroid disorders (2%) and Down’s syndrome (1.2%). In the case/control study 650 paired cases were analyzed. Having a first-degree relative with CD increases 2.5 times the risk for CD. No influence of nursery attendance or exanthematic disease was observed. Acute gastroenteritis multiplies the risk by 1.4 and muguet by 2.4 (statistically significant in the univariate but not in the multivariate analysis). Gluten introduction while the infant is still breast-fed reduces by 58–62% the disease risk and upper respiratory infections by 1.4 and muguet by 2.4 (statistically significant in the univariate and in one of the multivariate analysis).

Conclusion: Classic CD and onset at early ages are still the most characteristic features of CD in our milieu. In older children abdominal distension, hyporexia and ferropenia should prompt active search for CD. The observed protective role of mild respiratory infections has not been described in previous studies. We confirm the protective role of gluten introduction during breast feeding, thus this dietary recommendation should be advised especially in at-risk groups.

Disclosure of Interest: None declared.

PO-G-170

HLA-GENOTYPE DOESN’T INFLUENCE ON CELIAC DISEASE PHENOTYPE

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Objectives and Study: The HLA DQ gene dose effect has been widely studied, based on the T-cell capacity to produce a higher response depending on the antigen-presenting cells HLA-DQ and thus, this may have an influence on the CD phenotypes. Several papers have been published over this aspect with different results. Our aim is to establish the relationship between HLA genotype and phenotype in CD studying a large number of patients.

Methods: 396 children diagnosed with celiac disease in our unit between 1985 and 2008 in whom HLA genotype (DQB1 and DRB1) had been performed and data when diagnosis were available.

The children were divided in four groups based on the genotype relative risk of presenting celiac disease according to Vermeulen et al(*) that meets our data: 1) High: DQ2DR3/DQ2DR3, DQ2DR3/DQ2DR7 2) Substantial: DQ2DR3/DQ7DR5, DQ2DR7/DQ7DR5 3) Moderate: HLA DQ2DR3/DQ*DR different from DQ2DR3, DQ2DR7, DQ7DR5; 4)Low. Any other 78 variables were studied. Clinical information had been collected from an interview to the parents when diagnosis was made. We recovered from our Unit database (FileMaker 5.0 for Mac) data prior to diagnosis: anthropometric measures (z-score), nutritional and other plasma levels, CD specific and other autoimmune disease plasma levels, stool fats levels and anatomic pathologic results.

Results: The genotype risk children’s distribution were: High 168 (43%), Substantial 91 (23%), Moderate 115 (29.4%), Low 17 (4.3%) The mean age on diagnosis was 3.01 ± 2.73 years.

A few variables are shown in the table. We didn’t find any statistical difference between the HLA-risk groups in any of the studied variables.

Table:

<table>
<thead>
<tr>
<th>HLA-risk Variables</th>
<th>High</th>
<th>Substantial</th>
<th>Moderate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation of symptoms (months)</td>
<td>23.3 ± 21.8</td>
<td>19.6 ± 16.1</td>
<td>16.9 ± 13.8</td>
<td>25.8 ± 45.4</td>
</tr>
<tr>
<td>Diarrhoea at presentation (n an %)</td>
<td>75 (44.6%)</td>
<td>38 (47.9%)</td>
<td>54 (43.5%)</td>
<td>8 (39%)</td>
</tr>
<tr>
<td>Weight SDS at diagnosis</td>
<td>−0.97 ± 0.97</td>
<td>−1.01 ± 1.1</td>
<td>−1.27 ± 0.90</td>
<td>−1.35 ± 1.24</td>
</tr>
<tr>
<td>Ferritin levels (mg/dl)</td>
<td>16.6 ± 19.5</td>
<td>18.6 ± 22.9</td>
<td>16.8 ± 18.2</td>
<td>10.9 ± 6.8</td>
</tr>
<tr>
<td>Stool fat levels (g/24 h)</td>
<td>5 ± 3.9</td>
<td>4.3 ± 2.5</td>
<td>4.3 ± 2.6</td>
<td>6.9 ± 3.7</td>
</tr>
</tbody>
</table>

Mean and standart desviation of some variables.

Conclusion: Although some authors found a relationship between the HLA genotype risk and the phenotypic expression of CD, we haven’t found any difference in a large number of patients in a large number of variables, so we can conclude that, at least in our area, the HLA genotype don’t have an influence on the clinical symptoms, anthropometric measures, biochemical serum levels nor faecal fat levels, prior the diagnosis of CD.


Disclosure of Interest: None declared.
PO-G-171

PREVALENCE OF CELIAC DISEASE IN TURKISH SCHOOL CHILDREN

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Objectives and Study: Epidemiologic studies of Celiac disease (CD) in Turkey have been performed only within some regions of the country. The aim of this study is to determine the prevalence of CD in Turkish school children.

Methods: Between January 2006 and May 2008, serum samples were collected from 20190 students (age range, 6 to 17 years) in 139 schools in 62 municipalities from different regions of Turkey. CD was screened by using the anti-tissue transglutaminase IgA and total serum IgA. Subjects with selective IgA deficiency were further tested for anti-tissue transglutaminase IgA or IgG. The cutoff level for transglutaminase IgA defining a positive result was set at 20 RU/ml. Total serum IgA level was analyzed by using a routine nephelometric assay and serum levels below 0.05 g per liter were considered indicative of selective IgA deficiency. Serum samples which are positive for anti-tissue transglutaminase IgA or IgG were further tested for IgA anti-endomysial antibodies with indirect immunofluorescence method. Small intestinal biopsy was offered to all subjects with anti tissue transglutaminase antibody positivity.

Results: Of the 20190 subjects, 489 were positive for antibodies (only IgA anti-tissue transglutaminase antibody in 270, both IgG and IgA anti-endomysial antibody in 108 and IgG anti-tissue transglutaminase antibody in 4 patients). Selective IgA deficiency was detected in 108 patients and 4 of them were positive for IgG anti-endomysial antibodies. Intestinal biopsy was accepted by 215 subjects (tTG IgA positive: 110, tTG and EMA IgA positive: 104 and tTG IgG positive: 1). The biopsy findings of 95 children were consistent with celiac disease. Thus, the estimated biopsy-proved prevalence was 1 in 212 children. The positive predictive value for IgA tTG plus EMA was 75.9%. When only IgA tTG was used, positive predictive value was 44.3%.

Conclusion: We estimate that the prevalence of celiac disease is at least 0.47% in Turkish school children. Screening with IgA tTG plus EMA seem to give better results for diagnosis when compared with IgG tTG alone.

Disclosure of Interest: None declared.

PO-G-172

ASSESSING ACCURACY OF INTERPRETATION OF A RAPID CELIAC ASSAY IN A WARD SETTING

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Objectives and Study: Celiac Disease (CD) is a common autoimmune condition that can cause underdiagnosed clinical manifestations. To allow faster counseling and treatment, a prospective study was conducted between April 2008 and December 2009 in a Gastroenterology consultation ward to evaluate clinical accuracy of screening CD in high risk populations using a new point-of-care device.

Methods: Patients were enrolled at the Pediatric Department of the University Hospital of Geneva. Local ethical committee approval was granted. Criteria for inclusion were signed informed consent and clinical symptoms suggestive of CD, confirmed under gluten-free diet and first degree relatives of CD patients. Intestinal biopsy and genetic profile were performed in all CD patients. A multi-analytic lateral-flow immunochromatographic assay (CD-LFIA) based on detection of both IgA, IgG anti-transglutaminase and total IgA was evaluated. Whole-blood sample results were compared to anti-transglutaminase ELISA and total serum IgA determination.

Results: A total of 122 patients were sequentially submitted for CD testing using ELISA and CD-LFIA devices. A positive CD seroprevalence was found in 17 patients (13.9%) of which 10 were new CD patients and 7 known CD with poor diet compliance. CD-LFIA results were read by two independent observers. Using binary scores, an excellent concordance between observers was found with a Kappa coefficient of Cohen of 0.93 [0.84–1.00]. Sensitivity (equal to positive predictive value) of CD-LFIA compared to that of ELISA assays was 94.1% [71.3–99.9] and 88.2% [63.6–98.5], for each observer respectively. Two false negative results (15/17) belonged to CD patients under poor diet control with mean values (48U/ml) close to the threshold level. However, all new CD patients were correctly diagnosed with CD-LFIA with 100% sensitivity (10/10) for both observers. Specificity (equal to negative predictive value) of the CD-LFIA test for each observer was 99.1% [94.8–100.0] and 98.1% [93.3–99.8], respectively.

Conclusion: CD-LFIA was found to have the potential to be used outside routine laboratories and in less sophisticated clinical facilities. Result interpretation was found unambiguous for all new CD patients for both observers. The difficulties appeared in interpreting samples of weak reactivity exclusively linked to monitoring CD patients under gluten-free diet. For this specific group, another approach could be preferred using an automated, self-timed reader. However, with a very high negative predictive value of 99.1% [94.8–100.0], CD-LFIA test is highly suitable to rule out CD in screening high risk populations.

Disclosure of Interest: None.

PO-G-173

THE PREVALENCE OF CELIAC DISEASE IN PARENTS OF PRETERM OR LOW BIRTH WEIGHT NEWBORNS

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OBJECTIVES AND STUDY: Celiac disease (CD) may present with atypical symptoms including poor pregnancy outcomes such as preterm and low birth weight (LBW) deliveries. In that study, we investigated the frequency of CD in mothers and fathers of preterm or LBW newborns.

METHODS: 316 parents of 164 preterm or LBW newborns and 246 parents of 123 healthy newborns were included. CD was screened using tissue transglutaminase IgA(tTG). Endoscopic duodenal biopsy was provided in the seropositive cases.

RESULTS: Positive tTG was found in six (1.1%; 1/94) individuals (three mothers and fathers); five were from study group (1.6%; 1/63) and one from control group (0.4%; 1/246). CD prevalence in mothers, fathers and parents of preterm newborns was 1/57 (1.8%), 1/57 (1.8%) and 1/29 (3.5%), respectively. In LBW group, seropositivity in fathers was 1/50 (2%) with no seropositive mothers. Biopsy proven CD was found in 1/159 mothers (0.6%) and 1/79 fathers (1.3%). Mean birth weights of the newborns of seropositive mothers and fathers were 214 g (< 0.05) and 320 g lower than those of seronegative ones, respectively.

CONCLUSION: As the prevalence of CD in parents of preterm or LBW newborns seems higher than the healthy population (1/63 vs. 1/246), CD screening in that special group might be recommended.

DISCLOSURE OF INTEREST: This study was funded by Inonu University Scientific Research Projects Unit (No: 2007/03).

PO-G-174

FUNCTIONAL GASTROINTESTINAL DISORDERS: ROME II VERSUS ROME III CRITERIA

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OBJECTIVES AND STUDY: Research using the Rome II criteria provided the foundation for the updated Rome III criteria. Changes from the Rome II to the Rome III Criteria for pediatric Functional Gastrointestinal Disorders (FGIDs) include a reduction in the required duration of symptoms, the addition of new FGIDs categories (e.g., Functional Abdominal Pain Syndrome), changes to specific criteria for several FGIDs, and separate criteria defining. However, the implications of these changes for patient classification are so far unknown, to our knowledge.

The aim of our study was to evaluate the clinical validity and applicability of the Rome II versus Rome III criteria for paediatric FGIDs.

METHODS: A prospective longitudinal design study was used. Parents of children aged 0 to 4 and 4 to 17 years and for children aged 10 to 17 years, referred to three tertiary gastroenterology ambulatory centers, completed a detailed Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS) according to the Rome III criteria over a 3-month period.

RESULTS: A total of 572 patients (mean age 57.2 + 46.7 months, range 1–209 months, 284 males) were prospectively screened during this 3-month period. FGIDs were diagnosed significantly more often by Rome III than by the Rome II Criteria (133 (23.2%) vs 92 (16.1%), p = 0.002).

In comparison with the results from the Rome II criteria, the Rome III criteria classified a greater percentage of children as meeting criteria for Functional Constipation (6 (2.2%) vs 25 (9.4%), p = 0.0006) in the 4- to 17-year-old group, while a trend towards a higher rate was present in patients with Functional Abdominal Pain (1 (0.4%) vs 7 (2.6%), p = 0.06). The infant rumination syndrome and the Functional Dyspepsia were the most common diagnoses according to both Rome II and Rome III (9 (3.0%) vs 9 (3.0%), p = 1, and 6 (2.2%) vs 5 (1.9%), p = 1, respectively).

CONCLUSION: The Rome III Criteria show greater applicability than the Rome II Criteria for FGIDs, in particular in the 4- to 17-year-old group. Changes to the Rome II make the Rome III Criteria more inclusive. The significant overlap between different FGIDs, however, makes it unclear whether some of the diagnoses represent distinct disorders or artificial categories.

DISCLOSURE OF INTEREST: No declaration of interest.

PO-G-175

CELIAC DISEASE PREDISPOSES TO FUNCTIONAL GASTROINTESTINAL DISORDERS


OBJECTIVES AND STUDY: Previous reports have linked Irritable Bowel Syndrome (IBS) etiologically with various forms of mucosal inflammation. In children, whether the enteropathy of Celiac Disease (CD) could predispose to Functional Gastrointestinal Disorders (FGIDs) is unclear. The aims of our prospective study were to evaluate: 1) the prevalence of FGIDs in children affected by CD after one year from the diagnosis; 2) the putative relationship between the gluten free-diet and the development of FGIDs.

METHODS: The study population consisted of 100 consecutive children (M/F: 36/64; mean age: 6.6 years; range: 4–17 years), who received a diagnosis of CD from June 2008 to September 2008. To evaluate their GI symptoms and psychological traits, the Rome III Diagnostic Questionnaire for the Pediatric FGIDs (QPGS) and the Stait–Trait Anxiety Inventory for Children (STAIC) were filled by all the children at enrolment and after one year of gluten-free diet, if they were in remission. The two questionnaires were...
also completed by 56 age- and sex-matched healthy control children. 

Results: At enrolment, 76 of 100 (76%) celiac children were symptomatic. Among the symptoms, abdominal pain was the most prevalent (36%), followed by diarrhea (25%), failure to thrive (23%), weight loss (15%), constipation (15%), vomiting (14%) and lack of appetite (8%). Twenty-four/100 (24%) patients were completely asymptomatic. Overall, the patients without GI symptoms at the diagnosis were 39/100 (39%). Among the control group, 5/56 (9%) patients were affected by FGIDs (IBS, Functional Abdominal Pain [FAP] and Functional Dyspepsia [FD] in 3.5%, 3.5% and 1.8%, respectively). After one year of gluten-free diet, 25/100 (25%) celiac patients fulfilled the Rome III Criteria for FGIDs compared with 5/56 (9%) of the control group (P<0.01). Among the celiac children with FGIDs, Functional Constipation (FC) was the most prevalent disorder (16%), followed by IBS (6%), IBD (4%) and FD (2%). IBS, IBD and FD were also found in 3.5%, 3.5% and 1.8% of controls, respectively. At one-year follow-up, 4/39 (10.2%) children without GI symptoms at CD diagnosis developed a FGID (IBS 5%, FC 5%) while on gluten-free diet, whereas none of the controls developed any FGID (P<0.03). Celiac children showed significantly higher rates of anxiety and irritability compared to control group (P<0.001).

Conclusion: Our study suggests that, during gluten-free diet, children with celiac disease may develop FGIDs as well as psychological disturbances. Both mucosal inflammation or psychological factors associated with CD, such as anxious and/or irritable personality profiles, may predispose to FGIDs. Further studies are needed to evaluate the different role played by these two independent factors.

Disclosure of Interest: None declared.

PO-G-176

A DISCRIMINANT SCORE BASED ON IMMUNOHISTOCHEMISTRY OF JEJUNAL BIOPSIES FOR THE DIAGNOSIS OF CELIAC DISEASE

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Objectives and Study: It is widely accepted that, also from an histological point of view, celiac disease (CD) represents a spectrum which includes minor mucosal abnormalities. It is then necessary to have tools to correctly identify gluten-sensitive patients. Aim of this work was to evaluate the contribution of immunohistochemical analysis of jejunal biopsies to the diagnosis of CD.

Methods: Jejunal biopsies from 56 CD patients with Marsh 3 lesion and 56 controls were analyzed for CD3 and gamma-delta intraepithelial lymphocytes, gammadelta/CD3 ratio, CD25+ lamina propria cells. The data were statistically analyzed with SPSS and used to compute a discriminant equation. Using this score we evaluated blind 61 biopsies with normal mucosal architecture. In the latter cases the diagnosis of CD was retrospectively based on serology, biopsy, HLA and clinical response on a gluten free diet.

Results: All the immunohistochemical parameters were statistically different between CD and control patients. The combination of all four markers resulted in the following discriminant equation: score = (CD3 x 0.06) - (gammadelta x 0.119) + (CD25 x 0.112) + (gammadelta/CD3 x 0.131) - 4.709. Using this score patients were correctly classified as celiac or controls in 97.3% of cases: only 2/56 controls were classified as CD patients, and only 1 CD patient classified as control. When this equation was applied to patients with unknown diagnosis 13/14 (92.9%) with a positive score were correctly classified as celiac patients. However, only 27 of the remaining 47 (57.4%) were correctly classified as non-coeliacs, as 20 presented a positive CD serology (potential CD patients).

Conclusion: The discriminant score, resulted from the immunohistochemical analysis, represents a very specific tool for the diagnosis of CD; however, it lacks sensitivity in CD cases with minor histological abnormalities. Further research is needed to evaluate if in patients with the presence of serum CD-related antibodies and normal intestinal mucosa, the positivity of the immunohistochemistry discriminant score is predictive of evolution to villous atrophy.

Disclosure of Interest: None declared.

PO-G-177

IMMUNOGENICITY OF TWO OATS VARIETIES IN RELATION TO THEIR SAFETY FOR CELIAC PATIENTS

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Objectives and Study: Most of recent studies suggest that oats are well tolerated by CD patients. However, it is still possible that different oat cultivars may display different biological properties relevant for CD pathogenesis. Aim of our work was to investigate biological properties of two oat varieties in relation to their safety for celiac patients.

Methods: Genziana and Potenza varieties were used after having excluded any gluten contamination. Organ cultures of small intestinal biopsies from 11 active and 13 treated CD patients were established in the presence of each oat variety. In this system proliferation of epithelial cells, intraepithelial lymphocytes infiltration, and IL-15 induction both in the epithelium and in the lamina propria were assessed as evidence of innate immunity activation. Mononuclear cell activation in the lamina propria and INF-gamma release in
PO-G-178

LONG TERM EFFECTS OF GLUTEN FREE DIET ON BONE MINERAL DENSITY IN CHILDREN WITH CELIAC DISEASE


Objectives and Study: To evaluate effect of long term gluten free diet (GFD) on bone mineral density (BMD) in children with celiac disease (CD).

Methods: Thirty seven children with CD (20 classic CD, 13 atypical CD, 4 silent CD), diagnosed based on ESPGHAN revised criteria, were recruited. None of them had chronic illness or treated with a drug which effects bone metabolism. Serum total protein, albumin, total calcium (Ca), inorganic phosphorous (P), alkalen phosphatase (ALP), parathormone (PTH) and BMD in lumbar 2–4 vertebra (L2–4) by Dual Energy X Ray Absorbtionmetry method were evaluated at diagnosis and follow up. Bone mineral density in L 2–4 were compared with age and sex matched mean BMD in L2–4 of 143 healthy children.

Results: Mean BMD of celiac patients (0.5073 ± 1.14 g/cm2) was significantly lower than control group (0.5913 g/cm2) (P = 0.005) at diagnosis. Seventeen (45.9%) patients had osteopenia (9 patients with classical CD, 6 patients with atypical CD, 2 patients with silent CD) and 4 (10.8%) had osteoporosis (3 patients with classical CD, 1 patient with atypical CD) with respect to aged matched z score. Mean follow up period was 3.56 ± 2.29 years. BMD L2–4, aged matched z score significantly increased from −0.99 ± 1.1 to −0.43 ± 0.9 at the end of the first year with GFD (P = 0.001), however, there was no significant difference during follow up. Serum total protein, albumin, Ca, P, ALP and PTH values were not different during follow-up compared to baseline. Twenty one patients were strictly compatible to GFD, and 16 patients were partly on GFD. Among 17 patients with osteopenia at diagnosis, 9 patients who were on strict GFD, 5 patients improved, 4 patients remained osteopenic on follow up, while 8 patients who were partly on GFD, 7 patients improved, 1 patient remained osteopenic. Among the 4 patients with osteoporosis at diagnosis, 2 patients who were on strict GFD improved while other 2 patients who were partly on GFD were still osteoporotic at 1 year follow up. Two patients with normal BMD at diagnosis and who were partly on GFD developed osteoporosis at follow up.

Conclusion: Bone mineral disorders may be present in up to 50% of patients with CD at diagnosis. Bone mineral density is restored with strict GFD within the first year. We recommend evaluation of BMD in children with CD at diagnosis and follow up especially in patients who are on partly GFD.

Disclosure of Interest: None declared.

PO-G-179

EXPRESSION OF THE RECEPTOR CXCR3 AND ITS LIGANDS MIG AND IP-10 IN CELIAC DISEASE

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Objectives and Study: Celiac disease (CD) is an autoimmune disorder caused by gliadin in genetically susceptible subjects. The activation pathway of Natural Killer lymphocytes is as yet unknown in celiac disease. A possible mechanism is the activation of the chemokine receptor CXCR3 and the IFN-gamma inducible CXCR3 ligands Mig and IP-10.

Methods: 79 blood samples that were positive for the presence of at least one antibody to EMA, AGA or tTG were analyzed using ELISA for the expression of Mig and IP-10. Immunohistochemistry staining of small bowel biopsies for Mig from patients suspected of having CD was performed. CD3 T cells and CD56 NK cells collected from patients with positive biopsies with or without raised celiac antibodies had higher levels of Mig in their
Disclosure of Interest: None declared.

PO-G-180

DIAGNOSTIC USEFULNESS OF SINGLE BALLOON ENTEROSCOPY IN CHILDREN WITH GASTROINTESTINAL DISORDERS UNDEFINED AT CONVENTIONAL ENDOSCOPY

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Objectives and Study: Endoscopy of the small bowel (SB) is not uncommonly necessary when investigating patients (pts) with obscure gastrointestinal (GI) bleeding and those with disorders involving all the GI tract (i.e. inflammatory bowel disease [IBD], polyposis), for which assessment of SB can change disease management and course. Wireless capsule endoscopy (WCE) has gained acceptance as endoscopic tool for SB, however it does not permit histological diagnosis and therapy; furthermore it has some limitations (strictures, inability to swallow, GI dysmotility). Among adult’s gastroenterologists double-balloon, and more recently, single-balloon enteroscopy have allowed visualization of the entire SB. There are no pediatric data on the use of small bowel single balloon enteroscopy (SBSBE).

Methods: The single balloon endoscope (SIF-Q180, Olympus Optical Co., Ltd., Tokyo, Japan) consists of a 200-cm long video endoscope with an outer diameter of 9.2 mm and a flexible overtube with a length of 140 cm and an outer diameter of 13.2 mm. One single balloon is attached to the tip of the overtube. The SBSBE was performed in 30 patients (pts) (range age: 3–18 years, median age: 14.0) referred to our Unit for SB endoscopy. The procedure was performed under general anesthesia using iv propofol.

Results: The following groups of pts were investigated: A) 10 with suspected Crohn’s disease (CD) localized at the ileum (as revealed by previous WCE): in 8 SBSBE allowed histological confirmation of CD, whereas 2 had a diagnosis of probable CD. B) 9 pts had a previously established IBD: 5 were CD and 4 unclassified IBD (IBDU); of the 5 CD pts 3 had strictures that were successfully dilated, 2 had multiple ulcercations of the ileum and had previous surgery; of the 4 IBDU, 3 were reclassified as CD and 1 remained as IBDU. C) 5 with obscure GI bleeding (all with previous WCE): 3 had vascular lesions, 1 active ulcerations by NSAIIDs, 1 had a polyp: in all of them SBSBE allowed a therapeutic intervention. D) 6 with chronic enteropathy and unconcusive WCE: 2 were eosinophilic enteritis, 2 had jejunal celiac disease with normal duodenal histology, 1 had intestinal lymphangiectasia, 1 had CD after exclusion of tuberculosis. The procedure was well tolerated and no complications occurred.

Conclusion: These are the first reported pediatric data on the use of SBSBE. The latter is a feasible technique in pediatric gastroenterology for endoscopy of SB as well as for therapeutic intervention at that site. Studies are running to assess its diagnostic yield in comparison with other methods for evaluating SB. One important issue will be how to integrate this novel technique with WCE in the diagnostic algorithm of IBD pts.

Disclosure of Interest: None declared.

PO-G-181

INLET PATCH: CLINICAL PRESENTATION AND OUTCOME IN CHILDREN

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Objectives and Study: An inlet patch (IP) is defined as heterotropic gastric mucosa located in the proximal esophagus. Although considered fortuitous finding in adults, little information is available in children. The aim of this study was to evaluate the clinical, endoscopic, histological and evolutive characteristics of IPs in children.

Methods: This retrospective multicenter study included all cases of IP recorded in 7 tertiary French pediatric gastrointenstinal centers. Informations about demographics, clinical symptoms, endoscopic characteristics, histology, treatment and evolution were collected.

Results: Fifteen children were included (8 boys, 7 girls). The median age at diagnosis was 9.5 years (range, 3.3–15 years). Five children presented with esophageal atresia and 9 had gastroesophageal reflux. Only 1 child was asymptomatic. Digestive symptoms (dysphagia, food impaction) were noted in 14 patients and respiratory or ear, nose, and throat symptoms in 6. At endoscopy, IP was characterized by a small round salmon-pink lesion of the proximal esophagus. Helicobacter pylori were found in 2 patients. Proton pump inhibitor treatment was initiated in 14 children for a mean duration of 4.7 months (range, 1–12 months). Two patients
were lost to follow-up. Clinical symptoms disappeared in 5 patients and decreased in 3 others. One case of hematemesis was noted after a mean follow-up of 9 months. Recurrent symptoms were noted in 2 patients after treatment discontinuation.

Conclusion: IP is a rare, although probably underdiagnosed, pathology in children undergoing endoscopy and could be responsible for digestive and respiratory symptoms. Long-term longitudinal studies are required to assess the outcome.

Disclosure of Interest: None declared.

PO-G-183

DISCREPANCY BETWEEN MACROSCOPIC AND MICROSCOPIC FINDINGS ON ENDOSCOPY IN 40 CHILDREN WITH EOSINOPHILIC OESOPHAGITIS

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Objectives and Study: Eosinophilic Oesophagitis (EO) is a new clinicopathological entity and research evidence in the paediatric population is limited. The diagnosis of EO is based on strict histological criteria, but there is less published data on macroscopic and microscopic associations at endoscopy in this condition.

The aim of this study was to investigate macroscopic and microscopic findings on endoscopy in children with EO and to determine the proportion of children with EO who have no macroscopic abnormalities on endoscopy.

Methods: Institutional approval was gained to review clinical records for all children diagnosed with EO at one hospital over a 10 year period. Only children meeting strict histological criteria were included in this study; >20 eosinophils in one high power field (HPF) or >15 eosinophils in 2 or more HPF. The following data were extracted for all children included in this study: clinical features and history at presentation, macroscopic and microscopic findings at diagnostic endoscopy.

Results: 40 children (70% boys) were diagnosed with EO during the 10 year period; median age of diagnosis 6.5 (range 1–15). Clinical symptoms included vomiting in 26 (65%), abdominal pain in 16 (40%), paltering growth in 14 (35%), heartburn in 10 (25%), diarrhoea in 9 (23%) and dysphagia in 7 (18%). 30 children (75%) had a personal history of another allergic disease. All children met histological inclusion criteria and 9 children (23%) had >30 eosinophils per HPF. Macroscopic findings on endoscopy included normal mucosa in 25 (63%), oesophagitis in 7 (18%), white papules in 4 (10%), ulceration in 2 (5%), mucosal oedema in 2 (5%) and stricture in 2 (5%).

Conclusion: There is a discrepancy between microscopic and macroscopic findings on endoscopy in children with EO; most children with histologically defined EO will have no macroscopic abnormalities on endoscopy. Given these findings, we suggest that for patients with clinically suspected EO, multiple biopsies from the proximal and distal oesophagus should be taken, despite macroscopic findings at endoscopy.

Disclosure of Interest: None declared.

PO-G-182

TRANSORAL INCISIONLESS FUNDOPICATION FOR THE TREATMENT OF PAEDIATRIC GASTRO-ÖSEPHAGEAL REFLUX DISEASE: A FEASIBILITY STUDY

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Objectives and Study: A new transoral incisionless fundoplication (TIF, EsophyXTM) technique was evaluated for the treatment of paediatric gastro-öseophageal reflux disease (GORD) in a prospective feasibility clinical trial.

Methods: Prospective cohort study (December 2008-December 2009)

Inclusion Criteria: Chronic and symptomatic GORD, refractory to, or dependent, on high dose proton pump inhibitor therapy.

Exclusion Criteria: >18 years, dysphagia, obesity (BMI) >99th centile, previous upper intestinal surgery, or hiatus hernia >2cms.

Pre and post procedure (6 month follow up) assessment included upper GI endoscopy, 24 hour oesophageal pH with RI (reflux index), validated reflux quality of life score (QOLRAD). The TIF procedure was designed to partially reconstruct the antireflux barrier through augmentation of the gastroesophageal junction.

Results: Demographics-12 patients (8 Male), median age 12.5yrs (9–16), median weight 43.72 kg (28–91). The median duration of GORD symptoms in the patients was 45 months (24–70).

Median operative time was 42 minutes (range 25–94). In all patients a greater curvature of 3 cm, lesser curvature of 1 cm and a 270 degree wrap was achieved.

Adverse Events: Mild pharyngeal irritation & epigastric pain was seen in 3/12 patients. 1 of them had restrosternal chest pain & pneumomediastinum on CT chest & was treated for possible mediastinitis and discharged home after 5 days of intravenous antibiotics. Subsequently CO2 insufflation was employed & more rapid absorption resulted in no further mediastinal gas leak.

At 6 months: 10 out of 12 patients were followed up. Total QOLRAD (best 175) increased from a median of 84 (51–146) to 158 (25–175). Median RI improved from 13% (5.7–37) to 4% (2.2–27). Normalization of RI was seen in 50% (5/10). All other pH parameters also improved significantly. 8/10 did not require any further PPI use.
Conclusion: This is the first report of paediatric experience with a full thickness transoral endoscopic anti-reflux procedure and this shows that the TIF procedure using the EsophyX.TM. is feasible and safe with CO2 insufflation in children. Initial follow up also indicates that the TIF is an effective procedure, but further follow up is needed to demonstrate whether it’s sustained. This preliminary data is now the basis for a larger multi-centred randomized controlled study to evaluate the efficacy of TIF versus Laparoscopic Nissen’s fundoplication in treating GORD in children.

Disclosure of Interest: None declared.

PO-G-184

COMPARISON OF QUICK POINT OF CARE TEST FOR PAEDIATRIC SMALL BOWEL HYPOLACTASIA WITH BIOCHEMICAL LACTASE ASSAY

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Objectives and Study: The usefulness of a new quick test for endoscopic diagnosis of paediatric-type hypolactasia was tested in duodenal biopsies. In this test, an endoscopic biopsy from the postbulbar duodenum is incubated with lactose on a test plate, and a colour reaction develops within 20 min as a result of hydrolyzed lactose (a positive result) in patients with normolactasia, whereas no reaction (a negative result) develops in patients with severe hypolactasia.

Objectives: The aim of this study was to compare the Biohit® Lactose Intolerance quick (BLIQ) Test to the “gold standard” biochemical duodenal lactase (DL) activity assay in the paediatric population.

Methods: Two postbulbar duodenal biopsies were taken from 38 prospective children (0–16 years) who underwent upper GI endoscopy over a period of 1 year [June 08–May 09] at a single tertiary paediatric gastroenterology unit. The biopsies were used for the Quick Lactase Test (Biohit® PLC, Helsinki, Finland) and in biochemical disaccharidase (lactase, trehalase, sucrase, and maltase) assays.

Results: 38 children (19 male) of median age 5.45 years (0.3–14.8 years) had the combined testing. We further subdivided this group into those children that had their biopsies with a larger endoscope [XP, n = 26] and thus a bigger biopsy forcep and those children that had a smaller endoscope [XP, n = 12] and thus a smaller biopsy forcep. The results are tabulated below.

Table:

<table>
<thead>
<tr>
<th>Dissacharidase</th>
<th>Assay negative</th>
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<tbody>
<tr>
<td>positive (normolactasia)</td>
<td></td>
</tr>
<tr>
<td>Biohit +ve (normolactasia)</td>
<td>4</td>
</tr>
<tr>
<td>Biohit –ve (hypolactasia)</td>
<td>0</td>
</tr>
<tr>
<td>Biohit +ve (normolactasia)</td>
<td>2</td>
</tr>
<tr>
<td>Biohit –ve (hypolactasia)</td>
<td>0</td>
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</table>

USING SCOPE XP n = 12

[+ve predictive value = 57%] [+ve predictive value = 100%]

Conclusions: The Quick Lactase Test effectively identifies children with severe duodenal hypolactasia. These results are based on small numbers but tend to support findings in adult studies. The sensitivity and negative predictive value of the BLIQ was 100% on comparing it to DL. The specificity too appears to be high but variable (86% in XQ & 80% in XP groups). This would suggest a lower specificity perhaps, secondary to smaller size of the biopsies obtained and may warrant the need for 2 biopsies. In comparison with biochemical lactase assays, the sensitivity & specificity of BLIQ for indicating hypolactasia is very high and appears to be an effective point of care test for paediatric hypolactasia.

Disclosure of Interest: None declared.

PO-G-185

SINGLE BALLOON ENTEROSCOPY IN CHILDREN

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Objectives and Study: The feasibility and indications of Single balloon enteroscopy (SBE) in children is still to be determined. The aim of this study was to determine the safety, age/weight limitations and efficacy of SBE in identifying and treating occult disease present in the small intestine.

Methods: All children who underwent SBE were prospectively assessed at two referral centres. A total of 15 children underwent a total of 22 procedures. The indications, length of time of procedure, adjuvant radiology support, anaesthetic technique, length of stay and complications were all recorded. 12/15 children had undergone prior Video capsule endoscopy (VCE) and 1 prior mid bowel MRI.

Results: 15 children (9F, 6m, ages 2.8 – 15.8 yrs, mean 8.4 years, weight range 11.4kg-64 kg) had SBE performed. In all children the procedure was well tolerated with no major complications. Failure of procedure occurred twice (same child) due to gastric looping. All were completed as daycase procedures under general anaesthesia except one child who had unstable diabetes. The mean time to completion to terminal ileum was 104 mins (45–220 mins) with intubation of terminal ileum in 18 procedures. In 2 children SBE was performed for examination of Roux-en Y loops. Radiology
support for loop management was used in 6 children. Indica-
tions divided into 4 groups;
Group 1: Vascular lesions. 7 procedures completed and 2
failed procedures (gastric loops) completed in 2 children
for blue rubber bleb syndrome with 54 lesions injected
with adrenaline or sclerosant agent. Single procedures in a
further
4
children with bleeding ulcers identified by VCE were
treated but in one child no lesion was identified.
Group 2: Occult Inflammatory bowel disease, was diagnosed
in 4 children. Two had autoimmune enteropathy diagnosed
after SBE, one Crohns disease and one intestinal lym-
phangiectasias.
Group 3: Other conditions included B-cell lymphoma
was identified in one child following cardiac transplant. Two
children were assessed for patency of Roux en-y loops and
procedure was stopped after examination of Roux loops.
Group 4: Polyps. One child with Peutz-Jeghers and bleeding
had a bleeding polyp removed.
Conclusion: SBE is a well tolerated investigation in children
from 11 kg upwards. With over 90% completion rates SBE it
is safe and effective moreover it is important in both estab-
lishing new diagnosis including neoplasia and for therapeutic
interventions especially for occult mid bowel bleeding.
Disclosure of Interest: None declared.

PO-G-186

EFFECT OF LACTOBACILLUS GG ADDED TO AN
EXTENSIVELY HYDROLYSED CASEIN FORMULA
ON TOLERANCE ACQUISITION IN CHILDREN
WITH COW’S MILK ALLERGY

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Objectives and Study: Lactobacillus GG (LGG) modulates
immune function and has been proposed in the prevention
and treatment of pediatric allergic diseases. We investigated
whether the addition of LGG to an extensively hydrolyzed
casein formula (EHCF) could be able to influence the time of
tolerance acquisition in children affected by cow’s milk
allergy (CMA).

Methods: Children (1–36 months of age) affected by
IgE- or non-IgE-mediated CMA, confirmed by oral food
challenge, were enrolled in a double-blind trial and were
randomly assigned to 2 dietary interventions: 1. EHCF
(Nutramigen®, Mead Johnson,Italy), 2. EHCF containing
LGG (2.1x104 CFU/g of formula powder) (Nutramigen
LGG®, Mead Johnson,Italy). Oral food challenge was
performed to explore tolerance acquisition after six months.

Results: Fifty patients, 25 per group, were enrolled (30 male,
60%; age 8.6, 95%CI 6–11 months; body weight 9.9, 95%CI
9–11 kg; IgE-mediated CMA 21, 42%). At the diagnosis,
symptoms of CMA were gastrointestinal (63.9%), cutaneous
(44.2%), and respiratory (21.3%). After 6 months of dietary
intervention, tolerance was acquired in 6 out of 25 children
in group 1 (24%), and in 15 out of 25 in group 2 (60%,
P=0.01). Linear regression analysis revealed that the result
was positively influenced by the presence of gastrointestinal
symptoms (B=+2.2, P=0.26), but not by age at diagnosis, sex,
presence of extra-intestinal symptoms, and IgE or non-IgE
mediated mechanism.

Conclusion: Addition of LGG to an EHCF resulted in a
significant reduction of the time of tolerance acquisition in
children with CMA.

Disclosure of Interest: R.Berni Canani, Mead Johnson
Nutritional, Evansville, IN, USA, Grant Research Support.

PO-G-187

ANALYSIS OF ENTEROPATHY IN FOOD
PROTEIN-INDUCED ENTEROCOLITIS
SYNDROME: THE ROLE OF UP-REGULATED
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 in FPIES and to
determine the role of apoptosis and disrupted tight junction
in its pathogenesis.

Methods: Fifteen infants diagnosed with FPIES using stan-
dard oral challenge test and 5 controls were included.
Quantitative morphometric analyses of duodenal mucosa
were performed. Immunohistochemical stains of
TUNEL for overall apoptosis; CD3 for intraepithelial lymphocyte;
M30 for epithelial apoptosis; TNF-α expression and claudin-
1, claudin-4, and occludin for tight junction were also
performed. 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 the duodenal
mucosa of all FPIES patients (50–210 μm vs 305–380 μm
in controls, P<0.0001). TUNEL (P=0.043), CD3
(P=0.038), and M30 (P=0.042) were significantly higher
expressed in 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: These results suggest that FPIES is an enterop-
athy disorder. Villous atrophy is induced by enterocyte and
intraepithelial lymphocyte apoptosis which may be induced by up-regulation of TNF-α and disrupted tight junction.

Disclosure of Interest: None declared.

PO-G-188

RELATION OF TISSUE EOTAXIN AND IL-5 WITH THE ACTIVATION AND RECRUITMENT OF EOSINOPHILS IN FOOD PROTEIN-INDUCED PROCTOCOLITIS

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Objectives and Study: Food protein-induced proctocolitis (FPIPC) is a non-IgE mediated hypersensitivity disorder with peripheral blood eosinophilia in 25~50% of patients and histopathological eosinophilic infiltrations in all patients. Eotaxin and IL-5 are major cytokines to activate and recruit eosinophils in the peripheral blood or tissue. The aim of this study was to determine the relation of tissue eotaxin and IL-5 with eosinophils in the pathogenesis of FPIPC.

Methods: Data of 14 FPIPC patients who had been diagnosed on the basis of histopathology of rectal mucosal biopsy specimens and response to maternal diet elimination test, and exclusively breastfed were analyzed with 7 controls and divided into two groups; 7 cases with peripheral blood eosinophilia positive (≥ 500 cells/µL) (PBE+) group and 7 cases with peripheral blood eosinophilia negative (PBE-) group. Relation among peripheral blood eosinophil count, eosinophilic count in tissue (maximum eosinophil cells/high power field, HPF), eotaxin (expressed cells/10 HPF), and IL-5 (expressed cells/10 HPF) was analyzed using Pearson’s correlation coefficient.

Results: Peripheral blood eosinophil count (P = 0.001), tissue eosinophil (P = 0.001), eotaxin expression cells (P = 0.001), and IL-5 (P = 0.001) were significantly higher than the controls. However, these variables were not correlated with each other. Peripheral blood eosinophil count was 1,661 (630~4,480)/µL in PBE+ and 330 (150~497)/µL in PBE-. Eosinophilic count in tissue between two groups was 87 vs 34 (P = 0.012), but eotaxin and IL-5 staining were not significantly different in two groups.

Conclusion: Tissue eotaxin and IL-5 were significantly higher expressed in FPIPC than in the controls. This finding confirmed that FPIPC is an ‘extrinsic’ eosinophilic gastrointestinal disorder. However, no correlation among peripheral blood eosinophil count, tissue eosinophils, tissues eotaxin, and tissue IL-5 was identified. What has direct influence on the eosinophilic activation and recruitment in FPIPC?

Disclosure of Interest: None declared.

PO-G-189

ATOPY PATCH TEST IN CHILDREN WITH COW’S MILK PROTEIN ALLERGY

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Objectives and Study: Atopy patch test (APT) has been increasingly used in children with suspected cow’s milk protein allergy (CMA). We have recently published the results of the test standardization (1). However, diagnostic validity of the test has not been established yet. Aim of the study was to validate the APT by comparing it to the open food challenge test (OFC) in children with clinical symptoms consistent with CMA.

Methods: Data on 61 patients (30 girls; age 3 wks to 4 y, mean age 8.1 mo, median 5 mo) who presented with gastrointestinal (GI) symptoms suggestive of CMA (haematochezia, chronic diarrhea, abdominal colic and vomiting, chronic constipation, poor weight gain) were prospectively collected from January 1st 2008 to December 1st 2009. Beside GI symptoms, 24/61 (39.34%) patients had also symptoms of atopic dermatitis (AD). APT and OFC with cow’s milk based infant formula were performed in all patients. Allergen in the APT was 20 % concentrated milk powder in the petrolatum as a medium. Petrolatum alone was used as a negative control in all patients. The test result was graded as follows: negative (0) - no reaction; weakly positive (+) - erythema with infiltration; strongly positive (++) - erythema, infiltration and papules; and very strongly positive (+++) - erythema, infiltration, papules, vesicles. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for all patients. Results for patients with GI and AD symptoms were compared with patients who presented with GI symptoms alone.

Results: APT was positive in 31/61 patients (50.8%), and 11/31 (18.0%) patients had strongly or very strongly positive reaction. In all patients with positive APT, 22/31 had positive OFC. In children with negative APT, OFC has confirmed the diagnosis of CMA in 10/30 (33.33%, false negative). In general, APT yielded sensitivity of 68.75%, specificity 68.97%, PPV 70.97%, and NPV of 66.67%. However, sensitivity for strongly and very strongly reaction was 50%, specificity 95.23%, PPV 90.90%, and NPV was 66.67%. There was no difference in test efficacy in respect to the clinical presentation (P = 0.83, Table 1).

Table: Sensitivity, specificity, PPV, NPV in patients with GI+AD vs. GI symptoms alone

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
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<tr>
<td>GI+AD symptoms (n = 24)</td>
<td>60.0</td>
<td>77.8</td>
<td>81.8</td>
<td>53.9</td>
</tr>
<tr>
<td>GI symptoms alone (n = 31)</td>
<td>76.5</td>
<td>65.0</td>
<td>65.0</td>
<td>76.5</td>
</tr>
</tbody>
</table>

Conclusion: In comparison with OFC, only strongly and very strongly positive APT could be used as the diagnostic tool for CMA, irrespective of the clinical presentation.

Reference:
Disclosure of Interest: None declared.

PO-G-190

CASEIN AND RICE PROTEIN HYDROLYSATES: MOLECULAR WEIGHT DISTRIBUTION ANALYSIS AND IN VITRO POTENTIAL ALLERGENICITY ASSESSMENT
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Objectives and Study: Infant Formulas for infants with cow’s milk protein allergy (CMA) are based on extensively hydrolysed milk protein or hydrolysed rice protein. The goal of this study was to characterize molecular weight distribution of two casein and two rice hydrolysates and its IgE reactivity

Methods: Molecular size distribution was measured with HPLC Size exclusion chromatography (SEC) (GE Healthcare, Superdex 30 pg Column) with Phosphate Buffer 50 mM NaCl 0,15 M, pH= 7.2, Flux 1 ml/min), and detection at 214 nm. Absolute molecular weight was determined by the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry method (MALDI-TOF), a rapid and sensitive quantitative method with high resolution for peptides[1]. The IgE reactivity was evaluated using sera of patients with clinically demonstrated allergy to cows milk proteins that contains at least 20KU/L of specific IgE antibodies towards milk proteins, measured using FEIA-CAP System (Pharmacia diagnostics, Uppsala, Sweden). IgE binding was measured using an indirect ELISA coupled to a signal amplification system [2].

Results: SEC and MALDI-TOF allowed us to characterize hydrolysates in terms of peptide size abundance distribution. The percentage of peptides with a molecular weight under 2.000 Daltons (Da) varied from 85% to 95% Absolute maximum molecular weights detected by MALDI-TOF ranged from 1.968 to 2.685 Da. Hydrolysates presented no reactivity against IgE in serum of allergic patients when they were used at concentrations similar to native protein (0.0025 mg/ml). However, when they were used in concentrated form (1000x) they showed different degrees of reactivity

Conclusion: Precise molecular weight characterization and IgE in vitro reactivity may be useful tools to evaluate the appropriateness of protein hydrolysates for formula feeding of infants with cow’s milk protein allergy (CMA) as screening test previous to clinical trials in humans.

References:


PO-G-191

BENEFIT OF THE BASOPHIL ACTIVATION TEST IN DECIDING WHEN TO REINTRODUCE COW'S MILK IN ALLERGIC CHILDREN
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Objectives and Study: Oral challenges are required to establish the persistence or resolution of IgE-mediated cow’s milk allergy (CMA) in children. However determining the appropriate timing to offer a food challenge remains one of the most important and difficult issues of CMA management. The benefit of the basophil activation test (BAT) in predicting a child’s reaction to the oral challenge was evaluated and compared to the specific IgE and skin prick tests (SPT) results.

Methods: 112 consecutive children with CMA admitted for an oral challenge to reassess the persistence or resolution of their allergy were included. Allergen-induced basophil activation was detected by flow cytometry as a CD63-upregulation on basophils.

Results: Thirty-six children (32%) had a positive oral challenge. The percentage of activated basophils in patients with a positive challenge (mean = 20.7; SEM = 3.2) was significantly higher than that of patients with a negative challenge (mean = 5.1; SEM = 0.6, P < 0.0001). Among positive challenges, a significant correlation was found between the percentage of activated basophils and the eliciting dose of milk (P < 0.0001). The BAT had an efficiency of 90%, a sensitivity of 91%, a specificity of 90%, and positive and negative predictive values of 81% and 96% in detecting persistently allergic patients. The area under the ROC curve (AUC) was 0.866. These scores were higher than those obtained with SPT and specific IgE values, whichever positivity cut-point was chosen (AUC for SPT: 0.809; AUC for IgE values: 0.758). A decisional algorithm combining BAT, sIgE and SPT is suggested. Referring to this algorithm allowed the correct identification of 95% of patients as tolerant or persistently allergic to CMP in our cohort.

Conclusion: The BAT could be a valuable tool in the management of pediatric CMA in addition to specific IgE quantification and SPT, by contributing in determining whether an oral challenge can safely be undertaken.

Disclosure of Interest: Non declared.
PO-G-192

ENZYMATIC TREATMENT OF THE COW’S MILK ALLERGEN WHEY RESULTS IN DIFFERENTIAL INHIBITION OF MAST CELL DEGRANULATION COMPARED TO T CELL ACTIVATION

Objectives and Study: In cow’s milk (CM) allergic infants hydrolysates of CM in the diet are used. In hydrolysates the allergenic epitopes within the CM proteins are diminished by enzymatic treatment. In the current study we examined the immunological and allergenic properties of the whey fraction of CM during hydrolysis to evaluate the effect on established allergic responses.

Methods: During hydrolysis of whey, protein samples were obtained at 10, 15, 30, 45, 60, 75 and 90 minutes. Degradation of whey was checked by HPLC analysis. Allergenic potential was analysed by its IgE crosslinking capacity on human FcεRI-transduced rat basophilic leukemia cells (RBL-2B12, a kind gift of Dr. Teshima, Japan) sensitized with a serum pool of CM allergic patients. In addition, whey-sensitized C3H/HeOuJ mice were ear-challenged intradermally with whey or hydrolysates. Finally, T cell activating potential was tested on whey-specific human T cell clones and T cell lines at the level of proliferation and release of IL-4, IL-10, IL-13 and IFN-γ.

Results: After 10 minutes hydrolysis, the majority of the protein was already degraded resulting in 26% inhibition of mast cell degranulation, whereas 15 minutes treatment resulted in 92% inhibition. In the mouse model, ear swelling was markedly reduced after 10 minutes hydrolysis (68%), and further reduced (85%) at 15 minutes hydrolysis. In contrast, the T cell stimulatory capacity was affected less by the hydrolysis, and needed longer treatment of the whey. The average inhibition of human T cell proliferation was 8%, 11%, 57%, 74% and 79% for the 10, 15, 30, 45 and 60 minutes hydrolysates. The cytokine release by the T cells upon activation with the whey hydrolysate samples was inhibited to the same rate as T cell proliferation. No differential inhibition of the Th1/Th2/Treg cytokines was found.

Conclusion: We show using in vitro, as well as in vivo models the differential effects of hydrolysis of a CM allergen. The allergenic capacity of the whey hydrolysates analysed by mast cell degranulation and ear swelling in a mouse model is inhibited by a relatively low grade of enzymatic digestion compared to activation of human whey-specific T cells. This indicates an approach to actively induce tolerance in CM allergic patients by hydrolysates with reduced allergenic potential, but almost complete T cell activation properties.

Disclosure of Interest: Betty CAM van Esch, employee, affiliation 1 and 3 Johan Garssen, employee, affiliation 1 and 3.

PO-G-193

ORAL LC-PUFA’S CAN REDUCE THE DEVELOPMENT OF ALLERGEN INDUCED ECZEMA IN MICE

Objectives and Study: Dietary management of cow’s milk allergy include the use of extensive hydrolysed cow’s milk protein formulations. These formulations have clinically been proven to reduce the incidence and severity of allergic manifestations. Hypoallergenicity of the formulations can be assessed in vitro by evaluating reactivity against cow’s milk protein specific antisera. In the present study, however, we set out to study hypoallergenicity at a functional level in vitro.

Methods: In female ovalbumin sensitised BALB/c mice skin inflammation was induced by three ovalbumin patches accompanied by feeding a solid food containing DHA only, ARA only and a combination of DHA and ARA as well as a control diet without fatty acid supplementation. Total skin score was used to evaluate the symptoms. Thereby, skin lesion severity was assessed by clinical parameters and assigned into severity grades. In addition, immunohistochemical assessment of the skin lesions was performed, including analyses of cytokines and keratinocyte markers.

Results: Dietary ARA/DHA significantly improved the severity of allergen induced eczema. The total skin score was significantly reduced to 64 ± 29% compared with the control diet group (100 %). This clinical improvement by ARA/DHA supplementation was associated with increased numbers of Foxp3+ regulatory T cells, elevated IL-10 expression and a reduced epidermal expression of Ki-67, but not CD4 infiltration. Interestingly ARA or DHA supplementation alone was not efficient in reducing eczema.

Conclusion: Dietary intervention with ARA/DHA is effective in reducing the inflammatory immune response in the skin. The beneficial effect may be caused by alterations in cellular fatty acid profile that are involved local anti-inflammatory mechanisms. The present study suggests that the quality of the dietary fatty acid composition may be important for therapeutic application in human systemic allergic manifestations and atopic eczema.
PO-G-194

IMPACT OF GUT MICROBIOTA ON COW’S MILK ALLERGY IN MICE
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Objectives and Study: According to the hygiene hypothesis reduced exposure to microbial stimuli may be a major factor responsible for allergy development. Several clinical and experimental studies suggest a link between the development of atopy and intestinal microbiota composition. However, available epidemiological studies do not allow concluding which of dysbiosis or allergy appears first and influences the other. The aim of our study is to investigate in mice whether an early intestinal dysbiosis may be a cause of cow’s milk allergy.

Methods: We used a mouse model of cow’s milk allergy consisting of five oral sensitizations with whey proteins once a week and one oral challenge with ß-lactoglobulin (BLG), one of the major cow’s milk allergens. Allergic responses were monitored after BLG challenge in germfree (GF), conventional (CV) and gnotobiotic (Gn) mice through specific plasma markers of sensitization (IgE, IgG1), cytokines secretion of re-stimulated system anaphylaxis response (clinical scores, mMCP1), and Th1/Th2 balance (cytokines secretion of re-stimulated splenocytes). Gn mice were associated with a healthy infant microbiota selected for its dominance in Bifidobacterium and Bacteroides. Microbiota composition was analysed using culture and culture-independent method (DGGE) during the sensitization process and after BLG challenge.

Results: GF mice were more responsive to the sensitization and BLG challenge than microbiota-associated mice, independently of the microbiota composition, i.e. CV or Gn (infant microbiota) mice. GF mice displayed higher clinical scores of allergy, higher levels of BLG specific IgE, IgG1 and mMCP1 (showing massive mast cell degranulation), and a Th2 skewed profile as compared with microbiota-associated mice. Moreover, the allergic response was influenced by the gut microbiota composition as shown by lower levels of mMCP1 in Gn than in CV mice. Interestingly, differences in the gut microbiota composition were observed between CV mice displaying high and low allergic scores, with the high responders presenting significantly lower staphylococci levels. These differences were observed in caecum after challenge but not in faeces after sensitization.

Conclusion: We showed that (1) bacterial colonization of the gut had protective effect against sensitization and allergy response to BLG in mice (2) the intensity of the allergy response was linked to an alteration in the composition of the caecal microbiota.

Disclosure of Interest: Bertrand Rodriguez, EA 4065, Grant research Support from Nestlé research.

PO-G-195

A POTENTIAL ROLE FOR GALECTINS IN IMMUNE MODULATION UPON EXPOSURE OF HUMAN INTESTINAL EPITHELIAL CELLS TO NON-DIGESTIBLE CARBOHYDRATES AND TLR LIGANDS
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Objectives and Study: Early introduction of prebiotic non-digestible galacto- and fructo-oligosaccharides (scGOS/lcFOS) was found to reduce the incidence of atopic eczema in infants at risk. In addition, probiotic bacteria and in particular bacterial CpG DNA may support tolerance induction. Combined use of pre- and probiotics was most effective in the prevention of cow’s milk allergy in mice. In a novel in vitro coculture model the contribution of epithelial cells and epithelial derived galectins to the immune modulating effects of scGOS/lcFOS was investigated.

Methods: Human intestinal epithelial cells (IEC; HT-29) were cultured on transwell filters and exposed to 0.5% scGOS/lcFOS together with Toll-like receptor (TLR) 4 (LPS) or TLR9 ligand (CpG DNA) and co-cultured with anti-CD3/28 activated healthy donor peripheral blood mononuclear cells (PBMC) in the basolateral compartment. PBMC derived cytokines were measured by ELISA and T-cell phenotype was analyzed by flow cytometry. In addition, expression of galectins by IEC was studied by real time PCR and fluorescence microscopy. Apical and basolateral galectin function was blocked using lactose (100 mM). Sucrose treatment (100 mM) was used as control.

Results: TLR9 ligation of IEC resulted in enhanced TH1 type IFN-gamma secretion by activated PBMC in association with increased galectin-3 and -9 expression by IEC (P < 0.05). These responses were further enhanced after addition of scGOS/lcFOS (P < 0.01). TLR4 exposure of TLR9 agonist together with scGOS/lcFOS also increased the percentage of TH1 and regulatory T (Treg) cells. However, the TLR9-induced regulatory IL-10 secretion (P < 0.01) was not affected by scGOS/lcFOS. Basolateral blockage of galactins using lactose suppressed TLR9 induced IFN-gamma and regulatory IL-10 secretion while enhancing IL-6 (P < 0.05), IL-17 (P = 0.056) and TNF-alpha (P < 0.01) secretion by activated PBMC. TLR4 ligation of IEC enhanced epithelial galectin-4 expression as well as IL-12 and IL-17 secretion by activated PBMC which were both suppressed by scGOS/lcFOS (P < 0.01).

Conclusion: Upon epithelial exposure scGOS/lcFOS synergize with TLR9 ligand to support a TH1 and Treg type immune response and suppress pro-inflammatory responses induced by TLR4 ligation of IEC. scGOS/lcFOS
differentially modulate TLR-induced galectin expression by IEC which may contribute to immune regulation. Hence, intestinal epithelial cells may contribute to the protective effect of non-digestible carbohydrates like scGOS/lcFOS in the prevention of allergic disease.

Disclosure of Interest: This study was financed by Top Institute Pharma. J. Garssen is also affiliated at Danone Research B.V., The Netherlands.

PO-G-196

DIETARY NON-DIGESTIBLE CARBOHYDRATES INDUCE CD25+ REGULATORY T-CELLS THAT PROTECT MICE FROM DEVELOPING CASEIN ALLERGY

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Objectives and Study: Dietary non-digestible carbohydrates prevent the development of cow’s milk allergy in mice. In this study the contribution of CD25+ regulatory T-cells (Treg) was investigated using in vivo CD25+ depletion and adoptive transfer studies.

Methods: Mice were sensitized with casein and fed a diet containing 2% short-chain galacto-, long-chain fructo-, and acidic-oligosaccharides (GFA) or control diet. In vivo depletion of CD25+ Treg was performed using anti-CD25 (PC61). In addition, donor splenocytes of mice sensitized with casein and fed the GFA or control diet were adoptively transferred to naïve recipient mice in presence or absence of ex vivo depleted CD25+ Treg. Recipient mice were sham or casein sensitized and fed the control diet. The acute allergic skin reaction upon i.d. casein challenge and casein-specific immunoglobulins (Ig) and TH1 and TH2 counts were determined.

Results: The acute allergic skin reaction was reduced by GFA (P < 0.001) and in vivo anti-CD25 treatment abrogated this (P < 0.001). The GFA diet enhanced TH1 (P < 0.05) and tended to reduce the percentage of TH2 cells in the mesenteric lymph nodes. Splenocytes from casein-sensitized GFA fed donor mice prevented recipient mice from developing an acute allergic skin reaction and ex vivo depletion of CD25+ Treg prevented this without affecting Ig. The protection by the GFA diet was allergen specific since sham sensitized donor mice fed the control diet did not protect recipient mice from developing an allergic skin response.

Conclusion: CD25+ Treg were found to transfer tolerance, resulting in suppression of the allergic effector response occurring after dietary intervention with GFA in casein-sensitized mice.

Disclosure of Interest: This study was financed by Top Institute Pharma.

J. Garssen, B. van Esch and B. Schouten are also affiliated at Danone Research; L. Boon is affiliated at Bioscera and L. Knippels is affiliated at Danone Research.

PO-G-197

FAECAL CALPROTECTIN AS A MARKER OF INTESTINAL DISEASE IN PRETERM INFANTS: A SYSTEMATIC REVIEW

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Objectives and Study: Faecal calprotectin (FC) is a neutrophilic protein released upon localised gut inflammation. Its application in preterm infants is not yet established. Necrotising enterocolitis (NEC) is the most common devastating gastrointestinal disease of early life, with high morbidity and mortality. A quick, reliable, non-invasive faecal marker would aid early detection. We systematically reviewed the evidence base for the use of FC in preterm infants with intestinal disease.

Methods: Medline, Pubmed and Cochrane databases (1950 – December 1st 2009) were reviewed using SIGN guidelines (www.sign.ac.uk). Entry criteria comprised infants <37 weeks gestation. MeSH key word combination searches included: infant/preterm; very-low-birth-weight; FC; and NEC.

Results: 13 articles were identified, of which 7 were analysed further. 6 were higher evidence level (EL) controlled studies: 1- (1), 2- (5). The remaining case series was lower EL 3 (1). FC was measured by ELISA in all studies using 2 different manufactured kits (mcg/g). There was significant heterogeneity in description of cases, e.g. ‘NEC’, ‘focal intestinal perforation’, ‘need for abdominal surgery’, and ‘intestinal distress’. Controls were those without intestinal disease. 105 ‘cases’ (including 18 with NEC) and 211 ‘controls’ were identified. Of the 7 studies 5 demonstrated a higher FC in cases Vs controls, and 2 did not consider infants with intestinal disease. Sample timings in these 5 studies varied between single (n = 2), weekly (n = 4), and daily (n = 1). 2 studies included measurement in meconium, but only 1 quoted these (mean: 332, r:12–9386). Highest levels were recorded in definite NEC (≥Bell’s Stage I b), mean: 3755.13; (r:168–22,513) Vs mean: 166.38, (r:12–9386) in controls (P=0.053).

Conclusion: At present collective measurement of sensitivity and specificity of FC as a marker of intestinal disease and NEC in preterm infants is inappropriate given the heterogeneity of methodologies and case definitions, as well as the lack of serial measurements before, during, and after illness. These may also be affected by natural variation in levels with postnatal age. The effects of other confounders such as abdominal surgery require further investigation. Given the small numbers in these studies, appropriately powered current and future RCTs on the effect of
NEC-reduction strategies would be well placed to assess the role of FC in predicting and monitoring response to intestinal insults.

Disclosure of Interest: None declared.

PO-G-198

BACTERIAL ESTABLISHMENT OF GUT MICROBIOTA IN PRETERM INFANTS
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Objectives and Study: Littel information is available concerning the abnormal gut microbiota in preterm infants, which could be a risk factor of postnatal gastrointestinal diseases, including necrotizing enterocolitis, impaired nutritional status, and nosocomial infections. The aim of this study was to describe the gut microbiota of preterm infants at 1 mo of life infants using culture and culture-independent methods and to determine the main factors that influence its establishment.

Methods: This monocentric prospective longitudinal study enrolled from birth 73 preterm infants and 21 term infants. Perinatal factors were recorded. Faecal samples were collected at one month of life and analyzed by culture and qPCR.

Results: Staphylococci, enterococci and enterobacteria colonized circa 2/3 of the preterm infants. 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. By contrast, fullterm infants displayed a higher incidence of colonization by the anaerobic microbiota. Gestational age (GA) was the major factor influencing the bacterial establishment of preterm infants. In those born with a GA less than 28wks, the microbiota mainly comprised staphylococci and less than 1/2 of these infants were colonized by enterococci, enterobacteria, and clostridia. Neither bifidobacteria nor lactobacilli were detected. In infants born with a GA of 29–32 wks, the incidence of colonization by aerobic bacteria was between 81 and 95%. 87% of these infants were colonized by clostridia, but colonization by the other anaerobic genera was still dramatically low with only 13%, 11%, and 2% of these infants colonized by bifidobacteria, lactobacilli, and Bacteroides respectively. Preterm infants born at a GA of 33–36 wks had a microbiota pattern quite similar to fullterm infants, except a slightly lower incidence of bifidobacterial colonization (2/3 vs 95%).

Conclusion: Our data demonstrate very abnormal gut microbiota pattern in preterm infants at 1 mo of life compared to term infants. Gestational age is a major factor that influence the bacterial establishment of preterm infants. The important colonization rate of clostridia among a microbiota characterized by the paucity of species, in particular concerning bifidobacteria, a genus known for its health promoting properties, in the infants born before 32 wks of gestation may contribute to the higher risk for gastrointestinal diseases in these infants.

Disclosure of Interest: This study is supported by the French Agency for Research (ANR).

PO-G-199

COMPLIANCE TO (INTERNATIONAL) GUIDELINES FOR DIAGNOSIS AND TREATMENT OF CHILDREN WITH ACUTE GASTROENTERITIS. RESULTS OF A NATIONWIDE SURVEY IN PEDIATRIC DEPARTMENTS IN THE NETHERLANDS
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Objectives and Study: In this study we investigated compliance of Dutch pediatricians to guidelines for diagnosis and treatment of acute gastroenteritis (AG) in children. Compliance to these guidelines is considered important in order to increase quality of care and to reduce costs.

Methods: All pediatricians who are member of the Dutch Association of Pediatrics (‘NVK’) were informed about the survey through e-mail. In this e-mail message a direct link to a web-based Survey was presented. In the Survey pediatricians were asked to inform us about: 1. the number of admissions for dehydration in AG, 2. the percentage of children by whom the degree of dehydration was diagnosed on clinical grounds, and 3. the percentage of children in which diagnosis was made on the basis of laboratory investigations (blood sodium, blood gas analysis, glucose, urea, creatinin), 4. the way in which patients were rehydrated, 5. criteria for intravenous and oral rehydration, and 6. whether a published (inter)national guideline was used. Guidelines included: guideline of the American Academy of Pediatrics, the ESPGHAN guideline and a Dutch National Guideline (‘Compendium Kindergeneeskunde’).

Results: N=45 pediatric departments filled out the Survey (4 University Hospitals, and 41 General Hospitals). The number of admissions for dehydration in AG was 108 (25–400)(mean(range)). In 95% of cases degree of dehydration was assessed on clinical grounds; in 85% of cases laboratory investigations were performed. Five responders diagnosed dehydration on clinical grounds only, and 4 responders only used laboratory tests. The majority of responders used laboratory tests frequently (84% sodium, 73% blood gas, 49% glucose, 74% urea). Only 18% rehydrated orally in 4 hours, 49% in 6–12 hours, and 23% in 24 hours. Criteria for intravenous rehydration were: shock (46%), hypernatremia (19%) and persistent vomiting/failure of oral therapy (35%). Compliance to international guidelines was poor (4% used AAP; 20% ESPGHAN). Compliance to the National Guideline was...

Disclosure of Interest: None declared.

PO-G-200

NO EVIDENCE FOR A CAUSATIVE ROLE OF BLASTOCYSTIS HOMINIS IN CHILDREN WITH RECURRENT ABDOMINAL PAIN

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Objectives and Study: To investigate if recurrent abdominal pain (RAP) in children may be treated successfully by eradicating Blastocystis hominis (B.h.) with trimethoprim-sulfamethoxazole (TMP/SMX). Secondary outcome was the eradication rate of B.h. with TMP/SMX and metronidazole.

Methods: From October 2004 to December 2008 all patients referred to the Division of Paediatric Gastroenterology and Nutrition of the University Children’s Hospital Zurich because of RAP and detection of B.h. in stool samples as the only pathological finding after a standard work up (blood tests, Helicobacter pylori breath test, stool tests for parasites and bacteria) were offered to participate in the study. Patients were prospectively, randomly assigned into two groups. TMP/SMX (36 mg/kg/d) or placebo was given for 7 days in a double blind, placebo-controlled manner. Pain intensity was measured with a visual analogue scale either with numbers 0–10 or standardised face drawings, depending on the age of the patient. Two weeks after completion of treatment patients were followed clinically and three stool samples were collected. If B.h. was detectable in at least one of the stool samples, metronidazole (30 mg/kg/d) was given for 7 days and a further clinical and laboratory follow-up was arranged.

The study was approved by the local and regional ethical committee as well as the Swiss agency for therapeutic products. Procedures were conducted in accordance with the ICH Good Clinical Practice Guidelines.

Results: 43 patients met inclusion criteria, 40 patients were recruited and 37 finished the study (TMP/SMX n = 20, placebo n = 17). Demographic data showed no significant difference between the groups. The mean pain index after treatment patients were followed clinically and three stool samples were collected. If B.h. was detectable in at least one of the stool samples, metronidazole (30 mg/kg/d) was given for 7 days and a further clinical and laboratory follow-up was arranged.

The study was approved by the local and regional ethical committee as well as the Swiss agency for therapeutic products. Procedures were conducted in accordance with the ICH Good Clinical Practice Guidelines.

Results: 43 patients met inclusion criteria, 40 patients were recruited and 37 finished the study (TMP/SMX n = 20, placebo n = 17). Demographic data showed no significant difference between the groups. The mean pain index after treatment declined from 7.1 to 3.6 for all patients, with a decrease from 6.9 to 4.1 in the TMP/SMX- and 7.4 to 3.0 in the placebo-group, irrespective of detection of B.h. after treatment completion. Regardless of the precedent first line therapy metronidazole treatment led to a pain index decline from 3.7 to 1.9 in the remaining 25 patients. Eradication quotes were 35% in the TMP/SMX group, 29% in the placebo group and 44% with metronidazole as second line treatment.

Conclusion: In this randomized, double blind, placebo-controlled trial there was no difference in the eradication rate of B.h. between TMP/SMX and placebo. No difference in the decrease of pain index between the TMP/SMX and the placebo group could be observed. Furthermore, the decrease of pain index was irrespective of persistence or eradication of B.h. We conclude that there is no evidence for a causative role of B.h. in children with RAP in our study.

Disclosure of Interest: None declared.

PO-G-201

PROBIOTICS IN THE TREATMENT OF GIARDIASIS

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Objectives and Study: Giardiasis is the most common protozoa infection in children in Russia. It is the most often cause of abdominal pain, dyspepsia and protractible diarrhea. The results of the treatment of giardiasis are not satisfactory.

Aim: To improve the results of therapy of giardiasis

Methods: 129 children from 6 till 17 years old with giardiasis were randomized into 3 group according treatment received: 1 group (n = 43) used nitrafurat 15 mg/kg for 10 days; 2 group (n = 64) — metronidazol 20 mg/kg for 10 days; 3 group (n = 22) - albendazol 10 mg/kg for 7 days. 62 of these children also received probiotics with the main drug therapy: 36 patients received B.longum+E.feacium 107 2 times a day, 16 patients – B.bifidum+B.longum+L.gasseri 107 2 times a day, 20 patients – B.infantis+L.acidophilus+E.feacium 107 2 times a day for 2 weeks. The results of the therapy were assessed with PCR and microscopy of faeces. We provided an immunological study included assessment in biopsy specimens of duodenal mucosa the level of proinflammatory (IL-8,-INF-γ) and anti-inflammatory (IL-10) cytokines. We compared also results of microbial composition of faeces with cultural method. Study held twice: prior to treatment and in 2 weeks after.

Results: The efficacy of monotherapy with every of anti-protozoa drugs was very low: nitrafurat 21.4 %, metronidazol - 12.5 %, albendazol - 33%. Metronidazol had the highest level of adverse effects: vomiting (14%) and metallic taste in the mouth (18%). 1 child, consumed nitrafurat, had allergic rashes. Probiotic treatment with B.longum+E.feacium 107 according with nitrafurat improved treatment to 82%, with metronidazol – to 70.5%, with albendazol – to 87.5%. B.bifidum+B.longum+L.gasseri and B.infantis+L.acidophilus+E.feacium used only in combination with metronidazol, the efficacy of both was equal - 69%. All probiotics decreased the increasing IL-10 level and kept the same level of IL-8 and INF-γ, the ratio of IL-10/INF-γ has fallen from 6.7 to 3.4 (P < 0.05). Against this, monotherapy with
PO-G-202

ORAL REHYDRATION THERAPY WITH REDUCED OSMOLARITY ORAL REHYDRATION SOLUTIONS - AN EFFICIENT MANAGEMENT IN ACUTE DIARRHEA IN INFANTS

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Objectives and Study: Acute diarrhea, frequent in infant, may rapidly lead to dehydration. The first step in pathogenic therapy of diarrhea is represented by oral rehydration. The recent researches highlight the superiority of the Reduced Osmolarity Oral Rehydration Solutions (RORS). The objective of our study is to demonstrate the efficiency and the superiority of the RORS versus standard osmolarity Oral Rehydration Solution (standard ORS) in Oral Rehydration Therapy (ORT) of diarrhea in infant.

Methods: Between 2007 and 2008, we have made a prospective comparative randomized study, which has included 226 infants with acute diarrhea with/without mild or moderate dehydration. The patients included into the study were randomized in two groups, homogenous in terms of number and age of patients: the control group, 118 infants, rehydrated with standard ORS (311 mosm/l, sodium chloride 90 mmol/l, glucose 89 mmol/l) and the study group, 118 infants, rehydrated with RORS (230 mosm/l, sodium chloride 60 mmol/l, glucose 89 mmol/l). Oral rehydration was made according with World Health Organization recommendations and Endorsed Clinical Practice Guideline (2009). ORT was followed by precocious infant feeding. Infants with moderate dehydration received intravenous infusion 12–24 hours before ORT. The following clinical parameters were monitored: weight chart (between the admittance, the 3rd day and the discharged day), duration of diarrhea symptoms (average, minimum and maximum of duration), number of cases of remitted diarrhea/days, frequency of stool/day, days of hospitalization (average, maximum and minimum, total number of days of hospitalization).

Results: ORT with RORS versus standard ORS led to the following results: a decrease in frequency of stool starting with the 3rd day of treatment, with 58% (P < 0,001); a decrease in the mean duration of diarrhea (2,89 ± 0,76 days compared with 4,88 ± 1,17 days), with 40% (P < 0,001); a decrease in average number of days of hospitalization/case (5 ± 1,6 days compared with 6,91 ± 1,7 days), with 31% (P < 0,001); gain weight starting with the 3rd to discharged day (P < 0,001).

Conclusion: RORS decrease the intraluminal osmolarity, favouring the absorption of water and electrolytes by the solvent drag action, their use determining a decrease in duration of diarrhea, frequency of stool, hospitalization period, complications of dehydration, which represent economic and psycho-social important advantages.

References:

Disclosure of Interest: None declared.

PO-G-203

MANAGEMENT OF ACUTE GASTROENTERITIS IN FRANCE AND IN ALGERIA BY PAEDIATRICIANS AND GENERAL PRACTITIONERS: WHAT’S RECOMMENDED AND WHAT’S PRACTICED

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Objectives and Study: The ESPGHAN Working Group on acute diarrhoea and the French Speaking Group (GFHGNP) published recommendations with specific emphasis on oral rehydration solutions (ORS), early refeeding and avoidance of ineffective drugs. We conducted a study to determine if these treatment guidelines are closely followed by physicians in France and in Algeria.

Methods: Observational prospective study. France: 1 November 2003–29 February 2004. Algeria: 1 February - 30 June 2009. Children aged from 7 days to 3 years were included if they presented at least 3 watery stools per day. Physicians were fully free for their prescriptions.

Results: France: 695 children were treated by 332 general practitioners (GP) and 206 paediatricians (P). Algeria: 429 children were treated by 31 GP and 20 P. For children <18 months of age, ORS were better prescribed in Algeria (91,2%) than in France (83,8%). ORS were stopped before 12h in France and 38% of the cases and never before 24h in Algeria. Refeeding was initiated within 4h in Algeria and globally after 8h in France. The current milk was stopped in 66,4% of children in France and merely in 24,5% in Algeria. In these cases, formula was changed for a lactose-free formula (F = 63,8%, A = 58,6%), for a protein hydrolysate (F = 13,3%, A = 11,5%) and various formulas including probiotics (F = 22,9%, A = 29,9%). Both in the two countries, one drug at least was prescribed in 96% of children with a mean of 2,4 drugs per child: domperidone, racecadotril, probiotics and smectite were used in 92% of these cases.

Conclusion: Globally, P and GP in France all act similarly in both countries. Oral rehydration and milk refeeding were better managed in Algeria than in France. One more time, this study demonstrates that we are still far from the
recommendations for optimal management of acute gastroenteritis, particularly concerning drug’s prescription.

Disclosure of Interest: None declared.

PO-G-204

NOROVIRUS: PRIMARY CAUSE OF SPORADIC VIRAL ACUTE DIARRHEA IN CANARY ISLANDS (SPAIN)
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Objectives and Study: To determine the prevalence and clinical characteristics of norovirus acute diarrhea (AD) among hospitalized children in Canary Islands.

Methods: Prospective, transversal, descriptive and analytical study in younger than 5 years of age and admitted to our hospital with AD (3 or more liquid stools in the last 24 hours before admission) from May 2007 to October 2008. Patients with previous digestive pathologies or those who had received medical care in the previous week were excluded. A questionnaire was designed for data collection comprising sociodemographic, clinical, analytic and evolutive variables as well as a severity scale (Rauksa and Vesikari criteria). A stool sample from each child was screened for enteropathogenic bacteria and tested by reverse transcription (RT)-PCR for rotavirus, astrovirus, norovirus, and sapovirus and by immuno chromatographic methods for enteric adenoviruses. Subjects were then grouped on the basis of presence/absence of norovirus. Statistical study was based on the chi-squared test, Wilcoxon and multivariant logistic regression.

Results: 167 samples were collected (81 female / 86 male) (range: 4 months-5 years of age) (mean:16 months). In 14 samples (8.4) several viruses were isolated, with rotavirus being present in all of them, adenovirus in 10 and norovirus in 4. In 29 samples (17.4%), tests were negative. In the rest of the samples, only one type of virus was isolated: norovirus in 63 samples (37.7%); rotavirus, 54(32,3%); astrovirus, 3 (1.8%); and adenovirus, 4 (2,4%) No statistically significant differences were found for sociodemographic variables, clinical symptomatology or hidroelectrolytic alterations. In both groups, mean duration of diarrhea was 6 days and number of daily stools was 10. The mean severity score in both groups was 13, with severe cases being more frequent (89,4% in norovirus group and 85,7% in the rest). Norovirus is present throughout the year, with outbreaks in summer and winter. The other group follows a traditional seasonal pattern at the expense of rotavirus.

Conclusion: Norovirus is the most common viral cause of DA in children younger than 5 years of age and especially in infants younger than 6 months. Clinical symptomatology and severity are similar to those observed in other viral infections. It shows a seasonal pattern with outbreaks in summer and winter.

Disclosure of Interest: None declared.
PO-G-206

A SINGLE BLIND STUDY ON CLINICAL EFFICACY OF SACCHAROMYCIES BOULARDII OR METRONIDAZOLE IN SYMPTOMATIC CHILDREN WITH BLASTOCYSTIS HOMINIS INFECTION

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Objectives and Study: Although many Blastocystis infections remain asymptomatic, recent data suggest it also causes frequently symptoms. The goal of this study was to compare the natural evolution (no treatment) to the efficacy of S. boulardii or metronidazole.

Methods: Children presenting with gastrointestinal symptoms (abdominal pain, diarrhea, nausea-vomiting, flatulence) since more than 2 weeks and confirmed B. hominis infection were eligible for inclusion. Randomization was performed by alternating inclusion: group A: S. boulardii (250 mg twice a day, Reflor) during 10 days; Group B: metronidazole (30 mg/kg twice daily) for 10 days; Group C: no treatment. At day 15 and 30 after inclusion, patients were re-evaluated and stool samples were examined microscopically. On day 15, children that were still symptomatic and/or were still B. hominis infected in group C, were treated with metronidazole for 10 days.

Results: There was no statistically significant difference between three study groups for age, gender and the presence of diarrhea and abdominal pain. On day 15, clinical cure was observed in 77.7% in group A (n:18), in 66.6% in Group B (n:15) and 40% in Group C (n:15) (p Group A-C = 0.031). Disappearance of the cysts from the stools on day 15 was 80% in Group B, 72.2% Group A and 26.6% in Group C (P = 0.011 Group B-C; P = 0.013 Group A-C). Cure rate at Day 30 was similar for group A and B.

Conclusion: Metronidazole or S. boulardii have potential beneficial effects in B. hominis infection (symptoms, presence of parasites). These findings challenge the actual beneficial effects in B. hominis infection.

Disclosure of Interest: None declared.

PO-G-208

Fecal calprotectin levels as predictive marker for NEC in VLBW – interim results from a prospective multicentric trial

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Objectives and Study: Necrotising enterocolitis (NEC) is the most common gastrointestinal emergency in neonates with high mortality and morbidity particularly in very low birth weight infants (VLBW).

Methods: In order to assess the suitability of fecal calprotectin levels as predictive marker for NEC in VLBW we started a prospective multi-centre study in May 2008. Up to September 2009, 227 patients were included with complete data available in 168 cases. The mean gestational age was 29.1 weeks (23.0–34.1) and mean birth weight 1048 g (354–1490 g). 11 patients suffered from NEC defined as NEC-stage ≥ II (6.6%). 6 of those presented with classical and 5 with fulminant NEC defined as progression to NEC-stage III within 6 hours after onset of disease.

Results: The mean meconium calprotectin level in healthy VLBW was 158.5 μg/kg (5.8–310.8) and was significantly higher compared to preterms who eventually developed NEC (36.6 μg/kg;18.4–78.3; P = 0.018). In all cases calprotectin levels increased above 450 μg/kg. 5 out of 6 patients (83%) with classical presentation showed elevated calprotectin levels >250 μg/g 24h before clinical suspicion of NEC. In contrast, calprotectin levels in patients with fulminant NEC did not increase before laparotomy.

Conclusion: Fecal calprotectin seem to be a sensitive marker for classical NEC. However, patients with a fulminant NEC do not show an increase in calprotectin levels early in the disease which might indicate an impaired immunological response in such patients. Finally, VLBW who eventually developed NEC had significantly lower meconium calprotectin levels which might be suitable for early risk assessment of future NEC development.

Disclosure of Interest: None declared.

PO-G-209

MBL2 GENETIC VARIANTS ARE ASSOCIATED WITH INCREASED RISK FOR DEVELOPING CELIAC DISEASE IN ITALIAN PATIENTS

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Objectives and Study: Functional variants of the MBL2 gene encoding for the Mannose Binding Protein have been already associated with an increased risk for developing celiac disease (CD) in Italian patients (1, 2); a positive association was also found in a Finnish study (3). We replicated the analysis on a larger group of celiac patients from North Eastern Italy.

Methods: We screened for MBL2 functional polymorphisms in 1104 CD patients (707 F, 397 M; mean age 6.7 range 3–14) and 450 healthy blood donors (320 F, 130 M; mean age 23 range 19–41). HLA genotyping was performed using the PCR-SSP Kit AllSet (Dynal). Melting Temperature Assay has been used for the detection of MBL2 functional variants.

Results: MBL2 allele and genotype frequencies were similar between CD patients and healthy controls, but when
considering subjects characterized by not-DQ2/DQ8 HLA haplotypes (DR7 or without the DQ2/DQ8 heterodimer) a significant difference in the distribution of the 0 allele ($P=0.0092$) or 00 genotype ($p=7.879\times10^{-5}$) was found (see Table). In the not-DQ2/DQ8 CD patients the presence of the 00 genotype conferred a major risk (O.R. 4.09 CI = 1.95–8.41) to develop the disease.

**Conclusion:** We demonstrated that in absence of the main locus responsible for the susceptibility to CD MBL2 functional variants do strongly associate with the disease.

**References:**

**Disclosure of Interest:** None declared.

**PO-G-210**

**GASTROINTESTINAL INFLAMMATION IN CHILDREN WITH DI GEORGE’S SYNDROME**

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**Objectives and Study:** Di George’s syndrome is a clinical entity that describe the association of thymic hypoplasia or dysplasia with cardiac abnormalities, parathyroid hypoplasia and cleft palate. The majority of children with Di George’s syndrome have a hemizygous deletion of chromosome 22q11.2 and a significant number of patients have a variable degree of immune deficiency. Although different systemic abnormalisits have been described in association with Di Georg’s syndrome such as renal, neurodevelopmental and skeletal, there has been no description of the gastrointestinal features associated with it.

The aim of this study is to describe the gastrointestinal disorders in children with Di George’s syndrome and to determine whether these features are related to the degree of associated immune deficiency.

**Methods:** Patients with confirmed diagnosis of Di Georg’s syndrome and microdelition of chromosome 22q11.2 who were referred for gastrointestinal assessment and underwent endoscopic evaluation were studied. The presenting symptoms, the histology, total immunoglobulin, IgG subclasses, total lymphocyte count and T cell subsets were assessed.

**Results:** 12 patients (8 females and 4 males) were identified. The commonest presenting symptoms were failute to thrive and protracted diarrhoea (10/12). 6 had upper endoscopy, 5 had both upper and lower endoscopy, 11/12(92%)had identifiable pathology in their biopsies. The changes varied from pan eretic inflammatory process to isolated gastritis, oesophagitis or enterocolitis. The commonest features were plasma cell and lymphocytic infiltration (9/11) while one patient had eosinophilic oesophagitis.

Total immunoglobulins were low in 8/11 (73%) with low IgG and IgM needing immunoglobulin supplementation, while signs of immune dysregulation with raised IgG subclasses were seen in 3 patients. 11/12 patients had normal lymphocyte count. T cells were absent in one patient and slightly low in 2 patients.

**Conclusion:** This is the first study to describe the GI involvement in Di George’s syndrome. There seems to be clear association between GI inflammations in patients with Di George’s syndrome in this cohort. The association of gut inflammation and abnormal humeral response may suggest that this association is more common in patients with significant humeral immune deficiency and may suggest a GI autoimmune process. A larger study to look into this association and it’s mechanisms is warranted.

**Disclosure of Interest:** None declared.

**PO-G-211**

**LACTOBACILLUS RHAMNOSUS GG (LGG) AND ITS SOLUBLE FACTORS PROTECT AGAINST ALLERGIC SENSITISATION IN NEWBORN MICE**

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The aim of this study is to describe the gastrointestinal disorders in children with Di George’s syndrome and to determine whether these features are related to the degree of associated immune deficiency.

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Total immunoglobulins were low in 8/11 (73%) with low IgG and IgM needing immunoglobulin supplementation, while signs of immune dysregulation with raised IgG subclasses were seen in 3 patients. 11/12 patients had normal lymphocyte count. T cells were absent in one patient and slightly low in 2 patients.

**Conclusion:** This is the first study to describe the GI involvement in Di George’s syndrome. There seems to be clear association between GI inflammations in patients with Di George’s syndrome in this cohort. The association of gut inflammation and abnormal humeral response may suggest that this association is more common in patients with significant humeral immune deficiency and may suggest a GI autoimmune process. A larger study to look into this association and it’s mechanisms is warranted.

**Disclosure of Interest:** None declared.
PO-G-212

VARIATION OF THE IMMUNE PROFILE IN COLOSTRUM, EARLY AND MATURE MILK

Objectives and Study: The microbiota composition in the gut has been implicated in the development of allergic disease and asthma. It is known that the intestines of children with allergy are less often colonized with Lactobacillus and Bifidobacterium species. Rodent models of allergic sensitisation have shown specific protective effects of probiotic supplementation on the development of allergic disease. Furthermore, there is evidence that soluble factors produced by probiotic strains may also exert these effects. The aim of this study was to investigate specific protocols for LGG fermentation to generate soluble factors in order to prevent allergic disease in newborn mice.

Methods: The effects of Lactobacillus rhamnosus GG (LGG) were investigated in vitro using RAW274 mouse macrophages cell line and measuring pro- and anti-inflammatory cytokine production upon stimulation with LGG or LGG-derived supernatant fractions. LGG supernatant fractions were also treated with protease and sugar digesting enzymes to assess the contribution of these compounds to the observed biological effects. For in vivo studies, Balb/c mice were orally supplemented with LGG or LGG supernatant, from day two until week six of age, and then a protocol of acute allergic airway inflammation was applied. At the end of the experiment airway reactivity, BAL cytokines, serum immunoglobulins and lung histology were analyzed.

Results: In vitro experiments demonstrated that incubation of RAW274 cells with LGG bacteria or selected supernatant fractions resulted in increased TNFα and IL-10 production. Initial experiments revealed short heat treatment procedures to reduce the biological activity which however was preserved through ultra filtration and lyophilisation. Biological effects were abolished upon protease treatment and reduced after sugar digestion. In vivo treatment of newborn mice with viable LGG or selected supernatant resulted in less Th2 cytokines and OVA-specific IgE, lower eosinophil influx into the BAL, and significantly less lung inflammation and goblet cell numbers in comparison to treated mice.

Conclusion: We demonstrated that neonatal LGG supplementation may play a protective role in early allergic sensitization and acute experimental allergic airway inflammation later in life. Moreover, the studies support soluble factors from LGG to play a role in the transmission of this immunological effect early in life.

Disclosure of Interest: EAF van Tol, Mead Johnson Nutrition, employee.

PO-G-213

SALMON CONSUMPTION BY PREGNANT WOMEN REDUCES EX VIVO UMBILICAL CORD ENDOTHELIAL CELL ACTIVATION
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Objectives and Study: Inhibition of cell adhesion molecule (CAM) expression on endothelial cells (EC) is likely to ameliorate inflammatory and cardiovascular disease (CVD). In vitro exposure of EC to long chain (LC) n-3 polyunsaturated fatty acids (PUFA) has been shown to reduce CAM expression and leukocytic cell adhesion. Animal studies have shown similar effects. The aim of the current study was to assess whether salmon (rich in LC n-3 PUFA) consumption twice a week during pregnancy affects umbilical vein endothelial cell (HUVEC) activation.

Methods: HUVEC were isolated and cultured from a subset of participants (n=10) of the UK salmon in pregnancy study (SIPS). Cell surface expression of intercellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1) was assessed by flow cytometry in the presence or absence of 24 h LPS stimulation. In addition mediator secretion was measured by multiplex assay.

Results: The level of LPS induced ICAM-1 (P=0.006) and VCAM-1 (P=0.034) expression was significantly lower in the salmon diet group as compared to controls. Moreover, IL-6 secretion increased significantly upon LPS stimulation in the control group (P=0.003) but not in the salmon group, whereas TNF-alpha release was not affected by the salmon intervention. Furthermore, growth factor G-CSF, known to suppress ICAM-1 expression, was significantly enhanced by the salmon diet (P=0.009).

Conclusion: Increased dietary salmon intake was found to dampen EC activation, implicating a role for LC n-3 PUFA in suppression of inflammation and prevention of CVD in humans.

Disclosure of Interest: This study was sponsored by the Nutricia Research Foundation J. Gàrssen, Danone Research, employee.

PO-G-214

PRACTICAL OUTCOMES OF THIOPURINE METABOLITE MEASUREMENT IN PAEDIATRIC PRACTICE

Objectives and Study: Clinical response to Thiopurines is dependent on the concentration of its active metabolite, 6-Thioguanine Nucleotide (6-TGN). Dosing is, however, unpredictable because the concentration of 6-TGN is dependent on Thiopurine Methyl Transferase (TPMT) activity, an enzyme with common genetic polymorphisms. Because metabolite monitoring is not commonplace in the UK, some clinicians use proxy measures to assess response to thiopurines. We aim to evaluate how measuring thioguanine metabolites measurement influences clinical practice.

Methods: Thiopurine metabolites were measured in children who had been on medication for 3 months or more. For each measurement, data were collected on dosage, disease severity, concomitant use of 5-ASA, haematological and biochemical indices, and changes to management. Therapeutic 6-TGN levels were defined as 235–400 pmol/8 x 108 RBCs. Toxicity is defined as WBC <4 x 10^9/L, neutrophils <2 x 10^9/L, and AST/ALT >2 x elevated.

Results: 64 individuals studied, median age 14 years. Underlying diagnoses were 'IBD' (54/64) and 'other' (10/64). 59 treated with AZA, 5 with 6-MP. 95 separate measurements were made. TPMT phenotype was measured in 51/64 patients, 40/51 had ‘normal’ phenotype, and 11/51 had heterozygous TPMT mutations. Initial 6-TGN levels were higher in heterozygotes (median levels 836 vs. 328, P=0.001) at comparable doses of thiopurine (median 1.9 vs. 2.2 mg/kg, P=0.11). On first measurement, only 30% patients had 6-TGN levels within therapeutic levels. 30% were sub-therapeutic and 40% were supra-therapeutic. 9% had 6-TGN levels >800. Toxicity occurred in 7 cases (8%). Leucopenia (WBC<4) had a sensitivity of 2.5% in predicting therapeutic or supra-therapeutic 6-TGN levels. Concomitant use of 5-ASA did not significantly affect 6-TGN levels at comparable doses (median [6-TGN] 5-ASA 393 vs. 451 no 5-ASA, P=0.26).

In total, management was changed in 39 cases (41%). 6 cases of total non-compliance were exposed. 33/39 of these changes were adjudged to be exclusively or predominantly influenced by knowledge of the 6-TGN level.

Conclusion: Based on standard dosing regimens, clinicians can expect to achieve therapeutic levels of 6-TGN in a minority of cases. Measuring Thiopurine metabolites aids therapeutic dose alteration, detects potential toxicity, and identifies issues of non compliance that cannot be detected on routine blood monitoring.


Disclosure of Interest: None declared.

PO-G-215

CORRELATION OF SERUM VITAMIN D CONCENTRATION LEVELS WITH SEVERITY OF INFLAMMATORY BOWEL DISEASE

Objectives and Study: Vitamin D (25-OH D) may be implicated in the pathophysiology of inflammatory bowel disease (IBD) by regulating functions of inflammatory and immune cells. As in winter its synthesis is decreased in our region, we evaluated concentration levels of 25-OH D in correlation with IBD severity and seasonal variation.

Methods: We reviewed reports of patients who were referred to our unit for IBD in the last 5 years. Data collected included blood concentration levels of 25-OH D, albuminemia, erythrocyte sedimentation rate (ESR), and C-reactive protein...
Results: Among the 77 patients (mean age: 13 ± 0.3 years) included in the study, 49% and 51% were respectively admitted from November to April, and from May to October. Most patients had Crohn’s disease (90%) with a mean pediatric Crohn’s disease activity index of 29 ± 2 (range: 5–60). Mean levels of 25-OH D (65 ± 3 vs 59 ± 3 U), albuminemia (36 ± 0.7 vs 34 ± 0.7 g), ESR (29 ± 0.4 vs 32 ± 0.4 mm), and CRP (39 ± 6 vs 50 ± 6 mg) were not significantly associated with the season of admission. Mean 25-OH D levels were however inversely correlated with CRP (r = -0.5, P = 0.02). Albuminemia and ESR levels were not significantly correlated with 25-OH D (table 1).

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Conclusion: These results suggest that blood concentration levels of 25-OH D are inversely correlated with IBD severity, but without seasonal variation.

Disclosure of Interest: None declared.

PO-G-217

LONG TERM OUTCOME IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE
A. Batra*, B. Sandhu, C. Spray. Department of Paediatric Gastroenterology, Bristol Royal Hospital for Children, Bristol, United Kingdom.

Objectives and Study: The aim was to document the long term outcome of children diagnosed with inflammatory bowel disease (IBD) over a period of 15 years with particular reference to the response to treatment, growth, rate of relapse, need for surgery and identify predictors of outcome.

Methods: A prospective database of newly diagnosed children less than 16 years of age diagnosed with IBD has been kept at regional unit covering population of 5.2 million. Cases diagnosed between 1993–2003 were included (n = 241). Those cases who, after 16 years of age, were followed by adult gastroenterologist locally comprised 24% of total (58/241) and their initial data at diagnosis and subsequent case notes were analyzed.

Results: The average follow up duration was 8.6 yrs (5–13yrs). Mean age at diagnosis was 12.7 years. 50% (23/46) had Crohn’s disease (CD), 40% (23) Ulcerative colitis (UC), and 3% (2) Indeterminate colitis. 45% (26) were treated with steroids, 36% (21) with enteral feeds and 19% (11) were treated with 5 Aminosalicylates at initial diagnosis. Average number of relapses was 0.4/year with no difference between groups treated with steroid or enteral feeds. Time to 1st relapse was 9.1 months and 11.4months in groups treated with enteral feeds and steroids respectively. 23% (6/26) were steroid dependent and 7.5% (2/26) were resistant. Growth failure was seen in 13.7% and risk increased by 4.4 times in those with steroid dependence. Bone mineral density below -1.5 standard deviations was found in 14% (8/58), with equal distribution between CD and UC. This was increased in children of Asian origin (RR = 6.4), steroid dependence (RR = 4.4) and there was a correlation with disease activity (P = 0.02). Children treated with Azathioprine (AZA) had an absolute risk reduction for bone disease by 25% and for...
growth failure by 15%, 30% of patients required surgery and rates were similar for CD and UC. The mean duration of illness before needing surgery was 6.14 and 3.8 years in UC and CD respectively. There was a correlation between disease activity and need for surgery. 50% children with steroid dependence needed to undergo surgery. 6 patients with CD had resection of their terminal ileum (TI). The average duration of relapse following TI resection was 21.3 months with range of 8 – 36 months.

**Conclusion:** Time to 1st relapse after enteral therapy with range of 8 – 36 months.

PO-G-218

**ROLE OF MEASUREMENT OF 6TGN LEVELS IN CHILDREN WITH IBD ON AZATHIOPRINE**

A. Batra*, S. Protheroe. Department of Gastroenterology, Birmingham Children’s Hospital, Birmingham, United Kingdom.

**Objectives and Study:** Serious side effects are responsible for discontinuation of treatment with Azathioprine (AZA)in up to 18% children. TPMT deficiency fails to account for over 70% of these cases. There is insufficient data regarding role of 6TGN measurements in children.

The aims of the study were to look at the effectiveness of 6TGN levels as predictor of control of disease and risk of side effects in children with Inflammatory Bowel Disease (IBD) and its correlation with dose of AZA.

**Methods:** A case notes review was done. Children with IBD on AZA, who had their 6TGN levels measured between Jan to Dec 2008 were included. The cases were grouped into those with good control (Harvey Bradshaw Index (HB)>6, no relapse in last 6 months) and poor control (HB<7, relapse in 6 months). Data including 6TGN levels, dose of AZA and adverse effects were recorded.

**Results:** 42 patients fulfilled the above criteria. The mean age was 13.9 years (6 – 17 years). The male to female ratio was 1.6:1. 55% (23) were diagnosed as Crohn’s disease, 38% (16) as ulcerative colitis and 7% (3) as indeterminate colitis. All patients had their TPMT levels measured. 9.5% and 4.75% patients had TPMT levels above and below the normal respectively. The AZA dose ranged from 0.71 to 3.125 mg/kg/day (mean2.09 mg/kg/day). 9.5% (4) had adverse effects of AZA in the form of neutropenia (neutrophil count <1.5 x 109/L). 81 measurements of 6TGN were made (1–4/patient). The mean 6TGN level was 395.7 pmol/8x108 cells (range <50 - 1477 pmol/8x108 cells). The target range used by our lab for maximum efficacy is 235–450 pmol 6–6TGN/8x108 cells. We had 30.8% levels under, 30% levels above and 39.5% levels were within the target range. The data did not show a direct correlation between dose of AZA and 6TGN level (Correlation coefficient 0.167) irrespective of the TPMT level.

**Conclusion:** Better disease control was achieved when 6TGN levels were above the suggested range and this was not associated with any adverse effects. 6TGN could be used for adjusting the dose of AZA to achieve optimal efficacy. Dose/ body weight does not appear to determine 6TGN level. 6TGN measurement does not show a direct correlation between dose of AZA and disease activity. Treatment with AZA reduces risk of bone disease and growth failure but has no effect on need for surgical intervention.

**Disclosure of Interest:** None declared.

PO-G-219

**EFFICACY OF BIOLOGICAL THERAPY WITH ADALIMUMAB IN A PAEDIATRIC POPULATION**


**Objectives and Study:** Biological therapies have revolutionized the treatment of chronic systemic diseases in which the immune system disorders form a part of the disease mechanism. Adalimumab (ADA), a fully human anti-TNF-alpha monoclonal antibody, is an effective therapy for paediatric inflammatory bowel disease (PIBD). Recent evidence suggests that early treatment with anti-TNF agents and immunosuppressives may alter the natural history of the disease and prevent late complications.

**Methods:** The aim of this study is to evaluate the efficacy of ADA in PIBD considering the clinical, endoscopic and histological improvement.

**Methods:** Between January 2008 and December 2009 ADA was administered in 15 patients with PIBD. 11 patients suffered from Crohn’s disease (CD), 3 patients suffered from Ulcerative Colitis (UC), and 1 suffered from unclassified IBD (UIBD) with ocular autoimmune disease. The range of age varied from 4 years to 18 years and 11 patients were female. In 13 patients ADA was administered as a first biological therapy, in 2 patients ADA was administered after adverse reaction to Infliximab. Patients with CD presented in 5 cases ileal disease, 4 colic disease and 2 anal disease.
ADA was given subcutaneously every 2 wks according to the weight (<35 Kg: 80 mg wk; 0:40 mg wk 2 then 20 mg; ≥35 Kg: 160/80/40 mg). Azathioprine was continued after the beginning of ADA because of the severity of the disease, in 14 patients mesalazine was associated. An endoscopy with multiple biopsies was performed to evaluate the efficacy of the therapy about 12 weeks after the beginning of ADA. If no improvement was seen, an other endoscopy was performed after 24 weeks.

Results: Mean duration of ADA therapy was 9 months (range 1–20 months). The patient with UIBD switch to Infliximab because of no improvement. One patient with ileal CD and stenosis of ileal-cecal anastomosis presented only partial improvement of the ileal disease, but she underwent multiple endoscopic balloon dilatation because of the persistent stenosis. In 3 patients ADA was started about one month ago and no data about the efficacy are available. In 10 patients a clinical, endoscopic and histological improvement was seen in a mean time of 6 months (3 months to 12 months). No major adverse events happened, in one patient an isolated elevation of CPK was observed without any symptoms and therefore no therapy discontinuation.

Conclusion: ADA seems to be safe and efficient for the symptoms and therefore no therapy discontinuation. No major adverse events happened, in one patient an isolated elevation of CPK was observed without any symptoms and therefore no therapy discontinuation.

Disclosure of Interest: None declared.

PO-G-222

DEFB1 GENE 5’ UNTRANSLATED REGION (UTR) POLYMORPHISMS IN INFLAMMATORY BOWEL DISEASES

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Objectives and Study: The Inflammatory Bowel Diseases (IBDs) are multifactorial disorders associated with the production of nonspecific mediators of inflammation leading to the establishment of inflammatory processes and tissue destruction. The intestinal epithelium is the physical barrier that limits the access of enteric microbes and producing endogenous antimicrobial peptides, plays an important role in the protection from infection.

Human beta defensins are antimicrobial peptides constitutively expressed by epithelial cells of a wide variety of tissues including the intestinal mucosa. Since a decrease of human beta defensin 1 (encoded by the DEFB1 gene) expression in mucosa of IBDs patients was shown, and a correlation between DEFB1 expression and single nucleotide polymorphisms (SNPs) in the regulatory region of the gene was reported, we decided to verify the possible association of 5’ untranslated region (UTR) DEFB1 SNPs with susceptibility to develop IBDs.

Methods: Three DEFB1 5’UTR SNPs, G-52A (rs1799946) C-44G (rs1800972) and G-20A (rs11362), were analyzed in a group of 158 IBDs. Among the IBDs patients, 108 suffered from Crohn’s disease (mean age at diagnosis 36.52 ± 14.01) and 50 from ulcerative colitis (mean age at diagnosis 38.29 ± 15.71). 130 healthy adult blood donors (63 M/67F, mean age 31.3 ± 12.36) with no history of IBDs, from the same ethnic origin of IBDs patients, were recruited and used as controls.

Results: No statistically significant differences were found when comparing DEFB1 SNPs allele, genotype and haplotype frequency between UC patients and controls. Some trends of association were evidenced for DEFB1 SNPs between CD patients and controls, or CD patients with different anatomical localization of the disease.

Conclusion: Our results partly confirm findings previously reported by another research group (1), indicating that DEFB1 might be considered one of the genes contributing to the susceptibility to CD, and it’s role in IBDs and CD should deserve further investigation.

Reference:

Disclosure of Interest: None declared.

PO-G-221

CEACAM6 (CELL ADHESION MOLECULE 6 RELATED TO CARCINOEMBRYONIC ANTIGEN): A POSSIBLE ROLE IN PEDIATRIC CROHN’S DISEASE?

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Objectives and Study: Experimental studies indicate that intestinal bacteria are involved in the pathogenesis of Crohn’s disease (CD). Recent microbiological research in CD has mainly been focused on E.coli strains able to adhere and to invade cultured intestinal epithelial cells (AIEC, Adherent Invasive E.coli). surviving within macrophages and inducing secretion of high levels of TNF alpha. Adhesion of AIEC depends on the expression of specific surface receptor CEACAM6, that was shown to be abnormally expressed by ileal epithelial cells in adults with CD. Since there is a need for investigating CD in pediatric age, the aims of the present study were: 1) to assess expression levels of CEACAM6 in Caco2 cell line before and after induction with TNF alpha and INF gamma and in biopptic specimens of children with CD; 2) to evaluate in vitro the ability of the AIEC LF82 strain to alter CEACAM6 expression.

Methods: Colonic carcinoma cell line, Caco2, was cultured in D-MEM medium and incubated with TNF alpha and INF gamma for 24–48 hrs. Biopptic specimens were taken from 4 children with active CD and 4 healthy controls; mRNA expression was estimated by real time PCR and protein expression by western blot assay.

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Results: TNF alpha and INF gamma are able to increase the gene/protein expression of CEACAM6 after 24 hrs in undifferentiated and 48 hrs in differentiated Caco2 cell line. CEACAM6 expression is up-regulated in intestinal inflamed specimens of children with CD as compared to healthy controls. AIEC LF82 is able to induce in vitro CEACAM6 expression.

Conclusion: Our data show for the first time in pediatrics that CEACAM6 expression is up-regulated in intestinal inflamed specimens from CD subjects as compared to healthy controls. Expression of CEACAM6 is strongly influenced by specific pro-inflammatory cytokines. Results obtained might increase the knowledge about pathogenetic mechanisms underlying pediatric CD and identify new therapeutic targets in the management of IBD in children.

Disclosure of Interest: None declared.

PO-G-223

MANAGEMENT OF IBD IN CHILDHOOD:
ULTRASOUND VS. COLONOSCOPY

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Objectives and Study: To evaluate the role of Enterocolic Ultrasound (US) versus Colonoscopy for the diagnosis and the follow up of children affected by Inflammatory Bowel Disease (IBD).

Methods: We recruited 30 children aged 4 to 16 years (mean age: 10 years) admitted to our hospital for weight loss, rectal bleeding and abdominal pain from January 2009 to October 2009. 14 patients had already a diagnosis of IBD and were evaluated during the follow up: 5 were affected by Crohn’s Disease (CD) and nine were affected by Ulcerative Colitis. 16 patients received a new diagnosis of IBD during their hospitalization: 10 had a diagnosis of CD, 2 of UC and 4 of Indeterminate Colitis (IC). Firstly all patients underwent US, performed by an expert operator blinded about disease’s patients’ status. After that all children underwent Enterocolic Magnetic Resonance Imaging (MRI) carried out by the same operator. In the same day all patients underwent colonoscopy. Wall thickening, stenosis and wall inflammation were used to compare US, MRI and colonoscopy findings. The sensitivity and the specificity of ultrasonographic parameters versus colonoscopy were determined.

Results: No significant difference was shown between MRI and US findings. Evaluating all the study population, the sensitivity of US resulted 84% for wall thickening, 57% for stenosis and 20% for wall inflammation signs. Specificity of US was: 100% for wall thickening, 94% for stenosis and 100% for wall inflammation signs. In the follow up group US wall thickening had a sensitivity and a specificity of 100%, while US stenosis showed a sensitivity and a specificity of 67% and 100% and US wall inflammation signs a sensitivity of 50% and a specificity of 100%. In the diagnostic group, US detection of wall thickening showed a sensitivity of 73% and a specificity of 100%; US detection of stenosis had a sensitivity of 75% and a specificity of 100%, while US detection of wall inflammation signs showed a sensitivity of 87% and a specificity of 100%. We also estimated the mean sensitivity and specificity of US in CD, UC and IC which resulted respectively: 64% and 87%, 40% and 100%, 22% and 100%.

Conclusion: US is highly specific in detecting wall thickening, stenosis and wall inflammation signs compared to colonoscopy. We found a higher specificity of US in the follow up group compared to diagnostic group. Moreover US resulted more specific in children affected by UC and IC compared to children affected by CD. Therefore repeated ultrasonographic studies which are non-invasive and less expensive tools could replace colonoscopy during the follow up of patients affected by IBD. US is less sensitive and specific when performed at the diagnosis of IBD in children, but it can be used as a first step investigation.

Disclosure of Interest: None declared.
PO-G-224

INFLIXIMAB IN THE TREATMENT OF 171 PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A CANADIAN TERTIARY CENTER

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Objectives and Study: 1) Determine trends in the use of Infliximab (IFX) for the treatment of pediatric onset inflammatory bowel disease (IBD) over an 8 year period in a single tertiary pediatric center 2) Determine the effectiveness of IFX in patients with treatment-resistant and steroid-dependent inflammatory bowel disease.

Methods: A retrospective chart review of pediatric patients (18 years and younger) administered IFX for the treatment of IBD between 01/2000 and 12/2008. Analysis was divided in 2 time periods: 01/2000 to 12/2004 (N = 60) and 01/2005 to 12/2008 (N = 111). Treatments were scheduled maintenance (SM) (N = 109), episodic (E) (N = 22) or less than 3 infusions (<3) (N = 40).

Results: 171 patients: 99 males, 72 females; median age at diagnosis: 12, 4 years; Crohn’s disease = 145, ulcerative colitis = 11, indeterminate colitis = 15. Most frequent reasons for beginning IFX were failure or intolerance to immunomodulators and corticosteroids. Differences in the two periods of treatment were seen in the median time from diagnosis to beginning IFX: 27 months prior to 2004, 15 months after 2004. Before 2004, 21 patients received SM, 18 E, 21 <3 infusions. After 2004, 88 patients received SM, 4 E and 19 <3 infusions. 72 patients (42%) went into steroid free remission (<52 on SM). 69 patients (40%) were partial responders (<50SM.) 30 patients (17.5%) were non responders, 6 of which had fulminant disease at diagnosis. Severe anaphylactic reactions were observed in 10 patients. Minor allergic events and other adverse events were observed in 38 patients. 73 patients discontinued IFX due to loss of response, anaphylaxis or non response. Of these, 23 had surgery and 25 switched to adalimumab in the next three months.

Conclusion: Changes in trends of use of IFX were observed over time: fewer patients lost their response and more achieved remission when IFX dosing was scheduled and fewer patients received episodic therapy or less than 3 infusions. Overall response and remission rates were 82 % and 42 % respectively at 3 months consistent with the REACH trial.

Disclosure of Interest: None declared.

PO-G-225

INFLAMMATORY BOWEL DISEASE IN PATIENTS WITH CHRONIC GRANULOMATOUS DISEASE

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Conclusion: Chronic granulomatosis disease (CGD) is a rare inherited immune deficiency related to a defective oxidative burst in neutrophils. These patients are prone to recurrent and serious infections, but also to inflammatory lesions of the GI-tract.

Objectives: To analyze the type, frequency and evolution of inflammatory GI manifestations in a cohort of children with CGD (confirmed by a genetic analysis) comparing patients with and without GI symptoms.

Methods: Retrospective single center analysis including 111 CGD patients with a detailed immunological, genetic and GI-exploration including upper and lower endoscopy and histological analysis. Evolution and response to treatment were analyzed in a combined retrospective/prospective manner.

Results: 24 of 111 patients showed signs of inflammatory colitis and/or enteritis. In three of them, IBD was initially suspected (1 Crohn’s disease and 2 indeterminate colitis) before the diagnosis of CGD was made. On endoscopic examination, colonic inflammation was most frequent with pancolitis (55%), left-sided colitis (15%) and 12 children showed also peri-anal lesions. Upper GI-involvement was also observed in 7 patients (gastritis and/or esophagitis). One patient with pancolitis had also ileal ulcerations. Histological exam revealed a polymorphic inflammation composed of neutrophils an mononuclear cells and granuloma were seen in 70% of biopsies. CGD patients with GI-inflammation did not differ from those without with regard to age at diagnosis, their genotype or type of mutation, the NBT test at diagnosis or a particular susceptibility to bacterial or fungal infections. Response to anti-inflammatory or steroid based therapy was most often adequate and immunosuppressors were required in 2 patients.

Conclusion: This observations points out to a critical role of innate immune functions (neutrophils) in the control of mucosal homoestasis and the development of IBD. But a sole defect of neutrophil functions may not be sufficient to the development of chronic inflammatory ulcerations of the intestinal/colonic mucosa raising the question of additional factors involved.

Disclosure of Interest: None declared.

PO-G-226

OPTIMAL ASSESSMENT OF PAEDIATRIC IBD - A COMPARISON STUDY OF MRI AND BARIUM FOLLOW THROUGH


Objectives and Study: The current UK gold standard for assessing children with suspected Inflammatory Bowel

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Disease (IBD) following blood tests is upper endoscopy, ileocolonoscopy and Barium Follow through (BaFT). Significant doses of radiation, unpalatable contrast and volume intolerance are involved with BaFT. Adult practice in investigating Crohn’s Disease (CD) is changing with increasing use of Magnetic Resonance Imaging (MRI). The aim of this study was to compare BaFT and abdominal MRI in a paediatric IBD population.

Methods: All consecutive patients with a new diagnosis of IBD or a previous diagnosis requiring reassessment from September 2008 to November 2009 were requested to have both abdominal MRI and BaFT. Both investigations were performed to a specific paediatric IBD protocol. The studies were reported by non-blinded radiologists with an interest in gastrointestinal imaging. The reports were compared in conjunction with case-note review.

Results: 52 patients underwent both BaFT and an MRI abdomen according to the local paediatric Crohn’s disease protocol.

MRI:
- 44% (n = 23) no technical difficulties
- 39% (n = 20) partial small bowel underfilling with contrast
- 19% (n = 10) motion artefact
- n = 1 abandoned study - non tolerance

In comparing the two modalities:
- 71% (n = 37) MRI equivalent finding to BaFT
- 19% (n = 10) additional pathology on MRI not seen on the BaFT
- n = 1 BaFT detected pathology not seen on MRI
- n = 1 BaFT demonstrated gastro-oesophageal reflux, not seen on MRI
- n = 1 BaFT - terminal ileal inflammation. MRI - Normal (Lympho-nodular hyperplasia on ileo-colonoscopy).

Conclusion: MRI abdomen is a feasible, well tolerated investigation in paediatric IBD. In this cohort MRI reports were equivalent to BaFT and often demonstrated additional findings. This suggests that MRI should become one of the standard investigations in children with IBD with the important advantage of no radiation exposure.

Disclosure of Interest: None declared.

PO-G-227

USE OF MR ENTEROGRAPHY IN PHENOTYPING PAEDIATRIC IBD – A SINGLE CENTRE EXPERIENCE

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Objectives and Study: Accurate phenotyping of inflammatory bowel disease (IBD) and its extent has significant implications for treatment. Magnetic Resonance Enterography (MRE) is an obvious choice for studying small bowel, particularly in children because of lack of radiation, multi-planar imaging, better functional assessment, reproducibility, and superior soft tissue contrast. Our aims were to determine utility of MRE to confirm IBD type and clarify disease extent compared to endoscopic and histologic findings.

Methods: Endoscopic and histopathologic data on all children with IBD who underwent MRE during a 4 year period, August 2005 – September 2009 were reviewed. Inclusion criteria were a) MRE within a month of panendoscopy to avoid confounding effects of treatment b) MRE with sufficient intestinal distension with enteral contrast as collapsed loops may mimic wall thickening. Crohn’s disease (CD) on MRE was defined as bowel wall thickness (>4 mm) with transmural enhancement of ileum or jejunal pouch; stricture or fistulising disease with supportive features of extramural CD like fibrofatty proliferation, mesenteric lymphadenopathy, comb sign (prominence of mesenteric vascularity), Ulcerative Colitis (UC) on MRE was defined as continuous colonic disease with mucosal enhancement and proximal small intestine sparing.

Results: MRE was performed on 104 occasions in 64 IBD patients with mean age 12.35 yrs (3–18yrs) in the selected time period. All patients tolerated procedures well. 45 patients (20 CD, 20 UC and 5 IBDU), fulfilled study inclusion criteria by having MRE within a month of panendoscopy. Median time between endoscopy and MRE was 14 days (2–31 days) both for UC and CD. 16/20 CD patients had colonic involvement (7 Ileocolonic, 6 Ileocolonic + Upper GI, 3 isolated colonic). Disease distribution was modified in 3/20 of CD patients after MRE with evidence of increased small bowel disease. 5/45 children had their disease re-classified after MRE with 4/5 inflammatory bowel disease unclassified (IBDU) and 1/20 UC reclassified as Crohn’s. MRE however has poor sensitivity for detecting colonic disease compared to endoscopy with normal MRE findings in 3/20 children with Crohn’s colitis and in 50% of children with active UC.

Conclusion: MRE is a useful adjunct to endoscopy and histology in determining IBD disease classification and distribution; and a safe and effective method for disease monitoring but as expected has poor sensitivity for colonic disease.

Disclosure of Interest: None.

PO-G-228

INFLIXIMAB EFFICACY FOR STRICTURING PEDIATRIC CROHN’S DISEASE

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Objectives and Study: Infliximab is nowadays among the top-choice treatments for paediatric Crohn’s disease (CD)
within its different phenotypes [1,2]. Though a risk of bowel stenosis caused by anti-TNFα was initially feared, recent studies have validated Infliximab efficacy as anti-stenosing agent [3]. Aim: evaluation of Infliximab effect on the evolution of pediatric stricturing CD.

**Methods:** Retrospective and prospective descriptive analyses were made of data obtained from paediatric patients treated at the Pediatric Department of Padova University since the year 2000. All patients underwent upper and lower intestinal endoscopy, abdominal ultrasonography (US Technos Esaote, probe LA 523 13 Mhz) and magnetic resonance enterography (MR Philips Achieva 1.5 Tesla) to depict signs of active inflammation as well as complications such as bowel obstruction, fistulas and abscesses. In particular MR is able to distinguish active inflammation (mural post contrast hyperenhancement) from fibrostenotic stricture (low signal intensity wall thickening). Infliximab administration was performed according to the scheduled protocol (5 mg/Kg at week 0–2–6, then each 8 weeks).

**Results:** Among 40 patients, 18 were treated with Infliximab. Five of these Infliximab-treated patients (2 males; median age 10 ys) presented a luminal stenosis (3 ileal, one pre-pyloric, one large-bowel and one anorectal; mean time since CD diagnosis: 26 months, range ‘1–72’). At the time of stenosis finding, all patients presented a severe disease activity (PCDAI >20). One child with persistent disease activity developed ileal fibrotic stenosis (MR) after 6 Infliximab infusions: a surgical resection was required and Infliximab therapy was discontinued. The other 4 patients, with inflammatory stenosis (US and MR), all started Infliximab therapy and showed disappearance of the initially identified stenosing tract (mean follow-up: 12 months).

**Conclusion:** Our data – though limited – support Infliximab efficacy on pediatric CD, also as regards the stricturing phenotype. It is crucial for diagnosis and follow-up the use of adequate techniques to evidence the inflammatory component of the stenosing tract. MR enterography has revealed itself as an important and useful instrument for location assessment, disease monitoring and selection of appropriate treatment options.

**References:**

**Disclosure of Interest:** None declared.

**PO-G-229**

**DIAGNOSTIC WORK-UP OF IBD PATIENTS: CONCORDANCE WITH PORTO CRITERIA AND OTHER CHARACTERISTICS**


**Objectives and Study:** 1. To document if children are being diagnosed in concordance with ESPGHAN Porto criteria for diagnosing Inflammatory Bowel Disease (IBD) and compare with European data previously presented in 2009.
2. To document the current characteristics of IBD including disease distribution and presentation.

**Methods:** This study is based at the only regional centre which manages paediatric IBD in South West (SW) of England with a population of 5.2 millions. This centre has maintained a prospective database of all new IBD cases since 1990. This study is based on 2007 data only when data was also collected from all 13 paediatric centres in the region identifying newly diagnosed cases of IBD by using international diagnosis code (ICD10). This project was approved by the local audit committee.

**Results:** All 13 centres responded. 44 cases were identified. 42 diagnosed at the regional centre were on the database: 2 cases from 1 other centre were not.

**Concordance with diagnostic Porto Criteria:** All 26 CD had barium meal and follow through investigation. Upper gastrointestinal endoscopy was done in 24 CD, 15 UC and 3 IC cases. Two CD cases from single centre managed by adult gastroenterologist did not have upper endoscopy. All 44 patients had colonoscopy. Full colonoscopy with ileal intubation was seen in 21 CD (81%). 19% of IBD cases had incomplete colonoscopy without ileal intubation or biopsies; reasons being technical failure, poor preparation or very sick patients. See table.

Only 27% of CD cases presented with classic triad of diarrhea, weight loss and abdominal pain. 88% of CD and 57% of UC had upper gastrointestinal tract (UPGIT) involvement. Whole colon (right, transverse and left) was involved in 57% of CD cases. 73% of CD and 43% of UC had a time interval of more than 6 months from symptoms onset to diagnosis.

**Table:** Concordance with Porto Criteria compared with 2009 Europoean data (Eurokids)

<table>
<thead>
<tr>
<th></th>
<th>CD (%)</th>
<th>UC (%)</th>
<th>IC (%)</th>
<th>CD, UC, IC Eurokids (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD</td>
<td>26</td>
<td>14</td>
<td>3</td>
<td>66%</td>
</tr>
<tr>
<td>Upper endoscopy</td>
<td>24</td>
<td>14</td>
<td>3</td>
<td>82%, UC-72%, IC-79%</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>26</td>
<td>14</td>
<td>3</td>
<td>95%, UC-99%, IC-99%</td>
</tr>
<tr>
<td>Colonoscopy with ileal intubations</td>
<td>21</td>
<td>11</td>
<td>3</td>
<td>72%</td>
</tr>
</tbody>
</table>

**Conclusion:** This study shows good concordance with ESPGHAN Porto criteria with full colonoscopy with ileal intubation in 81% compared with 72% in EUROKIDS study. Over 90% cases are receiving specialist care at the regional
THE ROLE OF ENDOSCOPY OF THE UPPER GASTROINTESTINAL TRACT IN THE DIAGNOSTIC ASSESSMENT OF CHILDHOOD INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Upper gastrointestinal tract (UGT) endoscopy has become part of routine evaluation of children with suspected inflammatory bowel disease (IBD) in the Netherlands. However, no consensus exists with respect to diagnostic criteria of IBD of the UGT. The aim of this study was to describe the histological UGT abnormalities in children with Crohn disease, Ulcerative Colitis and non-IBD patients and to establish the role of UGT involvement in children with IBD at diagnosis.

Methods: Biopsies (colon, ileum, duodenum, stomach, esophagus) from children suspected for IBD who underwent endoscopy during the last 6-years were reassessed by a blinded, expert pathologist. Histological findings of the UGT were compared with the diagnosis based on ileocolonic biopsies. Histology of the UGT showing granulomas or histiocytic infiltrates confirmed the diagnosis of Crohn disease. Final diagnosis was based on endoscopic findings, histologic interpretation, imaging studies and follow-up data.

Results: A total of 172 children, aged 2.5 to 18 years, were enrolled in this study. Of these children, 70 had Crohn disease, 33 Ulcerative Colitis, 1 Indeterminate Colitis and 68 had no IBD. Granulomas in the UGT were found in 21 (30%) children with Crohn disease; 3 esophageal, 19 gastric and 2 duodenal. Focally enhanced gastritis (defined as presence of at least one foveolum/gland surrounded and infiltrated by inflammatory cells) was seen in 43 (61%) children with Crohn disease, compared to 6 (18%) children with Ulcerative Colitis and 5 (7%) children with no IBD. Specificity and positive predictive value of focal gastritis in Crohn disease were 89% and 80%, respectively. Crypt abscesses were only found in 6 (9%) children with Crohn disease, 5 gastric and 2 duodenal. Focal duodenitis was seen in 13 (19%) children with Crohn disease and in 1 child with no IBD. The child with Indeterminate Colitis had no histological abnormalities in the UGT. In 8 (11%) children with Crohn disease the diagnosis was solely based on UGT abnormalities; granulomas (n = 5) and histiocytic infiltrates (n = 3).

Conclusion: Focally enhanced gastritis, formerly suggested as a diagnostic marker for patients with Crohn disease, can also be found in children with Ulcerative Colitis and in non-IBD children. Therefore this finding does not differentiate between Crohn disease and Ulcerative Colitis. Granulomas and histiocytic infiltrates are exclusive found in children with Crohn disease. In 11% of the children with Crohn disease in our study the diagnosis was solely based on the detection of these findings in the UGT. We confirm that UGT endoscopy has an important role in the investigation in all children suspected of IBD.

Disclosure of Interest: None declared.

INCIDENCE AND PRESENTATION AT DIAGNOSIS OF INFLAMMATORY BOWEL DISEASES IN CHILDREN IN EASTERN FRANCE

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Objectives and Study: There is ongoing evidence that incidence of inflammatory bowel diseases (IBD) is still increasing especially in young children. Little is known about the overall epidemiology of IBD in France where studies have been performed mainly in the North. The aim of this work was to assess the incidence of IBD in children under 15 years of age in the region Franche Comté (located at the eastern part of France) during a 10 years study.

Methods: All children (<15 years) with a new diagnosis of Crohn’s disease (CD), Ulcerative colitis (UC) or Indeterminate colitis (IC) between January 2000 and January 2010 were included in this study. The study was in 2 parts:

*In the first part (retrospective)*, a mail was sent to all pediatricians and all gastroenterologist of the region requesting data about all cases of IBD diagnosed between January 2000 and December 2005.

*In the second part (prospective)*, an annual mailing record was established including all new cases of IBD diagnosed from January 2006 up to January 2010.

To ensure the exhaustivity of our data, we also contacted by mail all the anatomopathologist of the region requesting data of every cases of colitis diagnosed during the study period of time. All files were then reviewed (clinical, laboratory and radiological data) and classified according to Porto criteria.

Results: 70 children were diagnosed with IBD during the 10 years study. The sex ratio (m/f) was 1 for UC and 2 for CD. The annual incidence was: total IBD 3/105 children; CD 1.83/105; UC 1/105 and ICC 0.17/105. There was a slight increase in the incidence of CD between the first (1.7/105) and second period (1.9/105) while the incidence of UC remained constant. The mean duration between onset of symptoms and diagnosis decreased from 13 months during the first period to 8 months. 20% of patients had normal inflammatory data at diagnosis. All children had a colonoscopy at diagnosis and 77% also had an upper digestive endoscopy. 63% of the CD cases were located at the...
ileocolonic region and 71% of UC were pancolitis. More than 90% of children were followed up by a hospital physician. There was a significant change of follow up between the two periods with the arrival of a gastro-pediatrician in the region in 2005.

Conclusion: Incidence of IBD in Franche-Comte region is quite similar to that observed in Northen France. There is a slight increase of CD incidence during the ten years study while UC incidence remains constant. This study shows the impact of a specialized follow up by a gastro-pediatrician mainly on delay to diagnosis but also on modalities of diagnosis and follow up.

References:

Disclosure of Interest: None declared.

PO-G-232

COLECTOMY RATES IN PAEDIATRIC ULCERATIVE COLITIS OVER A 14 YEAR PERIOD IN A TERTIARY GASTROENTEROLOGY CENTRE
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Objectives and Study: The natural history and treatment options of paediatric ulcerative colitis (UC) is poorly understood and colectomy rates of up to 20% have been reported. The aim of this study was to review colectomy rates in our institution over a 14 year period.

Methods: We retrospectively reviewed the incidence for colectomies in 138 patients (69 female) diagnosed with UC at our tertiary Paediatric Gastroenterology Centre from 1996 to 2009 (Group 1: 1996–2002, n = 51, Group 2: 2003–2009, n = 87), median age at diagnosis 12 years, range 4–16, with a follow-up of up to 12 years, median 3y, range 0–12. All patients were diagnosed with UC according to standard clinical and histopathological criteria. Patients with indeterminate colitis were excluded.

Results: The total colectomy rate was 9/138 (6.5%). 5/138 (3.6%) of patients needed colectomies for non-responsive severe UC between 1996 and 2002, after failed treatment with 5-Aminosalizylates, corticosteroids, thiopurines (Azathioprine, 6-Mercaptopurine) and Ciclosporin, 4/138 (2.9%) patients had colectomies between 2003 and 2009, after additional failed treatment with monoclonal antibodies (Infliximab) and Methotrexate. All patients received Azathioprine. The median time to colectomy from diagnosis was 14 months (range 4–50). At diagnosis, patients who had a colectomy, 1/9 (11%) had distal colitis and 7/9 (78%) had severe pancolitis. 1/9 (11%) had mild to moderate pancolitis but severe arthropathy, which resolved after colectomy. This was before Infliximab was available in this patient in Group 1.

Conclusion: Aggressive initial treatment at diagnosis with corticosteroids, use of maintenance immune modulation with thiopurines and use of monoclonal antibodies have led, in our institution in the last 7 years, to a colectomy rate of only 2.9%. No lymphoproliferative disorders were recorded.

Disclosure of Interest: None declared.

PO-G-233

MICROBIOTA IN PEDIATRIC INFLAMMATORY BOWEL DISEASE
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Objectives and Study: The intestinal microbiota plays a crucial role in the aetiology of inflammatory bowel disease (IBD). However, changes of its various groups have not been studied extensively in children and related to disease activity.

Methods: Sixty-nine children and adolescents (median age 14 years) with IBD and 25 healthy controls (median age 14 years) were recruited for the study. The disease activity of the ulcerative colitis or Crohn’s disease was determined according to the pediatric ulcerative colitis activity index (PUCAI) or the Pediatric Crohn Disease Activity Index (PCDAI). Cell counts of nine bacterial groups and species were monitored in the faecal microbiota in all participants by real-time PCR analyses.

Results: With the primers used herein we were able to cover a median range of 90% of the total microbiota detectable with an universal primer. While no changes were observed in ulcerative colitis patients, numbers of F. prausnitzii and Bifidobacteria were reduced in children with active and inactive Crohn’s disease. Additionally, numbers of E. coli were increased in patients with active Crohn’s disease only.

Conclusion: The microbiota in children with Crohn’s disease is characterized by a decrease of F. prausnitzii and an increase in E. coli cell numbers, while no changes in the microbiota could be observed for ulcerative colitis.


PO-G-234

WHAT IS THE REAL SIGNIFICANCE OF UPPER GASTROINTESTINAL ENDOSCOPY IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)?
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PO-G-235

ANTI-GLYCAN ANTIBODIES ARE SIGNIFICANTLY INCREASED IN PEDIATRIC AND ADULT CROHN’S DISEASE PATIENTS AND THEIR FIRST DEGREE RELATIVES

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Objectives and Study: Disease specific antibodies have been described in patients with inflammatory bowel disease (IBD) and their first degree relatives. The recently described anti-glycan antibodies (AGA): anti-laminaribioside, chitobioside and mannobioside (ALCA ACCA and AMCA respectively) and anti-Saccharomyces cerevisiae antibodies (gASCA) specifically favor a Crohn’s disease (CD) diagnosis and prediction of disease behavior, however, little is known about their prevalence in healthy first degree relatives (FDR) and its significance. The aims were to investigate whether AGA will identify a specific IBD patients subgroup as well as their FDR.

Methods: IBD patients, their healthy FDR, control patients and their FDR (FDRc) were included. Demographic and disease data were recorded and correlated with inflammatory markers and AGA (Glycominds Ltd, Israel). Thirty five IBD patients (age 28.8 ± 15 years, 19 CD, 19 females) and 37 FDR were compared to 39/68 control patients/FDR.

Results: CRP (10.30 ± 17.9 mg%) and ESR (32.8 ± 26 mm/hour) levels were significantly higher in patients compared to FDR or control groups (P<0.06 and 0.01, respectively). AGA were detected in 15 (43%, 12 CD) patients (7 ALCA, 13 ASCA, 1 ACCA, 1 AMCA) and 12 (32%) FDR (9 CD-FDR, P=0.36), however, double AGA positive patients (7) only occurred in CD. 9 FDRc but no controls were AGA positive. ALCA levels were significantly increased in both CD patients and FDR (38.6 ± 24.8 and 34.6 ± 25.7 units, respectively), vs. control/FDRc, P=0.001. gASCA was significantly higher in CD patients (44.4 ± 44.2 units) vs. FDR (P<0.001) and controls/FDRc (P<0.001). Interestingly, positive compared to negative AGA IBD patients were significantly younger: 23.2 ± 8.3 vs. 33 ± 17.6 years (P=0.04) and had shorter disease duration: 3.6 ± 4 vs. 8 ± 8.3 years (P=0.06). Immunosuppressors/biologics had no effect on serologic response. Importantly, 40% AGA positive in contrast to 25% AGA negative IBD patients had AGA positive FDR.

Conclusion: AGA are significantly increased in CD patients and FDR compared to controls. gASCA best differentiated between CD and FDR. Positive AGA are associated with younger age and shorter disease duration. Thus, AGA panels contribute to CD diagnosis, prognostic stratification and may support either genetic anticipation or environmental exposures.

Disclosure of Interest: None declared.

PO-G-236

ONE YEAR OUTCOME OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE IN NORTHERN STOCKHOLM COUNTY

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1Department of Women and

Disclosure of Interest: None declared.
**Objectives and Study:** In recent years some studies have presented outcomes among larger cohorts of patients with paediatric inflammatory bowel disease (PIBD) [1,2]. Contrary to what is seen in adult studies, an increasing intestinal involvement over time and a more rapid progression to complicated forms of disease has been reported. A high prevalence of corticosteroid (CS) dependency and need for surgery has supported the hypothesis that PIBD represents a more severe phenotype of the disease.

In Northern Stockholm (NS) an endoscopic evaluation 6–18 months after diagnosis has been performed in almost all PIBD patients. There are few published data on the use of routine endoscopy to evaluate treatment and disease behaviour in a population based paediatric cohort.

**Methods:** Records of all patients diagnosed during 2002–2007 with PIBD in NS were examined. Patients were diagnosed according to the Porto criteria and classified within the framework of the Montreal criteria.

**Results:** A total of 135 children were diagnosed with PIBD. The initial diagnosis was changed in 8 of the 128 children that were re-endoscoped.

Among the 97 patients with Crohn’s disease (CD), two had intra-abdominal surgery within the first year after diagnosis. None of the 27 children with ulcerative colitis (UC) required an operation during the first year of follow up.

At follow up one year after diagnosis 78 (58%) of the patients with PIBD were judged to be in clinical remission.

At one year after diagnosis 19 (17%) patients received temporary oral CS. None of the children were dependent on CS.

At re-endoscopy, the disease location had extended among six patients with CD and the disease behaviour altered in one. Of the 5 patients with UC with localised colitis at presentation showed an increase in the extent of the disease territory at re-endoscopy. The median duration from diagnosis to re-endoscopy was 1.08 years (interquartile range 0.91–1.51 years).

**Conclusion:** Patients diagnosed with PIBD in NS seemed to have a mild disease course. The need for surgery during the first year and the CS dependency at one year after diagnosis were lower than reported from most other centres. Only a small number of patients had developed complicated forms of disease and showed an increasing intestinal involvement at re-endoscopy after one year.

**References:**


**Disclosure of Interest:** None declared.

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**PO-G-237**

**CORRELATION OF IBD ACTIVITY INDEXES AND EXTRASTINTESTINAL MANIFESTATIONS IN 264 NEWLY DIAGNOSED PATIENTS WITH IBD**

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**Objectives and Study:** The incidence of pediatric inflammatory bowel disease is increasing in the last few years. There is only limited information about the extraintestinal manifestation (EIM) in children. We report the frequency of EIM in children registered between 2008–2009 in our National Pediatric Inflammatory Disease Registry. Furthermore we analysed relationship between disease activity (Pediatric Crohn’s Disease Activity Index, PCDAI; Pediatric Ulcerative Colitis Activity Index, PUCAI) and EIM in 264 newly diagnosed children with IBD.

There has been no population-based study whether there is a relationship between these factors.

**Methods:** Twenty seven institutes serve data concerning newly diagnosed IBD patients to the National Pediatric IBD Register operating since January 1st, 2007. The questionnaire is about epidemiological data, initial therapy, disease extension and activity (PCDAI, PUCAI) as well as extraintestinal manifestation.

**Results:** 264 children (137 male, 127 female) were registered between January 1st, 2008 and December 12th, 2009. Mean age was 13,25 years (range 1.2–17.9), At the time of diagnosis or before 40 (15.2%) children were recorded with EIM. The extraintestinal manifestation was found more often in patients with Crohn’s disease than in patients with ulcerative colitis (28/169, 16.6% vs. 10/80, 12.5%). Mean age of children with EIM at diagnosis was 12.82 years (range: 1.2–17.9). Interestingly, more girls had EIM than boys (25 vs. 15, 62.5% vs. 37.5%). Skin (6.4%) and joint (3.8%) complaints were the most common EIM. Hepatic involvement was registered in eight cases (3%). Furthermore autoimmune thyroiditis, stomatitis aphthosa, mononeuropathy, involvement of vulvae, thrombophlebitis, autoimmune hemolytic anaemia were also found. Familial occurrence was nearly the same in children with extraintestinal manifestation and in children without extraintestinal manifestation (12.5% vs. 10%). There was no significant difference in disease localization compared children with EIM with children without EIM. Furthermore we couldn’t report difference in disease activity based on PCDAI/PUCAI at the time of diagnosis between newly diagnosed patients with or without EIM. Multiple EIM was verified in seven cases (2.7%).

**Conclusion:** Our data are concordant with the international data. It seems activity indexes have no significant effect for EIM at the diagnosis of IBD. Extraintestinal manifestations can suspect or confirm the diagnosis of IBD. Furthermore monitoring for extraintestinal manifestation of these children during control has remarkable importance due to quality of life of children and therapeutical decisions.

**Disclosure of Interest:** None declared.
THE FIRST STUDY OF INCIDENCE OF IBD IN CHILDREN IN A PORTUGUESE POPULATION

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Objectives and Study: Intro: Inflammatory Bowel Disease (IBD) is diagnosed before 20 years in 25 to 30% of all patients. Paucity of population-based data exits on the incidence of IBD in children in Portugal.

Objectives: To determine the incidence of IBD in northern Portugal (Minho), describe demographic data of the new diagnosed IBD in children and adolescents and characterize the inaugural episode in terms of clinical localization and extension of the disease following Porto’s Criteria.

Methods: Prospective multicentre study from May 1, 2008 to April 30, 2009. During this period all new diagnosed cases of IBD of children and adolescents with an age up to 18 years living in this region were reported (the all five public Hospital in Minho, the two pediatric gastroenterology units in Porto and all private adult gastroenterology doctors of Minho) and a prospective questionnaire was filled up. Data from the 2001 Portugal Census was used to determine the incidence.

Results: During the 12 months of the study, 17 cases of IBD were diagnosed, 11 CD and 6 Ulcerative colitis (UC). The overall incidence of IBD in Minho region was 6.4/100 000, CD 4.2/100 000 and UC 2.2/100 000. The median age was 13.59 years (SD ± 2.79 years) and 9 patients were males and 8 females. Mean time between the beginning of the symptoms and the diagnosis being made was 5.19 months (SD ± 5.86 months). The symptoms of the inaugural episode were: diarrhea in 5/6 UC and 10/11 CD, rectal bleeding in 4/6 UC and 6/11 CD, abdominal pain 3/6 UC and 9/11, weight loss 2/6 UC and 8/11 CD, fever 1/6 UC and 5/11 CD, malaise 1/6 UC and 8/11 CD, nausea and/or vomiting 1/6 UC and 7/11 CD and extraintestinal manifestations in 4/11 CD. Colonoscopies reveal pan-colitis in every UC cases and all the patients with CD present ileocolitis. The /17 of patients present with anemia in the first episode, as well as elevation of the inflammatory markers (erythrocyte sedimentation rate and C-reactive protein).

Conclusion: This was the first study in Portugal calculating the incidence of IBD in children. The incidence was similar to other reports in the European Population and there is, also, a predominance of CD over UC. The disease phenotype had no variety, all the patients with UC present pan-colitis and all CD had ileocolitis, as described for the IBD in children.

Disclosure of Interest: None declared.

LONG TERM EFFICACY OF INFlixIMAB IN INFLAMMATORY BOWEL DISEASE AT A SINGLE TERTIARY CENTER

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Objectives and Study: The chimeric anti-TNFα antibody infliximab (IFX) has been shown to be effective in inducing and maintaining short term remission in pediatric patients (pts) with Crohn’s disease (CD) and with ulcerative colitis (UC). However, data on long term outcome of IFX maintenance therapy in pediatric inflammatory bowel disease (IBD) are scanty.

Our objective was to evaluate the long term efficacy data of IFX in children with IBD that had received this agent for induction of remission.

Methods: All IBD treated with IFX and with follow up thereafter were enrolled. Data of patients (pts) were analyzed using the database for IBD pts of the Unit. Efficacy was evaluated by PCDAI and PUCAI clinical scores for CD and UC respectively. A total of 51 pts (39 CD, 12 UC) were enrolled.

Results: (mean ± SD). Age at first infusion was 14.4 ± 3.25 years, disease duration before IFX was 34 ± 32 months. Reasons for starting IFX were unresponsiveness to conventional therapies (42.5%) and perianal disease (37.5%) for CD, unresponsiveness to other therapies (33.3%) and steroid dependency or resistance (58.3%) for UC. Number of infusions was 7 ± 5.2 (range 2–20) for CD pts and 6 ± 5.4 (range 1–19) for UC. Mean therapy duration was for CD 11.8 ± 11.9 mts and for UC 10.4 ± 12.4 mts. At enrollment, 80% and 75% of CD and UC pts, respectively, were on concomitant immunomodulator (IM) therapy; 9.3% of CD pts and no UC pts stopped IM therapy during follow-up period. Mean PCDAI at 0, 3, 12, 24, 36 months and mean PUCAI at 0, 3 and 12 months are in the table. Among the 27 CD pts and 11 UC pts stopping IFX 13 CD pts and 3 UC pts stopped due to long term remission. At 12 months, of the 13 CD pts, 7 were still in remission, 5 restarted biologic therapy (3 Adalimumab, 2 IFX), 1 underwent ileal resection. Only 3 UC pts required colectomy for unresponsiveness. No serious adverse events or malignancies were reported.

Table:

<table>
<thead>
<tr>
<th>Months</th>
<th>T0 (CD 12 pts)</th>
<th>T3 (CD 6)</th>
<th>T12 (CD 4)</th>
<th>T24 (CD 7)</th>
<th>T36 (CD 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>of follow up</td>
<td>39 pts, UC 6</td>
<td>UC 6</td>
<td>UC 4</td>
<td>UC 4</td>
<td>UC 2</td>
</tr>
<tr>
<td>PCDAI</td>
<td>25.2 ± 13.8*</td>
<td>7.5 ± 6.1*</td>
<td>10.3 ± 10.8*</td>
<td>4.3 ± 4.7*</td>
<td>5 ± 0.5*</td>
</tr>
<tr>
<td>PUCAI</td>
<td>57.9 ± 27*</td>
<td>15 ± 19*</td>
<td>10 ± 5*</td>
<td></td>
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</tr>
</tbody>
</table>

*P < 0.001; **P < 0.05.

Conclusion: In our cohort of IBD pts, IFX maintenance therapy was a durable and effective treatment over a 3-year period in children with CD, it also appeared an effective therapeutic option to avoid or postpone colectomy in UC pts.

Disclosure of Interest: Non declared.
PO-G-240

EARLY USE OF INFliximAB IN TREATMENT-NAIVE PEDIATRIC CROHNS DISEASE
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3Pathology Dept, Akershus University Hospital, Lørenskog, 4Pediatric Dept, Oslo University Hospital, Ulleval, Oslo, Norway.

Objectives and Study: Crohns disease (CD) in children is characterized by an aggressive course with high risk of complications. Biologic therapy is an important therapeutic option. The aim of the study was to assess the outcome of early treatment with infliximab (IFX) over one year, and to compare baseline parameters with non-IFX treated patients.

Methods: Patients below 18 years of age, diagnosed with CD between 2005 and 2007, were invited to attend a prospective study with follow-up examination within 1.5 years after diagnosis. The catchment area comprised 18% of the Norwegian pediatric population. Patients were characterized according to the Porto criteria with upper and lower endoscopy, histology, MRI of the intestine, laboratory values, PCDAI (Pediatric Crohns Disease Activity Index) scores and recording of therapy. Treatment was decided individually.

Results: Thirty-seven children were diagnosed with CD, 30 (81%) met to endoscopic follow up. Nineteen (51%) patients received IFX during the first year after diagnosis. At diagnosis the mean age was 13.1 years in the IFX treated (IFX+) group compared to 11.5 in the non-IFX group. In the IFX+ group, the mean fecal calprotectin level was 2292 mg/kg compared to 855 mg/kg (P = 0.01) in the non-IFX group. The CRP was 40 and 22 mg/l (P = 0.01). There was a trend towards higher PCDIAI scores and shorter disease duration in the IFX+ group (ns). All IFX treated patients received concomitant azathioprine, 14 (78%) were treated with enteral nutrition and 7 (39%) received steroids. In the non-IFX group, 6 (55%) were on azathioprine, 2 (20%) on enteral nutrition and 6 (35%) received steroids. The mean time to IFX initiation was 2 months. None had to stop IFX due to side effects. Fifteen (83%) achieved clinical remission with IFX. Of the 3 non-responders, 2 required surgery, and one became steroid-dependant. At follow up 12 (67%) of 18 in the IFX+ group had ileal and colonic mucosal healing, but 10 (56%) of 18 patients had upper GI- involvement after one year with therapy. In the non-INX group, 3 patients had slightly elevated PCDIAI scores, the mucosal healing rate was 8 (66%) of 12 patients, with 5 (42%) of 12 patients having persistent upper GI findings.

Conclusion: Early top-down treatment with IFX was efficient and well tolerated. High CRP, ESR and fecal calprotectin levels were significantly associated with early IFX treatment. Future studies must clarify the prognostic role of persistent upper GI-involvement in spite of mucosal healing in the ileocolon.

Disclosure of Interest: None declared.

PO-G-241

CYCLOSPORINE TREATMENT FOR SEVERE STEROID RESISTANT ULCERATIVE COLITIS IN CHILDREN
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Objectives and Study: Severe ulcerative colitis (UC) non-responsive to steroids remains a clinical challenge. Cyclosporine A (CSA) has shown to establish an excellent short term response and avert the need for urgent colectomy. However, long term benefit and colectomy rate of CSA is questionable in children. The aim of this prospective study was to evaluate short and long term benefits as well as side effects of CSA in children with severe steroid resistant ulcerative colitis.

Methods: Thirteen patients with severe colitis (12 UC, 1 indeterminate colitis) were treated with CSA 5.6 ± 1.5 mg/kg/d. Severe colitis was defined as more than 6 bloody stools per day with one or more of the following signs: fever, anemia, tachycardia, raised erythrocyte sedimentation rate or low serum albumin. Prior to the study enrollment, all patients have used intravenous methylprednisolone for at least 10 days without response. Responders on CSA were discharged under a 6–12 months’ course of oral CSA. Follow-up evaluation was designed to define response, relapse and side effects at 3, 6, 9 and 12 months.

Results: Eleven patients (84.6%) responded with resolution of rectal bleeding and decreased stool frequency to less than 3 passages a day at median 7 days (4–12) with intravenous CSA. Remission maintained in 61.5% (n: 8), 30.7% (n: 4), 15, 3% (n: 2) and 15, 3% (n: 2) of patients at 3, 6, 9 and 12 months, respectively. All relapses occurred under oral CSA with serum concentrations of median 122 µg/l (98–200). Partial remission was obtained by combination of azathioprine in two cases. Colectomy was considered in 9 CSA non-responsive children; 3 colectomies were performed (overall colectomy rate at 1 year 23.1%, and n: 3/13), and treatment was switched to rescue therapy with other immunosuppressive agents in 6 patients who refused surgery. None of the patients had to discontinue CSA because of adverse effects. One patient had increased serum creatinine level which normalized after dose reduction. Hypertrichosis was observed in 4 children (30, 8%) and diseased after drug cessation.

Conclusion: Cyclosporine is safe and effective for short term in children with severe UC; however, relapse rate is high and it does not prevent colectomy.

Disclosure of Interest: None declared.

PO-G-242

MAGNETIC RESONANCE ENTEROGRAPHY FOR DIAGNOSIS AND FOLLOW-UP IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE
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Early top-down treatment with IFX was efficient and well tolerated. High CRP, ESR and fecal calprotectin levels were significantly associated with early IFX treatment. Future studies must clarify the prognostic role of persistent upper GI-involvement in spite of mucosal healing in the ileocolon.

Disclosure of Interest: None declared.
Objectives and Study: According to the Porto-criteria every child with suspected inflammatory bowel disease should undergo colonoscopy with ileal intubation, upper gastrointestinal endoscopy and (except definite ulcerative colitis) radiologic contrast imaging of the small bowel.

Aim of this case-series was to validate the clinical use of radiologic contrast imaging of the small bowel.

For the completion of diagnosis, contrast imaging of the colon as well as in the small bowel. There was excellent correlation with the findings of endoscopy and clinical follow-up with additional information about extraintestinal inflammation or fistulizing.

Conclusion: Endoscopy with multiple biopsies remains the unquestioned standard for initial diagnosis of pediatric IBD. For the completion of diagnosis, contrast imaging of the small bowel is requested.

MRE allows noninvasive assessment of the intestine, avoiding ionizing radiation exposure.

In our follow-up cohort MRE has proven to provide endoscopy-equivalent information about disease-activity, extent and localization with the additional benefit of detecting small-intestinal and extraluminal disease.

MRE may increase the diagnostic yield or replace the repeated endoscopy in selected cases.

Disclosure of Interest: None declared.
PO-G-244

MODULEN IBD EXERTS ITS ANTI-INFLAMMATORY EFFECT PARTIALLY THROUGH ACTIVATION OF OPIOID PATHWAY


Objectives and Study: Ulcerative colitis (UC) and Crohn’s disease (CD), commonly known as inflammatory bowel disease (IBD) affects 0.5 to 1% of the Western world’s population and is increasing in the developing countries. It is a chronic disease that requires lifelong treatment. Many patients do not respond or do not comply well with the recent medications. This, in addition to the high cost of these approaches, urges the scientific community to develop new treatments. Modulen IBD formula was developed by Nestlé to alleviate gut inflammation in Crohn’s disease patients. According to a series of publications, anti-inflammatory effect may be mediated by TGF-beta-enriched casein that is the main source of proteins in this product. Recently it was shown that high quantity of opioid peptides are also generated by casein digestion suggesting that anti-inflammatory effect of Modulen IBD could be also, at least in part, ascribed to activation of opioid pathway. In order to evaluate this hypothesis, the effect of Modulen IBD supplementation on inflammation was assessed in a preclinical model of intestinal inflammation.

Methods: Experimental colitis was chemically induced in C57BL/6J adult mice (n = 10), and the development of intestinal inflammation was assessed by body weight loss, macroscopic evaluation, and quantification of biomarkers. Role of opioid pathway activation was investigated using opioid receptor blocker given concomitantly with Modulen IBD supplementation.

Results: Modulen IBD supplementation improved body weight loss associated with intestinal inflammation; decreased macroscopic score, as well as markers of inflammation (e.g. COX-2, MPO, KC). The anti-inflammatory effect of Modulen IBD was significantly reduced by opioid receptor blocker.

Conclusion: In conclusion the anti-inflammatory property of Modulen IBD may be ascribed, at least in part, to activation of opioid pathway. In order to investigate this mechanism, the effect of Modulen IBD supplementation on intestinal inflammation was assessed in a preclinical model of intestinal inflammation.

Disclosure of Interest: None declared.

PO-G-245

INFLAMMATORY BOWEL DISEASE AND MUTATIONS IN THE INTERLEUKIN-10 RECEPTOR

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Objectives and Study: The molecular cause of inflammatory bowel disease is largely unknown. Recently homocysteine mutations in the IL-10RA or IL-10RB genes encoding IL10R1 and IL10R2 proteins were found in four patients with early-onset colitis.

Methods: We therefore investigated the IL10RA and IL10RB genes in our patients with onset of inflammatory bowel disease before the age of 10. The study was approved by the institutional review board and we obtained written informed consent from the parents.

Results: In a 10 year old girl with colitis indeterminate we found a heterocysogous pointmutation of the IL10RA gene and a heterocysogous pointmutation in the IL10RB gene.

Conclusion: Since the IL10R1 and IL10R2 form a heterotetramer to make up the interleukin-10 receptor we suggest that this may also lead to a disrupted interleukin-10-dependent “negative feedback” regulation. Further investigations are planned to proof this hypothesis.

Disclosure of Interest: None declared.

PO-G-246

NUTRITIONAL THERAPY FOR PAEDIATRIC CROHN’S DISEASE IN EUROPEAN COUNTRIES

C. Prell, S. Koletzko. Paediatric Gastroenterology, Dr. von Haunersches Kinderspital, Munich, Germany.

Objectives and Study: Exclusive enteral nutritional (EEN) is an established effective treatment in children and adolescents presenting with active Crohn’s disease (CD). However, neither the exact mechanisms nor the optimal performance are known. The aim of this survey was to gather the experience with EEN from different European centres as a baseline for future studies and protocol.

Methods: A standardized questionnaire was sent to the members of the IBD working group of ESPGHAN regarding indication, initiation and duration of EEN in paediatric CD, type and administration of formula, as well as the reintroduction of normal diet.

Results: Members from 18 centres representing 12 European countries (UK, Germany, France, Italy, Israel, Hungary, The Netherlands, Croatia, Denmark, Sweden, Portugal, and Spain) provided information. All but one centre use EEN for induction of remission, in 16 EEN is the first choice therapy for newly diagnosed active CD, but only 4 members reported routine use of EEN for relapse. The duration of EEN ranges from 6 – 8 weeks in 14 centres (n = 14), shorter in 3 and longer in 1 centre. In the majority (n = 12) a casein based whole protein isocaloric formula (1 kcal/ml) is the first choice formula, while 8 different isocaloric flavoured casein-whey mixed formulas are also applied, with aminoacid based formulas reserved for cow’s milk allergic CD patients. The addition of flavours, different food stuff and spices to the formula is allowed in 12 centres to improve the acceptance of EEN. In 12 centres the patient has the free choice whether to drink or to use a nasogastric tube for the administration of the formula. If a tube feeding is used, most centres (n = 10) administer EEN during day and night. After completion, a normal diet is allowed within 0 to 2 weeks.
(n=5) or is even more slowly reintroduced within 2 to 4 weeks (n=11). Special restrictions during this period are made in 4 centres (cow’s milk protein, gluten, egg, wheat and other food allergens). During EEN the patient is supervised and monitored by a paediatric gastroenterologist (n=18) and a dietician (n=15) or a nutritionist (n=5) on a regular basis. Full reimbursement of the costs is available in 10, and in part in the remaining 2 countries. 

Conclusion: Although EEN is frequently used for active CD in European countries, there are large differences regarding duration of treatment, type of formula, route of administration as well as the reintroduction of normal diet between the centres which may affect efficacy, acceptance, and relapse rate. Further research is needed to optimize EEN and to establish guidelines for less experienced physicians to promote this treatment option.

Reference: Christine Prell, Sibylle Koletzko- for the members of the IBD Working group of ESPGHAN.

Disclosure of Interest: None declared.

PO-G-247

RESPONSE TO AZATHIOPRINE IN ADULTS AND CHILDREN WITH INFLAMMATORY BOWEL DISEASE IS COMPARABLE WHEN PHENOTYPE IS CONTROLLED


Objectives and Study: Children and adolescents with inflammatory bowel disease (IBD) are more likely to have Crohn’s disease (CD) than ulcerative colitis (UC); their disease is more extensive and severe than in adults. Azathioprine (AZA) has been shown to be more efficacious in children than in adults; these studies, however, are confounded by differences in disease phenotype. We hypothesized that the efficacy of AZA in children with IBD would be comparable to adults if matched for disease type and extent.

Methods: The efficacy and tolerability of AZA in 32 paediatric IBD patients [18CD: 14UC] was compared to sex, disease type and extent (Montreal classification) matched adult IBD patients on AZA. Retrospective data was obtained by case note review. Clinical remission (CR), defined as asymptomatic steroid withdrawal with normalisation of CRP, was assessed at 3, 6 and 12 months.

Results: In the paediatric and adult patients, the median age (range) at diagnosis was 11 (5–16) and 28 (9–57) years, respectively. AZA was commenced earlier in paediatric patients (1.54 yrs (SD 1.48) after diagnosis) compared to adults (5.38 yrs (7.03)) (P < 0.01). At baseline, there were no differences in CRP and steroid use between groups. At 3 months CR was achieved in 5/29 (17%) paediatric patients and 7/28 (25%) adult patients (P = 0.5). Improvements in remission rates, although not different between groups, were seen at both 6 months (6/27 (22%) in paediatric patients versus 9/24 (38%) in adults (P = 0.4) and 12 months (10/28 (36%) paediatric and 13/28 (46%) adult patients (P = 0.6), but this was not statistically significant. Furthermore, no difference was seen in the subsequent use of anti-TNFs (6/32 (19%) paediatric and 5/32 (16%) adults (p = 1.0)) or surgery rates (5/32 (16%) paediatric (3 CD & 2 UC) and 4/32 (13%) (3CD & 1 UC) in adults (p = 1.0)). AZA was better tolerated in the paediatric patients with only 3/32 (9%) intolerant compared to 11/32 (34%) in the adults (P < 0.05).

Conclusion: When disease type and extent are adequately controlled for, there is no difference in the overall response to AZA between children and adults with IBD. Overall our remission rates are substantially lower than in previously published paediatric studies, but are comparable to results reported from the ongoing SONIC trial in adult CD patients (1).

Reference:


Disclosure of Interest: None declared.

PO-G-248

SINGLE-DOSE OF INFlixIMAB AND SHORT TERM RESPONSE IN RESISTANT ULCERATIVE COLITIS (CU)

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Objectives and Study: Early studies in Inflammatory Bowel Disease (IBD) have investigated infliximab (IFX) on Crohn’s Disease (CD). Initially the role of IFX was considered to be less predominant in CU. Recently it has been shown that IFX plays an important role even in CU. Initial uncontrolled studies have suggested efficacy of IFX in acute steroid refractory CU. More recently, in adult populations, Active Ulcerative Colitis Trials (ACT1 and ACT 2), have proved efficacy of IFX in inducing and maintaining remission in moderate or severe CU. Sands et al (1) demonstrated the efficacy of a single infusion of IFX without the need of maintenance therapy in severe active CU.

Methods: We report the experience of an open trial in 6 patients (pts) (aged 8–12) with severe, steroid refractory CU. Pts were considered eligible if classified as having pancolitis (E3) according to the Montreal Classification, if they had presented with the active disease for at least 2 weeks (wks) and if they had received at least 5 days of intravenous corticosteroids. A pediatric CU activity index (PUCAI) score was >65 in each patient (60–75) and >45 on day 5 after they had started CS therapy with positive predicting value of 95–100% for second line therapy. All six of these pts had
PO-G-249

GRANULOCYTE, MONOCYTE APHERESIS TREATMENT IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE: 1 YEAR FOLLOW-UP

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Objectives and Study: Granulocyte, monocyte/macrophage adsorption (GMA) treatment is a new and safe method that has given promising results in paediatric patients with inflammatory bowel disease (IBD). We evaluated the treatment at 1 year follow-up.

Methods: 38 children who had received GMA treatment and followed at least one year afterwards were included. 12 had Crohn’s disease (CD), 24 ulcerative colitis (UC), and 2 intermediate colitis (IC); 18 girls and 20 boys, age range 9–17 years (mean 13.5 yrs).

Results: At 2 wks 5/6 pts (83%) had responded to IFX with clinical remission (PUCAI <10). All these pts also had their steroids withdrawn for the 2 wks assessment period. The same percentage of remission was maintained after 8 weeks with complete discontinuation of corticosteroids therapy. One non-responder pt underwent colectomy 2 weeks after IFX infusion. There were no documented infusion reactions or adverse events.

Conclusion: The management of intravenous steroid-refractory CU is becoming more complicated and IFX has become an accepted treatment option according to recent data. Our data suggest that short-term efficacy following a single induction dose of IFX is superior to the ACT1 and ACT2 studies (83% versus 38% at 4 wks) without the need for regular maintenance infusions and with immunomodulatory continued therapy. This may favour the use of a single dose of IFX over cyclosporine as a rescue therapy in order to delay the need of surgery.

Reference:

Disclosure of Interest: None declared.
intradermally into ear with curdlan to induce hyperinflammation. Seven days later, the severity of inflammation was assessed on H/E stained slides of ears by a histological score (from 0–4, with 4 being the most severe inflammation) and ear thickness.

**Results:** Curdlan generated a mild inflammatory score in the wild-type mice (table 1), while CGD mice showed severe inflammation. Interestingly, genetic deletion of dectin-1 decreases significantly the severity of inflammation in CGD mice.

**Table:** Absence of Dectin-1 dampens CGD inflammation

<table>
<thead>
<tr>
<th></th>
<th>Inflammatory score (mean ± SEM)</th>
<th>Ear Thickness (mean ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>wild-type</td>
<td>1.6 ± 0.4</td>
<td>0.34 ± 0.1 mm</td>
</tr>
<tr>
<td>NOX2-deficient</td>
<td>3.3 ± 0.3</td>
<td>0.93 ± 0.01 mm</td>
</tr>
<tr>
<td>NOX2 and Dectin-1-deficient</td>
<td>2.1 ± 0.3</td>
<td>0.32 ± 0.16</td>
</tr>
</tbody>
</table>

**Conclusion:** Dectin-1 deficiency strongly diminished hyperinflammation in NOX2-deficient mice. However, our results were obtained in skin hyperinflammation and future research will have to investigate similarities and differences between hyperinflammation in the skin and the colon, especially with a trigger widely used as a food additive.

**Disclosure of Interest:** None declared.

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**PO-G-251**

**IMPROVEMENT OF BONE MINERAL DENSITY AFTER COMPLETED HEIGHT GROWTH IN ADOLESCENTS WITH IBD**

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**Objectives and Study:** Low bone mineral density (BMD) has been recognized as a potential problem in children and adolescents with inflammatory bowel disease (IBD). In a recently published cross-sectional population-based report (1), we investigated BMD in a group of 144 children and adolescents with IBD. The lowest BMD values were found in the lumbar spine (L2-L4). BMD mean Z-score of the lumbar spine in the whole group of IBD patients was significantly reduced compared to healthy references (mean Z-score –0.8 SD, range –5.9 SD – 3.7 SD, P < 0.001). Little is known about the development of BMD in this patient group, especially into early adulthood. Our aim was to describe the longitudinal development of BMD in IBD patients with completed height growth.

**Methods:** During a two-year period we followed the development of BMD in a group of patients (n = 32) who had completed their height growth (pubertal stage 5, height growth in the year before inclusion <1.5 cm) at the time of inclusion into the study. Of these 32 patients, 22 had ulcerative colitis, 7 Crohn’s disease and 3 indeterminate colitis (mean disease duration 51.2 months, range 3–123 months). To evaluate BMD all patients underwent a dual-X-ray-absorptiometry (DXA) of the lumbar spine (L2-L4). BMD values were expressed as Z-scores using pediatric reference data from Lunar. Bone age was estimated by a radiograph of the left wrist using the TW 2 method.

**Results:** At baseline, significant decreased BMD Z-scores were found both in males and females (table). In the group of the males, BMD Z-score improved significantly (P < 0.05) with 0.5 SD during follow-up. An improvement almost in the same range was seen in the female group (P = 0.059). Almost all patients had at baseline reached the maximum bone age.

**Table:** Male and female patients with IBD and pubertal stage 5 at both DXA measurements

<table>
<thead>
<tr>
<th></th>
<th>Males (n = 19)</th>
<th>Males (n = 19)</th>
<th>Females (n = 13)</th>
<th>Females (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td>Chronological age (years)</td>
<td>17.9</td>
<td>20.0</td>
<td>17.1</td>
<td>19.2</td>
</tr>
<tr>
<td>Bone age (years)</td>
<td>17.7</td>
<td>18.0</td>
<td>16.0</td>
<td>16.0</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>179.2 (±6.0)</td>
<td>179.6 (±6.1)</td>
<td>163.7 (±7.3)</td>
<td>164.3 (±7.5)</td>
</tr>
<tr>
<td>Height Z-score</td>
<td>–0.08 (±0.9)</td>
<td>–0.10 (±0.9)</td>
<td>–0.53 (±1.1)</td>
<td>–0.50 (±1.2)</td>
</tr>
<tr>
<td>BMD Z-score</td>
<td>–1.10 (±1.6)</td>
<td>–0.59 (±1.4)</td>
<td>–0.67 (±1.7)</td>
<td>–0.22 (±1.7)§</td>
</tr>
<tr>
<td>Lumbar spine (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05, §P = 0.059; compared to baseline.

**Conclusion:** There might be some evidence that the BMD of adolescents with IBD has the potential for “catch-up” into early adulthood.

**Reference:**

**Disclosure of Interest:** None declared.

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**PO-G-252**

**LONG-TERM OUTCOME OF TREATMENT WITH INFliximAB (IFX) IN PEDIATRIC CROHN’S DISEASE (CD): A POPULATION-BASED STUDY**

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**Objectives and Study:** This observational study assessed the long-term clinical benefit and safety of IFX in an
Inception population-based cohort of children <17 years and newly diagnosed with CD between 1988 and 2004.

**Methods:** Among 537 pediatric CD patients <17 years at diagnosis prospectively enrolled in the cohort, 120 (22%) received IFX and were included in this retrospective analysis. Patients still receiving IFX at last visit and patients who stopped IFX while in remission were considered as “IFX efficacy”. Primary or secondary non-responders to IFX were considered as “IFX failure”. The long-term effects of IFX on the course of CD were defined by the rate of surgery and nutritional catch-up. Nutritional catch-up was defined as a continuous variable corresponding to the difference between BMI Z score at maximal follow-up and at diagnosis.

**Results:** One hundred and twenty (69F, 51 M) patients received IFX. The median age at diagnosis and at IFX initiation was 14.5 years [Q1 = 12–Q3 = 16] and 17.9 years [16–21] respectively. The median follow-up was 110 months [75–161]. Fifty patients (42%) received episodic IFX and 70 (58%) scheduled (including 27 episodic converted to maintenance). Among the 120 patients, 39 (32%) were still receiving IFX at 1 and 3 years was 77%, 45% and 39% respectively. Sixty six (55%) patients were in continuous maintenance IFX at 1 and 3 years was 77% and 50% respectively. Sixty six (55%) patients were in the “IFX efficacy” group and 39 (32%) in the “IFX failure” group. The cumulative risk of surgery at 1 year and at 3 years was significantly reduced in the “IFX efficacy” group vs “IFX failure” group: 6% vs 29% and 13% vs 44% (P = 0.002). Within the “IFX efficacy” group, the cumulative risk of surgery at 1 year and at 3 years was smaller in patients with scheduled treatment (n = 43) vs episodic (n = 23): 0% vs 14% and 0% vs 23% (P < 0.005). Patients of the “IFX efficacy” group had a significant catch-up of nutritional status (P = 0.01) while those of the “IFX failure” group did not (P = 0.82). Twenty four patients presented adverse events including immediate and delayed hypersensitivity reactions (n = 19) and infections (n = 5).

**Conclusion:** In this population-based cohort of pediatric CD, treatment with IFX was efficacious in 55% of patients during a median follow-up of almost 3 years. Long term IFX responders had a lower rate of surgery and an improved catch-up of nutritional status.

**Disclosure of Interest:** None declared.

**PO-G-253**

**INCIDENCE OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE IN NORTHEASTERN SLOVENIA, 2000–2008**

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**Objectives and Study:** During the past few years an increasing incidence of inflammatory bowel disease (IBD) among children and adolescents has been reported in developed countries. There is only one study available on the incidence of paediatric IBD in southwestern Slovenia for the period of 1994–2005. So far, no studies have been carried out in northeastern (NE) Slovenia.

The aim of our study was therefore to assess the incidence of paediatric IBD in NE Slovenia.

**Methods:** All cases of Crohn’s disease (CD), ulcerative colitis (UC) or indeterminate colitis (IC) diagnosed from 2000 to 2008 in children and adolescents up to 18 years of age and resident in NE Slovenia were identified. In Slovenia pediatric patients (0–18 years) with suspected IBD are referred to, diagnosed and treated in 1 of the 2 tertiary medical centres for pediatric gastroenterology. Patients from NE Slovenia are referred to University Medical Centre Maribor (UMCM). Only a small proportion of these patients is being treated in regional hospitals by general pediatricians or internists. Therefore, case records were sought from UMCM as well as from the 4 regional hospitals in the study area. All patients were diagnosed on the basis of endoscopy, histopathology and small bowel investigations. Data on the background population (by sex, single-year age groups and calendar year) were obtained from Statistics Slovenia. The population aged 0–18 years in NE Slovenia declined by 15.8% from 173.811 in 2000 to 146.386 in 2008. The study covered 97.6% of the pediatric population (0–18 years) of Slovenia.

**Results:** In total, 95 cases of IBD were diagnosed during the study period (54 patients with CD, 36 with UC and 5 with IC). The mean annual incidence (per 100 000) was 6.6 (95% CI 5.3–8.0) for all IBD, 3.8 (2.5–4.8) for CD, 2.5 (1.7–3.3) for UC, and 0.3 (0.0–0.7) for IC. The incidence of IBD increased from 4.5 (95% CI 2.7–6.4) in the period 2000–02 to 7.4 (4.9–9.8) in 2003–05 and 8.3 (5.6–10.9) in 2006–08 (P = 0.061). The incidence of CD rose from 1.97 (95% CI 0.75–3.19) in the period 2000–02 to 4.42 (2.53–6.53) in 2003–05 and 5.15 (3.05–7.26) in 2006–08 (P = 0.028). The corresponding incidence of UC and IC, however, remained unchanged: 2.16, 2.63, 2.90 and 0.39, 0.42 and 0.22, respectively.

**Conclusion:** The incidence of IBD in children and adolescents increased in NE Slovenia during the study period. This was due to an increase in CD, whereas the incidence of UC remained unchanged. The increasing incidence is in accordance with reports from other European countries. In the present study, the incidence of CD and particularly of UC was higher than that reported from southwestern Slovenia, probably due to a more recent study period.

**Disclosure of Interest:** None declared.

**PO-G-254**

**DIAGNOSTIC VALUE OF MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY IN CHILDREN WITH INFLAMMATORY BOWEL DISEASES**

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1Department of Paediatrics, Section of Paediatric Gastroenterology, Division of Paediatric Surgery, Istanbul University Cerrahpaşa Medical Faculty, Istanbul, Turkey; 2Department of Paediatric Gastroenterology and Nutrition, Istanbul University Cerrahpaşa Medical Faculty, Istanbul, Turkey; 3Department of Paediatric Surgery, Istanbul University Cerrahpaşa Medical Faculty, Istanbul, Turkey

**Objectives and Study:** During the past few years an increase in the number of children and adolescents undergoing magnetic resonance cholangiopancreatography (MRCP) has been reported. The aim of our study was to determine the diagnostic value of MRCP in children with inflammatory bowel diseases (IBD).

**Methods:** The study included 41 children (21 boys, 20 girls) with IBD (20 Crohn’s disease, 21 ulcerative colitis) who underwent MRCP at the Division of Paediatric Gastroenterology and Nutrition, Cerrahpaşa Medical Faculty, Istanbul, Turkey. The demographic data, clinical symptoms, IBD activity and also MRCP findings were recorded. The sensitivity, specificity, positive and negative predictive values were calculated.

**Results:** The sensitivity, specificity, positive and negative predictive values of MRCP for the diagnosis of IBD were 95.2%, 95.2%, 95.2% and 95.2% respectively. The sensitivity, specificity, positive and negative predictive values of MRCP for the diagnosis of Crohn’s disease were 95.2%, 95.2%, 95.2% and 95.2% respectively. The sensitivity, specificity, positive and negative predictive values of MRCP for the diagnosis of ulcerative colitis were 95.2%, 95.2%, 95.2% and 95.2% respectively.

**Conclusion:** MRCP is a valuable diagnostic tool in children with IBD. It has a high sensitivity, specificity, positive and negative predictive values for the diagnosis of IBD and also for the diagnosis of Crohn’s disease and ulcerative colitis.

**Disclosure of Interest:** None declared.
Objectives and Study: Inflammatory bowel diseases (IBD) are often associated with extraintestinal manifestations. We aimed to evaluate the value of magnetic resonance cholangiopancreatography (MRCP) in diagnosing hepatobiliary manifestations of children with IBD.

Methods: Twenty-eight children [16 male, 57.1%; mean age 12.6 ± 2.1 (6–16)] with IBD diagnosed by endoscopic, radiologic and histologic criteria were evaluated with MRCP. Biochemical tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkalen phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin (tbil) and conjugated bilirubin (cbil) and serologic immune markers (including anti-neutrophilic cytoplasmic antibody (p-ANCA)) were measured.

Results: Sixteen patients were diagnosed as ulcerative colitis (UC), 9 as Crohn’s disease (CD), and 3 as indeterminate colitis (IC). MRCP performed without any complication was normal in 23 patients (82.1%) whose liver function tests were normal in all. The characteristics of 5 patients (17.9%, all with UC) with abnormal MRCP whereas it was positive in 8 patients with normal MRCP. Patient 1, 2 and 3 received ursodeoxycholic acid (UDCA) for sclerosing cholangitis as well as therapy for UC. Patient 1 and 3 have been followed up for 6 months after the beginning of therapy with UDCA.

Table:

<table>
<thead>
<tr>
<th>Gender/ Age</th>
<th>ALT/AST/ ALP/GGT/ cbil</th>
<th>MRCP</th>
<th>Liver histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1 M/14</td>
<td>85/85/460/377/0.5</td>
<td>Sclerosing-</td>
<td>Sclerosing-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cholangitis</td>
<td>cholangitis</td>
</tr>
<tr>
<td>Patient 2 M/12</td>
<td>391/148/262/122/0.01</td>
<td>Sclerosing-</td>
<td>Sclerosing-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cholangitis</td>
<td>cholangitis</td>
</tr>
<tr>
<td>Patient 3 M/10</td>
<td>266/165/889/362/0.3</td>
<td>Sclerosing-</td>
<td>Minimal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cholangitis</td>
<td>hepatitis</td>
</tr>
<tr>
<td>Patient 4 M/14</td>
<td>124/73/304/703/0.1</td>
<td>Irregular</td>
<td>Stenosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>bile duct</td>
<td></td>
</tr>
<tr>
<td>Patient 5 F/16</td>
<td>60/42/104/53/0.2</td>
<td>Chronic</td>
<td>pancreatitis</td>
</tr>
</tbody>
</table>

Conclusion: MRCP can be a valuable, noninvasive, radiation free tool in diagnosing extraintestinal hepatobiliary manifestations in children with IBD. A child with IBD and abnormal transaminase levels and/or pruritus should be evaluated for the presence of bile duct injury, in order to start UDCA for avoiding progressive liver disease.

Disclosure of Interest: None declared.

PO-G-256

CALPROTECTIN AS TRIAGE TEST TO AVOID UNNECESSARY ENDOSCOPY IN PATIENTS WITH SUSPECTED IBD

E116
Objectives and Study: In patients with suspected IBD confirmation of the diagnosis is done by endoscopy and histology. Many consider this invasive procedure as uncomfortable. Use of a triage test may reduce the number of unnecessary endoscopies. The aim of this meta-analysis was to evaluate whether faecal calprotectin (FC) to the diagnostic workup reduces the amount of patients subjected to endoscopy.

Methods: We searched MEDLINE and EMBASE for diagnostic accuracy studies with a prospective design and FC testing (index test) before endoscopy with histopathological verification (reference standard). Two review authors independently assessed quality and extracted data. Sensitivity and specificity of FC were estimated according to the most recent insights and methods for diagnostic meta-analyses.

Results: The final analysis included six adult (670 patients) (1–6) and seven paediatric studies (371 patients) (7–13). IBD was endoscopically confirmed in 32% of the adults and in 61% of the children. In the adult studies the pooled sensitivity and specificity of FC were respectively 0.93 (95% confidence interval 0.85 to 0.97) and 0.96 (0.79 to 0.99). In the paediatric studies we found respectively 0.92 (0.84 to 0.96) and 0.76 (0.62 to 0.86). The lower specificity in paediatric studies was significantly different from adult studies ($P = 0.048$).

Conclusion: Inferring from the pooled estimates we calculated the impact of FC testing on patient outcome. When only patients with an abnormal FC result continue the diagnostic pathway, 33 out of 100 suspected adults will undergo endoscopy, 2 IBD-cases will be missed, and 3 will be scoped unnecessarily. In a population of 100 paediatric patients 65 will undergo endoscopy of which 9 will not have IBD and 5 IBD cases will be missed. FC testing is a good triage tool for patients with suspected IBD to limit the number of unnecessary endoscopic procedures. These numbers should however be interpreted with caution. Despite a strict selection of studies based on proper patient recruitment and study design, there was considerable heterogeneity.

References:
1. Limburg et al (Am J Gastroenterol 2000)
2. Tibble et al (Gut 2000)
11. Sidler et al (Inflamm Bowel Dis 2008)
12. Ashorn et al (Inflamm Bowel Dis 2009)

Disclosure of Interest: None declared.
ROME III criteria, has never been established. This was the aim of this epidemiologic prospective study.

**Methods:** The prevalence of various FID was assessed among a cohort of children aged 0 to 4 years seen by their private pediatrician for regular follow-up over a given 4-weeks period. Some potential risk factors were moreover analysed.

**Results:** Among a global pediatric population of 100,000 children under 4, 1,211 children participated in the study after obtaining parental consent. 1,032 surveys were completed. The global prevalence of FID was 23.8%, with a slight male predominance. Given the age-dependent definitions of FID in children, the prevalence of regurgitations in infants under 1 year of age was 17.3%, that of colic in infants aged 0 to 4 months was 19% and the prevalence of dyschezia in infants aged 0 to 6 months was 5.6%. 6.7% of children under 4 were constipated and 1.7% had functional diarrhea. The prevalence of rumination and cyclic vomiting was extremely low (<0.6%). Among the putative risk factors, maternal smoking was slightly more frequent among colicky and regurgitating infants (NS). The global rate of breastfeeding was 60%. Breastfeeding was not significantly associated with an absence of FID. The mothers of children with constipation or functional diarrhea had more often themselves a FID.

**Conclusion:** This is the only pediatric study establishing prevalence of each type of FID according to age groups. Overall, the prevalence of FID is similar in children aged 0 to 4 years to that in adults, but with a male predominance. A greater frequency of FID was identified among parents of children with FID, thereby strengthening the hypothesis of the influence of heredity and parental behavior in the emergence of pediatric FID.

**Disclosure of Interest:** None declared.

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**PO-G-259**

**FUNCTIONAL GASTROINTESTINAL DISORDERS INDUCED BY NEONATAL STRESS: IS THE MODEL VALID IN HUMANS?**

U. Halac¹, M. Revillion², L. Michaud³, F. Gottrand², H. Labelle³, C. Faure¹.¹Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Hospital Sainte-Justine, Université de Montréal, Québec, Montréal, Canada, ²Unit of Gastroenterology, Hepatology and Nutrition, Clinic of Paediatrics, Hospital Jeanne de Flandre – CHRU de Lille, Université de Lille 2, Lille, France, ³Department of Paediatric Orthopaedics, Hospital Sainte-Justine, Université de Montréal, Québec, Montréal, Canada.

**Objectives and Study:** Functional gastrointestinal disorders (FGID) affect 15 – 20% of the general pediatric and adult population. Animal models suggest that a neonatal stress such as invasive procedures in the neonatal period could be responsible of visceral hypersensitivity and FGID later in the life.

The objective is to assess if children and adolescents with congenital esophageal atresia (EA), corrected during neonatal period, suffer from FGID more frequently than subjects without any neonatal history. Secondary aim is to study if EA’s characteristics and patient’s outcome are associated with FGID.

**Methods:** Subjects with EA and controls without any neonatal history, aged from 8 to 19, were prospectively enrolled in this multicentric case-control study. Gastrointestinal symptoms were assessed by a validated questionnaire and FGID diagnosis (irritable bowel syndrome (IBS), functional dyspepsia (FD), and functional abdominal pain (FAP)) was performed according to the pediatric Rome III criteria.

**Results:** Fifty three children with EA (25 girls, median age 12.3 years, range 7.8 – 19) and 72 controls (34 girls, median age 13.4, range 7.8 – 18.5) were included. 46 patients (87%) had a type C EA, and 29 (55%) presented >1 associated malformations. Complications during the first month after surgery occurred in 45% of patients, and included pneumothorax (14%), anastomotic stricture (14%), anastomotic leakage (8%) and secondary fistulization (4%). The median hospital stay duration was 16 days (range 7 – 154 days). Eleven children with EA (21%) presented a FGID (5 IBS, 5 FAP, 1 FD) as compared to 8 controls (11%) (3 IBS, 2 FAP, 3 FD)(P > 0.05; Chi square test). The presence of associated malformations, the occurrence of complications during the first month and a length of hospital stay >30 days did not influence the incidence of FGID.

**Conclusion:** Neonatal stress associated to surgical correction of an EA is not associated with FGID during childhood and adolescence. This suggests that visceral hypersensitivity secondary to neonatal stress in animal models may not apply in humans.

**Disclosure of Interest:** None declared.

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**PO-G-260**

**THE PSY-MED UNIT (PMU); A UNIQUE AND INTEGRATED APPROACH FOR CHILDREN WITH INVALIDATING FUNCTIONAL ABDOMINAL PAIN (FAP)**

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**Objectives and Study:** The PMU Emma Children’s Hospital, AMC Amsterdam, is a tertiary referral centre for children, ages 6–18 yrs, with invalidating functional complaints (at least two present): the complaints have impact on their social and family life’s,they have given up their hobbies, presence of school absenteeism Complaints; long-lasting (>3 months)and therapy resistant (earlier treatment not succesful) PMU-approach; an integrated approach starting at intake by paediatrician and psychiatrist/psychotherapist, seeing the patient together. During the intake the fact that body and mind belong together, you cannot divide them is explained to patient and family. Validation of complaints by full history/thorough physical examination; complaints are real, no doubt. Explanation of complaints by models (stress
model, brain-gut axis, sensitisation model) Individual treatment (rehabilitation, graded exercise, cognitive behavioural therapy etc.)

Aim: Evaluate effects of PMU treatment in children with FAP as major complaint.

Methods: Retrospective observational study in children with FAP as major complaint by measuring the invalidation level before and after treatment and persistence of complaints.

Results: 42 pt with FAP as major complaint, 27 girls (64%). Age at first visit; mean 13 yr 8 mnth (range 6–17) Before treatment: Duration of complaints >1 yrs in 23 pt (55%)/ >2 yrs in 16 pt (37%), 25 pt (60%) visited 3–5 care providers, 13 pt (31%) visited >5 care providers for this complaint before intake. School absenteeism 20–40% in 10 pt (23%)/40–80% in 5 pt (16%)/80–100% in 17 pt (40%)/.. 33 pt (78%) partially/completely given up their hobbies. 31 pt (74%) less developed social life. 13 pt (31%) no social life left. All patients had more than one complaint. At least 25 pt (60%) consulted alternative circuit before intake.

Treatment: 20 pt finished treatment, 13 pt still in treatment, 2 pt stopped treatment after intake. 2 pt no complaints at moment of intake, 5 pt one consult only to advise other care providers. 14 pt treated <1yr (70%)/ 6 pt (30%) treatment <3 months.

After treatment: 13 pt (65%) lost/minimized complaints, 13 pt no school absenteeism anymore (65%), 56% restarted hobbies, 14 pt (70%) normal social life after treatment.

Conclusion: PMU approach; good results for this serious invalidated patient group with therapy resistant functional complaints. Note: relative small group, not yet long-term follow-up.

Disclosure of Interest: None declared.

PO-G-261

CORTISOL DIURNAL RHYTHM AND STRESS REACTIVITY IN CHILDREN WITH FUNCTIONAL CONSTIPATION AND ABDOMINAL PAIN: THE GENERATION R STUDY


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Objectives and Study: The hypothalamus-pituitary-adrenal (HPA) axis is involved in the individual stress-response by releasing cortisol from the adrenal cortex. It has been suggested the HPA-axis may play a role in functional bowel disorders. The aim of this study is to assess the association between HPA-axis activity and functional constipation and abdominal pain in pre-school children.

Methods: This study was embedded in a subset of the Generation R Study, the Focus Cohort, a prospective cohort from early fetal life onwards. At the age of 24 months, parental derived questionnaire data on stool pattern and abdominal pain was available in 404 children. Functional constipation was defined according to the ROME II criteria (1). Abdominal pain was defined according to the Pain Response Inventory (2). Salivary cortisol diurnal rhythm (ie. after awakening, 30 minutes later, between 11am and 12 pm, 3pm and 4pm and at bedtime) and the cortisol stress reactivity after the stressful Strange Situation Procedure (SSP) were assessed at the age of 14 months. Logistic regression analyses were performed and were adjusted for baseline cortisol levels, age of sampling, gender, birthweight, gestational age, maternal alcohol consumption, smoking, parenting stress score, duration of breastfeeding and overweight.

Results: At the age of 24 months, 7.5% and 7.7% had functional constipation or abdominal pain respectively. Only 1.2% of the children had both symptoms of functional constipation and abdominal pain. No association between diurnal cortisol rhythm and cortisol reactivity with functional constipation was found.

Diurnal cortisol rhythm was not associated with the presence of abdominal pain, but cortisol reactivity to the SSP at 14 months of age was significantly associated with the presence of abdominal pain at the age of 24 months (OR: 1.10; 95%CI: 1.01 – 1.20).

Conclusion: These results do not support the role of circadian cortisol excretion in functional bowel disorders. However, the results do imply that the response of the HPA-axis to stress may be seen as a possible early indicator for sensitivity to abdominal pain in young children.

References:

Disclosure of Interest: None declared.

PO-G-262

LONG TERM HEALTH IMPACT OF OF INFANTILE SHORT BOWEL SYNDROME; MEDICAL ASPECTS


The Generation R Study Group, Erasmus Medical Center, Rotterdam, Netherlands.

Objectives and Study: In infantile short bowel syndrome (SBS), adaptation has been documented, but data on long-term effects are scarce. The aim of the study is to evaluate long-term medical consequences of infantile (<1 year age) SBS.

References:

Disclosure of Interest: None declared.
Methods: In a cross-sectional design, subjects with a history of infantile SBS, born between 1976 and 2001 (n = 40), were assessed for growth (weight and height for age, target height), nutritional status (four skinfolds, dual energy x-ray absorptiometry), dietary assessment (dietary record), defecation pattern and target height for height. Data were compared to reference values of healthy controls and presented as mean ± SD or median [range].

Results: Sixteen boys and 24 girls (mean age 14.8 ± 6.8 years) had received parenteral nutrition (PN) in their first years of life for a median of 110 [43–2345] days, following extensive bowel resection (mean residual bowel length was 71 ± 23.5 cm). Underlying diagnoses were small bowel atresia (n = 14), gastrochisis (n = 3), necrotizing enterocolitis (n = 8), volvulus and/or malrotation (n = 6), meconium peritonitis (n = 7), long segment M. Hirschsprung (n = 1) and ischemic small bowel e.c.i. (n = 1). Current mean weight for age and height for age Z-scores were −0.7 ± 1.2 and −0.9 ± 1.3 respectively in children (n = 31). Median BMI in adults (n = 9) was 19.9 [17–26] and height for age z-score was −1.0 [−2.5–1.5]. Target height (TH) Z-score was +0.3 ± 1.1 in children and +0.5 [−0.8–2.3] in adults. Height differed significantly from TH in children \( P = 0.00 \) and in adults \( P = 0.008 \). Most subjects had normal percentages of body fat. The average Z-scores for total body mineral density were normal in adults and children. However, in children the mean Z-scores for bone mineral content and lean body mass were −1.2 ± 1.4 and −1.2 ± 1.2 respectively. Mean energy intake was 91% of the estimated average requirements. Reported frequencies of defecation and bowel complaints were significantly higher than in healthy control subjects (\( P < 0.05 \)). All subjects were generally in good condition.

Conclusion: In the long term, the subjects have shorter stature than was expected from their calculated Target Height. The subjects have normal weight for height and body fat percentages, but bone mineral content is reduced.

Disclosure of Interest: None declared.

PO-G-263

CAN PARTIALLY HYDROLYZED GUAR GUM BE AN ALTERNATIVE TO LACTULOSE IN THE TREATMENT OF CHILDHOOD CONSTIPATION?


Objectives and Study: Constipation is common in children. Dietary fiber has important health benefits in childhood, especially in promoting normal laxation. One of the promising fiber sources is partially hydrolyzed guar gum (PHGG) because of its low viscosity, complete fermentation in the colon and tasteless and odorless characteristics. Here, we aimed to investigate the effect of PHGG in constipation and to compare with lactulose.

Methods: A randomized prospective controlled study on 61 patients was performed. Group I (31 patients, 45 % male, mean age: 7.3 ± 1.9) received PHGG (4–6 years: 3gr/day, 6–12 years: 4gr/day, 12–16 years: 5gr/day). Group II (30 patients, 53 % male, mean age 7.6 ± 2.5) received lactulose (1 ml/kg/day). PHGG was added into daily foods or drinks. Children were evaluated by bowel diary (defecation frequency, stool consistency, presence of soiling, rectal bleeding, flatulence and abdominal pain) at baseline and after 4 weeks of therapy. Stool consistency was evaluated by Bristol Stool Scale (1: hard stool to 7: liquid stool). Family questionnaire about the satisfaction and side effects of both groups were obtained.

Results: Age, gender and duration of constipation (group I: 8.0 ± 2.4 weeks; group II: 9.2 ± 2.1 weeks) were not different between two groups. Significant improvement in all parameters as compared to baseline was achieved in both groups. (Table) At the end of therapy, the bowel movement frequency was statistically higher in group II (6.0 ± 1.1) than group I (5.0 ± 1.7) (\( P < 0.001 \)). Other parameters including stool consistency, stool withholding, abdominal pain and rectal bleeding were not statistically different between two groups. Adverse effects were not different in both groups. Although statistically insignificant, flatulence was more frequent in group II than group I. In family questionnaire, bad taste, flatulence and necessity to ingest high amount of drug were noted in 54 %, 32 % and 68 % in group II, respectively. In group I, flatulence was noted in 22 %

Table:

<table>
<thead>
<tr>
<th></th>
<th>Group I Before</th>
<th>Group I After</th>
<th>Group II Before</th>
<th>Group II After</th>
<th>( p_1/p_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM frequency/week</td>
<td>4.0 ± 0.7</td>
<td>5.0 ± 1.7</td>
<td>4.0 ± 0.7</td>
<td>6.0 ± 1.1</td>
<td>0.005/0.001</td>
</tr>
<tr>
<td>BM consistency Abdominal pain (%)</td>
<td>2.8 ± 0.6</td>
<td>3.9 ± 0.7</td>
<td>3.1 ± 0.6</td>
<td>4.3 ± 0.6</td>
<td>&lt;0.001/0.001</td>
</tr>
<tr>
<td>Stool withholding (%)</td>
<td>49.2</td>
<td>38</td>
<td>16</td>
<td>50.8</td>
<td>0.01/0.013</td>
</tr>
<tr>
<td>Rectal bleeding (%)</td>
<td>24</td>
<td>20</td>
<td>0</td>
<td>24</td>
<td>0.001/0.001</td>
</tr>
</tbody>
</table>

Conclusion: Treatment with PHGG is as effective as lactulose treatment in constipation. Lactulose seemed to have more side effects including flatulence, and difficulties in ingestion such as sensation of bad taste and necessity of high volume.

Disclosure of Interest: None.

PO-G-264

THE ROLE OF SALIVARY PH AND BUFFER CAPACITY OF SALIVA ON PATIENTS WITH DIABETES VERSUS NON-DIABETIC PATIENTS IN PERIODONTAL DISEASE

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Disclosure of Interest: None.
Objectives and Study: There is evidence that salivary secretion and composition are different in patients with diabetes compared to non-diabetic subjects and that these changes are involved in the pathogenesis of periodontitis. The purpose of this prospective study was to evaluate some salivary parameters (flow and pH) and also the Streptococcus mutans levels in children with diabetes versus non-diabetic children.

Methods: The study took place between 2008–2009 and included 148 patients (62 diabetics and 86 non-diabetic children), with the age between 7–18 years. Were used Saliva-Check Buffer Kit and Saliva Check Mutans Kit to determine unstimulated and stimulated salivary flow and salivary pH.

Results: Children with diabetes had an unstimulated salivary flow average of 0.15 ml / min versus 0.36 ml / min for children without diabetes ($P < 0.00001$); 39 children with diabetes (63%) and only 1 non-diabetic child (1%) complained of dry mouth; 29 children with diabetes (47%) and 3 non-diabetic children (3.5%) had hyposalivation; 33 children with diabetes (53%) and 83 non-diabetic children (96.5%) had a normal unstimulated salivary flow. Average flow of stimulated saliva was similar in both groups: 2.2 ml / min in children with diabetes and 2.5 ml / min in non-diabetic children ($P < 0.01$); 57 children with diabetes (92%) and 85 non-diabetic children (99%) had a normal stimulated salivary flow (>2.0 ml / min); 5 children with diabetes (8%) and 1 non-diabetic child (1%) had a low stimulated salivary flow (<2.0 ml / min).

Diabetic patients have significantly lower salivary pH compared with non-diabetic patients. Ph average was 6.0 for children with diabetes and 7.0 for non-diabetic patients ($P < 0.01$); 19 children with diabetes (31%) and 1 non-diabetic child (1%) had a pH of 5.0; 53 children with diabetes (85%) and 8 non-diabetic children (9%) had a pH of 6.0; 3 children with diabetes (5%) and 77 non-diabetic children (90%) had a pH of 7.0.

Streptococcus mutans (SM) was detected in almost the same proportions (85% and 86%) in both groups. 53 children with diabetes and 74 non-diabetic children had levels above 500,000 cfu / ml of SM.

Conclusion: Increasing number of children with diabetes calls for proper assessment of salivary clinical parameters such as: spontaneous salivary flow, pH and default buffer capacity of saliva, obviously and statistically significant changes in our study at diabetic patients with known periodontitis potential. Towards SM the study does not reveal significant differences regarding the number of colonies in diabetic patients versus non-diabetics.

Disclosure of Interest: None declared.
Objectives and Study: The aim of this study was to evaluate the effect of yoga exercises on pain frequency, intensity and quality of life in children with functional abdominal pain.

Methods: 20 children, aged 8–18 years, with Irritable Bowel Syndrome (IBS) or Functional Abdominal Pain (FAP) were enrolled and received 10 yoga lessons. Outcomes were measured before the start of the yoga lessons (t = 0), the week before the yoga started (t = 1), directly after finishing the yoga lessons (t = 2) and 3 months after finishing the yoga-exercises (t = 3). Pain intensity and pain frequency were scored in a daily pain diary. Further instruments were: a Symptom Questionnaire based on the Rome III criteria, the Kidscreen quality of life questionnaire (KQoL).

Results: In the total group and the 11–18 years old patient group the pain frequency was significantly decreased at t = 2. (P < 0.001 and P = 0.004). In the 8–11 years old patient group both pain frequency and intensity were significantly decreased at t = 2 (P = 0.015, P = 0.031). After follow-up (t = 3) there still was a significant decrease in pain frequency in the younger patient group (0.04) and a borderline significant decrease in the total group compared to baseline (P = 0.052). Scores from the Symptom Questionnaire showed that almost all children reported less abdominal pain after the yoga-sessions (P = 0.002). Children as well as their parents reported a lower KQoL-scores at baseline than reference scores. Parents reported a significantly higher KQoL-score after yoga treatment on the dimension School and Peers. Three children didn’t complete the yoga sessions.

Conclusion: This is the first study that shows that yoga exercises are effective for children aged 8–18 years with FAP, resulting in significant reduction of pain intensity and frequency, especially in children of 8–11 years old. Avoid overlap.

Disclosure of Interest: None declared.
Kirkkale province. The study was carried out by applying questionnaire of 250 patients in a child population aged 5 to 18 years old calculated according to 43000 populations in this age group in Kirkkale and probable expected prevalence, around 20%, who were consecutive patients selected among those admitted to these primary care centers. All patients were enrolled into the study prospectively between October-December in 2009. Each family physician and paediatrician completed a detailed FD questionnaire designed on Rome-III criteria on these patients who were evaluated with their main symptom on admission and according to their parental features as well. The diagnosis of FD was based on the Rome-III criteria as epigastric discomfort or pain or prevalence of dyspepsia was calculated among the group.

Results: Among the 250 patients participating in the study mean age was 10±3 years and the male/female ratio was 1.6 (62.4% boys). Overall FD diagnosis was observed in 31% of the group (n:78). FD was higher in boys and also found higher with increasing age older than 10 years, but not significantly. Other most frequent symptoms following chronic abdominal pain were diarrhea, defecation disorders, painful defecation, fullness, functional constipation, and irritable bowel syndrome (31%, 27%, 20%, 19%, 17%, and 13% respectively). Most children who are brought to the primary care centers for chronic abdominal pain are unlikely to require diagnostic testing. All children who had a diagnosis of FD were evaluated for the natural history of the illnesses and their family histories. Abdominal discomfort was significantly higher in girls (28%, n:26 in females vs. 14%, n:22 in males) (P < 0.05). There was no statistically relationship between dyspepsia and parental gastrointestinal disorders, smoking or eating patterns. Medical management was the most common (48%) preference for treatment. Follow-up with no medications, but dietary modifications and alternative therapies such as herbal medicines and psychological approach were also other performing methods afterwards medical remedies.

Conclusion: Dyspeptic patients constitute a considerable part of patients admitted to primary health care centers in Kirkkale. The most frequent symptom is epigastric pain in dyspeptic children.

Disclosure of Interest: None declared.

PO-G-269

THERE IS A STRONG CORRELATIONS BETWEEN ESOPHAGEAL ACIDITY AND HEART RATE VARIABILITY

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Objectives and Study: It was shown that the Autonomic Nervous System (ANS) plays an important role in the Heart Rate Variability (HRV). We hypothesized that the esophageal acidity, by complex mechanisms, would also be found under the influence of ANS. The purpose of this work was to demonstrate, any possible correlations between the signal of electrocardiogram (EKG), considered as proxy of ANS balance, and esophageal pH (pHe).

Methods: The present study included twelve newborn babies hospitalized during 2007–2009 in neonates for gastroesophageal reflux (GER). None had severe disease (digestive, neurological, cardiac or pulmonary) or any treatment likely to interfere with the cardiac activity and the pHe. All patients underwent a polygraphic recording (EKG and 24 hour pHe monitoring). The sampling rate was 200 Hz for EKG signal and 1 Hz for pHe. All signals were resampled at 200 Hz.

Results: Our results supported this hypothesis, showing strong correlations between pHe and EKG.

Conclusion: Complementary studies would be necessary to specify the direction of this relation.

Disclosure of Interest: No declared.

PO-G-270

INTESTINAL MICROBIOTA COMPOSITION IN CHILDREN WITH CYSTIC FIBROSIS

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Objectives and Study: Intestinal inflammation is a frequent feature of children with Cystic Fibrosis (CF), which may be, at least in part, reduced by long term administration of the probiotic strain Lactobacillus GG. This suggests that microflora may be abnormal in CF children and may play a role in intestinal inflammation. Aim of this study was to investigate the composition of intestinal microflora of CF children and its relationship with intestinal and systemic inflammation.

Methods: CF children in stable conditions without acute intestinal or extraintestinal diseases were enrolled. The following parameters were obtained: sex, age, body weight, CF genotype. Intestinal inflammation was evaluated by fecal calprotectin concentration (CLP) and rectal nitric oxide (NO) production, using rectal dialysis. Systemic inflammation was evaluated by TNFα serum concentration. Intestinal microbiota evaluation was also performed using DGGE analysis, a molecular technique based on the analysis of the 16S rRNA gene sequences, and compared with age matched healthy controls.

Results: Twenty two children with CF were enrolled (median age 10 years; age range 7–18 years). Twenty children were dF508 homo/heterozygote, of which 4 were colonised with Pseudomonas aeruginosa. Increased CLP and NO concentrations were observed in 13/22 (59%) and 16/22 (73%) children respectively. Mean value of faecal CLP and rectal NO were significantly higher (171±152 vs. 61±69 μg/; P = 0.004; 18±14 vs. 2.3 ± 1.6 μmol/l; P < 0.001 respectively) compared to healthy controls. Increased TNFα serum concentration was observed in 10/17 children (59%). No significant correlation was observed.
between intestinal inflammation and age, gender, genotypes, or with systemic inflammation. Comparative analysis of intestinal microbiota showed that DGGE profiles of children with CF under 10 years of age were characterised by the absence of a band corresponding to Eubacterium rectale a strain which was detected in all age-matched healthy controls. In contrast in CF patient over 10 years of age the E. coli band was more evident compared to healthy children profiles.

**Conclusion:** Intestinal microflora is abnormal in CF children with an age-related pattern. Younger children lack species consistently detected in controls whereas in older children there is an abundance of selected species compared to controls. These results suggest a role of intestinal microflora in inducing intestinal inflammation in CF children and are consistent with targeting microflora as an adjunctive therapy in CF.

**Disclosure of Interest:** None declared.

**PO-G-271**

**POST-RESECTION INTESTINAL ADAPTATION SHOWS A TIME AND SEGMENT SPECIFIC PATTERN: A 3DIMENSIONAL STUDY IN A RAT MODEL OF SHORT GUT**

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**Objectives and Study:** Following massive intestinal resection, remnant bowel undergoes profound adaptive structural modifications that determines the chance of reaching intestinal sufficiency. We analyzed the time- and segment-related epithelial architectural changes in a rat model of small bowel resection.

**Methods:** Sprague-Dawley female rats (n = 32) were divided in 4 groups: 2-day, 7-day, 15-day post-resection groups, which had 75% of the jejunum removed, and the sham-resected control group (n = 10). Histological and morphometrical parameters in proximal to distal remaining intestinal segments, from jejunum to distal colon, were comparatively analysed in all groups. To set up a 3D geometrical model, we compared villi with cylinders of equal size and calculated absorptive capacity, expressed as cylinder surface lateral area.

**Results:** The combined analysis of morphometry and villi number/mm2 showed that the ileum undergoes major adaptive changes consisting in an increase in villus size associated with a relative reduction of their number compared with its basic architecture (table). In contrast, the jejunum undergoes minor changes in the early phase, with a substantial restoration of its basic epithelial tridimensional structure. However major architectural changes are observed afterwords, with a hypertrophic development of tridimensional structure, which however is not associated with a decrease in villus number.

**Conclusion:** Post resection intestinal adaptation is a segment and time related pattern which is highly functional to rapidly increase functional absorptive areas. Ileum more than jejunum undergoes extensive restructuring in the early post resection phase. Thus, sparing ileal segments during resection may substantially improve the outcome of patients undergoing extensive intestinal resection. The 3D model provides a tool for testing growth factors and other strategies to optimize post-resection intestinal growth.

**Disclosure of Interest:** None declared.

**PO-G-272**

**EFFICACY AND SAFETY OF POLYETHYLENE GLYCOL 3350 PLUS ELECTROLITES FOR THE TREATMENT OF FUNCTIONAL CONSTIPATION IN CHILDREN**

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**Objectives and Study:** Initial measures for the treatment of constipation include correction of lifestyle and dietary factors but when these fail, laxatives are needed. Compared to all other laxatives, polyethylene glycol 3350 plus electrolytes (PEG+E) achieves more treatment success. PEG+E efficacy has been validated in some studies but not many have evaluated it’s safety in children. The aim of our study was to evaluate the safety (biochemistry impairment, geometrical model, we compared villi with cylinders of equal size and calculated absorptive capacity, expressed as cylinder surface lateral area.

**Table:** Morphometrical analysis of villus structure and number (% modifications vs controls)

<table>
<thead>
<tr>
<th></th>
<th>Villus Height</th>
<th>Crypt Depth</th>
<th>N° of villi/mm2</th>
<th>Absorptive area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Jejunum - Ileum</td>
<td>Jejunum - Ileum</td>
<td>Jejunum - Ileum</td>
<td>Jejunum - Ileum</td>
</tr>
<tr>
<td>2 days</td>
<td>+1,0; +0,05</td>
<td>+0,02; +2,8</td>
<td>−1,4; −8,1</td>
<td>+2,54; +6,5</td>
</tr>
<tr>
<td>7 days</td>
<td>+6; +32,7</td>
<td>+15; +12,3</td>
<td>+1,3; −19,5</td>
<td>+5,06; +64,97*</td>
</tr>
<tr>
<td>15 days</td>
<td>+29; +43,9*</td>
<td>+30; +39,8*</td>
<td>+5,4*; −20,7*</td>
<td>+22,54*; +81,50*</td>
</tr>
</tbody>
</table>

* P < .05 vs control group.
malabsorption or excessive production of gas) and treatment’s efficacy of PEG-E in our paediatric population.

Methods: Fifteen patients who suffered functional constipation (Rome III criteria) were evaluated. Median age was 6.2 years (r 2–9). Patients with faecal impaction or who were being treated with other laxatives were excluded from the study. Blood sample (urea, creatinine, sodium and potassium) was obtained at baseline; All patients had normal renal function. PEG+E was administrated for 4 weeks as a powder in 6.9 g sachets containing: 6.56 g PEG 3350, 175.4 mg sodium chloride, 89.3 mg sodium bicarbonate and 25.1 mg potassium chloride. The mean dose was 0.44 g/Kg/day titrated according to age, weight and response. All patients had a 4 week follow-up (4WP). Urine screens (sodium and osmolality) were performed at the beginning and 4WP. Stool sample FENIR (faecal spectroscopy near infrared) and hydrogen breath test analysis samples were performed at 4WP. To analyse the efficacy of the treatment, the number of stools per week and stool form type (Bristol stool form scale: 1–7) were collected in the outpatient clinic.

Results: No statistical differences were obtained between urine sodium and urine osmolality values at the beginning and end of the study. After 4WP the FENIR median values were normal in all patients [fat 4.8% (r 3.6–7.09); protein 0.79% (r 0.4–1); starch 4.39% (r 0–8.2); water 68% (r 59–74)]. Median breath hydrogen test was 7 ppm (r 2–18). The number of stools per week was higher after 4 weeks (2.46 ± 0.71 vs 5.29 ± 1.68, P < 0.001) as well as the stool form score (2.47 ± 1.24 vs 4.5 ± 0.91, P < 0.001).

Conclusion: The use of PEG+E has been shown to be safe in our paediatric population. No adverse effects on biochemistry values nor digestive disturbances have been seen. PEG+E can be recommended for the treatment of functional constipation in children.

Disclosure of Interest: None declared.

PO-G-273

PANCREATIC TRAUMA IN CHILDREN
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Objectives and Study: To document the demographics, mechanisms and outcome of traumatic pancreatitis in children at a single large tertiary referral centre in Australia.

Methods: We undertook a 10-year retrospective audit of children admitted to the Royal Children’s Hospital [RCH], Melbourne, Australia with a hospital coded diagnosis which included pancreatic injury between 1993 and 2002. Data included patient demographics, source of admission, mechanism of injury, pancreatic complications, associated injuries, Intensive Care Unit [ICU] admission, results of any operative findings, results of any acute computed tomography (CT) and/or ultrasound (US) imaging of pancreas, selected laboratory findings and length of stay.

Results: We identified two distinct groups of patients in the 91 documented cases of pancreatic trauma (median age 8.0 yr, range 0.6–15.8 yr; M:F 2.5:1.0). Fifty-nine had a history of abdominal trauma and elevated serum lipase but no CT or ultrasound evidence of pancreatic injury (Group A). Thirty-two had a history of abdominal trauma, elevated serum lipase but also had CT scan and/or ultrasound evidence of pancreatic injury (Group B). Patients with “less severe” injury based on normal imaging had a lower initial lipase level [Group A, median 651 U/L (interquartile range 520–1324) vs, Group B, 1608 U/L (interquartile range 680–3526); P = 0.005] and shorter admission time [Group A, 9.0 days (interquartile range 5.5–15.5) vs Group B, 13.4 days (interquartile range 6.8 – 23.8), P = 0.04]. There were no differences with respect to mortality [Group A, 13.5 % vs Group B, 12.5 %] but patients with evidence of injury on imaging were more likely to have surgical intervention [Group A vs Group B, 0.0001]. The single most important cause of pancreatic trauma was involvement in a motor vehicle accident as a passenger or pedestrian. However, in children with high-grade ductal injury, bicycle handlebar injuries were most common. Associated injuries were common in both groups.

Conclusion: Significant pancreatic injury can occur in the absence of abnormality on medical imaging. Pancreatic trauma commonly occurs in the context of multiple injuries after motor vehicle accidents in children and bicycle handlebar injuries, especially in boys. Most children can be treated conservatively, with surgical intervention being limited to high-grade ductal injury.

Disclosure of Interest: None declared.

PO-G-274

ASSESSMENT OF MEDICAL STUDENTS USING A SCRIPT CONCORDANCE TEST AT THE END OF THEIR STAGE IN PAEDIATRIC GASTROENTEROLOGY

Objectives and Study: The Script Concordance Test (SCT) is a tool used to evaluate clinical reasoning in complex medical situations. Our aim was to create the first SCT in paediatric gastroenterology in order to objectively assess medical students.

Methods: We elaborated a SCT including 31 items divided into 10 clinical cases. Topics were chosen within the list of the academic national exam. In order to assess medical students, the reference panel was made by 10 residents to establish the scoring process. Answers were drawn up according to the Likert’s scale, ranging from −2 to +2. Scores are calculated based on the modal response. Depending on the variation of the experts’ answers to each item, we
classified the questions as correct, abnormal or uncertain. The SCT was also passed by 5 GI paediatricians. Results were given as mean / 20 ± SEM. Student t test was used to statistical analysis.

**Results:** Example: a 6-year-old boy, without any medical history, came at the emergency unit because of abdominal and joint pain. If you thought to “Schoenlein-Henoch disease” and “the US scan found an intussusception”.

The effect on the diagnostic hypothesis is:

-2: The hypothesis is quite improbable
-1: The hypothesis is less probable
0: The hypothesis is unchanged
+1: The hypothesis is more probable
+2: The hypothesis is quite certain

Scores were 15.35 ± 0.38 and 12.44 ± 0.58 (P = 0.0006), respectively for the reference panel and the 5 students. Scores were unchanged by suppressing abnormal or uncertain questions. But, the score of GI paediatricians was 13.37 ± 0.69, significantly lower than the reference panel (P = 0.01). The fiability of this SCT could be discussed. Students passed a SCT for the first time but they considered that this tool is appropriate and in concordance with the objectives.

**Conclusion:** If SCT is an interesting method, its elaboration can be difficult. It seems important to create a group of teachers to validate the process and to eliminate a wide variability.

**Disclosure of Interest:** None declared.

**PO-G-275**

**INTESTINAL INFLAMMATION IN CYSTIC FIBROSIS: LACK OF RESPONSE AFTER TREATMENT WITH MESALAMINE**

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**Objectives and Study:** There is some evidence of intestinal inflammation in patients with Cystic Fibrosis (CF) but little is known about the pathophysiology. Although the bowel mucosal architecture is usually considered to be normal in these patients, mucosal inflammation is detected and is desirable to revert this process.

The aims of this study were to assess the incidence of intestinal inflammation measuring faecal calprotectin (FC) in children with CF and to investigate whether 5-aminosalicylate (mesalamine) could modify the inflammation and the intestinal permeability (IP).

**Methods:** FC (µg/g) (n 25) and IP (n 23) were assessed in CF patients (age 9.4 ± 4.0 y). This study was also performed in a subgroup of these patients before and after 1 month of treatment with mesalamine (70 mg/kg/day). IP was measured by dual test with lactulose (L) (5 g) and mannitol (M) (1 g) made up to 100 mL of water. The urinary excretion of L (% L), M (% M) and L/M (% L/M) (index of IP) were expressed as percentage of the ingested dose. Fecal nitrogen and fat were obtained by FENIR (g/day).

**Results:** Mean FC was significantly higher in CF patients than in controls (288 ± 238 vs 40 ± 14) (P < 0.0001). The values of FC, % L, % M and % L/M after the treatment with mesalamine were not modified significantly. No changes were found in the faecal fat and nitrogen after the treatment.

**Conclusion:** Children with CF have evidence of intestinal inflammation detected by measuring FC. IP also is increased in an important number of cases of CF although without relation with the values of FC. The antiinflammatory treatment with mesalamine does not reduce the intestinal inflammatory state in CF patients.

**Disclosure of Interest:** None declared.

**PO-G-276**

**ROME III CLASSIFICATION OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN WITH CHRONIC ABDOMINAL PAIN**

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**Objectives and Study:** The updated Rome III classification of pediatric functional gastrointestinal disorders (FGID) associated with abdominal pain comprises: Functional Dyspepsia (FD), Irritable Bowel Syndrome (IBS), Abdominal Migraine, Functional Abdominal Pain (FAP), Functional Abdominal Pain Syndrome (FAPS). The aim of this study was to assess the prevalence of FGID in children with chronic abdominal pain using the current Rome criteria.

**Methods:** Participants were 439 consecutive new pediatric patients (192 boys and 247 girls) aged 4–18 years (mean age was 11.95 ± 3.89 years) referred to Pediatric Gastroenterology Department at Medical University of Lodz from
January 2008 to June 2009 for evaluation of abdominal pain of at least 2 months’ duration. After exclusion of organic origin children suspected of functional chronic abdominal pain were categorized with the use of Rome III criteria of FGIDs associated with abdominal pain (H2a-H2d1) and Questionnaire on Pediatric Gastrointestinal Symptoms (with the permission of Professor D.A. Drossman).

Results: In 278 patients (63.42%) medical evaluation did not confirmed organic etiology. 82.02% of children suspected of functional chronic abdominal pain met Rome III criteria for FGIDs associated with abdominal pain (FD, 9.82%; IBS, 13.44%; abdominal migraine, 3.42%; FAP, 15.49%; FAPS, 10.02%). 50 cases (17.98%) did not fulfilled criteria for subtypes of abdominal pain-related FGIDs allowing for strict classification - mainly due to different as defined by Rome III (once a week) frequency of symptoms’ presentation.

Conclusion: 1. FGIDs associated with abdominal pain are the most common reason of chronic abdominal pain in children. 2. To make Rome criteria more inclusive for functional chronic abdominal pain the defined frequency of symptoms’ occurrence should be more flexible.

Disclosure of Interest: None declared.

PO-G-277

GENOTYPE. PHENOTYPE CORRELATION IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: EVALUATION OF E148Q AND M694V MUTATIONS

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Objectives and Study: Familial Mediterranean Fever (FMF) is an autosomal recessive disorder characterized by self-limited episodes of fever and painful recurrent polyserositis that predominantly affects Mediterranean races. In recent years some reports have shown high prevalence of FMF in North-west Iran, with M694 V and E148Q being most frequent reported mutations. The aim of this study is to evaluate the clinical manifestations of FMF in patients with these mutations.

Methods: A cross sectional- descriptive study was performed in a 1 year period (January 2007. January 2008) 71 patients younger than 18 years with clinical diagnosis of disease proved in Children Hospital of Tabriz-Iran were referred to genetic lab for mutation analysis. ARMS-PCR & PCR-RFLP were used to detect mutations. Only 45 patients were shown to have identified mutations and 41 patients among them had M694V and E148Q mutations which were assessed for various clinical manifestations.

Results: M694V and E148Q mutations were seen in 55.7 and 35.5 patients respectively. Patients homozygous for M694 V were found to have earlier age of onset, longer duration of attacks, higher prevalence of positive family history and more complications. In our patients, prevalence of some manifestations differed from other ethnic groups reported previously.

Conclusion: M694 V mutation in FMF patients especially in homozygous state is accompanied with more severe disease and more complications.

Reference:

Disclosure of Interest: None declared.

PO-G-278

A NEW NONSYNONYMOUS RARE VARIANT OF APC GENE

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Objectives and Study: Familial adenomatous polyposis (FAP) is a syndrome inherited as an autosomal dominant trait. Genetic cause is germ line truncating mutations in the adenomatous polyposis coli (APC) gene. A milder form of FAP (attenuated FAP, AFAP) characterised by the presence of fewer adenomas (10–99) and later onset is observed in 8% of cases. Recently was identified bi-allelic germline mutations in the base excision repair (BER), gene MUTYH with recessive inheritance and multiple colorectal adenomas are usually associated with an attenuated polyposis phenotype. Rare inherited nonsynonymous variants of APC might act as low penetrance alleles and 61 different variants were sequenced in patients with adenoma that not carry conventional pathogenic mutation of APC or MUTYH.

Methods: Case Report: We report of female 17 yrs old with recurrent rectal hematochezia and bleeding episodes. Colonoscopy has shown 6 polyps, 5 pedunculated with short implantation base localizzated in sigma and ascending colon. Esophagastroduodenoscopy have shown 3 gastric polyps compatible about histology with hyperplastic type.

Results: The histology of colonic polyps was “adenomatous polyp with lower dysplasia” and “tubulo-villous polyp”. Peripheral blood DNA samples were sequenced for the entire open reading frame (ORF) and simple sites of APC and exons 7–13 for MUTYH. Genetic analysis described the presence of nonsynonymous variant of APC, G2502S.

Conclusion: 61 different rare nonsynonymous variants of APC gene have been identified. The variants III07K and E1317Q has been shown to be overrepresented in the germ-line of patients with high risk of somatic change and dysplasia. The G2502S variant identified in our study could be considered a new rare nonsynonymous variants even if the
true incidence and role in multifactorial inherited predisposition to colon cancer should be confirmed.

Disclosure of Interest: None declared.

PO-G-279

FIRST PRENATAL DIAGNOSIS FOR TUFTING ENTEROPATHY
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Objectives and Study: Mutation of the EpCAM gene has recently been identified as responsible for congenital Tufting Enteropathy (TE), a severe congenital diarrhea leading to parenteral nutrition dependency and sometimes to intestinal transplantation. EpCAM is a cell adhesion molecule implicated in numerous cellular functions contributing to cells and tissue organization. Our experience of reference center support a clinical heterogeneity as well as a genetic one, as we have found in only 10% of the studied patients a mutation of the coding sequence of EpCAM, mostly at a heterozygous status. A family of one child suffering from TE followed up in our center went on a third pregnancy and asked for prenatal diagnosis.

Methods: A girl referred to our centre with TE, onset of liver disease and multiple sepsis, underwent liver and gut transplantation at 4. She died at age 5 from a severe gram negative sepsis. Immunohistochemistry performed on intestine biopsy showed absence of the EpCAM protein. Study of EpCAM gene revealed a homozygous deletion of the whole exon 5. The RNA study confirmed the exon 5 deletion as we identified a junction fragment between exons 4 and 6. Her healthy parents are Caucasian, not related, and both heterozygous for the deletion. We used quantitative PCR on fetal DNA obtained after an amniocentesis at 18 GW, with parental consent.

Results: We identified that the fetus carried the deletion of the Exon 5 at a heterozygous status, which, in this family, is associated with a healthy evolution. Therefore the pregnancy was carried out to the term. The recent identification of the involvement of the EpCAM gene in TE allowed us to search for a mutation in the index case, to identify an exonic deletion and eventually to make the first prenatal diagnosis of this rare and severe disease in a family of a single case. The deletion is probably mediated by identified repeated sequences in introns flanking the Exon 5 of EpCAM gene. Nevertheless, not all the children known for suffering from TE have yet an identified mutation of the first gene related to TE. Other genes might thus be involved in this complex disease.

Conclusion: A third pregnancy in a family of one case of TE was prenatally diagnosed with a healthy fetus, thanks to the identification of a deletion of the exon 5 in the index case. This first published case of prenatal diagnosis for TE marks a practical turn for genetic counseling in this rare disease and should motivate further genetic studies to identify other involved genes.

Disclosure of Interest: None declared.

PO-G-280

FUNCTIONAL GASTROINTESTINAL DISORDERS (FGDS) IN HOSPITALISED CHILDREN: RATE AND POSSIBLE ASSOCIATED FACTORS
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Objectives and Study: To determine the incidence and duration of FGDS in hospitalised children and their relation with diagnosis at admission and intervention.

Methods: All children admitted from the end of January through March 2009 were enrolled in a randomised controlled trial in which they received an additional probiotic (LGG, Dicoflor 60, 6x10 9 c.f.u. per day), an additional antioxidant (red orange complex, Difensil Junior, Humana, 1 per day) or just standard treatment for underlying disorder causing the hospitalisation. FGDS were classified in agreement with Rome III criteria. A phone recall was made after 15 days, 1-3-6 and 9 months after admission by the same doctor who was unaware of the intervention received by the subjects. Analyses were based on allocated treatment.

Results: Data from 141 patients (57 F, mean age 51±5 SD 54 months, median 26 months) were included. At recruitment FGDS were present in 71/141 (50%) children without difference among the 3 groups. FGDS were reported in 52/141 (37%) children after 9 months from admission. During the follow-up FGDS disappeared in 29 patients: in 6/21 (29%) in the control group, in 4/23 (17%) in the antioxidant, and in 19/27 (70%) in the LGG group. FGDS occurred in other 10/70 (14%) "naive" children (5 in control, 1 in LGG and 4 in the red orange group), and followed an infection in all except one. In 7/10 patients antibiotic treatment for bacterial infection was used during the hospital staying. In 2 patients FGDS followed a gastrointestinal infection. In 7/10 patients the onset of FGDS occurred within 1 month from discharge. No significant difference were present in terms of age, diarrhea, number and kind of infections at admission among the 3 groups.

Conclusion: FGDS are common in pediatric age and may appear also after extra-intestinal infections. From our preliminary data is still unclear if probiotic (LGG) may play any protective role for pediatric post-infectious FGDS.

Disclosure of Interest: None declared.

PO-G-281

NEUROMUSCULAR STATUS PREDICTS GASTROINTESTINAL DYSFUNCTION IN PATIENTS WITH TYPE II AND III SPINAL MUSCULAR ATROPHY
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PO-G-282

CLINICAL OUTCOME IN CYSTIC FIBROSIS PATIENTS WITH OR WITHOUT MECONIUM ILEUS: A COMPARATIVE STUDY

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Objectives and Study: Meconium ileus (MI) is a form of neonatal intestinal obstruction due to an abnormal viscid meconium within the terminal ileum. MI is the presenting symptom in 15–20% of patients with cystic fibrosis (CF). Approximately half of these patients present with complex MI. The aims of the present study were to assess the clinical outcomes in cohorts of patients with complex meconium ileus at 5, 10 and 15 years in comparison to CF patients without MI.

Methods: CF patients presenting to our centre with MI were reviewed. Data on gestational age, weight, type and extent of surgery, duration of parenteral nutrition were recorded. Age, sex and genotype-matched controls were used for comparisons. In both groups, clinical status at 5, 10, and 15 years records were recorded from annual review records.

Results: A total of 23 (9 females) infants with MI were identified. Overall survival for both simple and complex MI - 92%. Of these, 75% had complex MI; 80% were born at term; and 50% were homozygous for ΔF508. 11 patients received TPN for median of 24 days (10–120 days).

In patients with complex MI, the median weight, height, BMI% for age (>50%), FEV1, FVC, abnormal live scan, Schwachman score at 5 years were 16.9 kg, 106.6 cm, 29.4%, 81.6%, 78.6%, 27%, 80; at 10 years were 27.4 kg, 133 cm, 40%, 68%, 83%, 70%, and 75; at 15 years were 43.3 kg, 155.2 cm, 33%, 74%, 84%, and 60. Of the controls, the mean weight, height, BMI% for age (>50%), FEV1, FVC, abnormal live scan, Schwachman score, at 5 years were 18.1 kg, 107.8 cm, 55.3%, 87% 92%, 44% and 86 (75–92); at 10 years were 31.7 kg, 136 cm, 53%, 80%, 88%, 33% and 82; and at 15 years were 48.5 kg, 154 cm, 54%, 82%, 89%, 58%, and 70 respectively. *p<0.05.

Conclusion: Compared with non-MI controls, children surviving complex disease tended to be smaller with lower BMI’s at all age points. Lung function (FEV1) was also worse. A higher % showed abnormalities on liver scans. Conflicting results from earlier studies may reflect the % of simple MI in the data sets.

With this limited study clear trends are emerging showing that the outcome for infants with complex MI is poorer both in terms of growth and lung function.

Disclosure of Interest: None declared.

PO-G-283

RELIABILITY AND VALIDITY OF THE CYSTIC FIBROSIS QUESTIONNAIRE-REVISED FOR CHILDREN AND PARENTS IN TURKEY

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Objectives and Study: Health-related quality of life (HRQOL) instruments are increasingly used as secondary...
outcomes for clinical trials in cystic fibrosis (CF) and for studies that document the natural progression of the disease. The purpose of this study was to translate the Cystic Fibrosis Questionnaire-Revised (CFQ-R) into Turkish for children with CF and evaluate its reliability and validity. Methods: Sixty-one children ages 6–13 years and 14 children aged 14 years of age and older with CF who presented to four centers in Turkey participated in the study. Demographic characteristics and disease severity parameters were recorded for all participants. All children completed the age-appropriate CFQ-R. Reliability analyses included internal consistency and item–total correlations. Construct and convergent validity were assessed using clinical parameters and correlations with KINDL scores, respectively.

Results: Mean age of children in the younger group was 9.8 ± 2.6 and mean age of the older group was 16.4 ± 1.7 years. Mean age of parents (83.3% female) was 36.3 ± 5.3 years. Most items were correlated with their intended scales, with a rho value of above 0.40 in the except for items 13 and 21 in the CFQ-R Child version. Cronbach’s alpha values were above 0.5 for all scales. For the CFQ-R Teen/Adult version, all item-scale correlations (Spearman’s rho) were above 0.40. In CFQR-Parent version, cronbach alpha values for all domains were above 0.60 except school performance. Analyses of construct and convergent validity were satisfactory.

Conclusion: Turkish versions of the CFQ-R Child, Parent and Teen/Adult versions are satisfactory questionnaires and can be integrated in the clinical evaluation and follow up of Turkish children with CF.

Disclosure of Interest: None declared.

PO-G-284

LOW-DOSE ERYTHROMYCIN IN THE TREATMENT OF GASTROESOPHAGEAL REFUX DISEASE IN INFANTS. A PILOT RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Objectives and Study: Gastroesophageal reflux disease (GERD) is defined as symptoms or complications of reflux of gastric content into the esophagus. Commonly used medications for the treatment of GERD include acid-suppressant and prokinetic drugs. Based on systematic review, the literature supports the use of erythromycin as a prokinetic agent, however most reviewed trials were conducted in preterm infants.

The aim of this study was to assess the effectiveness of low-dose erythromycin in the treatment of gastroesophageal reflux (GERD) in full-term infants.

Methods: This was a double-blind, randomized, placebo-controlled clinical trial. Subjects aged 1–11 months with symptoms of GERD confirmed both by 24-hours pH-monitoring and the Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R) were randomly assigned to receive either erythromycin at dose 1–3 mg/kg/dose or a comparable placebo. Both the active treatment and placebo were taken orally three times daily (20 minutes before meals) for 2 weeks. Parents were asked to fill out the I-GERQ-R at the study entry and at 2 and 4 weeks after enrollment.

Results: 24 infants were enrolled in the study, 12 in erythromycin group and 12 in placebo group; no significant difference was found between two groups. Difference in the I-GERQ-R score in erythromycin group compared with placebo group was statistically significant reduced (P = 0.000003) between beginning therapy and 4 weeks but was not between beginning therapy and 2 weeks (P = 0.07).

Conclusion: Erythromycin at dose 1–3 mg/kg/dose given three times daily was effective in treating GERD in full-term infants. Its effect seemed to be time-dependent.

Disclosure of Interest: None declared.

PO-G-285


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Objectives and Study: Eosinophilic oesophagitis (EE) is increasingly seen in children with GORD symptoms. There are reports of rare association in syndromes such as Rubenstein-Taybi syndrome. Although there is no clear association, EE has been seen in neurodisability children. Our aim is to study the epidemiology, co-morbidity, clinical presentation, investigations and response to treatment.

Methods: The case notes of children diagnosed with EE (2004–2009) were reviewed for co-morbidity, clinical symptoms, investigations, and response to treatment.

Results: From 2004–2009, 32 patients were diagnosed with EE in our GI clinic based on standard endoscopic and histologic criteria. The youngest was a male 16 month old, and the oldest was 15 years. The gender ratio was 25 males to 7 females. 26 patients had other associated disorders. 1 patient has Asperger’s syndrome and celiac disease confirmed on endoscopy. Another patient has ADHD, and 2 patients have global developmental delay with chromosomal abnormalities. 1 patient had arthrogryposis multiplex, 7 patients had asthma / eczema, and 3 patients with multiple food allergies. 1 patient with mastocytosis was shown on biopsy of a small skin lesion removed surgically from his anterior chest wall. Another patient had eosinophilic colitis as well as EE. 21 patients have high IgE levels, of which 19 had specific RAST test positivity. In 10 patients, the eosinophil count was mildly elevated in the peripheral blood. 24 of 31 patients improved clinically following treatment with swallowed fluticasone and montelukast. However, only 14 of 31 demonstrated
endoscopic improvement, of which 10 had an eosinophil count of less than 20/hpf.

**Discussion:** EE should be considered in patients with atopy, and food aversion or intolerance. Children with learning difficulties, chromosomal abnormalities, autism, and Asperger’s syndrome, should also be investigated for EE even if the symptoms are attributed to GORD.

**Conclusion:** Although most patients with EE respond clinically to medical treatment, endoscopic response should be sought, as it may be necessary to retreat, or to consider monoclonal anti-IL-5 antibody. Symptomatic children with allergy and a strong family history of atopy, and children with neurodisability should be investigated for EE. High IgE is a useful surrogate marker for EE in the presence of GI manifestations.

**Disclosure of Interest:** None declared.

**PO-G-286**

**SEQUENTIAL THERAPY IS NOT EFFECTIVE FOR THE TREATMENT OF HELICOBACTER PYLORI INFECTION IN CHILDREN**


**Objectives and Study:** Increasing resistance to clarithromycin dictates newer therapies for Helicobacter pylori (HP) infection. Sequential treatment has gained attention in recent years both in adults and children. The aim of this study is to assess the eradication rate of HP infection and to compare the side effects in children using a sequential treatment regimen compared with the classical lansoprazole-containing triple therapy.

**Methods:** Prospective, randomized, open-label study. Children aged 4–18 years with dyspeptic manifestations undergoing upper GI endoscopy were included if HP infection was proven by histology and urea breath test. Children with celiac disease, who have received proton pump inhibitors, H2-blockers or antibiotics during the 4 weeks preceding endoscopy were excluded. Children with HP infection in countries with high clarithromycine resistance. Because of complexity and ineffectivity of sequential treatment, it should not be used as first line treatment. New treatment alternatives must be explored for children with HP infection in countries with high clarithromycine resistance.

**Disclosure of Interest:** None declared.

**PO-G-287**

**THE PHENOTYPIC EXPRESSION OF GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN IS NOT RELATED TO THE TYPE OF REFLUX**


**Objectives and Study:** Gastroesophageal reflux (GER) is cause of recurrent symptoms and/or complications like esophagitis. Despite the presence of symptoms, the majority of patients do not have esophageal mucosal breaks and up to 70% of the patients are labeled as having non erosive reflux disease (NERD). We aimed at comparing the esophageal reflux pattern in children with erosive reflux disease (ERD) and NERD using 24hr-multichannel intraluminal impedance (MII)-pH monitoring.

**Methods:** A total of 20 children (median age 8.2 years; range 2.5–16.8) with ERD and 25 children (median age 9.2 years; range 3.6–13.2) with NERD were enrolled into the study. All patients underwent 24 hr-MII-pH monitoring. The following variables were analyzed: acid exposure time (AET), total number of reflux episodes (TN), number of long-lasting of reflux episodes (>5 min) (LR), number of reflux episodes according to pH (acid, weakly acid, weakly alkaline) and height.

**Results:** (mean ± SD). AET and LR did not differ between the two groups (ERD 7.6 ± 3.9, NERD 6.6 ± 4.5; ERD 5.8 ± 2.6, NERD 5.6 ± 7.9, respectively) (NS) as well as TN (ERD: 105.8 ± 54.16, NERD: 89.08 ± 35.91, NS). The two group did not differ neither for total numbers of acid (AR), weakly acid (Wac) and weakly alkaline (Walk) refluxes (ERD: 55.8 ± 38.49 AR, 16.5 ± 11.91 Wac, 11.7 ± 10.41 Walk;
NERD: 45.2 ± 26.22 AR, 12.76 ± 17.16 Wac, 8.64 ± 9.8 Walk, respectively) nor for the total number of reflux reaching the proximal, mid and distal esophagus (ERD: 56.55 ± 39.72, 17.85 ± 7.9, 9.6 ± 9.7. NERD: 40.36 ± 23.17, 14.4 ± 8.8, 5.08 ± 5.06, respectively) (NS). A subgroup analysis evaluating for each type of reflux (AR, Walk, Wac) the number of episodes reaching the proximal (PE), mid (ME) and distal (DE) esophagus, did not reveal any difference between the two groups (ERD: 39.05 ± 35.06 AR-PE, 11.35 ± 7.48 AR-ME, 5.4 ± 6.13 AR-DE, 11.45 ± 9.4 Wac-PE, 3.35 ± 2.05 Wac-ME, 1.7 ± 1.8 Wac-DE, 6.05 ± 5.69 Walk-PE, 3.15 ± 2.97 Walk-ME, 2.5 ± 3.15 Walk-DE; NERD: 31.44 ± 21.27 AR-PE, 10.4 ± 24 AR-ME, 3.36 ± 4.68 AR-DE, 5.44 ± 9 Wac-PE, 3.56 ± 4.95 Wac-ME, 1.4 ± 1.63 Wac-DE, 5.96 ± 6.63 Walk-ME, 1.88 ± 2.38 Walk-DE, respectively). The two groups did not differ for emesis, heartburn, regurgitation, asthma and epigastric pain whereas cough was more commonly detected in NERD (P < 0.01).

Conclusion: Our results fail to show significant differences in the pattern of reflux between the ERD and NERD patients that could be explain the different mucosal damage. Cough was more common among NERD patients. However, this data seems to suggest that other factors than the type of reflux, such as esophageal distension and visceral hypersensitivity, may underlie clinical expression of the disease.

Disclosure of Interest: None.

PO-G-288

THE RELATIONSHIP BETWEEN ENDOSCOPIC AND HISTOLOGICAL FINDINGS OF ESOPHAGUS IN CHILDREN WITH PRE-DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE

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Objectives and Study: The aim was to investigate the relationship between endoscopic and histological findings of esophagus in children with pre-diagnosis of gastroesophageal reflux disease.

Methods: A total of 213 children (mean age 8.4 ± 4.8, range 0.16 – 18) years) underwent diagnostic upper endoscopy, and their biopsy samples from distal esophagus were collected between January 2002 and December 2004. Patients were divided into two groups: with or without symptoms of gastroesophageal reflux disease. Endoscopic findings were classified according to Los Angeles, Savary-Miller, Hetzel, and Tytgat systems. Histologic findings were classified according to Knuff & Leape. The relationship between endoscopic and histologic findings were examined retrospectively.

Results: The relationship between the patients in gastroesophageal reflux disease symptoms and histological esophagitis was statistically insignificant. Prevalence of erosive reflux disease was 12.1 % in the group with symptoms of gastroesophageal reflux disease and 9.6 % in the other

PO-G-289

THE IMPACT OF LONG TERM LANSOPROZOLE TREATMENT ON SERUM IRON, CALCIUM, VITAMIN B12, BONE TURNOVER AND COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN

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Objectives and Study: Short term proton pump inhibitor use is generally well tolerated. But the impact of long term PPI on several vitamins, minerals, hematinic factors, bone turnover and immune system has not been very well studied in children. So the aim of this study was to evaluate the effect of long term lansoprazole treatment on serum hemoglobin, iron, ferritin, total iron binding capacity (TIBC), vitamin B12, calcium, phosphate, alkalenphosphatase level, calcium/creatinin ratio, bone turnover, community acquired pneumonia and acute gastroenteritis incidence in children.

Methods: We prospectively evaluated children who were diagnosed as gastroesophageal reflux disease and treated with lansoprazole and sodium alginate for six months duration. Serum levels of above mentioned parameters were measured at baseline and in two months intervals until the end of six months and compared with baseline levels. Patients were asked to communicate with our clinic in case of any previously educated sign of pneumonia and gastroenteritis. Data were analyzed with student t test and wilcoxon sign test.

Results: Forty five children aged between 4–17 years and treated with lansoprazole (1–1.4 mg/kg, max 60 mg), sodium alginate (0.25–0.5 mg/kg three times a day), were eligible for the study. Reduction of hemoglobin, iron and
ferritin level were observed in 28 (65.1%, P = 0.053), 18 (52.9%, P = 0.44), 15 (65.2%, P = 0.11) patients. Vitamin B12 level decreased in 15 (50%, P = 0.96) patients. Both serum calcium and phosphate levels decreased in 18 patients (41.9%, P = 0.98; 45%, P = 0.46 respectively). Alkalinephosphatase level increased in 19 (48.7%, P = 0.8) and calcium/creatinin decreased in 8 (21.1%, P = 0.8) patients. There wasn’t any significant change in terms of mean concentration of hemoglobin, iron, ferritin, TIBC, Ca, P, alkalinephosphatase, Ca/Cr and vitamin B12. Mean L1–4 concentration of hemoglobin, iron, ferritin, TIBC, Ca, P, and median duration of refluxes and symptom index (SI)

**Conclusion:** Six months duration of lansoprozole doesn’t have any unfavorable effect on serum calcium, iron, vitamin B12, bone metabolism, community acquired pneumonia and acute gastroenteritis.

**Disclosure of Interest:** None declared.

### PO-G-290

**THE INFLUENCE OF PEG ON GER EXONENTS BY MEANS OF MII/pH MONITORING IN NEUROLOGICALLY IMPAIRED CHILDREN – PRELIMINARY STUDY RESULTS**

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**Objectives and Study:** Neurologically impaired children demonstrate the high risk of malnutrition. At the same time they are prone to develop GER and its complications. Therefore some authors advocate for simultaneous fundoplication and PEG placement procedures. However, mainly due to different GER estimation methods and ethical drawbacks of randomised trials dedicated to this specific issue, published data are controversial and no commonly accepted guidelines were published. The aim of the study is to estimate the influence of PEG placement on exponents of gastroesophageal reflux with the use of Multiple Intraluminal Impedance (MII/pH) in neurologically impaired children qualified for home enteral nutrition (HEN).

**Methods:** The study comprised 14 children aged 4 - 16.7 years with chronic diseases of the central nervous system. All the children underwent 24-hour multiple intraluminal impedance (MII/pH, SLEUTH Sandhill Scientific) monitoring – basic one before PEG placement and second one between 6 – 8 months of HEN duration. Minimal MII/pH monitoring time was 22 hours. All impedance recordings were visually inspected for the typical MII pattern of GER. Acid, weakly-acid and non-acid reflux episodes, number and median duration of refluxes and symptom index (SI) comprising choking, coughing, emesis and regurgitation were calculated.

**Results:** Based on MII-pH results pathological GER was detected at pre-PEG monitoring in 6 subjects (42.65%): acid reflux in 2 and non-acid reflux in 4 cases. The median number of refluxes was 29.85 (range 1 – 79). The positive SI was observed in 1 child presenting with non-acid reflux. The second MII/pH revealed positive results in 2/14 children (14.3%): in non-acid and in weakly-acid reflux were detected. Positive SI was reported in one subject (the same as in pre-PEG monitoring). The median number of refluxes was 14.5 (range 2 – 76). Differences between indices of GER obtained by MII/pH before gastrostomy placement and on PEG feeding were not statistically significant. Enteral feeding improved clinical status (weight gain, frequency of regurgitation) of all patients with PEG regardless of MII-pH results. However one subject demonstrated severe esophagitis and was placed on PEG/PEJ.

**Conclusion:** The primary results of our MII/pH – PEG study suggest that the presence of GER doesn’t exclude good clinical response to enteral feeding via gastrostomy in neurologically impaired children. The choice of route of enteral feeding supply should rely on clinical tolerance and MII/pH results with symptom index.

**Disclosure of Interest:** None declared.

### PO-G-291

**LONG TERM OUTCOME OF CHILDREN WITH ESOPHAGEAL ATRESIA**

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**Objectives and Study:** The aim of this study was to evaluate the outcome of patients with esophageal atresia (EA), with a focus on the presence of late sequelae and quality of life.

**Methods:** One hundred three patients with EA were treated in our institution during a 10-year period. The study parameters included the patients’ demographics; type of EA; associated abnormalities; presence of gastroesophageal reflux disease (GERD) and digestive, respiratory, or orthopedic symptoms; results of a clinical examination to evaluate the nutritional status; spirometry results; and the quality of life assessed using the PedsQL 4.0 questionnaire.

**Results:** Of the original 103 patients, 63 patients (mean age: 13.4 years; range: 2.7) agreed to participate in the study. Ten died between 1 and 510 days of age. Thirty patients were not included (23 were lost to follow-up, 7 refused to participate). Nonparticipants (30%) presented with similar characteristics as the 70% of patients who participated. Eighty-two percent of the patients had EA type III, 35% underwent fundoplication, and 45% presented with anastomotic stenosis. Seventy-three percent had a normal nutritional status (16% were obese, 11% were undernourished). Only 13% of participants

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were free of any digestive symptoms; 65% had dysphagia and 35% had symptoms of GERD at the last follow-up. The main respiratory symptoms were chronic cough (19%) and dyspnea on exertion (33%). Only 38% of patients had no respiratory symptoms. Spirometry showed that 50% of patients had proximal obstruction and/or pulmonary distension, and 11% had restriction syndrome. The quality of life score was good but was lower than in healthy controls (80 vs 84, \( P < .05 \)) and lower in patients with associated congenital heart disease (71 vs 85, \( P = .01 \)) or respiratory symptoms (75 vs 87, \( P = .04 \)).

**Conclusion:** The high frequency of late sequelae in EA justifies regular and multidisciplinary follow-up through adulthood.

**Disclosure of Interest:** None declared.

**PO-G-292**

**GASTRO-OESOPHAGEAL REFLUX AND GASTRIC EMPTYING IN CHILDREN WITH CYSTIC FIBROSIS**

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**Objectives and Study:** Increased gastro-oesophageal reflux (GOR) is common in children with cystic fibrosis (CF). Gastric emptying (GE) can be normal, decreased or increased in children with CF. Delayed GE can be a possible mechanism of GOR in children. We studied GOR and GE in children with CF.

**Methods:** Twenty-two CF children (13 boys) with an age of mean +/- standard deviation (range) 6.1 \pm 4.3\ years (1.1–17.1\ years) presenting with gastro-intestinal and/or respiratory symptoms suggestive of GOR were studied. They underwent an impedance-pH monitoring for detection of GOR. Acid reflux parameters were regarded as increased if the total oesophageal acid exposure was above the 95th percentile of normal data obtained in healthy subjects (Vandenplas 1991). Furthermore, a 13C-acetate breath test to measure GE of liquids or a 13C-octanoic acid breath test to measure GE of solids using Non Dispersive Infrared Spectrometry to determine the GE parameters were performed. GE parameters were considered as increased if the gastric half emptying time was above the 95th percentile of normal data obtained in healthy subjects (Hauser unpublished data).

**Results:** Ten of the 22 children (45.5%) had increased acid GOR with a total acid exposure of mean \pm standard deviation (range) 6.6 \pm 6.7\ % (0.1–29.0\ %) for the whole group. Six of these 10 children (60.0\ %) had clinical symptoms suggestive of GOR. Eight of the 22 children (36.4\ %) had delayed GE with a gastric half emptying time of mean \pm standard deviation (range) 101 \pm 25\ minutes (79–134 minutes) for liquids and 239 \pm 204 minutes (88–911 minutes) for solids for the whole group. Two of these 8 children (25.0\ %) had clinical symptoms suggestive of delayed GE. Four patients had increased acid GOR and delayed GE (18.2\ %), 6 patients had increased acid GOR and normal GE (27.3\ %), 4 patients had normal acid GOR and delayed GE (18.2\ %), and 8 patients had normal acid GOR and normal GE (36.3\ %). Delayed GE was present in 4 of the 10 children with increased acid GOR (40.0\%) but also in 4 of the 12 children with normal acid GOR (33.3\%).

**Conclusion:** Increased acid GOR measured by impedance-pH monitoring and delayed GE measured by 13C breath test are present in respectively 45\ % and 36\ % of a population of children with CF presenting with gastro-intestinal and/or respiratory symptoms suggestive for GOR. Only 60\ % of these children with increased acid GOR have clinical symptoms suggestive of delayed GOR and only 25\ % of these children with delayed GE have clinical symptoms suggestive of delayed GE. Delayed GE is present in 40\ % of the children with increased acid GOR but also in 33\ % of the children with normal acid GOR.

**Disclosure of Interest:** None declared.

**PO-G-293**

**ASSESSMENT OF GASTRIC MOTOR FUNCTION BY MEANS OF A SATIETY DRINKING TEST IN CHILDHOOD FUNCTIONAL DYSPEPSIA: A SINGLE CENTER EXPERIENCE**

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**Objectives and Study:** Abnormalities of gastric motor function, in particular delayed gastric emptying and impaired gastric accommodation, have been implicated in the pathogenesis of functional dyspepsia (FD) symptoms, both in adults and in children. In previous publications, we have established normal values for the stable non-radioactive isotope gastric emptying breath test (Vandendriessche 2003) and slow nutrient drinking test in healthy children (Hoffman 2006). The aim of the study was 1) to evaluate the use of the gastric emptying breath test and 2) a slow nutrient drinking test to evaluate gastric motor function in consecutive FD patients seen at a pediatric tertiary care department.

**Methods:** A total of 24 children with FD (20 girls, mean age 12.9 \pm 3.0\ years) were studied. On two separate days, maximum one day apart, the patients underwent an octanoic acid gastric emptying breath test and a satiety drinking test. Prior to both tests, a dyspepsia questionnaire was filled out.

**Results:** The most prevalent dyspeptic symptoms were early satiety (96.1\%), postprandial fullness (88.4\%) and epigastric pain (80.7\%), followed by nausea (53.8\%). All dyspeptic children (n = 29) started the satiety drinking test and 24 children completed the test until a score of 5 was reached. Gastric emptying rate was slower than age-matched controls in 5 children (21\%). The maximum ingested volume during the satiety drinking test in FD was below the lower limit of normal for age-matched healthy children in 22 patients.
(92%). The endpoint of the satiety drinking test was significantly correlated with age (R = 0.60, P < 0.005) and body weight (R = 0.58, P < 0.005) but not gastric emptying rate. **Conclusion:** The satiety drinking test is a potentially useful non-invasive tool in the investigation of children with FD, and seems to have a higher diagnostic yield than gastric emptying testing.

**Disclosure of Interest:** I, Prof. Dr. Ilse Hoffman declares that there is no potential conflict of interest or no commercial role.

**PO-G-294**

**EXERCISE INDUCED BRONCHIAL HYPERREACTIVITY IN ASTHMATIC CHILDREN IS NOT RELATED TO GASTROESOPHAGEAL REFUX EPISODES**

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**Objectives and Study:** Bronchial asthma and gastroesophageal reflux disease (GERD) may coexist together. Exercise induced cough and bronchospasm are results of uncontrolled asthma but also they may be caused by GERD. **Aim:** The assessment of relationship between exercise and simultaneous reflux episodes (RE) and their implication in developing of cough and/or bronchospasm in asthmatic children.

**Methods:** 20 children with uncontrolled bronchial asthma and/or coexisting cough were enrolled into the study (12 boys, mean age 12.8 ± 3.3 yrs). 48-hour esophageal pH-impedance was performed in all children. The exercise test was done during pH-impedance monitoring. The records before and after exercise test were analysed, separately for pH-metry and pH-impedance. Asthma treatment were continued during the investigation.

**Results:** Acidic GER was diagnosed in 3 (15%) children based on pH-metry. Both, acidic and nonacidic GER were found in 10 (50%) children based on pH-impedance monitoring. The exercise test did not increase reflux episodes in 4 children with positive exercise test (decreased FEV1>10%) nor in 16 children with negative exercise test.

**Conclusion:** Gastroesophageal reflux episodes were not relevant with exercise induced bronchospasm and/or cough in studied group of asthmatic children. Short-lasting intensive exercise did not induce reflux episodes.

**Disclosure of Interest:** None declared.

**PO-G-295**

**DOES HELICOBACTER PYLORI INFECTION HAVE A ROLE IN THE PATHOGENESIS OF MESENTERIC LYMPHADENOPATHY IN CHILDREN WITH ABDOMINAL PAIN?**

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**Objectives and Study:** Although enlarged mesenteric lymph nodes are often seen in children, there are few studies in terms of the significance of this issue. It has been shown that each H. pylori infection and MLs can be associated with acute, chronic and/or recurrent abdominal pain. In this study, we aimed to define whether there is a relationship between H. pylori infection and ML in children with abdominal pain.

**Methods:** We retrospectively evaluated 123 children (64 male, 59 female; mean age 11.48 yr, range 1.5–17 yr) who admitted to outpatient clinic with abdominal pain during the 2-year period. The patients who had been completed certain laboratory investigations (serology for viral and bacterial agents, bacterial culture, serum immunoglobulins, microscopic stool examination, PPD test, chest radiography) for ML were selected for this study. Those children with ML which were defined as a cluster of three or more lymph nodes with diameter >5 mm detected by abdominal ultrasound were divided into two groups. Group I was composed of 64 children with abdominal pain and ML and group II was composed of 59 children with abdominal pain but without ML. H.pylori infection was diagnosed by both serology and 13C-urea breath test. In 22 cases upper gastrointestinal endoscopic examination was also performed.

**Results:** H. pylori infection was found in 31 (46%) of the 64 children in group I, and in 37 (62%) of 59 children in group II. The mean age was significantly higher in Group I than Group II (mean age 9.67 vs. 11.84 yr, p=0.000). The rate of detecting ML was significantly higher in male gender (p=0.000). There was no association between the presence of ML and H. pylori positivity. The final diagnosis in children with ML was intestinal parasitic infections in 10 (%15), gastroenteritis in 6 (%9), upper respiratory tract infection in 2 (%3), but in most of the patients the etiologic factor responsible for the ML could not be identified. The mean diameter of MLs was 12.15 ± 3.68 mm (range 7 - 25 mm) and the mean regression period of MLs was 4.4 ± 2.01 months.

**Conclusion:** These results suggested that H.pylori infection was not associated with ML in children who had abdominal pain. Additionally, it was difficult to determine the etiologic factors responsible for the MLs. Therefore advanced laboratory examinations may not be necessary in children with abdominal pain and MLs below 15 mm in diameter.

**Disclosure of Interest:** None declared.

**PO-G-296**

**THE FREQUENCY OF REFLUX ESOPHAGITIS IN CHILDREN WITH DYSPHAGIA**

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Objectives and Study: The aim was to evaluate the endoscopic and histologic findings of the esophageal mucosa for the diagnosis of reflux esophagitis (RE) in children with dyspepsia, to assess the clinical presentation of these patients and to investigate the relationship between Helicobacter pylori (Hp) infection and RE.

Methods: Between 2008 January and 2009 November, a total of 217 children [mean age 11.2 ± 3.9 years, 42.4 % male] underwent upper GIS endoscopy, for evaluation of dyspepsia. Questionnaire for dyspeptic symptoms (heartburn, early satiety, vomiting, nausea, nocturnal pain, belching, fullness, halitosis, anorexia and food intolerance), endoscopic and histopathologic evaluation were performed in all patients. Endoscopic RE was graded by Los Angeles classification. Histopathologic eosinophilic esophagitis was diagnosed based on the presence of papillary elongation, basal cell hyperplasia, dilated intercellular spaces, inflammatory cell infiltration (assessed separately for eosinophils, neutrophils and mononuclear cells), vascular congestion, erosion and ulceration. Patients were defined as Hp infected when histology was positive for Hp.

Results: Endoscopic RE was found in 11% of patients (24/217; Grade A:17 (70.8%); Grade B:7 (29.1%). Histopathologic eosinophilic esophagitis was found in 49.3% of patients (107/217). Endoscopy, when compared to histopathologic analysis had a sensitivity of 8%; specificity of 86%; positive and negative predictive value of 37.5 % and 49.2 % respectively; and accuracy of 47.9 % in diagnosing RE. Normal esophageal appearance in endoscopy failed to identify 98 patients (45.2%) with histopathologic RE. Conversely, amongst patients with endoscopic RE, 15 patients (6.9%) had normal histology. Hp infection was determined in 104 patients (47.9%). Hp infection was found in 57 (53.2%) patients with RE and in 47(42.7%) patients without RE (p = n.s). Comparing patients with or without RE there was no difference in age, gender, duration, frequency and type of dyspeptic symptoms.

Conclusion: RE is frequent in children with dyspepsia when the diagnosis is based on histopathology. However it is not possible to differentiate patients with and without RE on the basis of various dyspeptic symptoms and endoscopic findings. We conclude that biopsy is essential for diagnosing RE in children with dyspepsia. No significant association was found between Hp infection and RE.

Disclosure of Interest: None.

PO-G-297

FOOD ALLERGEN RESTRICTED DIET IN THE TREATMENT OF PAEDIATRIC EOSINOPHILIC OESOPHAGITIS

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Objectives and Study: Treatment of Eosinophilic Oesophagitis (EO) in children remains challenging. Elemental diet is the gold standard but it’s use is limited by palatability and long term compliance. Kagawalla reported significant improvement on standard 6 food elimination diet in 74% of patients (<10 eosinophils/HPF). The aims of the study were to assess the efficacy of 6 food elimination diet for 6 weeks in children with EO and the role of allergy testing.

Methods: Eligibility criteria included children with either a new diagnosis of EO (>15 eos/HPF) or previously diagnosed EO and on stable treatment for the prior three months. Patients with histologic evidence of other gastrointestinal diseases (except GOR) were excluded. Skin Prick Testing (SPT) for food and inhalant allergens using standard extracts was undertaken along with Atopy Patch Testing (APT) for egg, dairy, corn, soy, wheat, chicken and beef. Patients commenced a diet excluding cow’s milk protein, soy, egg, corn, wheat, seafood, peanuts and tree nuts for 6 weeks. At completion, repeat medical assessment including Endoscopy with biopsy was performed.

Results: 14 patients were enrolled and 13 patients completed the study protocol at time of presentation. Mean age 9 (1–15 years); 11 males and 2 females. Incidence of other atopic disorders requiring treatment was 10/13 (76%) and coexistent topical steroid therapy for EO was 4/13 (30%). On SPT, 7/13 (53%) had positive results (wheal >3 mm) with all 7 demonstrating sensitivity to aeroallergens and 2/7 to food allergens. On APT, 10/13 (77%) had positive results, the most common soy (6), cow’s milk, egg and corn (5). At conclusion of the diet 3/13 had complete histological remission, 2/13 had a significant histological improvement (3–10 eos/HPF), 2 had partial histological response (>50 reduction eos/HPF), and 6 were non-responders. Mean eosinophil count dropped from 47.3 to 30 per HPF. All patients reported subjective improvement in symptoms.

Conclusion: 53% of patients had positive histological response rate (RR) to the exclusion diet, 38% showing either significant histological response or entering remission. This histological RR was disappointing versus Kagawalla’s RR 74%. Reasons for a lower RR in our study include possible reduced compliance with prescribed diet and older study population. 53% study population displayed sensitivity to aeroallergens consistent with the observation of increasing aeroallergen sensitivity with age. Conclusions from our allergy tests are difficult with small sample population, but there was no clear correlation between positive SPT, APT and response to diet.

Reference:

Disclosure of Interest: None declared.

PO-G-298

COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE-PH-MEASUREMENT FOR DETECTION OF GASTRO-OESOPHAGEAL REFLUX IN CHILDREN; AN UPDATE FROM THE GERMAN PEDIATRIC IMPEDANCE GROUP G-PIG

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Objectives and Study: The new ESPGHAN/NASPGHAN guideline recommends the combined multichannel-intraluminal-impedance-pH-(MII-pH) monitoring as the standard test for GOR detection in children of all age groups.

The German Pediatric Impedance Group G-PIG was formed in 2005 by the first German children’s hospitals using the MII-pH-monitoring routinely in gastroesophageal-reflux-diagnostics with the aim to establish and standardize the use of the method in clinical practice.

Methods: All four G-PIG centres performed combined 24-hour oesophageal impedance-pH measurements in children presenting with symptoms suggestive of reflux. The patients were divided into three symptom groups depending on the main indication for the diagnostic procedure: patients with gastrointestinal symptoms (e.g. heartburn, abdominal pain, dysphagia), patients with pulmonary symptoms (e.g. chronic cough, chronic bronchitis, aspiration pneumonia, apnoe) and patients with neurological symptoms (e.g. dystonia, Sandifer-syndrom, tic disorder).

Results: Until now the group collected data from 700 patients (median age 4 years, range 3 weeks - 16 years; 291 females, 409 males). 329 patients presented with pulmonary, 325 with gastrointestinal and 46 patients with neurological symptoms. 270 of the measurements were considered abnormal: 101 (37%) showed abnormal MII and pH-study, 49 (18%) showed only pathological pH-measurements and 120 measurements (45%) had an abnormal MII-recording only. In our population extra-intestinal symptoms of GOR(D) tend to present more frequently in younger children (median age patients with pulmonary symptoms 2 years, with neurological symptoms 0.5 years, with gastrointestinal symptoms 2.5 years, with neuro-) and are more often related to a normal pH- but abnormal MII-study.

Conclusion: This is the largest systematically standardized data collection of MII-pH measurements in children worldwide. Our data show that 45% of the patients with abnormal gastro oesophageal reflux would not have been recognized by 24-hour-pH-measurement alone and confirm MII-pH as being superior to pH-monitoring alone in detecting an abnormal GOR in children.

Disclosure of Interest: D. Pilic: Tecnomatix Medical, Germany – speaker.
T.G. Wenzl: AstraZeneca – research support; Sandhill Scientific – consultant, research support; Tecnomatix Germany – speaker, research support; Reckitt Benckiser – speaker.

The other authors do not state any potential conflicts of interest.

PO-G-299

CLINICAL, PATHOLOGICAL & EPIDEMIOLOGICAL FEATURES OF PAEDIATRIC EOSINOPHILIC OESOPHAGITIS (EE) IN A SINGLE TERTIARY CENTRE IN THE U.K.

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Objectives and Study: To identify Primary- The clinical, endoscopic & histopathological features of paediatric Eosinophilic Oesophagitis (EE) presenting at our institution.
Secondary- The incidence of paediatric EE in the Humber region of United Kingdom & characteristics of a subgroup of patients with signs of both Gastroesophageal reflux disease (GORD) & EE.

Methods: The oesophageal biopsies with >15 eosinophils/HPF high power field (HPF) between January 1st 2007 & 31st December 2008 identified 24 patients whose notes were then retrospectively reviewed.

Results: 1046 children had an oesophagoscropy of which 15% had features of oesophagitis on histology & 2.1% (24/1046) had EE (13male).

Median age was 6 years (range: 0.5–15).

Clinical: The presenting symptoms were: feeding/swallowing problems (50%), other gastrointestinal symptoms (42%), & dietary allergy (33%). 6 patients had eczema +/-asthma. 4 children had refractory asthma & EE was diagnosed after a combined bronchoscopy & oesophagoscropy. Dietary elimination of proteins improved symptoms in 5 children.

In 17% (4/24) EE was associated with GERM, confirmed on pH study.

Macroscopy: The commonest findings were:
- Normal in 38%(9/24),
- Furrowing or trachealisation in 42%(10/24),
- ? Candida in 8%(2/24),
- oesophagitis in 8%(2/24) and
- No record/unknown in 4%(1/24)

Histopathology: Apart from the eosinophils/HPF which are tabulated below the other features seen in EE were various degrees of DIS: basa cell hyperplasia; papillary elongation and vacuolation of the epithelial cells. Microabcesses in the superficial mucosa were identified in 4 patients. An interesting finding of a cohort of patients with pH study proved GORD (4/24) was the otherwise rare presence of an increased number of so called squiggle cells (>6/HPF).

Table:

<table>
<thead>
<tr>
<th>Site</th>
<th>Median number &amp; range of e/HPF per biopsy site was</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal oesophageal biopses</td>
<td>24.5 (4–55)</td>
</tr>
<tr>
<td>Mid-oesophageal biopses</td>
<td>37.5 (22–55)</td>
</tr>
<tr>
<td>Distal oesophageal biopses</td>
<td>38 (20–57)</td>
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The median number of e/HPF was 32 (range:16–57).
Conclusion: EE should be suspected in any child with atopy &/or difficulty in feeding or swallowing. Suggestive macroscopy should prompt the endoscopist to obtain proximal oesophageal biopsies in addition to distal oesophageal biopsies as a high yield of e/HPF may help distinguish EE from GORD. pH study proved GORD & an increased presence of ‘squiggle cells’ in patients with EE suggests the possibility of an ‘overlap’ syndrome. The extra-polated population incidence of paediatric EE was 8/100,000 in our region. Severity of symptoms could not be correlated with e/HPF.

Disclosure of Interest: None declared.

PO-G-300

INCREASED YIELD IN DETECTION OF SYMPTOMATIC GASTRO-oesophageal reflux (GER) BY COMbined multichannel intraluminal impEdance (MII) and pH monitoring of the oesophagus – A single-centre experience

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Objectives and Study: MII monitoring is being established as an additional tool to conventional oesophageal pH monitoring. Clear-cut normal values for the number of bolus GER and the Bolus Exposure Index (BEI) still need to be determined in paediatric populations. The results of combined MII-pH testing are analysed to assess the increase in sensitivity for the detection of symptomatic GER.

Methods: From February 2008 through November 2009, combined MII-pH monitoring was performed in 64 symptomatic children and adolescents between 0.04 and 17.7 years of age (with a mean of 5.2 and a median of 2.2). 10 were on proton pump inhibitor (PPI) treatment, 1 on H2-blocker, and 1 on baclofen. Symptoms were recorded simultaneously by the patients or their caregivers. 8 patients didn’t notice any symptoms during 24-hour monitoring. The data collected with age-appropriate ComforTec® MII-pH catheters were manually edited and analysed with the help of the Sandhill’s BioVIEW® analysis software. Reflux Index (RI), Boix-Ochoa (up to 1 year of age) or DeMeester score (above 1 year), BEI, number of bolus GER within 24 hours, Symptom Index (SI), and Symptom Association Probability (SAP) were calculated as described in the literature.

Results: Out of 9 patients on PPI with a normal pH study, 2 showed a significant association between bolus GER on MII monitoring and gastrointestinal symptoms. 1 patient on PPI had a borderline pH study (RI 3.5%, Boix-Ochoa Score 16.6) and MII monitoring (BEI 2.8%, 76 bolus GER/24 h). The patient on H2-blocker had abnormal RI, DeMeester score, BEI, SI, and SAP. The patient on baclofen had only abnormal results on MII monitoring (BEI, number of bolus GER, SI, and SAP). Out of 52 patients off antireflux therapy, 1 infant had a borderline pH study (RI 4.9%, Boix-Ochoa score 19.7) and MII monitoring (BEI 4.4%, 76 bolus GER/24 h). 1 child had a pathologic pH study, but normal MII monitoring and didn’t notice any symptoms. Out of 50 patients with a normal pH study, 10 showed a significant association of bolus GER on MII monitoring with gastrointestinal symptoms, 2 with respiratory symptoms, and 1 with both.

Conclusion: MII monitoring was able to detect symptomatic bolus GER in about 25% of paediatric patients with a normal 24 h pH study. The increase in diagnostic yield was similar in patients on and off antireflux medication. The reliability of testing for symptomatic GER depends on accurate documentation of symptoms. Controlled interventional trials are needed to determine the exact significance of weakly or non-acidic bolus GER in oesophageal and respiratory disease.

Disclosure of Interest: None declared.

PO-G-301

EVALUATION BY BREATH TEST OF THE ERADICATION RATE OF HELICOBACTER PYLORI INFECTION IN TUNISIAN CHILDREN

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Objectives and Study: Evaluate using the breath test (BT) the eradication rate of helicobacter pylori (H.pylori) after triple therapy in symptomatic children presenting H.pylori gastritis.

Methods: Retrospective study of 100 children presenting chronic H.pylori gastritis, who had at least one proton pump inhibitor-based triple therapy and at least one BT to control eradication. We have studied epidemiologic and clinical data, the different triple therapies administrated and the results of the different BT.

Results: 100 children were included. The sex-ratio was 0.6. The median age was 10 years (2.5–15). The symptoms were dominated by abdominal pain (76%), followed by vomiting (56%), heartburn (12%) and hematemesis (16%). The endoscopic aspects were: nodular gastritis (68%), petechial gastritis (16%), congestive gastritis (8%), ulcerative bulbitis (4%) and duodenal ulcer in one case. Antral biopsies were performed in all cases. The histologic study revealed a follicular chronic gastritis in 65%, a superficial chronic gastritis in 35%. The H.pylori density was (2+) in 50% of cases, (+) in 40% and (+) in 10%. The initial triple therapy consisted in the association of amoxicillin, metronidazole and omeprazole (AMO) during 7 to 14 days in 72% of cases, and the association of amoxicillin, clarithromycin and omeprazole (ACO) during 7 to 14 days in 23%. One child who had a penicillin allergy received metronidazole, clarithromycin and omeprazole (MCO) during 10 days. 4% of children received sequential treatment (amoxicillin and omeprazole during 10 days associated to metronidazole during the first 5 days followed by clarithromycin during 5 days).
After the first treatment, the symptoms disappeared in 52% of cases, persisted in 38% and recurred in 10%. The BT was done at least 3 months after the treatment and was negative in 60%. A second triple therapy was administrated to the non eradicated children (N = 40). This therapy consisted in associating AMO during 14 days in 38% of cases, ACO during 10 days in 42%, sequential treatment in 18% and MCO during 14 days in penicillin allergic child. A second control BT was negative in 11 children (28%). The infection persisted after an average of 4 triple therapies in 29 children.

Conclusion: The eradication rate evaluated by BT after the first triple therapy was 60%. This rate increased to 71% after the second treatment. Bacteriologic studies and other therapeutic strategies should be proposed in children to ameliorate the eradication of H. pylori infection.

Disclosure of Interest: None declared.

PO-G-302

OBESITY IS A RISK FACTOR FOR GASTROESOPHAGEAL REFLUX IN CHILDREN

Objectives and Study: Gastroesophageal reflux (GER) is a very common disorder in obese adults. An association between high values of body-mass index (BMI) and GER symptoms has not been demonstrated in children. The implications of obesity in the etiology, management and outcomes in children with GER disease have become increasingly important due to the recent outbreak of obesity, particularly in childhood. The aims of our study were to evaluate 1) the prevalence of GER symptoms in overweight and obese children in comparison to general normal-weight population and 2) whether the GER symptoms are associated with the abdominal circumference (AC).

Methods: The study population consisted of 106 consecutive children (M/F: 53/53; mean age: 8.19 years; range: 2–17.7 years) referred to our Department for a well-child visit from June 2009 to December 2009. A detailed history and physical examination, including determination of height, weight, BMI and AC, was obtained from each patient. A questionnaire on reflux symptoms was completed by caregivers. On the basis of this questionnaire, a reflux symptomatic score, considering duration and severity of each referred symptom, was calculated.

Results: All of the 106 patients prospectively enrolled during the 6-month period were categorized according to BMI in normal-weight (BMI <85th pct), overweight (BMI from 85th to 95th pct) and obese children (BMI >95th pct) and according to AC in children with AC <75th, from 75th to 90th and >90th percentiles. The reflux symptomatic score resulted significantly higher (P < 0.005, for both comparisons) in obese than in normal-weight children (average score: 2.65 vs 0.64, respectively) as well as in children with AC >90th percentiles compared to those with AC <75th percentiles (average score: 2.90 vs 0.66, respectively). A trend towards a higher rate of reflux symptomatic score was present in patients with overweight (1.02 vs 0.64, respectively; P = 0.53) and this positive trend continued across all categories of both BMI and AC, including those less than 85th for BMI and 75th for AC.

Conclusion: Our preliminary data demonstrate that, also in childhood, overweight and obesity are risk factors for the development of GER symptoms. The risk of GER symptoms seems to rise progressively with the increase of both BMI and AC, even in normal-weight children. Our findings have important implications for future studies, since even moderate weight gain may cause or exacerbate GER symptoms.

Disclosure of Interest: None declared.

PO-G-303

COMPARISON OF MULTICHANNEL INTRALUMINAL IMPEDANCE-PHMETRY TESTING AND REFLUX SCINTIGRAPHY IN PEDIATRIC PATIENTS WITH SUSPECTED GASTROESOPHAGEAL REFLUX
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Objectives and Study: To compare the agreement of multi-channel intraluminal impedance (MII)-pHmetry and reflux scintigraphy in children referred for suspected gastroesophageal reflux disease (GERD).

Methods: Seventy five patients older than 6 months were evaluated by MII-pHmetry and 1 hour reflux scintigraphy. For impedance monitoring reflux was defined as if there was a sequential drop in impedance ≥50% of baseline value, starting distally and propagating retrogradely to at least next two more proximal measuring segments. Reflux index more than 4% for pHmetry, number of refluxes for 24 hours more than 50 for MII monitoring, and even one positive reflux frame for scintigraphy are accepted as positive. Agreement between 3 tests for diagnosis of GERD was evaluated as well as agreement of each reflux episode for scintigraphy and MII-pHmetry (kappa test).

Results: Sufficient data was obtained from 60 patients. Thirty-four (56.7%) of them were male and mean age was 8.7 ± 3.7 years. GERD was diagnosed in 34 (57.7%), 44 (73.3%) and 47 (78.3%) by pHmetry, MII, and scintigraphy pH and/or MII respectively. No agreement was found between pHmetry and scintigraphy, MII and scintigraphy, MII-pHmetry and scintigraphy for diagnosis of GERD (kappa values are 0.029; -0.042; -0.105 respectively). No agreement was found for refluxes found by MII and/or pHmetry and scintigraphy study during 1 hour period of scintigraphic study (kappa = -0.270; P < 0.0001).

Conclusion: No agreement was found between pHmetry, MII, MII-pHmetry and scintigraphy for diagnosis of GERD. Scintigraphy should be interpreted carefully and efforts
THE COMPARISON OF SEQUENTIAL TREATMENT WITH STANDART TRIPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION IN TURKISH CHILDREN
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Objectives and Study: The efficacy of standart triple treatment for Helicobacter pylori (H. Pylori) infection is decreasing worldwide including Turkey. Increasing antimicrobial resistance and falling eradication rates are the results of the widespread use of antibiotics. For this reason, several alternative regimens have been proposed. A novel 10 day sequential treatment with an eradication rate of 95% has been reported. However the efficacy of this therapy in children from different regions is not well known. As sequential treatment promise high effectiveness, good compliance and low treatment cost, it should be the ideal eradication therapy for children. The aim of the study was to investigate the H. pylori eradication rate of the sequential treatment and compare it with that of the standart triple therapy regimen.

Methods: Eighty-eight consecutive children with H.pylori infection were enrolled. Diagnosis of H.pylori infection was based on 14C -urea breath test and histologic analysis. Sequential treatment group received omeprazole 1 mg.kg \(^{-1}\) day \(^{-1}\) plus amoxicillin 50 mg. kg \(^{-1}\) day \(^{-1}\) for 5 days followed by omeprazole 1 mg.kg \(^{-1}\) day \(^{-1}\) plus clarithromycin 15 mg.kg \(^{-1}\) day \(^{-1}\) and metronidazole 20 mg.kg \(^{-1}\) day \(^{-1}\) for the next 5 days. Standart triple therapy group received omeprazole 1 mg.kg \(^{-1}\) day \(^{-1}\) for 1-month, plus amoxicillin 50 mg. kg \(^{-1}\) day \(^{-1}\) and clarithromycin 15 mg. kg \(^{-1}\) day \(^{-1}\) for 2 weeks. Eradication was assessed by 14C -urea breath test 6 weeks after therapy.

Results: The sequential therapy group consisted of 43 children (boys 46.5%; mean age \(\pm\) SD; 12.4 \(\pm\) 3.2). There was no statistical difference between two groups with regards to age and sex distribution. Patient compliance was good for all patients. Both of the treatments were well tolerated but as a side effect; nausea was more often in standart triple therapy group \((P=0.004)\). H. pylori eradication was achieved in 34 of 43 (79.1%) children receiving sequential treatment, and 23 of 45 (51%) children receiving triple therapy \((P=0.012)\). The cost of sequential treatment was lower than triple therapy.

Conclusion: Sequential therapy was associated with a higher eradication rate of H. pylori compared with standart triple therapy in Turkish children. In addition, sequential therapy had lower side effects and lower cost.

Disclosure of Interest: None.

PO-G-305

COMPARABLE HELICOBACTER PYLORI ERADICATION RATES IN CHILDREN FOLLOWING CLARITHROMYCIN RESISTANCE TESTING BY STOOL POLYMERASE CHAIN REACTION VS CONVENTIONAL INVASIVE METHODS
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Objectives and Study: Clarithromycin containing eradication treatment in case of infection with clarithromycin resistant Helicobacter pylori (H. pylori) most likely will fail. In a region where clarithromycin resistance is highly prevalent, the present study retrospectively assessed the eradication rate in children whose treatment was either based on the results of a real-time stool PCR allowing for the detection of clarithromycin resistance on a genetic basis in comparison to those who were treated according to the results of E-test applied to culture detected H. pylori strains.

Methods: Either stool PCR or esophagogastroduodenoscopy followed by E-test was conducted in dyspeptic children within a 2-year period. For eradication, a combination treatment (proton pump inhibitor, amoxicillin and either clarithromycin or metronidazole or levofloxacin) was given for 7 to 14 days. Negative results of stool PCR and 13C urea breath testing or monoclonal stool antigen EIA at least 6 weeks after end of treatment defined eradication success.

Results: 110 children were started on eradication treatment between 6/07 and 9/09 (mean age 11.5 years (range 3–18 years), m:f = 1:1.29). In those patients whose treatment was based on stool PCR results, eradication was successfully achieved in 49/64 (76.6%). If treatment was tailored according to E-test results, eradication rate was 33/46 (71.7%).

Conclusion: In an area with a high resistance rate to clarithromycin, eradication of H. pylori in children based on stool PCR results can be achieved in a similar percentage as compared to treatment according to conventional invasive resistance testing.

Disclosure of Interest: Christa Binder, Andrea Bruckdorfer, Heidemarie Gizci, Ulrike Graf, Karin Hammer, Albina Innerhofer and Andreas Vécsei have no conflicts of interest to declare. Alexander M. Hirschl and Athanasios Makristathis have received consultancy fees from In genetics.
PO-G-306

GASTROESOPHAGEAL REFLUX OR ASTHMA: WHICH COMES FIRST IN ATOPIC AND NONATOPIC CHILDREN?

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Objectives and Study: Gastroesophageal reflux disease (GERD) is one of the major problems in asthmatic children. However, exact condition in atopic or nonatopic asthmatic has not been clear. The aim of this study was to determine the frequency of GERD and the influence of GERD treatment on respiratory findings in atopic and nonatopic children with asthma.

Methods: Thirty two nonatopic, 24 atopic children with asthma were included. GERD related respiratory symptoms, inhaled steroid, bronchodilator and parenteral steroid requirement, exacerbations and hospitalizations during the 6 months prior to and after pH monitoring were recorded. 24 hour pH monitoring results and GERD treatment were also recorded.

Results: Mean age of atopic and nonatopic groups were similar (P=0.06). Frequency of proximal GERD was 71.9% in atopic, 70.8% in nonatopic group (P=0.93). Distal GERD frequencies were similar (66.7% and 68.8% in atopic and nonatopic groups respectively, P=0.87). All parameters improved in nonatopics after GERD treatment (P<0.01). However, only respiratory symptoms and hospitalization improved in atopics (P=0.002 and P=0.007 respectively).

Conclusion: Similar frequency of GERD in atopic and nonatopic children may suggest role of asthma in development of GERD. However, improvement in all clinical parameters in nonatopic children but not in atopic children might indicate that gastroesophageal reflux is the causal event in the association of asthma and GER in nonatopics whereas it is the result in atopics. These findings need to be supported by further prospective cohort studies.

Disclosure of Interest: None declared.

PO-H-307

AN OBJECTIVE METHOD TO QUANTIFY STOOL COLOUR IN NEONATAL CHOLESTASIS

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Objectives and Study: Biliary atresia (BA) is an important cause of neonatal cholestasis which requires early surgical intervention with the Kasai portoenterostomy. At presentation, 95.2% of infants with BA have pale stools. Currently stool colour is assessed subjectively, but pale stools are frequently unrecognised resulting in a delay in diagnosis and surgery which adversely affects the prognosis. We report early development of an objective means of measuring stool colour.

Methods: Normal and pale coloured stool specimens were collected from healthy infants and those presenting with liver disease. Stool colour was ascertained by two Paediatric Hepatologists and the colour was quantified with a spectrophotometer (specbos 1201, JETI GmbH) in a darkened room with a tungsten light source. The stool colour was expressed in CIE-Lab (International Commission on Illumination) coordinates. Logistic regressions were computed to determine a boundary that best accorded with the clinicians’ classification of stool colour.

Results: 25 stools were assessed (14 normal, 9 pale and 2 indeterminate). The diagnoses in the infants with pale and indeterminate stools were BA (4 cases), neonatal hepatitis (6 cases) and inspissated bile syndrome (1 case). The best classifier of a pale stool was a computed value L-0.90b greater than 53 with effectiveness assessed by computing the area under the ROC (receiver operating characteristic) curve as 89%.

Conclusion: This methodology can closely reproduce the ability of a paediatric hepatologist in distinguishing pale stools. A larger study will confirm the promise of our initial data.

Reference:

Disclosure of Interest: None declared.

PO-H-308

EXPRESSION OF EXTRACELLULAR MATRIX PROTEINS AND ADHESION MOLECULES IN CHILDREN WITH BILIARY ATRESIA

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Objectives and Study: The cause of biliary atresia remains largely unknown. Some authors hypothesise underlying defects in the morphogenesis of the biliary tract. We analysed the expression of the extracellular matrix (ECM) and of corresponding adhesion molecules in children with biliary atresia (BA), with cholestatic liver disease of other origin (CLD), and in normal control children to elucidate possible defects.

Methods: Liver biopsies were obtained from controls (n=8), infants with BA (n=13), or with CLD (n=6) and were immuno-histochemically stained. ECM proteins...
including basement membrane components Collagen type IV, Laminin subtypes, Perlecan, and Entactin. Adhesion molecules comprised of Integrin-alpha and -beta subunits. Statistical analysis was performed using chi-squared and Mann-Whitney tests. Results were defined as statistically significant if P < 0.05 in both tests.

**Results:** Laminin-beta1 was reduced in children with BA (23%) versus controls (80%). Its expression has been reported in foetal and neonatal liver and regeneration. Notably, adhesion molecule Integrin-beta1 was reduced on bile ducts of BA (61.5%) versus controls (100%). It has been attributed to morphogenesis and Laminin binding. Accordingly, Entactin was reduced around the biliary epithelium in BA (7.6%) versus controls (75%). On the contrary, Perlecan was increased in BA (84.6%) versus controls (25%). Perlecan has been reported enhanced during liver damage. Integrin-alpha3 was increased in the basal membrane of children with BA (76.9%) versus controls (12.5%). It has been associated with the development of immature, primitive bile ducts. These statistically significant results were restricted to children with BA.

**Conclusion:** The composition of the ECM in children with BA appears to be impaired. Reduction of Laminin, Entactin and Integrin-Beta1 may affect migration, matrix-epithelial binding, and differentiation. On the contrary, overexpression of Perlecan and Integrin-alpha3 could suggest ineffective proliferation of immature bile ducts. Our findings suggest the possibility of morphogenetic defects in the pathogenesis of biliary atresia.

**Disclosure of Interest:** None declared.

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**PO-H-309**

**APRI AS AN INDICATOR OF ADVANCED LIVER FIBROSIS IN CHILDREN WITH ALPHA-1-ANTITRYPSIN DEFICIENCY**

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**Objectives and Study:** Liver biopsy is regarded to be a golden standard in assessment of liver fibrosis in children with alpha-1-antitrypsin deficiency (ATD). Liver fibrosis due to HCV and HBV viral infections as well as alcoholic liver disease can be also assessed by a non-invasive marker - APRI (AspAT-to-Platelet Ratio Index). As prognosis and progression of liver disease in ATD is variable non-invasive markers are important tools for early diagnosis and follow up. The aim of the study was the evaluation of APRI as an indicator of advanced liver fibrosis in children with alpha-1-antitrypsin deficiency (ATD). Liver fibrosis due to HCV and HBV viral infections as well as alcoholic liver disease can be also assessed by a non-invasive marker - APRI (AspAT-to-Platelet Ratio Index). As prognosis and progression of liver disease in ATD is variable non-invasive markers are important tools for early diagnosis and follow up.

**Methods:** 45 children with liver disease due to PiZZ phenotype of ATD were included into the study. In all subjects APRI and liver histology were analyzed and compared.

**Results:** Liver biopsy was performed at the age of 0.25 years (0.17–0.67), median (Q1-Q3). Liver fibrosis was assessed according to 5 point scoring system (0–4). Points 2–4 were regarded as advanced fibrosis. Liver cirrhosis was also described. The best sensitivity and specificity of APRI was calculated based on ROC analysis and area under curve (AUROC) was assessed.

**Results:** In the studied group APRI was 0.22 (0.12–0.39), median (Q1-Q3). In 21 children advanced fibrosis was recognized and in 6 patients liver cirrhosis was described. The optimal cut-off value for APRI for advanced fibrosis was 0.26, and for cirrhosis 0.33. Respectively for advanced fibrosis and cirrhosis, sensitivity was 0.60 (95%CI 0.41–0.77); 0.83 (0.36–0.99), specificity was: 0.87 (95%CI 0.60–0.98); 0.31 (0.17–0.48), AUROC was: 0.74 (95% CI 0.58–0.89); 0.51 (95% CI 0.28–0.74).

**Conclusion:** APRI appears to be a sensitive but less specific indicator of cirrhosis in children with ATD. It seems to be a valuable marker of advanced liver fibrosis.

**Disclosure of Interest:** None declared.

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**PO-H-310**

**SERUM TRANSAMINASE ELEVATIONS IN INFANTS WITH ACUTE GASTROENTERITIS**

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**Objectives and Study:** To examine the frequency of hepatic transaminase elevations in infants with acute gastroenteritis.

**Methods:** Over a 8- weeks period, 35 of 130 infants admitted with acute gastroenteritis were found to have human rotavirus (HRV) gastroenteritis using stool antigen testing. Sera of infants were analyzed for alanine aminotransferase (ALT), aspartate aminotransferase, alkaline phosphatase, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), total and direct bilirubin, and creatinine.

**Results:** Thirty four infants (26%) had elevated ALT and AST. ALT elevations were 1–3 times the normal in 24(18%) and 6–20 times the normal in 10(8%) infants; the latter group showed the clinical and biochemical criteria of ischemic hepatopathy (severe dehydration,marked elevations of serum transaminase and LDH levels, elevated CPK and creatinine levels with coagulopathy followed by rapid decline in the absence of liver disease. In all infants transaminases normalized within 3–10 days. On admission 57% of infants with severe dehydration vs. 4% with no dehydration had elevated transaminase levels. Infant with severe dehydration had an estimated 31.5 fold higher odds of having elevated ALT & AST compared with those without dehydration.

14(40%) of HRV positive vs. 21(21%) of HRV negative infants had transaminase elevations and a border line significant association was detected between HRV positivity and elevated ALT&AST levels (odd ratio = 2.5 95%CI 1–3.2
Transaminase elevations were not significantly associated with age, sex, duration of gastroenteritis or with any of the following symptoms: fever (>38), vomiting and blood and/or leukocytes in the stools. Multivariate logistic regression analysis, showed that severe dehydration is still significantly associated with elevated Transaminase levels.

**Conclusion:** Our data suggest that liver injury during gastroenteritis in infants is quite frequent but always self limiting if the underlying perfusion disturbance caused by severe dehydration is corrected.

**Disclosure of Interest:** None declared.

**PO-H-311**

**RATIONALISATION OF SERVICES HAS FAILED TO IMPROVE OUTCOMES FOR BILIARY ATRESIA IN SCOTLAND. A REPORT ON BEHALF OF THE SCOTTISH SOCIETY OF PAEDIATRIC GASTROENTEROLOGY HEPATOLOGY AND NUTRITION (SSPGHAN)**

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**Objectives and Study:** Previously in Scotland kasais were performed for extrahepatic biliary atresia (EHBA) in three scottish centres. Following publication of data suggesting that outcomes were superior in those centres performing >5 Kasai procedures a year1 services were rationalised to three supraregional centres in England and Wales. No such directive exists for Scotland; however in 2002 an informal agreement was made within the SSPGHAN centres to refer all cases of EHBA to the three group A centres. The aims were to examine outcomes for patients with EHBA in Scotland since 2002 and compare this with the historical Royal Hospital for Sick Children Glasgow (RHSC)2 data and from the original paper describing outcome from centres performing >5 Kasai procedures a year (Group A)3.

**Methods:** A review of case-notes of all children with EHBA in Scotland Jan 2002-Oct 2009 was conducted from SSPGHAN units. Patient demographics and data regarding presentation, investigation, co-morbidity timing of Kasai, and Kasai centre, outcomes in terms of clearance of jaundice, transplant free survival (TFS) and survival were recorded for 6 months, 1yr and 2yr post Kasai. Clearance of jaundice was defined as conjugated bilirubin <20µmol/L.

**Results:** 26 children with EHBA were identified. A Kasai operation was performed in 24 (92%) infants and 2 (8%) had primary transplantation. 3 children had Kasai procedures in Edinburgh, and 1 patient moved to Scotland post-Kasai so were excluded from further analysis. 22 were referred to supraregional service and 20 had a Kasai procedure performed. Of these 22 children, 18 have reached 2 year follow up with 16 (89%) children had survived, 11 following liver transplantation and 6 with their native liver. 1 child died following transplantation.

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Age Presentation (kasai)</th>
<th>Clearance Jaundice (%)</th>
<th>2yr TFS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RHSC 1987–2000</td>
<td>20</td>
<td>40 (58)</td>
<td>13/20 (65)</td>
<td>13/20 (65)</td>
</tr>
<tr>
<td>Group A</td>
<td>57</td>
<td>44 (53)</td>
<td>33/52 (62)</td>
<td>33/57 (61)</td>
</tr>
<tr>
<td>SSPGHAN 2002–2009</td>
<td>22</td>
<td>49 (60)</td>
<td>9/20 (45)</td>
<td>6/18 (33)</td>
</tr>
</tbody>
</table>

significant difference \( P < 0.05 \).

**Conclusion:** Centralisation of Kasai services within the SSPGHAN group has failed to significantly improve outcomes for Scottish children presenting with EHBA. Despite now having surgery performed at Group A centres, 2yr TFS is significantly lower in the Scottish population than previously published UK data. Delay in presentation appears to be the key factor but additional delay from tertiary centre to surgery needs minimised to optimise outcomes.

**References:**
2. Ling S, RHSC Glasgow personal communication 2002

**Disclosure of Interest:** None Declared.

**PO-H-312**

**EOSINOPHILIC CHOLANGITIS: A NEW ENTITY OF SCLEROSING CHOLANGITIS, MANAGEMENT AND OUTCOME AT 1 YEAR**


**Objectives and Study:** Eosinophilic cholangitis (EC) is only described as case reports in adults. EC is characterized by eosinophilic infiltration of the biliary tract of unknown etiology. We report the first case of eosinophilic cholangitis in a child in the english literature.

**Methods:** A 14 year old girl presented with severe epigastric pain and deranged liver function. Investigation showed: total bilirubin 12µmol/L, aspartate aminotransferase (ALT) 93 IU/L, G-glutamyl transferase 307 IU/L. Eosinophilis were 1.51 x10^9/L. Investigations for other liver disease like infection, metabolic and autoimmune were negative. Stool was negative for ova and parasites. Ultrasound scan and MRCP showed bile duct dilatation. ERCP showed cholangiopathy of the major ducts. A liver biopsy specimen showed features of acute cholangitis and pericholangitis with predominant eosinophilic infiltrate. A gastric and small bowel biopsy also showed eosinophilic gastritis. Hence, in view of the presence of eosinophilia, eosinophilic infiltration in the
biliary epithelium, eosinophilic infiltration of stomach and bowel a diagnosis of EC was entertained.

**Results:** The patient was treated with prednisolone (2 mg/kg/day) and was weaned to 5 mg/day over 6 months. In addition she was started on Ketotifen. Clinical and laboratory remission was achieved in 6 months. A repeat liver biopsy at 6 months showed significant improvement in the liver histology. Liver function tests normalised in addition to both her eosinophilia and inflammatory markers.

**Conclusion:** Eosinophilic cholangitis should be considered in the differential diagnosis of the other forms of sclerosing cholangitis in children. Management with steroids and Ketotifen is effective, the long-term outcome remains to be determined.

**Disclosure of Interest:** None declared.

**PO-H-313**

**WILSON’S DISEASE IN CHILDREN: MONOCENTRIC EXPERIENCE WITH ANALYSIS OF 114 CHILDREN OVER A 18 YEARS PERIOD**


**Objectives and Study:** Wilson’s disease (WD) is a rare autosomal recessive disorder of copper metabolism with a highly variable spectrum of clinical manifestations in childhood. We evaluated the clinical and laboratory characteristics of 114 children with WD to determine clinical presentation, diagnostic course and outcome.

**Methods:** The medical reports of 114 children (63 boys) whom were diagnosed as WD between 1991 and 2009 were reviewed retrospectively. Physical examination, laboratory tests and liver biopsies of patients were evaluated.

**Results:** The mean age at diagnosis was 9.5 ± 3.2 years (1.5–16 years). There was consanguinity in majority of the parents (81, 71.1%). Eighty seven (76.3%) patients were diagnosed as symptomatic cases including 12 patients whom presented with acute liver failure. Twenty seven patients were diagnosed by family screening. Overall 80 patients presented with hepatic, 5 with neurologic, and 17 both hepatic and neurologic features. Hepatomegaly was the most common clinical finding, in 41 patients, while splenomegaly, icterus and ascites were found in 26, 25 and 24 patients respectively. Kayser–Fleischer rings were present in 63 of 109 patients (57.8%) while serum ceruloplasmin level was below 20 mg/dl in 97 of evaluated 114 patients (85.1%). Urinary copper excretion was above 80 μg/24 hours in 85 of 102 patients (83.3%). Liver copper above (250 μg/g dry weight) was found in 53 (67.0%) of 79 patients. Cirrhosis and chronic hepatitis were the most common findings of liver biopsy (23/79, 29.1% for each). All the patients with acute liver failure died except one who had liver transplantation. Ninety seven non-fulminant WD patients were treated with D-penicillamine and zinc sulphate at diagnosis. A total of 6 children were converted to trientine due to adverse reactions of penicillamine (nephrotic syndrome in 2, deterioration of liver functions in 2, Stevens-Johnson reaction in 1, allergic rash in 1 patient). Five patients had liver transplantation during follow-up. Seventy six non-fulminant WD patients had been followed up for 5.0 ± 3.7 years (3 months-14 years). Five patients died during the follow-up because of end stage liver disease. Eighteen patients who were nonadherent to chelation therapy had poor outcome.

**Conclusion:** Wilson’s disease in children may present in different forms and needs extensive investigation for diagnosis. Drug treatment is helpful for a stable or improved course of non-fulminant disease. Fulminant WD is almost mortal without liver transplantation.

**Disclosure of Interest:** None declared.

**PO-H-314**

**EXTRAHEPATIC PORTAL VEIN OBSTRUCTION. THE ETIOLOGY, TREATMENT OPTIONS AND PROGNOSIS**


**Objectives and Study:** Extrahepatic portal vein obstruction (EHPVO) results in portal hypertension and is a common cause of upper gastrointestinal bleeding in children. Etiological factors are diverse and commonly include umbilical catheterization, hypercoagulable states and congenital portal vein abnormalities. The aim of this study is to describe the clinical characteristics and treatment results of children with EHPVO.

**Methods:** Retrospective study. Case files of children who were diagnosed as EHPVO between 1982 and 2009 were retrospectively reviewed.

**Results:** There were 43 children (19 female/24 male) diagnosed as EHPVO in 27 years. The mean age at the admission was 5.9 ± 3.4 years (9 months to 15.5 years). The median follow-up time was 4.4 years (1 month to 16.7 years). Most common presentation pattern was upper gastrointestinal bleeding (n = 18, 41.8%). Other presentation patterns were abdominal distention (n = 10, 23.2%), splenomegaly on physical examination (n = 9, 20.9%), growth retardation, jaundice, thrombocytopenia, deep vein thrombosis, and abdominal pain. Fourteen patients had neonatal problems that might have resulted in portal vein obstruction. Sixteen patients had low thrombocyte counts (< 150,000), 15 patients had low albumin levels (< 3.5 g/dL) at presentation. Ten patients have developed coagulopathy at the follow-up. No deaths were observed during the follow-up period. There were 4 patients with concomitant splenic vein obstruction. Liver biopsy was performed in 16 patients. Two patients had factor V Leiden mutation (1 heterozygote, 1 homozygote), 5 patients had methylene tetrahydrofolate reductase
Extrahepatic portal vein obstruction is generally results from problems in neonatal period such as umbilical vein catheterization, sepsis, and omphalitis. Thrombophilia might accompany EHPVO. Both band ligation and endoscopic sclerotherapy seems to be effective in reducing rebleeding. Overall the prognosis is good and recurrence of varices is rare once eradicated. Early diagnosis of EHPVO by following the high-risk patients and starting medical/endoscopic treatments early in the course of disease might improve the patient care by preventing the first episode of bleeding.

Disclosure of Interest: None declared.

PO-H-316

ELEVATED SERUM GAMMA-GLUTAMYL TRANSPEPTIDASE PREDICTS THE FUTURE DEVELOPMENT OF CIRRHOTIC CYSTIC FIBROSIS LIVER DISEASE

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Objectives and Study: Cirrhotic cystic fibrosis liver disease (CCFLD) develops in 5–10% of CF patients. To date CCFLD is mostly diagnosed based on physical examination in combination with ultrasound (US) of liver and spleen. Unfortunately, these diagnostics can not predict which patients will develop CCFLD in the future. Currently, ursodeoxycholic acid (UDCA) is the only treatment employed to prevent CCFLD. It might be beneficial if UDCA could be administered in an early phase to patients with a high risk of CCFLD. We aimed to determine if liver biochemistry, in particular a solitary serum Gamma-glutamyl transpeptidase (GGT) elevation, could predict the development of CCFLD.

Methods: We reviewed medical records of pediatric CF patients in follow up at 1–1–2007 (age: 0–18 years; n = 280) in our two CF centers. CCFLD was defined as a heterogeneous and nodular aspect of the liver on periodic US in combination with clinical or US proven splenomegaly. The date that patients first met this definition was used as date of diagnosis. GGT results 2 years prior to the diagnosis were evaluated. We used as controls historical GGT results of CF patients with normal liver US and no signs of splenomegaly at the age of 15 years (n = 50 patients, available GGT results: mean: 9, range 1–27). We excluded elevated GGT values if additionally alanine transaminase (ALT) was increased (>2xULN).

Results: 15 patients met our definition of CCFLD (4.5%). All had established CCFLD before the age of 15 years. We calculated mean, median and peak GGT values. At least 2 GGT results were available in the 2-year period before the diagnosis CCFLD in 12/15 patients (80%). Using ROC analysis, the mean GGT value of the available results was identified as the best predictor for CCFLD (AUC: 0.89). Consecutive cross tab analysis showed that a mean GGT value >30 IU/L (based on at least 2 measurements), in the absence of ALT elevation was a significant independent predictor for the development of CCFLD in the period of 2 years.

Disclosure of Interest: None declared.

PO-H-315

NON-ALCOHOLIC FATTY LIVER DISEASE INVESTIGATED BY MAGNETIC RESONANCE SPECTROSCOPY AND CORRELATED TO BMI SDS AND LIVER PARAMETERS IN SERUM OF 73 OBESE CHILDREN IN DENMARK

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Objectives and Study: To investigate the presence of non-alcoholic fatty liver disease (NAFLD) in obese children. To establish correlation of the amount of fat in the liver with elevations in measurements of liver parameters and BMI.

Methods: Liver fat was assessed by Magnetic Resonance Spectroscopy (MRI). NAFLD was defined as a liver fat percentage above 9%. Weight and height were measured in light indoor clothes. Body mass index (BMI) standard deviations score (SDS) was calculated with adjustment for age and gender. Fasting blood samples were analysed for lipids and hepatic enzymes.

Results: Seventy-three Danish children (thirty-eight boys), with a mean age of 13.5 ± 2.7 SD (range 6 - 20 years) and with a median BMI SDS of 3.1 ± 0.5 SD were investigated by MRI. Twenty-eight % (n=21) showed evidence of NAFLD. Sixty-two % of the children with NAFLD were boys. For those with NAFLD, the median liver fat % was 27.5 % (range 9.4 % - 64.4 %). Children with NAFLD had significantly higher BMI SDS (P=0.001) and higher levels of alanine aminotransferase (ALT) (P=0.001) compared to the children with liver fat % less than 9 %. The degree of fat in the liver was positively correlated to BMI SDS, gender, triglycerides (TG), ALT, gamma-glutamyl transferase (GGT) and lactate dehydrogenase (LDH) (r²=0.58).

Conclusion: BMI SDS is positively correlated with NAFLD and the degree of fat in the liver is associated with ALT, GGT, TG and LDH concentrations.

Disclosure of Interest: None declared.
0–2 years prior to the diagnosis. A GGT >30IU/l predicted CCFLD with a sensitivity of 83%, specificity of 92% and a PPV and NPV of 71% and 96%, respectively. Based on these results the odds ratio for a CF patient age 2–15 years with a persistent GGT >30 U/l, in the absence of ALT elevation, for developing CCFLD in the following 2 years was 60 (95% CI: 10–374).

Conclusion: Our results, in a large cohort of CF patients, strongly indicate that isolated serum GGT elevation could predict the development of the cirrhotic form of CF liver disease. Our results provide a perspective for targeted prophylactic treatment for CCFLD.

Disclosure of Interest: None declared.

PO-H-317

INVESTIGATION OF LATENT CARDIOMYOPATHY AND ITS PREDISPOSAN FACTORS IN CHILDREN WITH PORTAL HYPERTENSION

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Objectives and Study: Cirrhotic cardiomyopathy (CCMP), which is a condition characterized by electrophysiological, diastolic and/or systolic dysfunction of the heart, is a well-defined entity in adults. However, pediatric data is limited. To determine the rate and risk factors of CCMP in children with portal hypertension (PHT).

Methods: This study included 50 children (age 8.4 ± 4.8 years; 54% male) with cirrhotic (40/50) and non-cirrhotic (10/50) PHT as the study group and 50 healthy children (age 8.8 ± 4.6 years; 54% male) as control. Recorded data were evaluated retrospectively. Electrocardiography (ECG) and echocardiography (conventional/Doppler) was used to evaluate cardiac functions. QTc ≥ 0.45 was accepted as prolonged on ECG. The study group was divided into subgroups as cirrhotic/noncirrhotic groups, groups with ascites/without ascites, Child groups (A-C), Group 1 (QTc ≥ 0.45)/Group 2 (QTc <0.45). After the causes of prolonged-QTc and cardiomyopathy (CMP) other than cirrhosis in childhood were excluded, Group 1 was described as CCMP group. By Logistic Regression analysis, the risk factors for CCMP; such as sex, age, duration of the disease, PELD and CHILD score/severity of ascites were evaluated.

Results: In study group, none of the cases had cardiac symptom, except the cyanotic one with hepatopulmonary syndrome. Although mean QTc of the noncirrhotic children was statistically higher compared to the controls (0.41 ± 0.02 vs 0.38 ± 0.03, P < 0.01), none of them had a QTc>0.45. Ten patients (20%) with prolonged-QTc constituted the group with CCMP (Group 1). All children in Group 1 were cirrhotic, either in the stages of Child B (1/10) or Child C (9/10) and most of them had ascites (9/10). Moreover, mean cardiac linear sizes and diastolic dysfunction indices (E/A, Em, Am) of Group 1 were higher than in control group. Similary, these parameters were also impaired in groups with ascites. Sistolic dysfunction (low EF and FS) was found only one case in Group 1. Also this case was in group with ascites. While this case (2%) was described as manifest CCMP, other nine cases (18%) were described as latent CMP. When risk factors for CCMP were evaluated, it was determined that sex, age and duration of disease were not the risk; severity of ascites was the most important risk factor. [P = 0.001, OR: 9.4 (2.5–35.2)].

Conclusion: Cardiomyopathy is a complication of severe PHT affecting the sinusoids. Therefore, detailed cardiac examination should be made in children with cirrhotic PHT, especially the cases with ascites and high Child score.

Disclosure of Interest: None declared.

PO-H-318

ASSESS THE RISK OF SEVERE HYPERBILIRUBINEMIA IN BREAST-FED INFANTS

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Objectives and Study: In recent years, the increased prevalence of breastfeeding in conjunction with early discharge practices has increased the risk for marked hyperbilirubinemia in term infants. The aim of this study was to investigate the risk factors for significant hyperbilirubinemia in Taiwanese breast-fed infants.

Methods: A prospective study was designed to investigate the effects of these factors [birth body weight, gender, mode of delivery, glucose-6-phosphate dehydrogenase (G6PD) deficiency, variant UDP-glucuronosyltransferase 1A1 (UGT1A1) gene and a suspicious analog organic anion transporter 2 (OATP 2) gene] on significant hyperbilirubinemia in Taiwanese breast-fed neonates. Those full term infants with a positive Coombs test or with concurrent neonatal illness requiring intensive care were excluded. Umbilical cord blood samples have been collected for study of UGT1A1 and OATP2 gene. The PCR-restriction fragment length polymorphism (RFLP) method was applied to detect the known variant sites in the UGT1A1 (promoter area, nucleotides 211, 686, 1091, and 1456) and OATP2 gene (nucleotides 388 and 521) in Taiwanese. The blood samples for the analysis of total serum bilirubin (TSB) level were obtained at the time of the routine metabolic screen before discharge. Significant hyperbilirubinemia was diagnosed if a full term infant needed phototherapy and had a bilirubin level ≥256.5 μM (15.0 mg/dl) in serum within 1 week after birth. We analyzed the risk factors for significant hyperbilirubinemia using univariate logistic regression models.

Results: A total of 252 full term breast-fed infants were enrolled in this study. Of these, 59 (23.4%) infants received phototherapy with significant hyperbilirubinemia. G6PD deficiency, vaginal delivery and the variation at nucleotide
211 of the UGT1A1 gene were significantly different between the hyperbilirubinemia and control groups. The results of univariate logistic regression revealed odds ratios (ORs) of 12.24 [95% confidence interval (CI): 1.08–138.62; \( P < 0.05 \)], 3.55 [95% CI: 1.64–7.66; \( P < 0.001 \)], and 2.48 [95% CI: 1.29–4.76; \( P = 0.006 \)] for neonates who were G6PD deficiency, vaginal delivery and carry the variant UGT1A1 gene at nucleotide 211, respectively. Thirty two (54.3%) breast-fed infants with severe unconjugated hyperbilirubinemia had at least one mutation of the UGT1A1 gene. Variation at nucleotide 211 is the most common mutation.

**Conclusion:** In conclusion, breast-infants who are G6PD deficiency, vaginal delivery and carry the 211 variants in the UGT1A1 are at high risk to develop severe hyperbilirubinemia.

**Disclosure of Interest:** None declared.

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**PO-H-319**

**AGE DEPENDENT PARAMETERS AND THE DIAGNOSTIC ACCURACY OF THE SCORING SYSTEM IN PEDIATRIC WILSON DISEASE**

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**Objectives and Study:** Wilson disease (WD) is an autosomal recessive disorder of copper metabolism resulting in accumulation of copper in the liver and other organs. There is no single diagnostic test that can exclude or confirm WD with certainty. Recently, molecular biological methods play important role in WD confirmation. However, WD is often diagnosed by clinical findings and biochemical tests in many clinical units because genetic analysis is not yet universally available and sometimes inconclusive. We evaluate the efficacy of the scoring system, which was proposed at the 8th International Meeting on Wilson disease and Menkes disease in Leipzig, and the difference in diagnostic accuracy by age.

**Methods:** Genetic analysis was performed on 114 WD patients (mean age, 9.2 ± 3.8 years; range, 19 months–19.6 years); 2 mutations in 92, 1 mutation in 20 and no mutation in 2 patients. The laboratory findings and clinical parameters in the scoring system except molecular testing were applied in 112 patients. We discriminated younger children (<6 years) from older ones (>6 years) to assess the difference in scoring between two groups (n = 26 vs. n = 86).

**Results:** In the 112 patients, 103 (92.0%) had a score of ≥ 4, which is diagnosis established score in this scoring system. Kayser-Fleischer rings were detected in 36/112 patients (32.1%). Neurologic symptoms and coombs-negative hemolytic anemia were present in 21/112 (18.8%) and 8/112 patients (7.1%), respectively. Serum ceruloplasmin concentration was low (≤20 mg/dL) in 110/112 patients (98.2%).

**Conclusion:** The scoring system proposed at the international meeting in Leipzig seems to be highly useful for the clinical and biochemical diagnosis of WD when the genetic testing is not available. More attention is needed particularly when the scoring system is applied without genetic testing for the diagnosis of WD in preschool children who usually do not show the definite diagnostic cut-off values of conventional laboratory tests.

**Disclosure of Interest:** None declared.

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**PO-H-320**

**DATA MINING APPROACH OPTIMIZES DIAGNOSIS OF WILSON DISEASE IN CHILDREN**

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**Objectives and Study:** In Wilson disease (WD) the top priorities of the diagnostic process are to identify all patients with WD and simultaneously to have proper diagnosis as soon as possible. The first line of diagnosis of WD consists of laboratory tests: serum ceruloplasmin concentration, total and free serum copper concentration, 24 h urinary copper excretion (available, inexpensive and no time-consuming). The aim of the study was to optimize interpretation of results of WD diagnostic test with approach of advanced data mining techniques.

**Methods:** 62 patients with WD were included to the study group. All of them had serum ceruloplasmin concentration [mg/dL], total and free serum copper concentrations [ug/dL], 24 h urinary copper excretion [ug/24 h] measured. The reference group (RG) consisted of 69 patients with other cause of liver injury. The results of tests performed were analyzed with Weka environment. Weka was created in 1993 at University of Waikato in New Zealand. It comprises large, coherent collection of tools for data analysis. The following analysis are possible: to store and handle data, to perform operation on data tables, effective statistic analysis, application of data mining algorithms, graphical facilities for data analysis and display.

**Results:** DTNB algorithm (patients with urine copper over 49.17 or patients with ceruloplasmin less than 15.5 and urine copper over 9.55 are classified as WD) produced optimal sensitivity – 0.98 and NPV – 0.98, and can be used for screening of WD.

**SMO algorithm with line classifier:**

**0.5239** (standardized) ceruloplasmin

**+1.6479** (standardized) total serum copper

**-2.0764** (standardized) urine copper
-0.315* (standardized) free serum copper +0.3945; result >0 classified as WD) produced optimal specificity – 1 and PPV – 1, which allowed for proper diagnosis in 53 WD patients (sensitivity 0.85, NPV – 0.88). Algorithms used each after other provide proper diagnosis in 85% of WD patients after first line biochemical tests and decrease the number of patients requiring further expensive or invasive diagnostic tests to 16 (9 WD and 7 RG).

Conclusion: The first line diagnostic tests supported by data mining approach seem to be very efficient in screening and establishing the final diagnosis of Wilson disease.

Disclosure of Interest: None declared.

PO-H-321

ACUTE LIVER INSUFFICIENCY CAUSED BY HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS - EXPERIENCE OF CHILDREN'S MEMORIAL HEALTH INSTITUTE IN WARSAW

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Objectives and Study: Haemophagocytic lymphohistiocytosis (HLH) is a life-threatening condition, caused by congenital or acquired defects in cellular cytotoxicity, manifesting with fever, hepatosplenomegaly, duo- or pancytopenia, coagulopathy, hyperferritinemia. Acute liver insufficiency (ALI) may be its 1st clinical presentation. The aim of the study was to summarize experience in diagnosing and treating children with ALI due to HLH.

Methods: We present 6 children (3 girls + 3 boys), aged from 6 mo to 4 yo, with ALI complicating HLH.

Results: They manifested fever, jaundice, hepatosplenomegaly, accompanied by anaemia, thrombocytopenia, coagulopathy (INR 1.8 - 4.0), hypofibrinogenemia, hypertransaminasemia. Neurological symptoms included irritability, seizures, coma. Hyperferritinemia and increased erythropoagocytosis in bone marrow were found in all children. Cytotoxic activity of NK cells, evaluated in 5 children, was low in 4. Perforin expression in NK cells was normal in 5 tested patients. We established the diagnosis of HLH secondary to CMV-infection in 2 boys and due to EBV in the 3rd one, FHL type 3 or 4 in girls. Hyperferritinemia and increased erythropoagocytosis in bone marrow were found in all children. Cytotoxic activity of NK cells, evaluated in 5 children, was low in 4. Perforin expression in NK cells was normal in 5 tested patients. We established the diagnosis of HLH secondary to CMV-infection in 2 boys and due to EBV in the 3rd one, FHL type 3 or 4 in girls. Five children received treatment according to HLH-2004 protocol (dexamethasone, cyclosporin A, etoposide), a girl with multi-organ failure only DXM. The boys were given Gancyclovir to treat co-existing infection. Patients treated with immunochemotherapy avoided liver transplantation due to improvement of liver function. The girl cured with DXM and the boy with EBV-HLH died from multi-organ failure, 2 girls died from HLH- reactivation; a boy suspected of XLP died after MUD-HSCT. Only 3 yo- boy with CMV-associated HLH is free of symptoms. We confirmed FHL due to MUNC13-4 mutation in one girl. Genetic evaluation towards FHL type 3 and 4 is ongoing in 2 girls.

Conclusion: 1. Both, genetic and secondary HLH should be considered in children with ALI of unknown origin.
2. Immunochemotherapy, based on HLH-2004 protocol, is an effective treatment of ALI caused by HLH and may be recommended instead of LTx.

Disclosure of Interest: None declared.

PO-H-322

MORTALITY OF BILIARY ATRESIA IN CHILDREN NOT UNDERGOING LIVER TRANSPLANTATION


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Objectives and Study: Orthotopic liver transplantation (OLT) has become a life saving treatment for children with end stage liver disease due to biliary atresia (BA). It is known, however, that not all BA patients undergo OLT. We assessed the mortality of BA patients without OLT in a national database of BA in The Netherlands.

Methods: We quantitated and characterized the mortality of non-transplanted BA patients under the age of five years, using the Netherlands Study group of Biliary Atresia Registry (NeSBAR) database. We included children born between 1987 and 2006. To determine whether mortality had changed over time, we compared the cohort 1987–1996 (n = 98) with that of 1997–2006 (n = 99). Causes of mortality were obtained from patient charts. Clinical condition at the time of assessment for OLT was expressed in the Pediatric End-stage Liver Disease (PELD) score.

Results: Mortality of non-transplanted BA children decreased from 27% (26/98) in 1987–1996 to 15% (15/99) in 1997–2006 (P = 0.04). In cohort 1987–1996, mortality was predominantly based on BA patients who had not been evaluated or accepted for OLT (17%:17/98 vs. 7%:7/99 in cohort 1997–2006; P = 0.02). Sepsis was the prevailing cause of death in both cohorts (29%;12/41). PELD-scores at time of assessment were higher in our cohorts 1987–1996 and 1997–2006 compared to international data (26.0 ± 5.1 and 22.3 ± 6.8, respectively, vs. international data: range 11.7–13.3), indicating more advanced liver disease.

Conclusion: Our national data indicate that, between 1987 and 2006, liver transplantation has increasingly been considered as treatment option for BA, resulting in decreased non-transplant mortality in The Netherlands. Ongoing mortality of BA patients without OLT is mainly due to sepsis and is attributable to assessment of BA patients for OLT in an already clinical advanced condition. We hypothesize that
non-transplant mortality in The Netherlands for BA patients can be further reduced by earlier listing for OLT.
* also on behalf of NeSBAR (Netherlands Study group for Biliary Atresia Registry).

**Disclosure of Interest:** None declared.

**PO-H-323**

**CHOLELITHIASIS IN CHILDREN WITH DOWN SYNDROME**

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**Objectives and Study:** Down syndrome (DS) is a chromosomal disorder most often observed in the newborn period. Various facial, limb and internal abnormalities are found in this disorder. There are no any studies of cholelithiasis in children with DS in Turkey. The aim of this study was to determine the association between DS and cholelithiasis.

**Methods:** Between 2007 and 2008, we evaluated 37 children admitted to Ataturk University, Faculty of Medicine, and Department of Pediatrics because of DS diagnosed by cytogenetic and clinical investigations. Of 37 infants, 24 (64.9%) were girls, 13 (35.1) were boys. The age range enrolled in this study was from 2 to 12 years old (4.43 ± 2.62 years old).

**Results:** Of the 37 patients with DS who underwent abdominal ultrasound examination, nine (24.5%) were found to have cholelithiasis, three (8.1%) were found to have biliary sludge. Spontaneous resolution was observed in 27.02% of the patients with cholelithiasis. One patient had undergone cholecystectomy. Hypothyroidism was seen in 16 out of 37 patients with cholelithiasis. One patient had undergone cholecystectomy. Hypothyroidism was seen in 16 out of 37 patients (43.2%) of which 6 (66.7%) had cholelithiasis while 6 months, then one stopped the therapy with corticosteroids, the other continued with budesonide 3 mg/24 h. 6 months. They achieved remission on special diet + immunosuppressive therapy. The both children stopped the immunosuppressive treatment & they had no relapses until now.

**Conclusion:** AIH might remain undiagnosed because of lack of symptoms, because of absence of liver-specific autoantibodies, or because of a misdiagnosis of CD. Acute hepatitis in celiac patients should induce one to suspect an autoimmune origin. Patients with AIH might have a hidden CD too.

**Disclosure of Interest:** None declare.

**PO-H-325**

**VACCINE ESCAPE MUTANT CHRONIC HEPATITIS B INFECTION IN A CHILD**

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**Objectives and Study:** The most important strategy to prevent hepatitis B virus (HBV) infection and its consequences is the universal vaccination of all newborns. However, an important and well-known consequence of population vaccination is the emergence of vaccine escape mutations. These mutations are stable and replication competent, escape from host immune response, and may cause breakthrough infections. Such mutant HBV infections sometimes occur despite adequate antibody response to vaccination. Here, we report the first case of vaccine escape mutant in immune competent child in Turkey.

**Methods:** A retrospective survey was made for the period 1989–2008 in the Department of Pediatrics in Varna (population of the region 2 000 000). Among 25 pediatric patients with CD we identified 2 with AIH.

**Results:** Diagnosis of CD preceded the diagnosis of liver disease in these patients, but elevation of aminotransferase activity was present. They had liver-related non-organ-specific autoantibodies. Any viral markers & metabolic disorders were not diagnosed. Liver histology showed inflammatory lesions with features of autoimmune damage and different degrees of fibrosis in both. They were on gluten-free diet (until now) + prednisolon 2 mg/kg/24 h. 6 months, then one stopped the therapy with corticosteroids, the other continued with budesonide 3 mg/24 h. 6 months. They achieved remission on special diet + immunosuppressive therapy. The both children stopped the immunosuppressive treatment & they had no relapses until now.

**Conclusion:** AIH might remain undiagnosed because of lack of symptoms, because of absence of liver-specific autoantibodies, or because of a misdiagnosis of CD. Acute hepatitis in celiac patients should induce one to suspect an autoimmune origin. Patients with AIH might have a hidden CD too.

**Disclosure of Interest:** None declared.

**PO-H-324**

**AUTOIMMUNE HEPATITIS ASSOCIATED WITH CELIAC DISEASE IN CHILDHOOD**

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**Objectives and Study:** Autoimmune hepatitis (AIH) are frequently associated with celiac disease (CD). This is a rare condition & occurs predominantly in young people. CD is an autoimmune disorder, with an onset in childhood. In some cases two or more autoimmune diseases can occur in one patient. The aim of this study was to describe the clinical features of children and adolescents presenting with an AIH associated with CD.

**Methods:** A retrospective survey was made for the period 1989–2008 in the Department of Pediatrics in Varna (population of the region 2 000 000). Among 25 pediatric patients with CD we identified 2 with AIH.

**Results:** Diagnosis of CD preceded the diagnosis of liver disease in these patients, but elevation of aminotransferase activity was present. They had liver-related non-organ-specific autoantibodies. Any viral markers & metabolic disorders were not diagnosed. Liver histology showed inflammatory lesions with features of autoimmune damage and different degrees of fibrosis in both. They were on gluten-free diet (until now) + prednisolon 2 mg/kg/24 h. 6 months, then one stopped the therapy with corticosteroids, the other continued with budesonide 3 mg/24 h. 6 months. They achieved remission on special diet + immunosuppressive therapy. The both children stopped the immunosuppressive treatment & they had no relapses until now.

**Conclusion:** AIH might remain undiagnosed because of lack of symptoms, because of absence of liver-specific autoantibodies, or because of a misdiagnosis of CD. Acute hepatitis in celiac patients should induce one to suspect an autoimmune origin. Patients with AIH might have a hidden CD too.

**Disclosure of Interest:** None declare.
Liver biopsy demonstrated histologic findings of chronic HBV infection. Mutation analysis performed by direct sequencing method yielded glycine to arginine change at codon 145 (G145R) which is the most common vaccine escape mutation pattern. No any vaccine escape mutation pattern was detected in mother’s DNA.

Conclusion: This case underlines the importance of the epidemiologic studies regarding the rate and pattern of vaccine escape mutation in post vaccination era. Together with the presumption of non-horizontal transmission, vaccine escape mutant species may become the dominant species in the infectious viral population in future. It poses a potential threat to the long term success of vaccination programmes. So, consideration should be given to incorporating into the current hepatitis B vaccine of additional antigenic components which will confer protection against infection by vaccine escape mutants if dictated by studies.

Disclosure of Interest: None declared.

PO-H-326

ACUTE-ON-CHRONIC LIVER FAILURE IN CHILDREN WITH BILIARY ATRESIA

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Objectives and Study: Acute-on-chronic liver failure (ACLF) has been recently described in adults. We reviewed the etiology, outcome and prognostic factors in children with biliary atresia (BA) with ACLF, which was defined as an acute liver insult with a rise in serum bilirubin and INR complicated within 4 weeks by ascites and/or encephalopathy.

Methods: Demographic, clinical and laboratory data were collected retrospectively in children diagnosed with BA in our centre from 1990–2009 with ACLF (group 1) or already compensated liver disease and listed for liver transplantation (LT) (group 2-control).

Results: 54 children (26 M and 170/62 M) with median ages of 6 months [range, 2–96] and 10months[0.4–13yrs] were identified in group 1 and 2 respectively. Median values for group 1 at 3 months prior to ACLF and at time of event and group 2 at listing were for serum bilirubin 261µmol/L[3–936], 229[54–803] and 185[11–457], INR 1.1[0.9–1.6], 1.8[1.2–4.8] and 1.1[0.7–2.82], albumin 34 g/L[22–45], 31[19–50] and 32[17–48] and sodium 137mmol/L[125–142], 136[127–164] and 137[123–158] respectively. The median Hepatic Artery Resistance Index (HARI) was 1.0[0.82–1.2] for both groups. Between groups 1 and 2 growth failure was recorded in 13(24%) and 78(49%), age <1yr in 41(74%) and 91(53%) and days from listing to LT 59[range, 4–242] and 664[486] respectively. Precipitating factors for ACLF were sepsis in 25(47%) children, gastrointestinal bleeding in 23(43%) leading to hepatic encephalopathy in 16(30%), worsening ascites in 18(33%) and hepatorenal syndrome in 6(11%). Eight children had confirmed bacterial and/or fungal sepsis and 4 had serological evidence of viral infection. 31(57%) children were admitted to Intensive Care with ACLF with a median time of 45 days[2–100] prior to LT. 18(33%) children required mechanical ventilation, 6(11%) continuous haemofiltration (CVVH) and 3(5%) exchange transfusion. 42(78%) children received a cadaveric LT; 3 had a living related LT. 5 children normalised their INR and 7 their serum albumin. All 12 recovered from ACLF. 19(35%) children died in group 1, 10 pre-LT compared to 19(11%)in group 2, 10 pre-LT. Independent factors at time of ACLF that showed a significant association with mortality were CVVH (P<0.01), ventilation (P<0.03) and hepatorenal syndrome (P<0.03).

Conclusion: ACLF group has a higher mortality rate with preserved growth but affecting mostly the <1yr old children compared to control group. Sepsis and variceal bleeding are the predisposing factors. Renal decompensation is a poor prognostic factor and early intervention could optimise the outcome.

Disclosure of Interest: None declared.

PO-H-327

SEVERE LYSOSOMAL LIPID STORAGE DISEASE OF THE LIVER IN MONOSOMY1P36: NEW PRESENTATION EXTENDING THE PHENOTYPE

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Objectives and Study: Monosomy 1p36 has been increasingly recognized as a distinct chromosome deletion syndrome in the past few years. Monosomy 1p36 is mostly associated with severe mental retardation, developmental delay, behavioral difficulties and self-injury. There are several distinct dysmorphic features, including large anterior fontanelles, microcephaly, brachycephaly, deep-set eyes, flat nose, nasal bridge and pointed chin. In contrast to the “classical” phenotype, several children with a 1p deletion have had overgrowth and hyperphagia with a clinical presentation similar to Prader –Willi syndrome (PWS).

Methods: Here we describe an 11-year-old girl with 1p36 deletion demonstrating the classical dysmorphological features, having developed an uncontrolled voracious appetite and severe truncal obesity. Gastroenterological evaluation revealed elevated liver enzymes. Liver biopsy disclosed severe fatty liver: in addition to medium-size triglyceride droplets, hepatocytes showed excessive lipofuscin.
accumulation. A most unusual feature was the presence of frequent, extremely large lipolysosomes, never previously reported in this condition.

**Results:** Oligonucleotide-based microarray analysis was performed using a 105K-feature whole-genome microarray. It showed copy-number loss of 177 oligonucleotide probes from the short arm of chromosome 1 at 1p36.33p36.32, approximately 2.2 Mb in size.

**Conclusion:** We suggest that the chromosome segment 1p36.33–36.32 harbour a critical region for the manifestation of obesity and hyperphagia. We also suggest that monosomy 1p36 syndrome should be considered in patients with hypotonia, developmental delay, obesity, hyperphagia, behavioral disorders, learning difficulties and a negative genetic test for PWS, even in the absence of the striking facial features of the syndrome.

**Disclosure of Interest:** na

**PO-H-328**

**QUANTITATIVE ASSESSMENT OF LIVER FIBROSIS USING NON-LINEAR OPTICAL MICROSCOPY ACROSS LIVER SURFACE**

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**Objectives and Study:** Liver fibrosis mostly presents clinically till an advanced or cirrhotic stage[1], therefore the availability of accurate measurement of hepatic fibrosis on the progressing is an essential issue in anticipation of new anti-fibrotic therapies and treatment of chronic liver disease. Due to the major alternation of ECM during fibrogenesis[2], the most direct way of quantifying fibrosis is to directly monitor the fibrogenic collagen content and morphology change in the liver organ. Combining SHG and TPEF microscopy, we aim to develop a fully automated quantification system for liver fibrosis assessment based on signals collected from type I collagen and liver cells as quantification marker to represent the degrees of fibrosis development across the liver surface[3].

**Methods:** Treated rats liver slices were obtained by the nonlinear optics microscopy system and imaged using SHG/TPEF microscopy. Liver capsular and sub-capsular regions are defined in the images using algorithm developed. After the capsular region is defined, the average width of the capsular region, the collagen percentage in capsular region and in sub-capsular region are quantified. Morphological features in the sub-capsular region are also quantified accordingly.

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**Disclosure of Interest:** None declared.

**PO-H-329**

**ALPHA-1 ANTITRYPSIN DEFICIENCY WITH LIVER DISEASE IN SPANISH CHILDREN**

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**Objectives and Study:** Identification of early prognostic data in children with alpha1 antitrypsin (AAT) deficiency.

**Methods:** Review of 79 patients with signs of liver disease and AAT deficiency (PiZZ = 73, S = 6). Neonatal cholestasis developed in 56 (71%), the other 23 patients had physical/analytical disturbances detected later in life. Probability of survival with own liver according to initial symptoms was assessed. Children with neonatal cholestasis had clinical/biochemical data recorded at age 12 months, which were studied as predictors of outcome.

**Results:** 1. Survival was influenced by clinical onset. Patients with neonatal cholestasis (54 PiZZ, 2 PiSZ) had a mean follow-up of 10 years, 44.6% died or underwent liver transplantation (LT), including 1 PiSZ patient. Patients without neonatal cholestasis were followed (mean ± SD) 16±6 years, none died or had a LT.

2. Neonatal cholestasis group: Low birth weight affected 59%, initial Bilirubin averaged 7.8 ± 3.2 mg/dL. Early biopsy (n = 30) showed ductopenia in 8, ductal proliferation in 6, Giant cells in 6 and unspcific cholestasis -fibrosis in 13. At age 12 months, 57% had an enlarged spleen, 21% showed abnormal bilirubin (>1.5 mg/dL), ALT was
>100 U/L in 74.5% and GGT >150 U/L in 62.5%. Any of those characteristics negatively influenced survival. Persistent high bilirubin led to the worst prognosis (5-year survival:30%). GGT>150 U/L was particularly useful for prognostic purposes (survival with own liver was 72% in 5,10 and 15 years, respectively, as compared to 92% at 5 and 15 years in children with GGT<150 U/L). Low birth weight or duodenal stenosis did not influence survival.

3. Overall, 27 children were listed for LT, all had neonatal cholestasis. Two died in the waiting list. Twenty-three patients underwent LT, 3 of them before 1 year of age. Post-LT survival was 91.3% at 1 and 10th year.

Conclusion: Overall prognosis of children with neonatal cholestasis was 59% survival with own liver at 10 years, compared to 100% in children identified in later ages. Those with neonatal onset who display GGT<150 U/L at 1 year (38% of the cases) had usually good outcomes. Liver transplantation achieved 91% long-term survival.

Disclosure of Interest: None declared.

PO-H-330
ASCITES AND GASTROINTESTINAL BLEEDING IN PATIENTS LISTED FOR LIVER TRANSPLANTATION

Objectives and Study: Evaluation of incidence and management of complications of advanced liver disease in children.


Median follow-up after listing was 60 days, median age was 1.5 years. Diagnosis were biliary atresia (BA) in 41 (51.8%), other chronic liver disease (OCLD) in 35, acute failure (ALF) in 3. PELD at the end of follow-up was <13 in 41 (51.8%), 13 to 22 in 17 (21.5%) and >23 in 1 (26.4%).

Results: 1. Ascites developed in 45 children (57%), gastrointestinal (GI) bleeding occurred in 27 (34%); 23 children had both complications.

2. ASCITES: affected all ALF, 66% BA, 43% OCLD. Incidence was 27% in PELD <13 group compared to 89% in PELD >13 group. Children with ascites showed significant lower albumin and sodium and higher bilirubin and INR compared to non-ascitic patients. Among children with ascites, 25% showed Na<130 mEq/L, 61% had fever or SIRS and 30% a marked aminotransferase elevation; treatment was spironolactone (100%), furosemide (64%), plasma or albumin (57%), terlipressin (22%), paracentesis (13%), dialysis or hemofiltration (4%).

3. GI-bleeding: occurred in 1 of 3 ALF, 36.5% BA and 31% OCLD; in 19.5% PELD<13 compared to 50% PELD >13.

Albumin was lower and INR higher in children with haemorrhage. Treatment was ranitidine or omeprazole (all), plasma or clotting factors (44%), somatostatin (44%), endoscopy (15%), haemodynamic support (22%).

4. Ascites and GI-bleeding influenced survival in the waiting list, all 6 deaths occurred in children affected by both complications.

5. LT was performed in 63 children (37 had ascites). Post-LT 1-year graft and patient survival was 71% and 85.5% in children with ascites, compared to 92.3% and 96.1% in non-ascitic (graft: P=0.09, patient: ns).

Conclusion: Ascites and GI-bleeding were related to derangement of liver function tests. The risk of mortality was increased in affected candidates; with unaffected patient outcome after LT.

Disclosure of Interest: None declared.

PO-H-331
INSULIN RESISTANCE, LIPID METABOLISM AND FATTY ACID PROFILE IN CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE
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Objectives and Study: The aim of the study was to verify whether non-alcoholic fatty liver disease (NAFLD) in overweight/obese children is associated with specific disturbances in insulin resistance, lipid metabolism and plasma fatty acids.

Methods: 14 patients with NAFLD aged 14.4 (13.5–16) yrs with BMI 27.4 (25.4–27.8) and 14 healthy overweight/obese children aged 15 (14–16.3) yrs with BMI 26.5 (25.2–26.9) yrs [median(Q1-Q3)], matched for absolute BMI (±0.5 yrs) and gender were compared. Parameters of insulin resistance, lipid metabolism as well as fatty acid concentrations in plasma phospholipids were measured and compared using statistic analysis.

Results: There were no significant differences between NAFLD and healthy overweight/obese children in fasting glucose, insulin, HOMA-IR, LCAT, ApoA1, ApoB, ApoE, total cholesterol, triglycerides, lipoprotein A, LDL, VLDL, HDL, glutathione and glutathione peroxidase. However we found that NAFLD patients had, in comparison with healthy children:

- higher monounsaturated fatty acids (MUFA): 19 (17.8–21) vs. 16.6 (14.57–17.75) %wt/wt, P=0.013;
- lower polyunsaturated fatty acids (PUFA): 30.3 (29.57–32.54) vs. 34.6 (33.27–35.67) %wt/wt, P=0.004;
- lower total n-3 fatty acids: 3.3 (2.81–3.47) vs. 3.5 (3.32–3.76) %wt/wt, P=0.016;
- and lower total n-6 fatty acids: 21.4 (20.12–22.62) vs. 24.5 (22.98–25.67) %wt/wt, P=0.004 [median(Q1-Q3)].
Conclusion: Decreased concentrations of polyunsaturated fatty acids in overweight/obese children are associated with a risk of fatty liver disease. Other parameters of lipid metabolism and Insulin resistance seem not to distinguish between NAFLD and healthy overweight/obese children.

Disclosure of Interest: None declared.

PO-H-332

ACUTE LIVER FAILURE AMONG DANISH CHILDREN DURING A 5 YEARS PERIOD
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Objectives and Study: Acute liver failure (ALF) in childhood is a rare condition reported to have 30–50% mortality in patients not having liver transplantation (LTX). In about half of the patients no definite diagnosis is achieved. Identification of children who need liver transplantation (LTX) is a challenge and prognostic markers are still under discussion. We present a prospective study of diagnosis, outcome and biochemical markers in children with ALF, seen at our centre from January 2005 to January 2010. ALF was defined as INR >2 and elevated ALT without known pre-existing liver disease.

Methods: All Danish children with ALF are admitted to the Copenhagen University Hospital and they were all prospectively enrolled in the database. Data on age, diagnosis, treatment, outcome, and biochemical markers at admission and peak levels were registered.

Results: 36 children (age 15 days to 15.1 years) fulfilled the inclusion criteria. In 26 children a specific diagnosis was established (table); only 10 children (27%) remained without a diagnosis. Peak INR and peak bilirubin were higher in the group without a diagnosis (P = 0.009 and P = 0.02), but peak ALT was higher in the PCM group (P = 0.05). 11 patients were considered candidates for LTX, whereof two were not listed due to later emerging contraindications. Peak INR and peak bilirubin but not peak ALT were higher among candidates for LTX, whereof two were not listed due to later emerging contraindications. Peak INR and peak bilirubin but not peak ALT were higher among candidates for LTX, whereof two were not listed due to later emerging contraindications. Peak INR and peak bilirubin but not peak ALT were higher among candidates for LTX, whereof two were not listed due to later emerging contraindications.

Conclusion: In this population, we did find a diagnose within more children than expected based on previous studies (ref). Overall survival was 86%, with 70% survival in the not-transplanted group, which is similar to previously published data(ref). Children with metabolic disease and children without a diagnosis had a higher risk of death or LTX.

Reference:

Disclosure of Interest: None declared.

PO-H-333

NONALCOHOLIC FATTY LIVER DISEASE IN CHILDREN WITH HYPOPITUITARISM
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Objectives and Study: It has been reported that children with hypopituitarism have features of metabolic syndrome. The aim of this study was to investigate the clinical features and liver histology of pediatric nonalcoholic fatty liver disease (NAFLD) associated with hypopituitarism.

Methods: We reviewed the clinical data and liver histology of eleven children diagnosed as having hypopituitarism and NAFLD. Diagnosis of NAFLD was based on evidence of a fatty liver from abdominal computerized tomography (CT).

Results: The mean age at the time of diagnosis of hypopituitarism was 10.4 years and the mean age at the time of diagnosis of NAFLD was 13.1 years. Craniofacial hypopituitarism was the most common cause of pituitary dysfunction. At the time of diagnosis of NAFLD, nine patients (82%) had a body mass index greater than the 85th percentile, four patients (36%) had elevated fasting blood glucose levels and seven (64%) had hypertriglyceridemia. Of the six patients biopsied, one was cirrhotic, two had nonalcoholic steatohepatitis (NASH) with bridging fibrosis, two had NASH with mild portal fibrosis and one had simple steatosis.

Conclusion: Children with hypopituitarism are at risk of short stature, obesity, hyperlipidemia and NAFLD. Early diagnosis of NAFLD is important in children with hypopituitarism because NASH is common.

Disclosure of Interest: There is no conflict of interest to declare.

Table:

<table>
<thead>
<tr>
<th>Table:</th>
<th>PCM intoxication (n=10)</th>
<th>Other (n=10)</th>
<th>Metabolic (n=6)</th>
<th>Unknown (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>13.4 (0.9)</td>
<td>5.3 (1.6)</td>
<td>2.8 (2.3)</td>
<td>3.4 (1.7)</td>
</tr>
<tr>
<td>LTX/death before LTX</td>
<td>3.5 (0.6)</td>
<td>2.6 (0.2)</td>
<td>5.0 (1.1)</td>
<td>5.8 (0.8)</td>
</tr>
<tr>
<td>INR peak</td>
<td>5707 (1630)</td>
<td>1822 (643)</td>
<td>175 (65)</td>
<td>3057 (1211)</td>
</tr>
<tr>
<td>Bilirubin peak (µmol/L)</td>
<td>50.9 (14.7)</td>
<td>148.3 (51.1)</td>
<td>98.8 (23.1)</td>
<td>243.4 (57.9)</td>
</tr>
</tbody>
</table>

*2 children were not LTX candidates **1 child died after LTX.
PO-H-334

INTERFERON AND ZINC COMBINATION THERAPY IN CHILDREN WITH CHRONIC HEPATITIS B INFECTION

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Objectives and Study: Host immune response plays an important role in chronic hepatitis B infection (CHB). It is known that zinc has immune-enhancing role on especially infectious diseases. This prospective open study reports the results of zinc and interferon-alpha-2a (IFN) therapy in children with chronic hepatitis B infection (CHB).

Methods: 21 naive, HBeAg positive children (9 female, mean age 10.2 ± 4.5) received IFN, subcutaneous 9 mega-units /m2 for six months and peroral zinc (7.5 mg/day for <10 years and 10 mg/day for >10 years) for 12 months. Serologic, viologic, and biochemical response ratios were evaluated at the end of therapy and 6 months after completion of therapy. Sustained response was defined as HBeAg negativity and HBV DNA <10,000 copies/mL at 6 months after treatment. Liver biopsy was performed at baseline and 6 months after completion of therapy. Histological response was defined as decrease in Knodell histological activity index (HAI) score by at least 2 points compared to baseline.

Results: Pretreatment mean ALT, log HBV DNA, HAI (Knodell) and serum zinc level were 126.1 ± 85.2 U/L, 8.6 ± 0.5 copy/mL, 8.4 ± 2.9 and 88.1 ± 10.7 mcg/dl, respectively. End of therapy ALT level and log HBV DNA were significantly lower than pretherapy (P = 0.002 and P = 0.001), while zinc level was not different. End of therapy normalization of ALT, HBV DNA <10 000 copies/mL, HBeAg negativity and HBsAg negativity were 35%, 5%, 15% and 5%, respectively. Six months after completion of therapy, normalization of ALT, HBV DNA <10 000 copies/mL and HBeAg negativity occurred in 26.3% of patients. HBsAg negativity was 5.3%. There was no difference between pre and posttreatment HAI score. Sustained and histologic response were 26.3% and 50% respectively.

Conclusion: As a first study investigating the effect of zinc and IFN therapy in children with CHB, sustained and histologic response rates were not different than previously reported monotherapy or combination therapies.

Disclosure of Interest: None declared.

PO-H-336

EFFICACY AND TOLERANCE OF ZINC IN THE TREATMENT OF WILSON DISEASE

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Objectives and Study: Transaldolase deficiency, an hereditary disorder of pentose phosphate metabolism, was reported in only few patients. Liver disease began at birth, with other symptoms and a variable evolution. We report here 8 other patients, in order to further understand this disease, and help for the diagnosis and follow-up.

Methods: The polyols were measured in urines. The diagnosis was made on elevated erythritol, arabitol, ribitol, sedoheptulose and sedoheptulose-7P, and confirmed with enzymatic or molecular analysis. In 3 children with a liver biopsy, the respiratory chain was also studied.

Results: These 8 patients are from 3 families, one Turkish (4 children), two African (Mauritania and Gabon). In the 1st family, anasarca developed in the 2nd pregnancy, that was interrupted; the foetus had liver fibrosis. The other children from two families (3 boys, 2 girls) presented a neonatal liver failure, with hepatoplenomegaly and hemolytic anemia. Some of them had also dysmorphic features, cutis laxa, hypertrichosis, urogenital malformations, heart malformations. In the 3rd family, both children (1 boy, 1 girl) presented a liver disease, with elevated transaminases and hepatoplenomegaly, in the first months of life. One of these 7 patients (1st family) died of liver failure at 5 months of age. His brother has a mild liver fibrosis, and a moderate renal failure at 10 years of age. The other children have cirrhosis, some of them with liver failure. A respiratory chain deficiency was found on 2/3 liver biopsies.

Conclusion: Transaldolase deficiency should be suspected in children with early fibrosing liver disease, associated with hematological abnormalities or other symptoms (urogenital, heart, skin). The diagnosis is easy with the urinary dosage of polyols. The lesions may result from the osmotic power and toxicity of accumulated sugars, and also from a secondary respiratory chain deficiency.

Disclosure of Interest: None declared.

PO-H-335

TRANSALDOLASE DEFICIENCY: A METABOLIC DISORDER WITH NEONATAL LIVER FAILURE AND CIRRHOSIS

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Objectives and Study: Transaldolase deficiency, an hereditary disorder of pentose phosphate metabolism, was reported in only few patients. Liver disease began at birth, with other symptoms and a variable evolution. We report here 8 other patients, in order to further understand this disease, and help for the diagnosis and follow-up.

Methods: Twenty six WD patients treated with zinc acetate were included in this multicenter study. Clinical
and biological data were collected via a questionnaire: age and symptoms at diagnosis of WD, age at beginning of zinc therapy, efficacy on biological parameters, side effects.

**Results:** At presentation, 23 patients (88%) were asymptomatic, mostly diagnosed during a familial work-up; 23 patients (88%) had liver disease, and one (4%) had neurological symptoms. A Kayser-Fleischer ring was present in 15% of cases. Diagnosis of WD was made at a median age of 8 years (0.8 – 16.1). According to the centre, the percentage of WD patients treated with zinc varied from 8.5 to 61.5%. D-penicillamin was associated in 18 patients (69%), trientine in 4 (15%), and 3 patients (11%) received the 3 drugs. Zinc therapy was initiated at the time of diagnosis in 12 patients (46%), as the only drug in 8 cases. Median age at the beginning of zinc therapy was 10.8 years (2.3–12.3) and 2.6 years after the diagnosis of WD. In children who received only zinc, it was started at the age of 7 years (2.3 – 11.1), 5 months after the diagnosis of WD.

Zinc was started at the recommended dosage in 11 children and progressively increased in 15 patients. A dosage above the recommended doses was used in 5/6 patients under 5 years of age, 10/19 in patients between 6 and 15 years, and 1/1 patient above 16 years. After the beginning of the treatment, the median ALT and urine copper values normalized in 5 months. Thereafter, urine copper values remained under 50 μg/24 h in all patients but one patient with a poor compliance. Epigastralgia (n = 4), vomiting and diarrhea (n = 1), leucopenia (n = 1) and transient increase of serum lipase (n = 1) were observed.

**Conclusion:** Although rarely used in the treatment of WD, zinc acetate effective and well tolerated. The guidelines regarding the dosage and the monitoring should be more closely followed.

**Disclosure of Interest:** None declared.

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**PO-H-337**

**QUALITY OF LIFE IN CHILDREN AFTER A PARTIAL EXTERNAL BILIARY DIVERSION FOR PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS OR ALAGILLE'S DISEASE**

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**Objectives and Study:** Progressive familial intrahepatic cholestasis (PFIC) and Alagille syndrome (AGS) are disorders which can present with progressive cholestasis. Main symptoms are jaundice and often intractable pruritus beginning in infancy. When medical treatment fails, partial external biliary diversion (PEBD) has evolved as symptomatic treatment for intractable pruritus. We aimed to determine quality of life (QOL) in children with PFIC/AGS who underwent PEBD as compared to healthy peers. We also examined the relationship between severity of pruritus and QOL.

**Methods:** Using a prospective PFIC/AGS database, we identified all patients who had undergone PEBD and were now between six and eighteen years of age. Patients and their parents were invited to participate. The age-appropriate Dutch-version of the PedsQL 4.0 survey and Infant Dermatitis scale were used to assess QOL resp. pruritus. Pearson’s correlation was computed for total QOL and severity of pruritus.

**Results:** Eight of 11 eligible patients (7 in 1; 4; median age 9.2 years, range 6.3–14.5; median follow-up 5.0 years, range 4.6–6.8) and their parents participated. Both self-reported and parent-proxy overall QOL, physical health and psychosocial summary scores (range 0–100) were decreased compared to healthy peers (difference ≥1SD, see table 1). Children’s median score for severity of pruritus (1 = none to 5 = severe) was 2.5, which was significantly strongly correlated to overall QOL (r = 0.74).

**Table:** Overall, physical and psychosocial mean sum scores (±SD).

<table>
<thead>
<tr>
<th></th>
<th>Patient self report</th>
<th>Parent proxy report</th>
<th>Healthy peer self report</th>
<th>Healthy peer parent proxy report</th>
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</thead>
<tbody>
<tr>
<td>Overall QOL</td>
<td>57 ± 10</td>
<td>51 ± 13</td>
<td>83 ± 14</td>
<td>88 ± 12</td>
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<tr>
<td>Physical</td>
<td>61 ± 8</td>
<td>54 ± 14</td>
<td>84 ± 17</td>
<td>89 ± 16</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>55 ± 12</td>
<td>48 ± 16</td>
<td>82 ± 16</td>
<td>87 ± 12</td>
</tr>
</tbody>
</table>

**Conclusion:** Pediatric PFIC/AGS patients with PEBD have a considerably reduced QOL when compared to healthy peers. QOL is closely related to the severity of pruritus. Whether there is an increase in QOL compared to pre-PEBD due to a reduction of pruritus needs to be further investigated.

**Disclosure of Interest:** None declared.

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**PO-H-338**

**ASPARTATE TRANSAMINASE TO PLATELET RATIO INDEX IS NOT CORRELATED WITH SEVERITY OF FIBROSIS OR WITH TRANSPLANT-FREE SURVIVAL IN CHILDREN WITH BILIARY ATRESIA**

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**Objectives and Study:** The Aspartate Transaminase to Platelet Ratio Index (APRI) is postulated as non-invasive, easily available surrogate marker for the severity of liver fibrosis in adults. We aimed to determine whether pre-Kasai APRI correlates with severity of fibrosis or transplant-free survival in children with biliary atresia.

**Methods:** All children with type III biliary atresia who underwent liver biopsy followed by Kasai hepatopancreatoduodenostomy examined the relationship between severity of pruritus and QOL.

**Discussion:** None declared.
in the UMC Groningen between 1987 and 2009 were included. Fibrosis was graded mild (portal fibrosis without septa), moderate (portal fibrosis with septa), severe (bridging fibrosis) or cirrhotic (nodular regeneration). APRI was computed as follows: \( \text{APRI} = \frac{\text{ASAT}}{\text{upper limit normal}} \times 100 / \text{Platelets} \), using values obtained just before hepatopancreatobectomy. Data are medians and range, unless stated otherwise.

**Results:** Complete data was available for 31 of 37 eligible patients (13 M, 18 F). Severity of fibrosis was mild (n=7), moderate (n=9), severe (n=9) or cirrhotic (n=6) in preoperative biopsies. Median preoperative APRI scores in these fibrosis groups were comparable: 1.3 (0.9–5.7), 1.4 (0.7–7.2), 1.4 (0.8–4.0) and 1.3 (0.0–4.8) resp. Median potential follow-up was 8.3 years (1.2–16.4). Median pre-operative APRI scores were similar in patients who were still alive with native liver [1.3 (0.7–5.1), n=10], and in patients who underwent liver transplantation [1.2(0.8–7.2), n=11] or who died [1.4 (0.6–3.6), n=10]. Median pre-Kasai APRI scores were also similar between patients who underwent OLT before the age of 6 months, between 6 months and 2 years and patients who survived more than 2 years without transplantation.

**Conclusion:** In this retrospective study in children with biliary atresia, APRI did not correlate with either preoperative severity of fibrosis, nor with transplant-free survival. It remains to be determined whether APRI could be useful for longitudinal monitoring of the development of fibrosis in individual pediatric patients with biliary atresia.

**Disclosure of Interest:** None declared.

**PO-H-340**

FEATURES OF AUTOIMMUNE LIVER DISEASE ASSOCIATED WITH CELIAC DISEASE IN CHILDREN: A SINGLE CENTER EXPERIENCE

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**Objectives and Study:** Celiac disease (CD) has been frequently reported to be associated with pediatric autoimmune liver disease (ALD). Aim of this study is to report on ALD associated with CD followed between 1995–2009 in our center. Methods: Retrospective analysis of medical records of 116 patients with ALD (75 with autoimmune hepatitis (AIH), 21 with autoimmune sclerosing cholangitis (ASC) and 20 with AIH/ASC overlap syndrome) and screened for CD at onset or during follow-up.

**Results:** Among these 116 patients, 16 (13.7 %; 14 female; mean age at presentation 54 months, range 6–126) had CD. At onset, 8 patients were asymptomatic, 4 had clinical malabsorption and 4 an acute hepatitis. Aminotransferase activity was elevated in all (ALT mean 24 x N, range 2–65, serum IgG in 9 and liver-related autoantibodies were present in 12 (ANA/SMA in 9 e LKM in 3). Percutaneous liver biopsy showed in all interface hepatitis, lobular necrosis and variable fibrosis (F1–F3). Inflammatory bile duct damage were present in 5, all with ANA/SMA serum reactivity. All patients were put on gluten free diet (GFD) and treated with prednisone and azathioprine except for a patient with IDDMM treated with cyclosporin. Ursodeoxycholic acid was added in the 5 cases with bile duct lesions. Mean total follow-up is 73 months (range 7–165) and all patient are in clinical and biochemical remission. Immunosuppressive treatment could be stopped in 6 patients (37.5%) from a mean period of 65 months (range 2–150) in comparison to 10 of 100 patients with ALD (10%); p = <0.01 chi square test.

**Conclusion:** ALD in children is confirmed to be strictly associated with CD. Normal IgG values and seronegative autoantibody pattern do not exclude diagnosis of ALD. Elevation of aminotransferase activity lasting more than 3 months after starting of GFD, justifies a diagnostic work up for ALD. All patients with ALD and CD responded to immunosuppressive therapy and to GFD with an high number of patients who could stop safely the treatment compared to patient with ALD without CD suggesting a possible better long term prognosis and a possible long term adjuvant effect of GFD.

**Disclosure of Interest:** None declared.
4 required 65–100% PN. Mean duration of PN to liver biopsy was 8 mo. (SD ± 9.0, range 1–24). Liver histology included cholestasis in 7 biopsies, portal fibrosis in 5, bridging fibrosis in 4, bile duct proliferation in 3, steatosis in 2, cirrhosis in 2, portal inflammation in 2. ALK and TB correlated with the liver biopsy changes specifically cholestasis. ALK, TB, albumin and INR showed significant improvement between the termination of PN and end of study. ALT did not correlate with liver histology or weaning of PN and fluctuated during the entire study period especially during intercurrent illnesses. The laboratory data (mean ± SD) are given in the table below:

**Table:** Laboratory data during study

<table>
<thead>
<tr>
<th></th>
<th>ALT (U/L)</th>
<th>TB (mg/dL)</th>
<th>ALK (U/L)</th>
<th>Albumin (mg/dL)</th>
<th>INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>83.6 ± 44</td>
<td>8.8 ± 7</td>
<td>484 ± 283</td>
<td>2.8 ± 0.6</td>
<td>1.3 ± 0.2</td>
</tr>
<tr>
<td>Biopsy</td>
<td>97.8 ± 59</td>
<td>3.5 ± 3.6</td>
<td>471 ± 87</td>
<td>3.0 ± 0.5</td>
<td>1.4 ± 0.4</td>
</tr>
<tr>
<td>End of PN</td>
<td>101.5 ± 54</td>
<td>1.3 ± 2</td>
<td>491 ± 232</td>
<td>3.1 ± 0.6</td>
<td></td>
</tr>
<tr>
<td>End of study</td>
<td>81.4 ± 32</td>
<td>0.3 ± 0.3</td>
<td>340 ± 154</td>
<td>3.6 ± 0.5</td>
<td>1.1 ± 0.2</td>
</tr>
</tbody>
</table>

**Conclusion:** Significant liver disease with diverse histological findings including cirrhosis is associated with IFALD. Serum ALT is not a good marker for liver histology. Aggressive medical management and a vigorous effort to reduce or wean off the use of PN will prevent advancement of IFALD to a great extent.

**Disclosure of Interest:** None declared.

**PO-H-341**

**HEPATITIS B VIRUS GENOTYPES IN ITALY:**

**EPIDEMIOLOGY IN A PEDIATRIC POPULATION**

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**Objectives and Study:** A genetic classification of Hepatitis B Virus (HBV) has identified worldwide eight genotypes, from A through H. The differences are based on an intergroup divergence of 8% or more in the complete nucleotide sequence. The distribution of HBV genotypes varies geographically. Genotypes A and D occur frequently in Africa, Europe, and India, while genotypes B and C are prevalent in Asia and Oceania. Genotype E is restricted to West Africa, and genotype F is found in Central and South America. The distribution of genotypes G and H is less clear. Different HBV genotypes appear to be associated with distinct virological characteristics; besides, a relationship between HBV genotypes, response to antiviral therapy and clinical outcome has been described. Since the introduction in Italy of universal HBV-vaccination in 1991, HBV infection has become virtually absent in native children; on the other side, recent migrations and international adoptions have increased the number of infected children coming to Italy from foreign countries, where the infection is endemic and the vaccination is not available.

The objective of our study was to assess the distribution of HBV genotypes in 27 children of different ethnic origins, living in Italy.

**Methods:** 27 HBsAg-positive children (median age: 10.6 yrs, range: 3–18 yrs, male/female ratio: 19/8) followed in the period 1992–2009 at the Pediatric Liver Unit of Hospital Policlinico in Milan were included. HBV genotypes were determined by INNO-LIPA.

**Results:** Genotype distribution was as follows: genotype A: 6 patients (4 Africa, 1 Italy; 1 East-Europe); genotype B: 1 patient (Asia); genotype C: 2 patients (Asia); genotype D: 17 patients (7 East Europe, 4 North-Africa, 3 India, 3 Asia); genotype C+D: 1 patient (Asia).

**Conclusion:** The distribution of HBV genotypes in our pediatric population shows a strong correlation with the prevalence of HBV genotypes reported in the native countries for adult patients. About one third of the patients showed a non-D genotype, characterized by different natural history and response to antiviral treatment; as in Italy, at the moment, the great majority of HBV adult carriers shows the genotype D, in the next years, when these children with non-D genotypes grow up, heterogeneous clinical patterns of infection are predictable.

**Disclosure of Interest:** None declared.

**PO-H-342**

**PREVELANCE OF HEPATITIS D CO-ENFECTION IN CHILDREN WITH HEPATITIS B INFECTION:**

**CROSS-SECTIONAL ANALYSES FROM EGE REGION**

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**Objectives and Study:** Effective hepatitis B virus (HBV) control has warranted a decline in HBV prevalence over the world with a relevant reduction in HBV associated delta hepatitis. However, despite the dramatic decline in HDV infection rate and the hope for vanishing the disease, no further decrease was recorded after 2000. This cross-sectional study aims to search: I-The prevalence of HDV co-infection in children with HBV infection in Ege region II-The influence of national infant HBV vaccination on HDV co-infection rate III-The impact of HDV co-infection on prognosis of liver disease.

**Methods:** Serological markers of hepatitis B and D virus infection were determined by ELISA in patients with chronic hepatitis and cirrhosis. Delta co-infection rate was evaluated in two groups, children born before and after national neonatal mass vaccination has started (before and after 2000). Viral load, serum ALT and histological grade were evaluated in co-infected cases.
Results: Overall hepatitis delta virus infection rate was 1.6% (3/179). Neither of the chronic HBV (n:149) patients had HDV co-infection. All three children with delta hepatitis had cirrhosis and delta virus prevalence among cirrhosis was 10% (3/30). Among children born before neonatal HBV vaccination program, HDV prevalence was 1.2(2/167). Annual admission of newly diagnosed pediatric HBV infection to the hospital declined from 10.5 patients per year to 1.2 patients per year before and after 2000, respectively, and delta hepatitis was detected in one patient (1/12) born after millennium. Hepatitis e antibody was detected in two patients with delta co-infection (11 and 6 years old) and all mothers of delta hepatitis cases were chronically HBV infected.

Conclusion: Delta hepatitis is rare among HBV infected children in Ege region of Turkey. Besides the national vaccination program, delta hepatitis is not vanishing and it has a grave prognosis evolving to early cirrhosis.

Disclosure of Interest: None declared.

PO-H-344

ACUTE HEPATOTOXICITY CAUSED BY ORAL YELLOW PHOSPHORUS INTAKE FROM TOY FIREWORKS: A REPORT OF THREE PEDIATRIC CASES

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Objectives and Study: The aim of this study is to draw attention to the toxicity caused by yellow phosphorus, an extremely hepatotoxic agent that is found in toy fireworks made with gunpowder.

Methods: Case 1: A 5.5-year-old girl was admitted with icterus, ascites and lethargy. Laboratory tests revealed ALT 1875 IU/L, AST 2956 IU/L, total bilirubin 24 mg/dL, direct bilirubin 21 mg/dL, INR 2.3 and hyperammonemia. EEG data was consistent with stage two hepatic encephalopathy and no acute hepatic failure etiology was found. The patient underwent a living related donor liver transplantation on her 14th day after the admission. Histopathology of the explant liver demonstrated massive hepatic necrosis and hepatosteatosis. Toy fireworks ingestion on the 4th post-transplant day has been reported in the patient history. The patient is now healthy in her first year after the transplantation.

Case 2: A 7-year-old girl was admitted with icterus and lethargy on the third day of the yellow phosphorus containing toy fireworks ingestion. Laboratory tests disclosed ALT 1150 IU/L, AST 1747 IU/L, total and direct bilirubin 19 and 13.9 mg/dL, INR 3.8, hyperammonemia. EEG data was consistent with stage two hepatic encephalopathy. On the sixth day of the follow-up, liver transplantation from a living related donor was performed. Histopathology of the explant liver revealed confluent necrosis and hepatosteatosis. The patient is now well in her second year after the transplantation.

Case 3: A 4-year-old boy was admitted with vomiting, somnolence, icterus and hepatomegaly two days after the toy fireworks ingestion. Laboratory tests demonstrated ALT 69 IU/L, AST 88 IU/L, total and direct bilirubin 4.1 and 2.7 mg/dL, INR 3.8, hyperammonemia. EEG data was consistent with stage one hepatic encephalopathy. Under supportive therapy, his clinical and laboratory findings have completely ameliorated and he was discharged from the hospital 14 days after his admission.

Results: Yellow phosphorus is extremely toxic. An ingestion of 1 mg/kg dose may lead to a fatal poisoning. After a few hours from ingestion, from 69% to 73% of total ingested dose concentrates in the liver, where the most severe complications develop. Acute fulminant hepatic failure and
mortality rates have been reported as 27% and 23–73%, respectively. Currently, there is no antidote available and cases with acute hepatic failure unresponsive to medical treatment require liver transplantation.

**Conclusion:** Since it is extremely hepatotoxic and lethal when ingested, indiscriminate sale of toy fireworks to children must be prevented in our country.

**Disclosure of Interest:** None declared.

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**PO-H-345**

**HEPATIC FOCAL NODULAR HYPERPLASIA IN CHILDREN- IS THERE A NEED FOR FOLLOW-UP ?**

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**Objectives and Study:** Focal nodular hyperplasia (FNH) of the liver is a rare benign tumour of uncertain etiology. Diagnostic methods and management strategies have not been standardised and the natural history is unclear. We describe the clinical and radiological characteristics, associated conditions and outcome of children with focal nodular hyperplasia.

**Methods:** A retrospective analyses of 14 children diagnosed with FNH in a single centre between Aug 1996 to March 2009 was performed. Data including clinical characteristics, diagnostic imaging, treatment, follow-up and outcome was recorded.

**Results:** There were 9 females (M:F = 1:1.8) and mean age at diagnosis was 10.7 yrs (range 6–16 yrs). FNH was incidentally diagnosed in 9/14 (64%). Coexisting medical conditions included previous malignancy(n = 3), McCune Albright Syndrome(n = 2),portal vein malformation(n = 2), Alagille’s syndrome(n = 1) and ovarian cyst(n = 2) while one patient was on oral contraceptives. Abdominal pain was the commonest presenting symptom in the symptomatic group(n = 3/5). The diagnosis was based on radiological investigations including MRI in 10/14 with histological confirmation in 7/14. Typical FNH radiological lesions (solitary, less than 5 cm) were seen in only 4/14. Multiple FNH lesions were noted in four cases while lesion size greater than 5 cm was present in eight patients. Mean follow-up period was 32.7 months (range 6–108 months). Three underwent surgical resection due to large tumour size and one had recurrence of FNH. The remaining eleven children were conservatively managed with close clinical and radiographic monitoring. Serum alpha-fetoprotein levels were normal in all patients at diagnosis and follow-up. Progressive increase in lesion size was noted in five with distortion of vascular structures but no complications. Size progression was more likely in those with atypical lesions on imaging.

**Conclusion:** FNH is a benign tumour in childhood which rarely may have complications including progression to malignancy. Management should be conservative with close follow-up indicated in patients with atypical radiologic findings. Surgical resection is rarely indicated except for very large tumours as recurrence may occur.

**Disclosure of Interest:** None declared.
Conclusion: In the first year after its placement TIPSS arrested progression of PH and its consequences on spleen and oesophageal varices. If this is confirmed by further follow up pre-emptive TIPSS can be promising if timed early, at the first signs of progressive LF, before splenic enlargement and oesophageal varices are established.

Disclosure of Interest: Boelaert Hilde, None declared.
De Bruyne Paulien, None declared.
Defreyne Luc, None declared.
Robberecht Eddy, None declared.
Voet Luc, None declared.

PO-H-347

LONG-TERM IMMUNOGENICITY OF HEPATITIS B VACCINATION IN EGYPTIAN CHILDREN

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Objectives and Study: The aim of the work is to detect the long-term immunogenicity of the vaccine in children after five and ten years of vaccination, also to test for anamnestic reaction to determine whether or not a booster dose is needed.

Methods: This study included 200 healthy children. Before being included in the study children were screened for the presence of HBV infection. The children were divided into two groups according to age (each group contains 100 children). Their data are included. Group ‘A’ included 53 males and 47 females, around 6 years old, all children were vaccinated 5 years ago. Group ‘B’ included 27 males and 73 females, around 11 years old. All children vaccinated 10years ago. HBsAb titre was tested in their blood, booster dose of the vaccine was given to children whose HBsAb was <10 mIU/ml, then one and half months later, another blood sample from each of them was retested for HBsAb to evaluate the response to this booster dose of vaccine.

Results: When testing the serum of the children in both groups (A&B) for HBsAb and its titre, both groups have a wide range concerning the level of HBsAb (2–1000) mIU/ml. Our data proves the decline of antibodies titre with time, and there was significant difference between the two groups in the level of HBsAb. There was no significant difference in anti-HBs between girls and boys in group A in contrary to group B. In group A, from the nineteen children who needed a booster vaccination dose, 14 were vaccinated. Serum sample was taken from 10 children after one and half month from vaccination, out of these 10, 9 (90%) responded by increased level of HBs antibodies and only one child did not respond, Six (66.6%) of the nine showed an adequate response. In group B, fifty two children in this group had antibody titre <10, forty eight were vaccinated. After one and half month, 34 children were tested again for HBsAb. Two out of the thirty four children did not respond (5.8%) and 32 (94.2%) responded by an increase in the antibody titre. Of those responded, 19 had adequate response (HBsAb ≥ 100) and 13 had hypo-response (HBsAb lies between 10–100). Therefore, 80% of the boys who were retested for HBsAb after vaccination responded adequately while 51.7% of the corresponding girls responded adequately. There was no significant difference in antibodies titre responding to the testing dose with p value = 0.814.

Conclusion: Hepatitis B vaccine is an effective and successful way for preventing HBV infection. There is persistence of protective antibodies after primary vaccination in most of children with decline of the levels over time. Even so, no need for booster dose at least for 10 years after vaccination.

Disclosure of Interest: None declared.

PO-H-348

HEPATOPULMONARY SYNDROME IN CHILDREN WITH CIRRHOTIC AND NON-CIRRHOTIC PORTAL HYPERTENSION: A SINGLE CENTER EXPERIENCE

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Objectives and Study: Hepatopulmonary syndrome (HPS) is defined as an arterial oxygenation defect induced by intrapulmonary vascular dilatation (IPVD) associated with hepatic disease. The prevalence and clinical characteristics of HPS in portal hypertensive children is not well characterized. The aim of this study was to investigate the prevalence and clinical characteristics of HPS in 40 portal hypertensive children.

Methods: We studied 40 children (11 girls and 29 boys; mean age; 111 ± 52 months; range; 24–216 months) with portal hypertension (24 cirrhotic, 16 non-cirrhotic) for the presence of HPS using pulse oximetry, blood gas analysis, contrast enhanced echocardiography (CEE) and/or Tc99m macroalbumin aggregated (MAA) scintigraphy. Clinical and laboratory characteristics of patients were recorded. HPS was considered to be present in a patient with elevated arterial-alveolar oxygen gradient (PAAO2 ≥15mmHg) and positive CEE and/or scintigraphy.

Results: Elevated arterial-alveolar oxygen gradient was detected in 7 of the 24 patients with cirrhotic and 2 of the 16 patients with non-cirrhotic portal hypertension. Six patients in cirrhotic group and one patient in non-cirrhotic group showed IPVD with CEE. Intrapulmonary shunt in Tc99m-MAA was shown in one patient besides CEE in CPH group. Only four patients in cirrhotic group fulfilled the HPS criteria. The cirrhotic patients without IPVD had significantly better hepatic function and lower PELD scores.

Conclusion: HPS occurs especially in cirrhotic portal hypertensive patients with severe hepatic dysfunction.

Disclosure of Interest: None declared.
PO-H-349

SUCCESSFUL TREATMENT OF DIFFUSE HEPATIC INFANTILE HAEMANGIOENDOTELIOMA WITH PROPRANOLOL

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Objectives and Study: Infantile haemangioendothelioma is the most common tumor of the liver in the first year of life. Although the clinical course is often self-limiting, multifocal and diffuse variants could be life-threatening because of high-output cardiac failure due to arteriovenous and portovenous shunting. Current medical treatment consists of high dose prednisone, interferon and/or vincristine. Efficacy of medical treatment is poor, leading often to consider more aggressive approaches. Propranolol has recently been reported to be effective and well tolerated in newborns with severe cutaneous infantile hemangioma.

Methods: We treated with propranolol an infant with diffuse infantile haemangioendothelioma, pulmonary valve stenosis and incipient high-flow cardiac overload.

Results: A 4-month-old girl with a diagnosis at birth of pulmonary valve stenosis with transvalvular gradient of 30 mmHg, presented with hepatomegaly and a previous history of prolonged neonatal jaundice and thrombocytopenia. Several cutaneous hemangiomas were noted. Ultrasonography and Magnetic Resonance revealed diffuse vascular lesions with a minimal proportion of normal parenchyma. Cardiologic assessment revealed an increased transvalvular gradient to 63 mmHg, enlargement of all cardiac chambers with mild mitral and tricuspidal insufficiency. The baby was fidgety and poorly feeding. Treatment with propranolol was thus decided and administered at initial dose of 1 mg/kg and rapidly increased at 2 mg/kg. Discoloration and reduction in size of cutaneous lesions was noted within two weeks, the baby progressively improved his feeding and behaviour. Pulmonary transvalvular gradient reduced to 48 mmHg after 4 weeks of therapy and to 30 mmHg at age 7 months. At that time a Magnetic Resonance of the liver revealed dramatic reduction of number and size of vascular lesions. No adverse effects of propranolol therapy were recorded.

Conclusion: We first treated a 4-months infant with a life-threatening hepatic haemangioendothelioma with propranolol obtaining within 3 months dramatic improvement of hepatic imaging and regression of cardiac overload. If these results will be confirmed in other patients, treatment with propranolol could change the natural history of this potential severe disease of the newborn.

Disclosure of Interest: None declared.

PO-H-350

PEGYLATED INTERFERON AND RIBAVIRIN TREATMENT FOR CHILDREN WITH HEPATITIS C.

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Objectives and Study: In childhood, hepatitis C virus (HCV) infection is relatively uncommon, occurring mostly in high-risk patients, primarily those affected by hematologic diseases and through maternal transmission which is the major source of the infection in the pediatric age group. Treatment strategies have evolved over the years and a combination therapy with ribavirin and Pegylated interferon (IFN) alfa is currently the treatment of choice for both children and adults. There are very few studies reporting the efficacy of this combination treatment in children. We therefore aimed to review our experience with this combination therapy in children.

Methods: We retrospectively reviewed charts of children who had been treated with a combination therapy with ribavirin and Pegylated IFN alfa for chronic hepatitis C. Patients were treated with either SC Pegylated interferon alpha 2A (6 patients) once a week (180mcgxBSA/1.73m2) and ribavirine 15 mg/kg/day BID or SC Pegylated interferon alpha 2B (7 patients) once a week (1.5mcg/kg) and ribavirine 15 mg/kg/day BID. Treatment was for 24 weeks for patients with genotype 2 and 3 and 48 weeks for patients with genotype 1.

Results: Complete information was available for 13 patients, 9 males and 4 females, ages 3–16 years (mean 12.5±4 years). The source of infection was blood transfusions in 5 patients, vertical transmission in 4 and one had accidental infected needle sting. The source was unknown for 3 patients. Nine patients had viral genotype 1 (1B in 7, 1A in 1, unknown in one), one patient had genotype 2 and three had genotype 3A. Viral load was between 134,000–3,440,000IU/ml. ALT levels before treatment were between 41–142IU/L (mean 76±32). Adverse events were common (85%) and were mainly constitutional and tended to improve with time. None of the patients had severe bone marrow suppression. Viral load was negative after 12 weeks for 11 patients (85%). Sustained viral response (SVR) 6 months after end of therapy was achieved for 9 patients (69%). All of them had negative viral load after 12 weeks. Therapy was successful in 5/9 (55%) patients with genotype 1, and in all 4 patients (100%) with genotype 2 and 3. No differences were noted between the two drugs.

Conclusion: According to our series, combination therapy for hepatitis C in children is successful at least as in adults. Although adverse events were common, the treatment is usually well tolerated.

Disclosure of Interest: None declared.

PO-H-351

THE NON-INVASIVE 13C METHACETIN BREATH TEST DIFFERENTIATES BILIARY ATRESIA FROM OTHER CAUSES OF NEONATAL CHOLESTASIS
Objectives and Study: Extrahepatic biliary atresia (EHBA), an inflammatory sclerosing cholangiopathy, is the leading indication for liver transplantation in children. Distinguishing biliary atresia from other causes of prolonged neonatal cholestasis (NC) may be challenging. The non-invasive BreathID® 13C-Methacetin breath test (MBT, Exalenz Ltd.) is a novel method to determine liver function in acute and chronic liver disease. 13C Methacetin is metabolized uniquely by the liver and 13CO2 is measured in the exhaled breath. Because breath collection and analysis is continuous and passive through a nasal canula, compliance is not needed. Our aim was to assess the ability of the 13C-MBT to differentiate EHBA from other causes of neonatal cholestasis.

Methods: MBT was preformed in infants with NC before any invasive procedure. Percent dose recovered (PDR) per hour peak and time to peak were correlated with age, bilirubin levels, transaminases, degree of fibrosis and Pediatric End-Stage liver Disease (PELD) scores.

Results: Five of the 10 infants with NC studied were eventually diagnosed as EHBA. GGTP levels were significantly higher in infants with EHBA (809 ± 357 vs. 218 ± 187). No difference in bilirubin levels was measured. The mean age of the infants at the time of testing was 49 ± 11 days. MBT showed that infants with EHBA did not reach the PDR peak value during the test time of one hour, while all infants with neonatal hepatitis(NH) reached the peak after 43 ± 5 minutes (P < 0.006). Time to PDR peak correlated significantly with GGTP levels (r = 0.78, 95% CI: 0.66 – 0.97) (P = 0.0388). Degree of fibrosis, quantified by modified Ishak score (values 1–6), significantly correlated with time to PDR peak (r = 0.91, 95% CI: 0.35 – 0.99, P = 0.0131). Follow-up tests after KP showed a correlation between MBT values and clinical outcome. In four infants with EHBA, PDR peak became similar to infants with NH, which correlated with decreased bilirubin levels. In one patient, bilirubin levels remained elevated with no change in MBT results. This infant was listed for liver transplant at the age of 5 months.

Table: Response to treatment and genotypes

<table>
<thead>
<tr>
<th>Treatment Group (n)</th>
<th>Genotype A (n = 19)</th>
<th>Genotype B (n = 9)</th>
<th>Genotype D (n = 37)</th>
<th>Previous treatment</th>
<th>Median (range) follow up(months)</th>
</tr>
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<tbody>
<tr>
<td>Interferon (20)</td>
<td>50</td>
<td>0</td>
<td>36</td>
<td>None</td>
<td>74 (15–127)</td>
</tr>
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<td>67</td>
<td>50</td>
<td>70</td>
<td>None</td>
<td>74 (15–127)</td>
</tr>
<tr>
<td>Lamivudine (2)</td>
<td>33</td>
<td>50</td>
<td>58</td>
<td>2-Int; 1-Pred/Int</td>
<td>93 (82–105)</td>
</tr>
<tr>
<td>Adefovir (7)</td>
<td>33</td>
<td>0</td>
<td>25</td>
<td>1-Lamivudine</td>
<td>18 (3–37)</td>
</tr>
</tbody>
</table>

Table: Response to treatment and genotypes

Conclusion: This pilot study shows that MBT can differentiate between EHBA and other causes of neonatal cholestasis by time to peak of Methacetin metabolism. Furthermore, in children with established EHBA MBT correlated with clinical and laboratory assessment of liver disease and thus may serve as a non-invasive tool for follow-up of EHBA. Larger scale studies should be conducted to confirm our initial observations.

Disclosure of Interest: Y. Ilan, Medical Director, Exalenz.

PO-H-352

DOES GENOTYPE PREDICT RESPONSE TO TREATMENT IN CHILDREN PERINATALLY INFECTED WITH HEPATITIS B

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Objectives and Study: Hepatitis B genotype is now thought to correlate with outcome and response to treatment. We have compared viral genotype with treatment response in children infected perinatally with hepatitis B who had been treated with either oral antiviral drugs (Lamivudine or Adefovir) or subcutaneous Interferon (IFN) with and without Prednisolone priming (Pred/IFN).

Methods: All children who took part in clinical trials in this unit since 1990 were included. The hepatitis B genotypes were determined using a commercial line probe assay (InnoLipa), which was validated against direct sequencing.

Results: 62 children were included, some of whom had more than one course of therapy: 60 children had single genotypes, two children had mixed genotypes. The genotype results agreed with the geographical origin of the families of the children, with the majority of South Asian children having genotype D and European and Afro-Caribbean children having genotype A. See Table 1. Overall response to treatment was better in children with genotypes A 9/19 (47%) and D 19/37 (51%), compared to those with B and C for all forms of treatment. No response was observed in children with Genotype C. Although the response to Interferon alone was better in children with genotype A (50%) compared to D (36%), prednisolone priming improved the response in both genotypes to 67%
& 70% respectively. The response to oral anti viral therapy was (3/9) 33% for genotype A and (8/16) 50% for genotype D.

**Conclusion:** Overall response to treatment was similar in children with genotypes A & D but was significantly improved following therapy with Pred/IFN. Children with genotype A did less well on lamivudine compared to genotype D.

Assessment of genotype in children pre treatment may provide a guide to potential response and improve information and choice for families. If interferon therapy is being considered then prednisolone pre-treatment should be reconsidered as an adjunct to interferon treatment.

**Disclosure of Interest:** None declared.

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**PO-H-353**

**ALPHA-FETO PROTEIN IN NEONATAL CHOLESTASIS**


**Objectives and Study:** Alpha-feto protein (AFP) is an oncofetal glycoprotein that is normally present in significant amounts in the serum of fetus. AFP level is known to increase in hepatoma, malign germ cell tumors in childhood. It may also be elevated in acute/chronic hepatitis, neonatal hepatitis, biliary atresia and some hereditary disorders. The aim of this study was to determine AFP levels of infants presenting with different etiologies of neonatal cholestasis.

**Methods:** Patients were evaluated with appropriate laboratory tests for differential diagnosis as well as serum AFP levels.

**Results:** Fifty-three infants with neonatal cholestasis with a mean age of 83.4 ± 63.9 days were enrolled. Causes of neonatal cholestasis are shown at Table 1. The mean AFP level of all patients was 46969.9 ± 78924.8 IU/ml. Twenty one patients had AFP values higher than normal range according to the age. There was no difference between groups in terms of ratio of patients with elevated AFP level. No correlation was found between AFP levels and ALT, GGT, bilirubine, albumine and INR levels.

**Conclusion:** AFP levels were elevated in 39.6% of patients. Although statistically insignificant the ratio of patients with elevated AFP levels seems to be higher in metabolic diseases and idiopathic neonatal hepatitis. Although the predictive role of AFP in diseases of neonatal cholestasis is uncertain, for patients with elevated levels of AFP metabolic disease and idiopathic neonatal cholestasis should be kept in mind.

**Disclosure of Interest:** None declared.

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**PO-H-354**

**FEASIBILITY OF ROUX-EN-Y LOOP ENTEROSCOPY IN CHILDREN WITH LIVER DISEASE**

www.jpgn.org

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**Objectives and Study:** Postoperative problems in roux-en-Y (RNY) loops including bleeding are problematic to diagnose and treat. In adults, diagnostic and therapeutic procedures in the RNY loop have been reported using balloon enteroscopes (1). We report the first paediatric case of RNY loop examination using a single balloon enteroscope.

**Methods:** A 13 year old boy weighing 35 kg presented with severe intermittent gastrointestinal bleeding after portoenterostomy (PE) for biliary atresia aged 15 days. Clinical examination and ultrasound examination confirmed portal hypertension. Oesophago Gastro Duodenoscopy revealed grade II oesophageal varices without evidence of bleeding or other abnormality. Capsule endoscopy and colonoscopy to terminal ileum were also normal. Total enteroscopy including RNY loop enteroscopy was performed using a single balloon Olympus enteroscope (SIF type Q260) and outer tube ST-SB1 (Olympus) by the ante-grade approach under general anaesthesia. Total length of the scope was 200 cm and inner diameter was 2.8 mm in size. Outer tube’s length was 140 cm and the diameter was 13.2 mm.

**Results:** Small bowel was examined as far as the caecum in 70 minutes. The RNY then was identified at 50 cm from the duodenum-jejunal flexure; the surgical anastomotic site and the portal enterostomy surface were examined. Good biliary drainage was observed but no bleeding point was identified. No complications or difficulties were encountered during this procedure.

**Conclusion:** Single balloon enteroscopy can be used safely and successfully after biliary atresia surgery in children to examine the entire small bowel including the previously inaccessible RNY loop.

**Reference:**


**Disclosure of Interest:** None declared.

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**PO-H-355**

**LIVER TRANSPLANTATION FOR PROPIONIC ACIDAEemia IN CHILDREN**

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**Objectives and Study:** Propionic academia (PA) is a rare inherited metabolic disorder, despite improvements in conventional management, long-term outcome for these
PO-H-356

SYMMETRIC DIMETHYLARGININE (SDMA) AS A PLASMA BIOMARKER OF RENAL FUNCTION IN CHILDREN WITH LIVER DISEASE

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Objectives and Study: SDMA is formed during post translational modification of nuclear proteins and released following proteolysis. SDMA is considered an end-product of metabolism and relatively physiologically inert. The meta-analysis reporting plasma SDMA as an endogenous biomarker of glomerular filtration rate (GFR) (Kielstein et al, Nephrol Dial Transplant, 2006) suggested a potential alternative for monitoring GFR in children with liver disease. Plasma creatinine is particularly unreliable in liver disease because of reduced synthesis and bilirubin interference and formal GFR measurement (51Cr-EDTA clearance) is time consuming and susceptible to errors. Cystatin C is established as a marker of GFR in children with liver disease.

Methods: Plasma SDMA was measured by fragmentation specific stable isotope dilution liquid chromatography electrospray tandem mass spectrometry (MSMS) (API4000, Applied Biosystems, Warrington, UK). 62 children (30 male), previously reported by Samyn et al 2005, who had undergone liver transplantation (LT) at a single centre between 1989 and 2000 were included. Median (range) age at LT was 3.1 years (0.6–18.7 years); the commonest indication for LT was biliary atresia (47%). Previously described measurements, on 79 occasions, on this cohort, included 51Cr-EDTA plasma clearance and plasma cystatin C. Further plasma samples, stored at −80°C were available for SDMA analysis. A control group of 15 normal children (8 male), median age 15 years (6.5–18.5 years) was used.

Results: Plasma SDMA was significantly higher in children with liver disease, 0.41 micromol/l (0.32–0.60) vs 0.58 (0.44–1.12) (P < 0.001). There were highly significant correlations between SDMA and both 51Cr-EDTA GFR, r² = 0.65 (P < 0.001), and cystatin C, r² = 0.60 (P < 0.001).

Conclusion: The capability to measure plasma and/or dried blood spot SDMA by MSMS emphasises the requirement for formal validation studies. SDMA is a potential plasma biomarker of GFR and may prove useful in monitoring renal function in children with liver disease.

Reference:

Disclosure of Interest: None declared.

PO-H-357


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Objectives and Study: This study objective was to determine the outcomes of Croatian children with biliary atresia.

Methods: Health records of infants born in Croatia between January 1, 1992 and December 31, 2006 who were diagnosed with biliary atresia and treated at a single university center
PO-H-358

THE METABOLIC PREDICTION MODEL OF NONALCOHOLIC FATTY LIVER DISEASE IN CHILDHOOD
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Objectives and Study: Several metabolic disturbances are regarded to be associated with non-alcoholic fatty liver disease in children, still different factors were indicated in different studies. The purpose of this study was to evaluate the role of numerous metabolic factors in the prediction of non-alcoholic fatty liver disease (NAFLD) in children using data mining approach.

Methods: The study included 195 children: 75 children with NAFLD aged 12.05 ± 3.6 compared to 120 healthy children aged 11.2 ± 3.9. Children with simple obesity aged 15.8 ± 1.7 and 24 healthy controls aged 14.9 ± 3.6. NAFLD was diagnosed based on ultrasound and ALT increase (both criteria fulfilled). Twenty-three lab parameters describing lipid metabolism, insulin resistance, oxidative stress and adipocytokines were included in the data mining and statistical analyses.

Results: Besides serum concentrations of TG, oxyLDL, ApoE, Lp(a), LCAT, GSH, leptin and leptin receptor no other parameters appeared to be significant to construct prediction model of NAFLD. The model consisted of two rules. The first one is described by concentrations of TG (>82 mg/dl), concentrations of GSH (>598 µmol/l) and concentration of lp(a) (<17 mg/dl) which were associated with NAFLD. The second rule included concentration of GSH (between 519 – 736 µmol/l) and concentration of leptin (<13.6 pg/ml). The model was able to predict nearly 80% of all instances. Positive Predictive Value (PPV) was 95.5% while Negative Prediction Value (NPV) was 100%. Specificity and sensitivity was equal to 95.3% and 100% respectively.

Conclusion: The results obtained indicate the role of selected parameters of lipid metabolism, glutathione and leptin in prediction of NAFLD. These disturbances seem to be very specific for fatty liver disease.

Disclosure of Interest: None declared.

PO-H-359

ASSOCIATION OF PLASMA PHOSPHOLIPID FATTY ACID CONCENTRATIONS WITH NON-ALCOHOLIC FATTY LIVER DISEASE
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Objectives and Study: Non-alcoholic fatty liver disease is caused by obesity and disturbed energy balance. Still, it was postulated that it is not only intake of energy and quantity of fat but also the fat quality in the diet which may play the role by influencing fatty acid metabolism.

The purpose of this study was to evaluate the association of fatty acid profile with non-alcoholic fatty liver disease (NAFLD).

Methods: The study included 195 children: 75 children with NAFLD aged 12.05 ± 3.6 compared to 120 healthy children aged 14.2 ± 3.1 (59 obese children and 71 lean children). NAFLD was diagnosed based on ultrasound and ALT increase (both criteria fulfilled). Plasma phospholipid concentrations of fatty acids were measured with gas chromatography and expressed as wt/wt% of all fatty acids analyzed in all subjects studied. Forty-nine parameters (concentrations of 37 fatty acids and variables calculated from the source data) were included in the data mining and statistical analyses of associations with NAFLD compared to healthy controls.

Results: Besides total n-6 polyunsaturated fatty acids (PUFA) other parameters poorly predicted the diagnosis of NAFLD. Simple predictive model with cutoff point of total n-6 PUFA equal to 22.195 was found. NAFLD was associated with decreased total n-6 fatty acids. The model was able to correctly predict nearly 86% of all instances. The Positive Predictive Value (PPV) was 88.3% while Negative...
PO-H-360  

THERAPEUTIC PLASMA EXCHANGE IN CHILDREN WITH LIVER FAILURE: SAFETY & EFFICACY

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Objectives and Study: Therapeutic plasma exchange (TPE) is often performed in children with acute liver failure (ALF). However, there is no data about the effect of TPE on laboratory parameters in children. The aim of this study is to analyze the safety and expected effect of TPE on biochemical and coagulation parameters. Additionally, we aimed to investigate if it has a role among the other prognostic factors for children awaiting for liver transplantation.

Methods: In this retrospective study, we enrolled all children who were admitted to pediatric intensive care unit with diagnosis of ALF and received TPE between December 2005 and December 2009. One TPE session period was 4 hours. In one period, 1.5 times of patients plasma amount was changed. Serum prothrombin time (PT), international normalized ratio (INR), total (TB) and direct bilirubin levels (DB), aminotransferases and serum ammonia values (NH3) were recorded before and after TPE sessions.

Results: Twelve patients (M/F, 4/8, median age 8 years) underwent a total of 35 TPE sessions (2.9 session per patient, median 3). ALF was induced by viral hepatitis in 5 cases, by Wilson disease in 4 cases and by toxins in 3 cases. Overall, there was significant improvement in serum PT (mean 44.5 vs 22.6 s, \( P = 0.0003 \)), INR (mean 4.4 vs 1.9, \( P = 0.0002 \)), ALT (median 122.5 vs 87.5 U/L, \( P = 0.000 \) mean 15.4 vs 12.6 mg/dL, \( P = 0.0006 \), mean 15.4 vs 12.6 mg/dL, \( P = 0.0001 \), respectively), and NH3 (mean 135.7 vs 114.7 \( \mu \)mol/L, \( P = 0.0003 \)) after TPE, when compared with baseline. Five of the twelve patients (42%) died in the pediatric intensive care unit, 2 patients survived with their own liver and 5 patients underwent successful liver transplantation (ltx). When the degree of change in the parameters was compared between the survivors without ltx and the others, similar improvement was observed in some parameters in children who died. (change in INR 2.15 vs 3.17, after each session respectively) No serious adverse effect of TPE was observed in the patients during or after completion of TPE.

Conclusion: TPE is effective in improving liver tests in children with liver failure. The degree of improvement is not an indicator for the possibility of surviving with the native liver. It corrects coagulopathy effectively independent of the severity of the liver failure. Expected changes in laboratory parameters after TPE must be considered while planning for liver transplantation.

Disclosure of Interest: None declared.

PO-H-361  

PFIC THE FIRST REPORT FROM SOUTH IRAN

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Objectives and Study: PFIC (progressive familial intrahepatic cholestasis) refer to a heterogenous group of autosomal recessive disorders of childhood that present with pruritus, jaundice, hepatomegaly and growth failure. The exact prevalence of this rare disease remains unknown, but the estimated incidence varies between one in 5000 and one in 100000 births. Although PFIC is a rare disease and only a few cases from middle east is reported, it seems to be frequent in IRAN. So we carried out a retrospective study to evaluate the clinical presentation of PFIC in south IRAN.

Methods: During a period of 5 years from January 2004 to January 2009 in our center 50 children with final diagnosis of PFIC were managed and followed. We reviewed the patients for age of distribution, clinical presentation, extrahepatic features, parents consangunity, paraclinical datas and clinical courses.

Results: Among 50 patients with PFIC, the mean age at presentation was 12 months, 47 patients had consangunity in parents and 7 patients had positive family history of liver disease in their families. The most common symptoms were jaundice and pruritus. Among extrahepatic manifestations, short stature (18 patients) and chronic cough (11) patients was the most common. 38 patients had good clinical course with only medical therapy (ursodesoxy cholic acid, rifampin, fat soluble vitamins, etc), 9 patients underwent liver transplantation and 3 patients had chronic liver disease without transplantation. Overall mortality of these patients was 3(6%).

Conclusion: PFIC is not so rare disease in south IRAN, therefore it should be included in the differential diagnosis of infant cholestasis. To distinguish between PFIC1 and PFIC2 immunostaining for bile salt export pump (BSEP) is recommended. Significant percentile of patients (76%) had good clinical response to medical therapy alone without liver transplantation, so we may have milder form of PFIC than other part of world.

Disclosure of Interest: None declared.
PO-H-362

GLOMERULAR AND TUBULAR FUNCTION FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION IN CHILDREN TREATED WITH TACROLIMUS

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Objectives and Study: Nephrotoxicity is the most notable side effect of tacrolimus (TAC) use in long term solid organ recipients. The aim of this study was to evaluate the impact of TAC on medium term renal function in a series of pediatric liver transplant recipients treated with TAC. We hypothesized that nephrotoxicity would be less than in a historical cohort on cyclosporine (CsA).

Methods: Glomerular and tubular indices were retrospectively analyzed from routine follow up visits in 24 consecutive OLT recipients, aged 6 months to 16 years (mean 4.0 ± 0.958 years), over a 3-yr interval (2 retransplantations). All patients received TAC as primary immunosuppression. Steroids, mycophenolate, and diuretics or antihypertensive treatment were used as needed. Laboratory values examined included serum creatinine, blood urea nitrogen and TAC trough levels. Creatinine clearance (CrCl) was determined using a 24-hour urine collection and considered abnormal below 90 ml/min/1.73m2. Tubular reabsorption of phosphate (TRP), calcium/creatinine ratio (UCa/Cr), protein/creatinine ratio (UPr/Cr), sodium excretion fraction (FeNa) were determined using conventional formulas. SPSS 17.0 was used for generating statistical data (P < 0.05 = significance).

Results: Subjects diagnoses at transplant were similar to those previously reported, and actuarial patient survival was 90%. CrCl increased significantly each month post OLT (P = 0.003), with a trend toward significance between pre-OLT and 36 months (P = 0.17). The inverse correlation between CrCl and TAC levels did not reach statistical significance (P = 0.783). There was a significant difference in prevalence of patients with a GFR <90/ml/min/1.73m2 between 1 and 24 months (P = 0.045). No patient had GFR <60 ml/min/1.73m2 at 36 months vs. 21% pre-OLT. TRP values were normal throughout the study (mean values = 89–91%). UPr/Cr decreased over time (p = ns), and correlated significantly with TAC trough levels (P = 0.031). UCa/Cr values normalized by the third month post OLT, decreasing significantly over the time (P = 0.00) but no significant correlation with TAC troughs (P = 0.588) was observed. We did not observe any effect of time (P = 0.926) or of TAC troughs (P = 0.421) on FeNa. 4.2% of the patients needed antihypertensive therapy before OLT; 62.50% at 3 months post-OLT and 20.83% at 36 months post-OLT.

Conclusion: Despite nephrotoxic side effects in the early postoperative phase, this study shows that 65.5% patients had a normal renal function by 3 years post OLT. No patient had a GFR <60 ml/min/1.73m2 after 2 years. Tubular indices correlated with TAC trough levels. In our cohort, TAC appears to have fewer nephrotoxic side effects than CsA.

Disclosure of Interest: None declared.

PO-H-363

OUTCOME OF LIVER TRANSPLANTATION FOR AUTOIMMUNE HEPATITIS IN CHILDREN

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Objectives and Study: Liver transplantation (LT) is the final therapeutic option in patients with cirrhosis associated with autoimmune hepatitis (AIH) who do not respond the medical treatment. The aim of this study is to evaluate the long-term outcome of children who underwent LT for cirrhosis associated with AIH.

Methods: Pretransplant and posttransplant data of the children with AIH transplanted between April 1997 and December 2008 were respectively analyzed. During this period 158 LT was performed to 148 patients (median: 4.6 years, range: 6 months-17 years).

Results: 15 LT (11 cadaveric) were performed to 12 children which constitutes the 9.4% of all liver transplanted children. Serological analyses identified patients with AIH type 1 (n = 9), type 2 (n = 2) and autoimmune sclerosing cholangitis (n = 1). Median PELD score was 29 at the time of transplantation. Immunosuppression regimens include Tac (n = 7) and CyA (n = 5) along with long duration steroids. Patients were followed for mean 70 ± 45 months (2–135 months). Rejection episodes were experienced in 6 patients (4 acute) (50%) that were managed by pulse steroid therapy. Liver histology revealed bile duct loss and foam cell arteriopathy (chronic rejection) in one patient who required re-transplantation. Recurrence of AIH (diagnosed by biochemical, serological and histological evidence of graft hepatitis) was seen in 5 patients (41.6%) (two in the early period) managed by mycophenolate mofetil or dose increments of steroids. Nodular sclerosing Hodgkin’s lymphoma was developed in one patient 9 years after LT that was successfully treated with chemotherapy, and one patient developed diabetes mellitus 6 years after LT. Three patients (25%) underwent retransplantation due to early surgical complication in one, and chronic rejection and recurrence of AIH in the late period in other two patients. Only one patient died, and 5yrs and 10 yrs survival rate after LT was 91.7%.

Conclusion: Despite high frequency of disease recurrence, rejection episodes and morbidity, LT for cirrhosis associated with AIH has an excellent outcome in children.

Disclosure of Interest: None.
PO-H-364

H1N1 INFECTION IN SEVEN PEDIATRIC LIVER TRANSPLANT PATIENTS
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Objectives and Study: H1N1 virus infection is currently a significant threat for individuals. Pediatric liver transplant (LTX) recipients are in the risk group for H1N1 virus associated mortality and morbidity. Post LTX immunosuppression and pretransplant state of poor health are contributors to morbidity and/or mortality associated with H1N1 infection in pediatric LTX recipients. Here we present 7 pediatric LTX recipients infected with H1N1 virus.

Methods: Retrospective chart analysis of 7 patients, diagnosed with H1N1 infection in our hospital between October and November 2009 was included in this study. LTX patients with fever, rhinorhea, cough and myalgia seen in the transplant clinic have been evaluated for H1N1 infection. Liver enzymes, CBC, tacrolimus (TAC) and CRP levels were assessed. Some patients did not have H1N1 swab (PCR) sent as per local Infectious Disease Committee and/or shortage of swab material. Patients with suspected but not documented H1N1 infection are not included in this study.

Results: 7 patients, all boys, aged between 9 and 155 months (mo), are diagnosed with H1N1 infection. Mean time from LTX was 14.7 mo. Mean age at the time of LTX was 72.7 mo. All but one were on TAC. None of them received steroids at the time of infection. One of the patients was on both TAC and MMF. All patients had fever (mean 39 °C, axillary), rhinorhea, and cough. 2/7 patients had myalgia. 6/7 patients were admitted to the hospital. Mean hospitalization time was 5 days. Oseltamivir was commenced for all patients. Immunosuppression has not been decreased in patients with recent LTX but patients were monitored closely for either rejection or aggravated infection. 4/7 patients received ampicillin/subactam for associated pneumonia and/or pleural effusion. Further laboratory details are summarized in the table below. Overall incidence of H1N1 infection in our cohort was 7.1% (n = 7/99). All admitted patients have been discharged without complications. No mortality or morbidity was observed among our patients with H1N1 infection.

Table:

<table>
<thead>
<tr>
<th>TAC level (mean ng/ml)</th>
<th>Pre-H1N1 Infection</th>
<th>During H1N1 Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (mean 10^9/l)</td>
<td>6212</td>
<td>4445</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>NA</td>
<td>34.4</td>
</tr>
<tr>
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<td>41.8</td>
<td>45.7</td>
</tr>
<tr>
<td>AST</td>
<td>44.4</td>
<td>56.7</td>
</tr>
</tbody>
</table>

* Not Available.

Conclusion: H1N1 virus infection is well tolerated among the pediatric liver transplant recipients. Although we did not reduce the dose of immunosuppressive treatment, H1N1 infection did not cause any mortality or morbidity in our cohort. LTX patients receiving significant immunosuppression with H1N1 infection may be followed with the same amount of immunosuppression and antiviral treatment with close monitorization of clinical and laboratory findings.

Disclosure of Interest: None declared.

PO-H-365

ATTITUDES ABOUT ORGAN TRANSPLANTATION AMONG THE MEDICAL STUDENTS IN EASTERN TURKEY
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Objectives and Study: Organ transplantation has become one of the most efficient ways to save lives for people with end-stage organ failure. But the incidence of organ failure has been increasing all over the world; many patients are dying while waiting on the list. In Turkey, many transplantations are performed from living donor. Because many social and religious myths against cadaveric transplantation. The aim of this study was to analyze the opinion, attitudes and beliefs related to organ transplantation and organ donation of medical students living in eastern of Turkey. There is a lack of information about how Turkish medical students perceive organ donation, and what they know about organ donation and transplantation.

Methods: 233 medical students voluntarily completed a questionnaire concerning organ donation and transplantation. The questionnaire included a test that was used to assess knowledge of and attitudes about organ donation.

Results: The intention to become a post mortem or living donor was of 31.8% and 17.2% respectively. Religious belief about organ donation affected significantly willingness to donate. Of 233 medical students, 9.9 % were believed that organ donation was not in accord with Islamic believes. None of the students had organ donation card.

Conclusion: This data show that the willing of the medical students about organ donation is inadequate.

Disclosure of Interest: None declared.

PO-H-366

H1N1 INFLUENZA IN CHILDREN WITH LIVER TRANSPLANTS

Objectives and Study: Novel Influenza A virus led to actions for diagnosis/treatment in liver transplanted children. Characteristics of the infection were reviewed.
PO-H-368

GROWTH AND OBESITY AFTER LIVER TRANSPANTATION IN CHILDREN

Objectives and Study: It is well established that chronic liver disease (CLD) leads to malnutrition and 80% of children show good evidence of catch up growth after liver transplantation. However, there is concern in adult transplant programmes that obesity and development of the metabolic syndrome are becoming more prevalent.

Aims: 1. Assess post liver transplant weight gain and linear growth in our paediatric population.
2. Determine frequency of obesity in this population.

Methods: Clinical, anthropometric and demographic data on all children who underwent liver transplantation at Leeds Teaching Hospitals between November 2000 and December 2007 were obtained from a prospective database and hospital notes. Patients were grouped into diagnostic categories: acute liver failure (ALF), chronic cholestasis, non cholestatic CLD, tumours and non cirrhotic metabolic liver disease (MLD). Anthropometric data was collected pre-transplant, at 6 months post transplant and annually to 5 years. Children with a BMI standard deviation score (SDS) of greater than 2 or at least 2 visits were classified as obese.

Results: 109 liver transplants were performed on 98 children during the study period. 10 children were excluded from analysis as they died within a year of their transplant and two children were excluded as they were retransplanted outside
the study period. Of the remaining 86 children, 13 (15%) were categorised in the ALF group, 38 (44%) in chronic cholestasis group, 26 (31%) in non cholestatic CLD group, 6 (7%) had tumours and 3 (3%) had MLD. The median follow up was 5 years (range 0.75–5 years). As expected, for the whole cohort the median SDS scores for weight, height and BMI were low (−1.39, −1.25, −1.27) at pre-transplant assessment and improved to near normal by 12 months post transplant (−0.17, −0.82, 0.54), without ongoing increases over the following years. This was most notable in children with chronic cholestasis, tumours or MLD. Children transplanted for ALF maintained normal anthropometry before and after transplant. However, children with non cholestatic CLD became increasingly overweight post transplant (median BMI SDS score 0.10 pre-transplant, 2.74 five years post transplant). Overall, 13 (15%) children had a BMI SDS score >2 on 2 occasions and of these 9 were in the non cholestatic CLD group. Five of the 13 children had a BMI SDS score >2 at pre-transplant assessment. Three of the 5 children transplanted for α1 antitrypsin deficiency became obese post transplant.

Conclusion: We have confirmed good catch up growth post transplant for children with CLD. A cohort of children with non cholestatic CLD are at risk of obesity post transplant. Identification of the factors responsible for post transplant obesity would require a larger study.

Disclosure of Interest: None declared.

PO-H-369

INCREASE IN DE NOVO ALLERGIES AFTER PAEDIATRIC LIVER TRANSPLANTATION; THE BRISBANE EXPERIENCE

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Objectives and Study: To identify the incidence of reported De Novo allergies in children post Orthotopic Liver Transplantation (OLT) by the Queensland Liver Transplantation Service (QLTS) over the last 11 years.

Methods: Comprehensive review of medical records of all OLT recipients during study period via cross-checking procedural and electronic laboratory results and documented Immunology specialist referral and diagnosis.

Results: In the 11 years from 1st July 1998 to 1st August 2009 78 children received 85 cadaveric liver transplants (OLT); 60 children survived. Of 78 children transplanted 12 (15.4%) have had significant drug reactions and 13 (16.6%) significant food reactions. 9/13 (69%) children with severe food reactions and 2/12 children with significant drug reactions were aged 3 years or younger. 12 significant allergic reactions to food were De Novo reactions and 8 of these patients were infants. 6 of 60 (10%) surviving children with food reactions carry an Epipen.

Only 31/60 (51%) of survivors are currently followed in Queensland and all patients diagnosed are in this cohort. Many patients are followed elsewhere hence our reported incidence of severe allergic reactions in the total population of liver transplant survivors is a gross underestimate.

Conclusion: Serious atopic disease is clinically important in the post OLT community, particularly infants. These children should be targeted for specialist Allergist referral and risk management for anaphylactic episodes.

Disclosure of Interest: None declared.

PO-H-370

EXPERIENCE WITH SIROLIMUS IN PEDIATRIC LIVER TRANSPLANTATION

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Objectives and Study: Immunosuppressive therapy with calcineurin inhibitors (CNIs) is the standard regimen after liver transplantation (LT). However, CNIs-associated adverse effects have been reported such as nephrotoxicity, de-novo malignancy, and infectious diseases in children. Sirolimus (SRL) side effect profile differs from that of CNIs. The aim of this study was to review our experience with SRL in pediatric LT recipients.

Methods: Between 2001–2009,127 children with end-stage liver disease underwent LT in Baskent University Faculty of Medicine, 13 of them received SRL therapy. Median age of patients (7 M/6F) receiving SRL was 7.5 y (range, 9 m–15 y). 11 patients converted to SRL from CNIs therapy. Indications for SRL conversion were posttransplant lymphoproliferative disease (PTLD; n = 2), nephrotoxicity (n = 3), steroid resistant acute rejection non responding to ATG treatment (n = 4), hypertrophic cardiomyopathy (n = 1), and de-novo inflammatory bowel disease (n = 1). SRL was commenced to 2 patients with hepatocellular carcinoma (HCC) as primary immunosuppressive therapy. Median time from LT to conversion of SRL was 14 months (range, 5 m–4 y). Median duration of follow-up period was 3 years (range, 5 m–4.5 y). Sirolimus dosage ranged between 0.25–4 mg/d. Target therapeutic SRL blood trough levels ranged between 5–5 ng/dL. For each patient receiving SRL, we reviewed serial biochemical parameters. Any occurrence of side effects were documented.

Results: In patients with HCC no tumor recurrence was observed. ECHO showed regression of interventricular septum hypertrophy 6 months after therapy. Chronic diarrhea, abdominal pain symptoms improved in the child with de novo inflammatory bowel disease. Glomerular filtration rates (GFR) improved significantly after conversion in 2 patients (GFR 62 to 124 and 52 to 153) Renal function remained stable in the 3rd child (GFR 41 to 39). No recurrence occurred in 2 PTLD patients. However T-cell PTLD occurred in allograft liver in a patient 14 months after SRL therapy. Steroid resistant acute rejection was controlled.
Disclosure of Interest: None declared.

PO-H-372

PREDICTING THE OUTCOME OF CONGENITAL INTESTINAL FAILURE

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Objectives and Study: The inherited intractable diarrhoeas of infancy are uncommon. The best characterised are Congenital Tufting Enteropathy (CTE) caused by mutations in the EpCAM gene and Microvillous atrophy (MVA) by defects in the MYOB5 gene. There have been reports of both conditions recovering spontaneously avoiding the need for intestinal transplantation. The aim of this study was to identify genotypes in CTE and MVA that correlate and predict these recovering phenotypes.

Methods: Both CTE and MVA usually require lifelong parenteral nutrition (PN) or intestinal transplantation. Our experience and isolated case reports recognise that some patients may develop enteral tolerance and wean from PN. All children with either diagnosis were identified, notes and dietetic charts reviewed and long term outcome assessed. 41 children (15 CTE, 26 MVA) had DNA assessment by direct sequencing of PCR amplified products of all exons and splice sites on an ABI DNA analyser. Clinical assessment was performed in all to identify children showing significant enteral tolerance >50% of calorie requirements.

Results: 6/15 CTE children fitted this criteria with 3/6 off PN Mutation screening in 5/6 recovering CTE children showed splice site mis-sense mutation leading to a deletion of exon 5. All were Maltese in origin. One child was from Afghanistan with a Hom 657+1G>A of exon 5 had >50% enteral tolerance but very poor venous access, a feature seen in one other genetically identical child with similar enteral tolerance but had died from thrombosis at a young age. Of the 5 Maltese children 3/5 had come off PN in their late teens, the other 2/5 were aged 12 and 14 yrs. In the nonrecovering CTE children mutations were found in the coding sequence of exon 5 most commonly Hom 499_500insC and Hom 492_-2A>G. 4/26 MVA were off PN managed on specialised diets but in only one was a mutation identified in the 40 exon coding regions and this showed no difference in from the other 22 mutation positive. The 3 recovered MYOB5 negative children had characteristic EM changes

Disclosure of Interest: None declared.

PO-H-371

THE EFFICACY OF HEPATITIS A VACCINATION AFTER LIVER TRANSPLANTATION IN CHILDREN

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\textsuperscript{1}Pediatric Gastroenterology, \textsuperscript{2}General Surgery, Baskent University Faculty of Medicine, Ankara, Turkey.

Objectives and Study: Hepatitis A virus (HAV) infections occur throughout the world, but are most commonly found in developing countries. Hepatitis A is a vaccine-preventable disease. It is shown that vaccination against hepatitis A is safe and efficient (94%) in healthy children and chronic liver disease patients. However, experience with vaccine administration in immune-compromised children is limited. The purpose of our study is to evaluate the efficiency of inactivated hepatitis A vaccine in children who underwent liver transplantation.

Methods: Between 2001–2009, 125 children, underwent liver transplantation in Başkent University Ankara Hospital. Patients, who were not under steroid therapy, were followed up at least 6 months after transplantation, and with normal liver function tests were included into the study. Patients with negative AntiHAV IgG received HAV vaccine 2 times with a 6 month interval. To evaluate the immune response, antiHAV seroconversion was assessed after 1 and 7 months from the first vaccination.

Results: 89 patients were included into the study, 28 (31%) of them had negative anti HAV IgG levels. Of these patients, 24 were under tacrolimus, 3 under cyclosporine, 1 under sirolimus therapy. 15 of them were male, and 13 of female, with median age of 4 1/2 years (23 months–18 years). AntiHAV IgG seroconversion was provided after the first dose of vaccination in 15 (53%) out of 28 patients. The second dose of vaccination was completed in 23 (82%) patients. Anti HAV IgG seroconversion was provided in 17 of 23 patients after the second dose (74%). There was no significant difference between seroconverted and non-seroconverted patients in terms of lymphopenia (<1000/mm\textsuperscript{3}) during the vaccination period lasting six months (2/17 versus 1/6). No local or systemic side effects were seen.

Conclusion: In our study, seroconversion rate against HAV vaccination obtained in liver transplanted children (74%) was satisfactory. Total lymphocyte count was not useful predicting serologic response to hepatitis A vaccination.

Disclosure of Interest: None declared.

in all 4 patients after SRL therapy. One child developed neutropenia and neutropenic sepsis that resolved discontinuation of SRL. Oral and genital aphths developed in one patient. Transient peripheral edema developed in lower extremities in one child. Mild hyperlipidemia observed in two patients.

Conclusion: SRL has been effective in certain situations such as CNIs associated nephrotoxicity, steroid/ATG resistant acute rejection, hypertrophic cardiomyopathy, de-novo inflammatory bowel disease after LT in our patients. Although SRL has antitumoral effects T-cell PTLD occurred under SRL therapy. We didn’t observe major complications except neutropenic sepsis.

Disclosure of Interest: None declared.
although in 2 children (siblings) these EM changes fluctuated from biopsy to biopsy.

**Conclusion:** In conclusion in MVA genetic phenotype correlation is not of benefit in identifying children that may recover from MVA. However in CTE splice sites mis-sense mutations deleting exon 5 in Maltese children may predict recovery from parenteral nutrition dependency and also help predict children and also a greater predisposition to loss of venous access.

**Disclosure of Interest:** Institute Of Child Health Grant. Jeans for Genes Pump priming Grant.

**PO-N-373**

**INCREASING CURRENT NEED FOR HOME ENTERAL TUBE FEEDING IS UNRELATED TO FORMATION OF A NUTRITION SUPPORT TEAM**

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**Objectives and Study:** Introduction: Home enteral tube feeding (HETF) is increasingly used to support patients with chronic childhood conditions, but with little data published regarding the prevalence and outcome of paediatric HETF. The British Artificial Nutrition Support Survey report of 2008 (1) is estimated to have captured only 59% of paediatric HETF patients.

**Aims:** 1. To identify the true prevalence and incidence of children receiving HETF during a 13 year period after the introduction of a regional Nutrition Support Team (NST). 2. To describe the characteristics of these children (age, sex, diagnosis, route of feeding). 3. To describe complications, duration and outcome of HETF.

**Methods:** Retrospective review of all aged <19 yrs receiving HETF in a defined UK region from 1/5/97 – 30/04/09 (stable population of 1.25 million people). Data was obtained from the Enteral Feeding Database (data from district general hospitals and the regional tertiary centre). Hospital computerised records, and medical and dietetic notes were accessed where necessary.

**Results:** 661 patients (51% male) were identified. Point prevalence rose rapidly from 33 on 01/05/97 to 141 on 01/05/01, followed by a period of stability, and then a further increase from 2007 onwards. The incidence of new HETF starts followed a similar pattern. Median (range) age at HETF start was 2.1 (0.0 – 18.9) years. Median (range) length of time on HETF was 2.6 (0.1 to 21.2) years. The most common primary diagnoses was neurological (32.2%). Only 5.3% of patients required jejunal feeding. At study end, 29.1% of patients remained on active HETF, 10% were transferred to adult services on HETF, 41% returned to full oral feeds, and 15% died on HETF (none due to HETF complications).

**Conclusion:** Following formation of a regional NST, a large number of children requiring HETF were identified, resulting in rapid increase in prevalence of patients on HETF, followed by stability and then a more recent increase. Just under half of patients return to oral feeding. These trends provide valuable information to aid development and funding of HETF services.

**Reference:**


**Disclosure of Interest:** R Ardill, none.

S Lawrence, none.

HL Min, none.

C Paxton, none.

L Eyles, none.

DC Wilson, Numico, speaker.

DC Wilson, SMA Nutrition, speaker.

DC Wilson, SHS-Nutricia.

DC Wilson, Wyeth, Grant/Research - Support.

**PO-N-374**

**MATERNAL SERUM VITAMIN B12 AND FOLATE LEVELS AND CONSUMPTION OF ANIMAL PRODUCTS IN LOW SOCIOECONOMIC GROUP**

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**Objectives and Study:** Vitamin B12 and folate deficiencies in pregnancy, which can cause neurological damage and developmental delay of infants, are important issues of public health. In these babies, evaluation of the mother’s vitamin B12, folate levels and diet is important. In this study, the frequencies of vitamin B12 and folate deficiency and their relationship with animal product consumption were investigated.

**Methods:** The pregnant women in the last trimester were included into the study from February through June 2008. A questionnaire with 17 items gathering information about socio-demographic status, consumption of meat, egg, milk-dairy products, multivitamin supplementation was used. Once a week or less consumption of animal product groups (meat, milk, egg) was inadequate, 2–3 times per week or more were considered to be sufficient. Vitamin B12 and folate levels were studied by chemiluminescence method (Normal values: vitamin B12, 193–982 pg/ml, folate; 3–17 ng/ml). The babies of mothers who had Vitamin B12 deficiency were evaluated after their birth. Serum B12 levels of babies were determined and Denver Developmental
Screening Test was used to assess the cognitive and behavioral status of infants.

**Results:** Vitamin B12 and folate levels were evaluated 210 pregnant women in last trimester. Average of vitamin B12 and folate levels in pregnant women 181.5 ± 44.4 (median 163) pg/ml, 8.87 ± 5.04 (median 8) ng/ml, respectively. Vitamin B12 levels were below 150 pg/ml in 40% of pregnant women (n = 84). Animal food consumption was inadequate about half of pregnant women and vitamin B12 levels in these women were significantly low (Table 1). The folate deficiency was observed in 18 pregnant women (8.7%). Infants of 40 mothers whose B12 vitamin levels were <150 pg/ml, were followed-up and low levels of vitamin B12 were determined in 13 (32.5%) infants. Denver Developmental Screening Test was abnormal in 7 (17.5%) infants. The percentage of pregnant women who had received multivitamin supplementation during pregnancy was 57%, but vitamin B12 and folate levels were not different between the groups with or without multivitamin supplementation (P = 0.08).

**Conclusion:** Vitamin B12 deficiency in pregnant women in low socio-economic conditions is a serious problem. This situation can be explained by widespread vegetable consumption and insufficient animal food consumption. Vitamin B12 supplementation also must be emphasized as well as folate supplementation during pregnancy.

**Disclosure of Interest:** None declared.

**PO-N-375**

**THE CHARACTERISTICS AND EATING HABITS OF 2 TO 6-YEAR-OLD CHILDREN WITH FOOD REFUSAL**

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**Objectives and Study:** Poor appetite is defined as eating less than expected or complete refusal of eating one or more specific food. These children should be evaluated in terms of eating habits, relations with parents, the socio-demographic characteristics of the families, mother and child interaction and the effects of eating disorder on the growth of children. In this study, the characteristics of children with food refusal was evaluated.

**Methods:** Study population included the children of 2 to 6 years of age with no acute or chronic illnesses who presented to the hospital between March 2008 and August 2009. A questionnaire of 34 items was filled by the parents and/or mothers of the children. The questionnaire reflected information about the demographic characteristics of children, weight and height percentiles, the education level and the age of the mother, the number of siblings, the eating habits of the children and their families (selective eating, anorexia, junk food etc...), nutritional information since birth (breast feeding, supplementary foods, preparation of foods). Body Mass Index (BMI) was calculated for each case.

**Results:** The study included 211 children (112 (53.1%) boys, 99 (46.9%) girls; with a mean age of 4 ± 1.5 years. The mean age of mothers was 30.6 ± 5.8 years. One hundred and seventy-nine children (84.8%) were primarily taken care of by their mothers. Only 17.1% of the mothers had a job and most of the mothers (56.4%), were primary school graduates. The percentages of children who had previous medical examination and used medication for food refusal were 58.3% and 56.9%, respectively. The average duration of breastfeeding was 13 ± 8.3 months, and a significant relationship was found between the beginning of nutrition problems and the termination of breastfeeding (r = 0.19, P = 0.03). Junk food eating was observed in 88% of the children while 43% refused to sit around the dinner table when eating, and 80% of them were forced to be fed. Percentile values of BMI were within normal limits in 63.1% of children (Table 1).

**Table:** Grouping of children according to BMI percentiles

<table>
<thead>
<tr>
<th></th>
<th>Underweight child (n = 53; 25.1%)</th>
<th>Normal weight children (n = 133; 63.1%)</th>
<th>Overweight child (n = 25; 11.8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length SDS (Mean±SD)</td>
<td>−0.14 ± 1.41</td>
<td>−0.37 ± 1.3</td>
<td>−0.55 ± 2</td>
</tr>
<tr>
<td>BMI (Mean±SD)</td>
<td>12.9 ± 0.9</td>
<td>15.45 ± 1.0</td>
<td>18.7 ± 1.6</td>
</tr>
<tr>
<td>BMI SDS (Mean±SD)</td>
<td>12.9 ± 0.9</td>
<td>−0.33 ± 0.7</td>
<td>1.8 ± 0.7</td>
</tr>
</tbody>
</table>

**Conclusion:** Even though food refusal was perceived as a problem by most of the parents, growth was not affected significantly. Termination period of breastfeeding was a risk factor for nutrition problems in our study. In this group, the rate of wrong eating habits was quite high.

**Disclosure of Interest:** None declared.

**PO-N-376**

**HELCOBACTER PYLORI INFECTION: RELATION TO PROTEIN LOSING ENTEROPATHY IN MALNUTRITION**

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**Objectives and Study:** To study the prevalence of Helicobacter pylori (H-P) infection in malnourished children and to prove the association -if any- between H-P infection and protein losing enteropathy (PLE) in these children.

**Methods:** Stool samples of 120 studied children (40 underweight children, 40 marasmus children and 40 age- and sex-matched, well nourished children as a control group)
were tested for H-P antigen and faecal concentration of alpha 1-antitrypsin (FA-AT) using ELISA technique. Estimation of both parameters was repeated in H-P positive children 6 weeks after eradication therapy of H-P infection.

**Results:** The prevalence of H-P infection amounted to 66% of malnourished children compared to 20% of control group (P = 0.0001). The mean values of FA-AT in H-P positive children (both malnourished and control group) were significantly higher than in those with negative infection (P = 0.0001), following the eradication of H-P infection, the mean values of FA-AT in malnourished infants showed a significant decrease (P = 0.0001). However, these values were still higher than those in the control group (P = 0.0001) as shown in the table.

**Table: Faecal concentration of alpha 1-antitrypsin (FA-AT)**

<table>
<thead>
<tr>
<th>FA-AT (ug/dl)</th>
<th>under weight children</th>
<th>marasmus children</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-P negative children</td>
<td>67.05 ± 13.38</td>
<td>71.84 ± 7.63</td>
<td>24.60 ± 2.44</td>
</tr>
<tr>
<td>H-P positive children</td>
<td>146.76 ± 16.36</td>
<td>169.25 ± 4.94</td>
<td>31.90 ± 0.00</td>
</tr>
<tr>
<td>H-P positive after H-P eradication</td>
<td>74.44 ± 6.62</td>
<td>74.11 ± 9.39</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** H-P infection has a high prevalence in malnourished children and may be an important co-factor in the pathogenesis of PLE in those children and its eradication can reverse some of this finding.

**Disclosure of Interest:** None declared.

**PO-N-377**

**SYSTEMATIC REVIEW OF MEDICAL AND NUTRITIONAL THERAPIES FOR PAEDIATRIC INTESTINAL FAILURE CONFIRMS THE EXPANDED EVIDENCE BASE FOR THE USE OF NOVEL LIPIDS**

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**Objectives and Study:** Intestinal failure (IF) affects an increasing number of paediatric patients. Parenteral nutrition (PN) is the mainstay of therapy, but is associated with the development of IF associated liver disease (IFALD). There has been much recent interest in the potential for novel intravenous lipids in PN to ameliorate the course of IFALD. The authors aimed to review the evidence base for medical and nutritional therapies in paediatric IF with specific focus on the evidence base for novel lipids.

**Methods:** Systematic review of data involving studies with patients aged <18yrs and requiring >28 days PN. Outcome measures sought included; improvement in intestinal function; intestinal adaptation; growth; prevention and treatment of IFALD; mortality. The Cochrane Database, Medline (1950- Nov 2009) and CINAHL (1982- Nov 2009) electronic database searches were conducted using keywords and subject headings (MeSH). IF; short bowel syndrome (SBS); Child. Major reviews from agreed experts in the field were reference checked as were all potential studies. Papers were excluded if it was impossible to separate childhood and adult data. Two authors independently assessed the level of the evidence (EL) using the Scottish Intercollegiate Guidelines Network (SIGN: www.SIGN.ac.uk) methodology.

**Results:** From 1607620 hits, combination keywords of IF/Child and SBS/Child identified 762 potential citations. 61 potential studies were reviewed for eligibility with 36 being included in the review. 2 studies were EL 1- 7 were EL 2- and 27 were EL 3. Strategies included; growth factors (4), bile analogues (6), dietary manipulation (6), bacterial manipulation (7), multidisciplinary team (3) and PN manipulation (10). 7 studies described the use of novel lipids, 4 being of higher EL; There were no Cochrane systematic reviews. Of the 10 studies published since 01/01/2006, 6 described the use of novel lipids.

**Table:** Higher EL studies describing novel lipid use in paediatric IF

<table>
<thead>
<tr>
<th>Study</th>
<th>Lipid type (regimen)</th>
<th>Number in Rx group</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goulet et al 1999</td>
<td>Clinoleic (2g/kg/d)</td>
<td>1- 9</td>
<td>Reduced LDL in Rx</td>
</tr>
<tr>
<td>Gura et al 2008</td>
<td>Omegaven (1g/kg/d)</td>
<td>2- 18</td>
<td>Reduced IFALD in Rx</td>
</tr>
<tr>
<td>Lee et al 2009</td>
<td>Omegaven (1g/kg/d)</td>
<td>2- 18</td>
<td>Reduced TRGs in Rx</td>
</tr>
<tr>
<td>Puder et al 2009</td>
<td>Omegaven (1g/kg/d)</td>
<td>2- 42</td>
<td>Reduced death in Rx</td>
</tr>
</tbody>
</table>

**Conclusion:** The evidence base for medical and nutritional therapies in paediatric IF remains limited. However there has been a recent significant expansion in the data relating to novel lipids in established IFALD. Well designed RCTs will help establish the role of such therapies in both the prevention of IFALD and in the treatment of established disease.

**Reference:**


**Disclosure of Interest:** D Wilson Grant/Research support: Wyeth, SHS Nutricia.

**PO-N-378**

**ASSESSMENT OF NUTRITIONAL STATUS IN CHILDREN WITH CHRONIC LIVER DISEASE**


**Conclusion:** The prevalence of H-P infection amounted to 66% of malnourished children compared to 20% of control group (P = 0.0001). The mean values of FA-AT in H-P positive children (both malnourished and control group) were significantly higher than in those with negative infection (P = 0.0001), following the eradication of H-P infection, the mean values of FA-AT in malnourished infants showed a significant decrease (P = 0.0001). However, these values were still higher than those in the control group (P = 0.0001) as shown in the table.

**Disclosure of Interest:** None declared.
Objectives and Study: To study the nutritional aspect of Chronic liver disease (CLD).

Methods: Dietary history and detail anthropometry assessment done with standard procedure and equipment. Whole body DEXA scan done to know the total body fat %. Data of all patients prepared and analyzed using epi – info software (CDC-2000) with nutritional assessment software. Centile charts also used for some results.

Results: Total 50 children were enrolled. Mean age 9.2 (range 1–22) years, 80% boys. Total 50 children were enrolled. Mean age 9.2 (range 1–22) years, 80% boys. Etiology wise Wilson’s Disease 24%, Autoimmune Liver Disease 18%, CLD (Undetermined etiology) 26%, Chronic Hepatitis B Infection 14%, Cryptogenic 6%, Biliary Arteria 4%, PFIC 6%, PILBD 2%. 25 (50%) of 50 children were underweight (Z score < -2SD). 22 (44%) patients out of 50 were stunted (Z score < -2SD). 19 (38%) were both undernourished and stunted. 20 (40%) having low BMI (Z score < -2SD) which 7 (65%) children having Mid Arm Circumference (MAC) < 12 cm indicating malnutrition more in smaller children with CLD. 36 (72%) patients having calorie intake just 50–80%. 14 (28%) patients had only low fat estimated by US fat centile charts. Total body fat % by DEXA shows that patients with CLD having body mainly protein deficiency due to poor synthetic functions of liver. In majority of patients the body fat was relatively preserved in comparison with protein.21 (42%) children having triceps skin fold < 5th centile using US centile charts. Arm circumference and arm muscle area (AMA) falls below 5th centile in 44 (88%) children using centile charts. Indicating more muscle mass depletion indicating more protein deficiency.

29 (58%) children having low total Serum protein value and 36 (72%) patients having low serum albumin. Overall 11 (22%) patients have both low value of protein and albumin. Low value may be attributed to decrease food intake in combination with poor synthetic functions of liver. Children with CLD who are becoming nutritionally depleted should be identified quickly and nutritional intervention should be done properly to prevent further malnutrition and to improve nutritional status.

Conclusion: Around half of the children were undernourished and stunted. Malnutrition was more in smaller children. Decompensated children with CLD were more malnourished. Fat was relatively preserved in comparison with protein. Synthetic function of liver affected in two third patients. To conclude further studies with more patient data is needed with dietary interventions and to see its out come.

Disclosure of Interest: None declared.

PO-N-379

NUTRITIONAL FOLLOW-UP IN SURGICAL NEONATES AFTER HOSPITAL DISCHARGE

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Objectives and Study: Neonates who have undergone major gastrointestinal (GI) surgery are complex. They often require prolonged artificial nutritional support and hospital stay. Suboptimal early nutrition and prolonged hospitalisation may be associated with short and long term morbidity. Little is known about the nutritional and growth outcomes of surgical neonates (SNs) post hospital discharge. The aim of this study was to evaluate the prevalence of “failure to thrive” (FTT) in SNs after discharge from hospital.

Methods: A retrospective analysis was done at Chelsea and Westminster Hospital, a tertiary referral centre for neonatal surgery. Babies who had major GI surgery over an 18-month period (1st Jan 2006 - 31st July 2007) were identified from the unit’s database. Further data were collated from medical case notes, dietetic records, parental satisfaction survey and physician feedback. FTT was defined as weight decreasing over 2 centile lines using unit’s standardized growth centile chart.

Results: Sixty-five of 80 eligible infants were analysed. The key surgical diagnosis in this group included necrotizing enterocolitis, duodenal stenosis, Hirschsprung’s disease and exomphalos. Nineteen SNs (29%) developed FTT, 12/19 as inpatients (4 with further growth impairment post-discharge) and 7/19 after discharge/transfer to local hospital. Twenty SNs (30.8%) were referred for dietetic follow-up after discharge for associated comorbidity e.g. FTT, gastroesophageal reflux, and milk intolerance and in 22/65 (33.8%) they required milk change by the dietician post-discharge e.g. to a hypoallergenic or hypercaloric formula. Post-discharge FTT was common if babies only had surgical without co-existing neonatal follow-up. Neurodevelopmental data were unavailable for the majority.

Conclusion: SNs are shown to be at high risk of FTT even after discharge from hospital, and they require significant dietetic input during their hospital stay and after discharge. We recommend increased awareness of the potential comorbidities. Ongoing provision of dedicated multidisciplinary nutritional, growth and neurodevelopmental support for early identification and intervention is vital.

Disclosure of Interest: None declared.

PO-N-380

PREVALENCE OF MALNUTRITION AND RISK FACTORS IN YOUNG CHILDREN WITH CONGENITAL HEART DISEASE: A PROSPECTIVE STUDY

M. Bouhabib1, C. Lambe1, F. Bajolle1, D. Bonner2, D. Sidi2, O. Goulet1, V. Colomb1.

Objectives and Study: Malnutrition and failure to thrive have been known for long as consequences of congenital heart diseases (CHD) in children. Risk factors for nutritional imbalance are insufficient food intake and increased energy demand due to heart disease. The aims of the study were to assess prospectively the prevalence of malnutrition in young
children with CHD, to identify disease-related risk factors and to show the effect of nutritional support.

**Methods:** All children with CHD aged 1 month to 2 years consecutively admitted for at least 48 h over a 6 month-period at the paediatric Cardiology unit were studied. The following parameters were collected: age (A), features of the CHD, medical and surgical treatments, weight (W), height (H), arm circumference (AC), head circumference (HC), food intake (compared to recommended dietary allowance, RDA). Nutritional support was proposed according to nutritional condition and food intake.

**Results:** 54 children with CHD aged 6.6±6.9 months (including 28 infants aged 1 to 3 months) were studied: 25 CHD (46%) with pulmonary hypertension (PHT) and 29 CHD without PHT. Curative (32 cases) or palliative (16) surgery has been performed in 89% of the patients. In the whole population, the W was −2.5±0.7 SD, H: −1.6±0.7 SD, W/H: 81±6, AC/HC: 0.26±0.2 DS. Moderate to severe malnutrition according to the Waterlow classification (W/H <80% and/or H/A <90%) was present in 50% of children. In children with PHT, W/A (72.5±6.4 vs 68.7±9.4) and W/HT (82.8±5.4 vs 79.3±7.0) were significantly lower than in those without PHT (P<0.05). Cyanosis or age lower than 3 months were not significantly associated with malnutrition. Food intake at admission were estimated as 62±21 % of RDA for age (57±16% in children with PHT vs 68±19% in the others, P<0.01). If expressed per ideal W for H, food intake was 57±15% RDA in children with PHT vs 68±17% in the others, (P<0.01). Nutritional support was proposed to 100% of children (oral hypercaloric feeding 59%, enteral feeding 41%). The mean supply was 130 kcal/kg/d, range 0.8–1.6 kcal/ml, 130 ml/kg/d and 1.4 mmol NaCl/kg/d, with a good tolerance in all the children.

**Conclusion:** Children with CHD are often malnourished, more wasted than stunted. PHT appears as a risk factors for malnutrition. Spontaneous food intakes do not meet the specific needs of the CHD. Therefore, nutritional support should be proposed in children with CHD, especially before and after cardiac surgery.

**Disclosure of Interest:** None declared.

**PO-N-381**

**NUTRITIONAL ASSESSMENT, MANAGEMENT AND CODING BY A NUTRITION SUPPORT TEAM: PREVALENCE OF MALNUTRITION IN HOSPITALISED CHILDREN AND IMPLICATIONS FOR DRG-BASED REIMBURSEMENT**

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**Objectives and Study:** Malnutrition is common in hospitalised patients. It is associated with higher morbidity and mortality and increased medical expenses. Systematic malnutrition screening and optimal management improve patients prognosis. In diagnosis related group (DRG) based health care systems, malnutrition coding should allow reimbursement of medical resources and economic expenses related to the screening and management of malnutrition. But the coding of malnutrition is far from optimal for diverse factors. The aim of this study was to screen for malnutrition in hospitalised children, initiate treatment and to code all cases of malnutrition in order to evaluate the economic impact of such practices.

**Methods:** This prospective study was conducted by a nutrition support team (NST) over a three months-period in 2009 in two wards (pediatric neurology and pediatric orthopedic surgery) of a tertiary care pediatric hospital whose malnutrition coding in 2008 was 2% and 0% of stays respectively. All children with a length of stay of at least two days were included in the study. A dietitian collected the data (weight, height, growth charts, clinical history) and each case was reviewed by a pediatrician specialized in nutrition to assess the nutritional status (mild, moderate or severe protein-energy malnutrition, obesity, and absence of nutritional pathology), initiate nutritional management and code as appropriate according to the international classification of disease -10th version. The economic impact for hospital reimbursement was then calculated.

**Results:** 348 children were studied. Malnutrition prevalence was 20%. The systematic coding of all 68 malnutrition cases led to an increase of 127 745 Euros in reimbursement to the hospital.

**Table:**

<table>
<thead>
<tr>
<th>Nutritional status</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
<th>obesity</th>
<th>No nutritional disease</th>
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<tr>
<td>Neurology</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td>37</td>
</tr>
</tbody>
</table>

**Conclusion:** This study confirms there is still a high prevalence of malnutrition in hospitalised children. Nutritional assessment and appropriate management by specialized nutrition teams allows coding of malnutrition and leads to considerable reimbursement for hospitals. Screening, management and coding of malnutrition by specialized nutrition teams (NST) should be encouraged and developed to improve patient care and cost effectiveness.

**Disclosure of Interest:** None declared.

**PO-N-382**

**INFLUENCE OF BODY COMPOSITION ON FEV(1), FEV(6), FEV(1)/FEV(6) AND PEAK EXPIRATORY FLOW RATE**

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**Objectives and Study:** Body composition analysis is currently accessible to clinician. In adults, it was shown the
The aim was to determine if respiratory parameters (Peak expiratory flow rate (PEF), VEMS, VEMS/CV...) were influenced by body composition.

**Methods:** We included patients less than eighteen years of age admitted to the department of pediatrics during the 1st six-month period of 2009. Children were excluded if they were taking medications, or suffering from diseases known to affect body composition or cardiopulmonary function (cardiac failure, cystic fibrosis, renal disease, dehydration, diuretics, perfusion, artificial nutrition...). Anamnestic and anthropometric data were collected. FEV(1), FEV(6), FEV(1)/FEV(6) (=VEMS/CV), PEF were determined using a PiKo-6™ device. Body composition was measured by multifrequency bioelectrical impedanceometry.

**Results:** 29 children (24 girls and 5 boys) were included. The mean age was 15.2 ± 1.5 years, BMI 22.5 ± 4.6 kg/m², oximetry SpO2 99.01 ± 0.19%, PEF 365.5 ± 42.4 L/min (88.1 ± 7.5%) and FEV(1)/FEV(6) 0.8 ± 0.1. Mean FFM/weight was 0.8 ± 0.1, mean FM/Weight of 0.2 ± 0.1 and MCA/height 2 9.4 ± 1.7 kg/m².

We found a negative correlation between BMI and PEF and BMI and FEV(1)/FEV(6). It was also found a negative correlation between FFM and PEF and between FFM and FEV(1)/FEV(6).

**Conclusion:** Our study confirms negative association between FM and respiratory status. Overweight children with obstructive symptoms would improve their respiratory status by losing weight.

**Disclosure of Interest:** None declared.

**PO-N-384**

**RELATIONSHIP BETWEEN FEEDING TYPES AND FECAL CALPROTECTIN LEVELS IN INFANTS**

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**Objectives and Study:** Fecal calprotectin (FC) is potentially important clinical test as a marker of inflammation in the gastrointestinal tract. The aim of our study was to evaluate association between feeding types in infants and FC levels in addition to the factors affecting feeding with breast milk in the community. It is also considered that the gained FC levels can be used as references for future studies.

**Methods:** The study includes healthy 80 infants who use different feeding types. Group 1 consists of infants fed with only breast milk, group 2 consist of infants fed with breast milk+formula, group 3 consist of infants fed with only formula with probiotic, group 4 consist of infants fed with only standard formula. Of all infants, 41 of them are female, 39 are male. Mean age is 2.9 ± 1.3 months (1–5.5 months). FC levels in stool were studied by ELISA method (Immuno- nodiagnostic, Germany).

**Results:** Mean FC level in our study was 5.97 mg/L (9.32–27.51 mg/L), 9.57 mg/L (4–15.6 mg/L), 6.04 mg/L (5.75–28.9 mg/L), 16.08 mg/L (5.75–28.9 mg/L), 7.3 mg/L respectively. There were no statistically significant difference between the group 1-group 2 and group 1-group 3 in FC levels of infants. But FC level of the group 4 was significantly higher than group 1 (P=0.0001), group 2 (P=0.0001), and group 3 (P=0.002).

**Conclusion:** We investigated intestinal inflammation using FC levels and the lowest level was determined in the infants feeding with only breast milk. The results of this study that formulas formula supported with prebiotics have more influence between body composition and respiratory function. But there is little data in children.

**PO-N-383**

**PREVALENCE OF OVERWEIGHT AND OBESITY IN SAUDI CHILDREN AND ADOLESCENTS**

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**Objectives and Study:** There is limited information on overweight and obesity in Saudi children and adolescents. The aim of this report is to establish the national prevalence of overweight and obesity in Saudi children and adolescents. The data set of the 2005 Saudi reference was used to calculate the BMI for age for children 5 to 18 years. Using the 2007 WHO reference, the prevalence of overweight, obesity and severe obesity in all age groups was 23.1%, 9.3% and 2% respectively. Boys had a significantly higher prevalence of obesity (10.1% vs 8.4%; P < 0.001) and severe obesity (2.3% vs 1.6%; P < 0.001), but girls had higher prevalence of overweight (23.8% vs 22.4%; P = 0.014).

**Conclusion:** This report establishes the national prevalence of overweight, obesity and severe obesity in Saudi children and adolescents, indicating intermediate levels between developing and industrialized countries consistent with the socioeconomic status of the country. Measures should be undertaken to prevent further increases of prevalence and associated health hazards.

**Disclosure of Interest:** None declared.
positive physiological effects and more healthy intestinal colonization formation than standard formulas.

**Disclosure of Interest:** We investigated intestinal inflammation using FC levels and the lowest level was determined in the infants feeding with only breast milk. The results of this study that formulas formula supported with prebiotics have more positive physiological effects and more healthy intestinal colonization formation than standard formulas.

**PO-N-385**

**NUTRITIONAL SUPPLEMENTATION IN CHILDREN ON PERITONEAL DIALYSIS: A SINGLE CENTER EXPERIENCE**

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**Objectives and Study:** Protein-energy malnutrition is a common problem in children on chronic peritoneal dialysis (PD). Nutritional supplementation (NS) has proved to be useful in increasing nutritional intake, but there is a lack of consensus about efficacy, indications, methods of supplementation and timing.

**Methods:** We retrospectively studied the prevalence and outcome of NS in children younger than 10 years who underwent PD.

Out of 25 children (18 males), median age 1.6 yrs (0.4–9), seventeen underwent NS (Group A) because of protein energy wasting and 8 were not supplemented (Group B) because of poor family compliance (4 pts) or normal nutritional status (4 pts). Methods of NS in Group A were oral supplements (11 pts), nasogastric tube (5) or gastrostomy (1).

Daily energy intake (DEI, %RDA), weight (W) SDS, height (H) SDS, serum albumin, haemoglobin, base excess were assessed for each case at the beginning and at the end of the follow-up (FU) period (transferred to hemodialysis (HD), transplantation, still on PD). Non parametric between-group tests were used and P < 0.05 was considered statistically significant.

**Results:** Median FU was 20.2 months (5.8–58) and 25.8 months (4–69) in Group A and B respectively. Median age at the start of FU were 1.4 yrs (0.4–8.9) in Group A and 5.0 yrs (0.7–9) in Group B (P < 0.005); no differences for the other tested parameters were present at the start of FU. Mean DEI, as %RDA, during FU was significantly higher in Group A than in Group B (100.63 ± 14.65 vs 75.6 ± 18.4, P < 0.01).

During FU, Group A showed a significant improvement in W SDS (from −1.9 ± 1.1 to −1.4 ± 1.0, P < 0.05) but no change in H SDS (from −2.0 ± 1.3 to −1.9 ± 0.9, ns), whereas in Group B W SDS remained stable (from −1.7 ± 1.0 to −1.6 ± 1.0, ns) and H SDS slightly decreased (from −1.8 ± 1.2 to −2.0 ± 1.0, ns).

No significant differences were observed for the biochemical parameters in the two groups.

**Conclusion:** Nutritional supplementation, irrespective of the use of oral supplements, nasogastric tube or gastrostomy, can be useful in increasing energy intake and improving protein energy wasting in children on PD.

**Disclosure of Interest:** None declared.

**PO-N-386**

**ACHIEVING ENTERAL AUTONOMY FOLLOWING SURGERY FOR SHORT BOWEL SYNDROME**

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**Objectives and Study:** Paediatric short bowel syndrome (SBS) carries significant morbidity and mortality. Patients undergoing bowel reconstructive surgery for short bowel syndrome have poor enteral tolerance immediately post surgery. The nutritional status is often maintained solely by parenteral nutrition (PN). Enteral feeds are started as early as possible to stimulate intestinal adaptation, which is a vital phase in achieving enteral autonomy. Published data is limited for the nutritional progression of these patients.

**Objective:** To assess the nutritional and clinical outcomes of infants with intestinal failure following autologous reconstruction surgery and identify factors associated with the resumption of a normal dietary intake.

**Methods:** This was a retrospective study of 20 patients (60% males, gestational age range 24 – 38 weeks) undergoing autologous reconstructive surgery at Royal Manchester Childrens Hospital from 2000 to 2009. Aetiology of SBS were gastrochisis, small intestinal atresia, mid gut volvulus, malrotation and necrotizing enterocolitis. Forty five percent had more than one congenital gastrointestinal condition.

**Results:** The patients underwent longitudinal intestinal lengthening and tailoring procedure (n = 13) and tapering enteroplastic (n = 7) for SBS. Post-operative survival rate was 95%. PN was required post surgery (mean 536 days, median 193 days). Enteral autonomy was achieved in 40% of patients (mean 520 days, median 414 days) while 1 patient remains dependent on nutritional supplements and 8 patients continue to progress with food reintroduction. Two patients developed intestinal and liver failure and required transplantation. Another patient died perioperatively as a result of multi-organ failure. All patients who have achieved enteral autonomy gained weight to higher percentiles post surgery.

**Conclusion:** PN is required post reconstruction surgery for extended periods. Oral intake is gradually increased as tolerated. Potential factors associated with successful resumption of normal dietary intake include early eating experience, short duration on PN prior to surgery, early surgical intervention and using hydrolysed formula as the initial feed.

**Disclosure of Interest:** None declared.
PO-N-387

FEELING OF BURDEN, PSYCHOLOGICAL DISTRESS AND ANXIETY AMONG PRIMARY CAREGIVERS OF CHILDREN WITH HOME ENTERAL NUTRITION


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Objectives and Study: To examine the relationship between several psychological and demographic factors with the feeling of burden experienced by caregivers of children with home enteral nutrition (HEN).

Methods: A prospective observational study was carried out between one year at a multicenter level. Fifty-six primary caregivers of paediatric patients with chronic diseases requiring long-term HEN were recruited. They were asked to respond to specific questionnaires about their anxiety symptoms (STAI), psychological distress (SCL-90-R) and feeling of burden (Zarit). The study was approved by the Ethics Committee of each hospital. Written parental informed consent was obtained.

Results: A statistically significant association was found between caregivers’ feeling of burden and psychological distress (r = 0.516, P < 0.001) and anxiety symptoms (r = 0.376, P = 0.005). No correlation was found between maternal burden related to age and familial socioeconomic status and her child’s diagnosis. Psychological distress mediated the relationship between anxiety symptoms and caregivers’ burden.

Conclusion: Caring for a child with chronic disease often has a significant impact on the child’s immediate environment and a great impact on the family, especially on the primary caregiver. These effects become apparent in both their physical and psychological state of health and often curb their social, cultural and professional opportunities and diminish their quality of life. In our study we found that psychological distress and anxiety increase caregivers’ feeling of burden and may disrupt family well-being. We believe that professionals who attend these patients should be aware and detect high-risk situations in order to plan specific psychosocial aid efficiently.

Disclosure of Interest: No declared.

PO-N-388

SCHOOL ATTENDANCE IN CHILDREN ON LONG-TERM TREATMENT WITH PARENTERAL NUTRITION (PN) AT HOME


Objectives and Study: Incidence of school absenteeism in chronic diseases is approximately twice that of healthy children (Charlton, 1991). Continuing improvements in treatment have enabled children with chronic health problems to be discharged home on “hi tech” treatment and to attend full time school. This study investigates absences of children with severe intestinal failure on long term PN at home (HPN). The aim was to identify if improvements in medical treatment and coordination between health professional and schools has enabled children with intestinal failure requiring HPN to attend school and compare attendance with the national average.

Methods: Details of absences from the attendance registers in the children’s schools were obtained for all HPN children attending our unit and for all children in the United Kingdom and Ireland in full time education between 5–16 years old, for the academic years 2005–2006 and 2008–2009. Age, sex and underlying disease of HPN children were recorded and analysed.

Results: In 2005–2006, 21 children (female: male 12:9) at home on PN treatment were in full time education. 18 were at school and 3 were educated at home with a tutor (all 3 had gut dysmotility). The average absenteeism of children during the year was 15.9% (range 3 – 34%) compared with national average 6.8%. No significant difference noted between secondary/primary school and sex. There was a significantly higher rate of absence (P = 0.01) in children with motility disorders.

In comparison, in 2008–2009, 15 of the 21 children (female: male 8:7) were still on HPN of which 11 were still at school and 1 home educated. Five children were no longer on treatment and had weaned onto enteral feeds, 1 had had an intestinal transplant, 2 had progressed to university education and one was in full time employment. The average absenteeism of patients in 2008 was 18.8% (range 8 – 38%) compared with national average 6.2%.

Conclusion: Children on HPN have higher absences than the national average (with motility disorders significantly worse), although they still have good attendance levels and an excellent level of achievement. Absence level is in keeping with other chronic diseases. School attendance is an important indicator of quality of life with children proving they can do academically well as demonstrated by progressing to university education.

Children who suffer chronic disease should have the opportunity to have a future career. The importance of school should be remembered in a child’s medical management.


Reference:

Disclosure of Interest: None declared.
PO-N-389

ANTICOAGULANT THERAPY WITH WARFARIN DOES NOT INTERFERE WITH BONE MINERAL DENSITY AND GROWTH OF CHILDREN ON HOME PARENTERAL NUTRITION
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Objectives and Study: Warfarin is used in some home parenteral nutrition (HPN) dependent children to prevent embolic events. It has been described that warfarin might affect growth and bone mineralization by interfering with osteocalcin and protein S synthesis. We aimed to evaluate warfarin therapy effect in growth and bone mineral density (BMD) of our HPN dependent children.

Methods: 18 children (10 boys) aged 5.5 to 18 years, median 12, who were on HPN for longer than 5 years were included in the study. 6 children had been receiving warfarin for a median of 9.2 years [2.4 – 13]. Height, weight and BMD were analyzed along with the following variables: sex, age, underlying disease, age at HPN onset, length on HPN, immunsuppressant therapy and warfarin therapy.

Results: 8 children (44%) had normal height, weight and BMD for age. Having a mucosal enteropathy increased the risk of short stature among children on HPN (p = .031). No other variables had significant effect on growth or BMD.

Conclusion: Long-term warfarin therapy does not have adverse effects on BMD and growth of children on HPN. Almost half of children receiving HPN grow normally. Having a mucosal enteropathy is the main risk factor for short stature among these children.

Disclosure of Interest: None declared.

PO-N-390

PARENTERAL NUTRITION (PN) WITH A LOW-FAT, HIGH CALORIE CONTENT REVERSES LIVER AFFECTION IN LONG TERM PN DEPENDENT INFANTS
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Objectives and Study: Parenteral nutrition associated liver disease (PNALD) is a well known and feared complication of long term parenteral nutrition. Especially the lipid content has been suspected to contribute to the aetiology of the liver disease. In many conventional, commercial PN bags, lipids provide a substantial amount of the calories, which infants are dependent upon to ensure sufficient weight gain and growth. In adults a low-fat PN regime has been shown to be effective in avoiding and reversing PNALD. In the present study we report the use of a low-fat PN regime adapted from adults, with calorie content comparable to PN with fat, in 10 infants less than 1 year with signs of liver affection and a need for long term PN.

Methods: All infants dependent on long-term PN admitted to Hans Christian Andersen Children’s hospital, Odense, Denmark during the period January 2007 to December 2009 were started on low-fat PN regime when showing a significant rise in s-bilirubin. A fat-free PN was provided 5–6 times a week. In order to provide essential fatty acids and fat soluble vitamins, PN with fat was given 1–2 times per week. The fat-free PN contained (0.73 kcal/ml) with the calories provided mainly by carbohydrates.

Results: 10 infants were included of which six had intestinal failure due to NEC, one had gastrochisis and small intestinal atresia, one had unrecognized anal atresia, leading to intestinal necrosis and resection, and two had midgut volvulus.

Conclusion: A low-fat PN regime but with a high caloric content known in adults to prevent PNALD is well tolerated and is in an uncontrolled study suggested to reverse liver affection in PN-dependent infants.

Disclosure of Interest: None declared.
Objectives and Study: Low dietary fiber and fluid intake are often considered as important causative factors in the development of childhood constipation. However, studies investigating this relation are contradictory. Most studies that did find a difference expressed fiber or fluid intake in g/day (g/d), while most that did not find a difference expressed intake in g/MJ/d. Therefore, we investigated in a single study dietary fiber and fluid intake in constipated and healthy children and expressed the intake in these groups as g/d as well as g/MJ/d.

Methods: In a cohort of patients with childhood constipation in the Netherlands, food intake was recorded using a 3-day food diary. Dietary fiber, fluid, energy intake were compared with the intake of a large cohort of age matched healthy children (boys 489, girls 515). In addition, dietary fiber intake was compared with the Dutch Guideline on Dietary Fiber Intake.

Results: Ninety-one constipated children (1–12 years; boys 40, girls 51) completed the diary. Fiber intake expressed in g/d was significantly lower in the constipated children (boys: 12 ± 4 g/d vs. 15 ± 6 g/d, P < 0.01, girls: 13 ± 4 g/d vs. 14 ± 5, P = 0.03). However, when expressed in g/MJ/d, intake was similar (boys: 2.1 ± 0.6 vs. 2.0 ± 0.6, P = 0.48, girls: 2.1 ± 0.5 vs. 2.0 ± 0.7, P = 0.11). Water intake expressed in g/d was significantly lower in constipated children (boys: 1.1 ± 0.3 vs. 1.3 ± 0.4, P < 0.01, girls: 1.1 ± 0.3 vs. 1.2 ± 0.3, P < 0.01). Again, when expressed in g/MJ/d, water intake was similar (boys: 1.9 ± 0.05 vs. 2.0 ± 0.02, P = 0.15, girls: 1.9 ± 0.04 vs. 2.0 ± 0.02, P = 0.27). Finally, energy intake (MJ/d) in constipated children was significantly lower (6.0 ± 1.4 vs. 7.6 ± 2.2, P < 0.01, girls: 6.0 ± 1.1 vs. 7.0 ± 2.0, P < 0.01). There was no significant weight (kg) difference (boys: 23.4 ± 9.5 vs. 24.4 ± 9.3, P = 0.69, girls: 23.0 ± 8.1 vs. 25.3 ± 9.8, P = 0.10). Moreover, neither constipated nor non-constipated children met the Dutch recommendations.

Conclusion: Absolute intake of dietary fiber and fluid are significantly lower in constipated children. However, when related to the amount of energy consumed no difference is found with controls. As results seem to depend on the unit used (g/day or g/MJ/day), this could be an explanation for the contradictory data in the literature. However, it remains uncertain if a low fiber or fluid intake is an important factor in the development of childhood constipation.

Disclosure of Interest: F.T.M. Kokke, Danone Research, Grant Research Support.

PO-N-392

CAUSES OF REMOVAL OF TUNNELED CENTRAL VENOUS CATHETER IN CHILDREN RECEIVING HOME PARENTERAL NUTRITION – FIVE-YEAR SINGLE CENTRE EXPERIENCE IN 184 PATIENTS

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Objectives and Study: Parenteral nutrition in children is associated with the risk of complications. Many of them are related to a placement of tunneled central venous catheter. Sometimes it is necessary to remove the catheter due to these complications.

Objective: The aim of this study was to analyze causes and frequency of removal of tunneled central venous catheter in children fed parenterally at home.

Methods: Cases of removal of tunneled central venous catheter in children fed parenterally at home from the 1st of March 2004 to the 28th of February 2009 remaining under the care of the Children’s Memorial Health Institute were retrospectively analyzed.

Results: During the five-year period, from the 1st of March 2004 to the 28th of February 2009 there were 184 patients fed parenterally at home with implanted either Broviac or Groshong type catheter for 163267 days in total. Indications for catheter removal occurred in 78% of exit-site and tunnel infections observed with the frequency of 0.36/1000 catheter-days, representing 30% of all removals. Indications for catheter removal due to blood stream infections occurred in 11% of sepsis with an incidence of 0.12/1000 catheter-days, representing 11% of all removals. Catheter removals occurred in 67% of catheter thrombosis complications with the frequency of 0.1/1000 catheter-days, which represented 8% of all removals. In 45 cases (0.27/1000 catheter-days, 23% of all removals) catheter was removed due to the decision to wean off parenteral nutrition. There were 21% of all removals caused by other reasons such as an incorrect location or a damage of the catheter. There were 14% cases of all catheter removals connected with unplanned weaning off parenteral nutrition secondary to central venous catheter complications.

Conclusion: The survival of central venous catheter was mainly determined by the type of complications. The most frequent cause of the catheter removal was the exit-site or tunnel infection, while the most common catheter related complication was blood stream infection. Planned weaning off parenteral nutrition was the third indication for the catheter removal. It is worth noticing that 14% of all removals (all caused by central venous catheter complications) resulted in the unplanned decision to quit parenteral nutrition program.

Disclosure of Interest: None declared.

PO-N-393

25OH-VITAMIN D3 STATUS IN CELIAC DISEASE: COMPARISON BETWEEN CHILDREN IN ISRAEL AND SPAIN AND THEIR ADULTS’ COUNTERPARTS

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Medical Center, Sachler Faculty of Medicine, Tel-Aviv University, Tel-Aviv; 2Pediatric gastroenterology and nutrition unit, Carmel Medical Center, Haifa, Israel; 3Servicio Immunologia, Hospital Universitario Marques de Valdecilla, Santander, Spain.

Objectives and Study: The relationship between Celiac disease (CD) and bone mineral density (BMD) are obscure. Since reduced BMD is frequently found especially in adult CD and dietary guidelines favor vitamin D supplementation in adults and children with CD, 25(OH) vitamin D3 (25(OH)D3) serum levels were investigated in CD children in order to challenge its routine supplementation in CD.

Methods: Israeli (51), Spanish (59), CD children (group1 and 5, respectively) were compared to children with non specific abdominal pain (54), their parents (80) and a Spanish adult CD patients (22) (group 2,3,4, respectively). All CD patients fulfilled the accepted diagnostic criteria. 25(OH)D3 was checked by Liaison chemiluminescent-immunoassays (DiaSorin, Italy).

Results: Groups 5 and 1 had the highest levels (30.3+/-12.3 and 25.6+/-9.7 ng/ml, respectively) compared to groups 4 and 3 with the lowest levels (20.2+/-10.5 and 20.7+/-10.7ng/ml). The levels in groups 1 and 2 were comparable (25.6+/-9.7 and 24.9+/-11.4ng/ml). Concerning 25(OH)D3 sera levels in the 5 groups, only the difference between group 5 and 4 were significant (30.3+/12.3 and 20.2+/10.5ng/ml, respectively P = 0.003). However, when serum vitamin D level was split above and below 20ng/ml level, 54.5% of Spanish adult CD had vitamin D deficiency, compared to 16.9% of the local CD children (P = 0.001). 29.6% of group 2 had deficient levels compared to 50% of their parents (P = 0.019).

Conclusion: Vitamin-D sera levels negatively correlate with age. Most probably it is the age, more then CD itself that impacts 25(OH)D3 levels. It is rather adult CD more then children that should be assessed for vitamin D levels and supplemented accordingly.

Disclosure of Interest: Non declared.

PO-N-394

NUTRITIONAL RISK IN HOSPITALISED CHILDREN: AN ASSESSMENT OF TWO INSTRUMENTS

Objectives and Study: The relationship between Celiac disease (CD) and bone mineral density (BMD) are obscure. Since reduced BMD is frequently found especially in adult CD and dietary guidelines favor vitamin D supplementation in adults and children with CD, 25(OH) vitamin D3 (25(OH)D3) serum levels were investigated in CD children in order to challenge its routine supplementation in CD.

Methods: In a cross-sectional study two trained investigators applied STAMP and STRONG respectively to eligible inpatients. Demographic data, clinical information, dietetic input and measurements of weight and height were recorded.

Objectives and Study: The relationship between Celiac disease (CD) and bone mineral density (BMD) are obscure. Since reduced BMD is frequently found especially in adult CD and dietary guidelines favor vitamin D supplementation in adults and children with CD, 25(OH) vitamin D3 (25(OH)D3) serum levels were investigated in CD children in order to challenge its routine supplementation in CD.

Results: Groups 5 and 1 had the highest levels (30.3+/-12.3 and 25.6+/-9.7 ng/ml, respectively) compared to groups 4 and 3 with the lowest levels (20.2+/-10.5 and 20.7+/-10.7ng/ml). The levels in groups 1 and 2 were comparable (25.6+/-9.7 and 24.9+/-11.4ng/ml). Concerning 25(OH)D3 sera levels in the 5 groups, only the difference between group 5 and 4 were significant (30.3+/12.3 and 20.2+/10.5ng/ml, respectively P = 0.003). However, when serum vitamin D level was split above and below 20ng/ml level, 54.5% of Spanish adult CD had vitamin D deficiency, compared to 16.9% of the local CD children (P = 0.001). 29.6% of group 2 had deficient levels compared to 50% of their parents (P = 0.019).

Conclusion: Vitamin-D sera levels negatively correlate with age. Most probably it is the age, more then CD itself that impacts 25(OH)D3 levels. It is rather adult CD more then children that should be assessed for vitamin D levels and supplemented accordingly.

Disclosure of Interest: Non declared.

PO-N-395

EFFECT OF EXTENSIVELY CASEIN HYDROLYZED FORMULA (EHPF) ON GASTROESOPHAGEAL REFUX (GER) IN SYMPTOMATIC PRETERM INFANTS.

Objectives and Study: Feeding intolerance characterized by vomiting, large gastric residuals, abdominal distension is common in preterm infants. Human milk (HM) feeding has been shown to be associated with less feeding intolerance and is the first-choice milk in very low birth weight infants.

Statistical analysis used weight-for-height (height <120cm) and BMI (height>120cm) as proxies for acute undernutrition and height-for-age for chronic undernutrition. Correlation of assessed risk and two factors predictive of nutritional risk: anthropometric nutritional status and presence of nutritional intervention, were used to evaluate validity of the instruments.

Results: 43 children (mean age 6 years and 4 months) were assessed by STAMP and STRONG. Using STAMP the population was classified as 44% high risk, 28% medium risk and 28% low risk. Using STRONG, 25% were high risk, 46% were medium risk and 29% low risk. For validity, STAMP scores correlated to weight-for-height (P < 0.01) and height-for-age (P < 0.01) but correlation was not significant for body-mass-index (P > 0.05). STRONG correlated to all anthropometric measures (P < 0.01). For STAMP and STRONG 60% and 83 % respectively of children ranked as high risk received nutritional intervention. Both tools identified all of the acutely malnourished (Z score <2 weight-for-height, or body-mass-index) and 7 of 8 chronically malnourished children (Z score >2 height-for-age). STAMP took 10–15 minutes to apply, and involved measuring children’s weight and height, and STRONG took 5–10 minutes.

Conclusion: In terms of validity; STAMP correlates less closely to anthropometric assessment of nutritional status and identifies considerably more children who receive nutritional intervention as high risk than STRONG. This suggests STAMP over-diagnoses nutritional risk. In terms of ease of use STAMP involves measurement of each child’s weight and height. Only 12.5% of inpatients had heights recorded. STAMP takes approximately ten minutes longer than STRONG. Both for validity and ease of use STRONG was superior to STAMP.

References:
1. www.stampscreeningtool.org

Disclosure of Interest: None declared.

PO-N-395
In formula-fed infants, hydrolyzed cow’s milk protein has been shown to promote gastric emptying, to accelerate the gastrointestinal transit of formula and to induce frequent loose of stools if compared with native cow’s milk protein. Recent studies suggest that protein hydrolysate improved the feeding tolerance in preterm infants compared with standard preterm formula: no studies have reported its effect on GER, which is common in preterm infants. Multichannel intraluminal impedance (MII) is a technique that detects GER, regardless of its acidity, as electrical impedance changes occurring inside esophageal lumen. Combined pH-MII allows the detection of both acid and non acid GER episodes and could be useful to evaluate GER features in preterm infants, whose gastric pH is often buffered by frequent milk meals.

The aim of the present study was to test the efficacy of extensively casein hydrolyzed formula (eHPF) on GER in symptomatic preterm infants.

Methods: Sixteen preterm infants (EG <33 weeks; mean birth weight 1193 g) with symptoms of GER (frequent regurgitations and/or postprandial desaturations) were enrolled in the study. At the time of enrolment, all infants were fed an eHPF (Nutramigen). Each patient underwent a 24 hour, continuous and simultaneous measurement of intra-esophageal pH and impedance (pH-MII). During the study period, each patient was fed 8 meals: 4 meals of preterm formula (PF) or HM and 4 meals of the eHPF. GER features in the post-prandial periods after the eHPF administration were compared with those of the post-prandial periods after HM or PF administration by Wilcoxon’s test.

Results: A mean of 30.7 acid-GER (22.5 by pH-monitoring: 8.19 by MII) after eHPF, and a mean of 39.4 acid-GER (30.8 by pH-monitoring: 8.56 by MII) after HM/PF were detected. The difference in GER episodes detected by pH-monitoring was statistically significant (P = 0.041).

Conclusions: Feeding preterm infants with an eHPF reduces acid GER indexes. The study population needs to be enlarged in order to confirm this result.

Disclosure of Interest: None declared.

PO-N-396

EFFECTIVENESS OF SPECIFIC NUTRITIONAL SUPPORT IN PATIENTS WITH TYROSINEMIA TYPE 1

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Objectives and Study: A low phenylalanine-tyrosine (Phe-Tyr) diet is recommended in patients with tyrosinemia type 1, since therapy with 2,2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanidion (NTBC) is not able to prevent all possible complications related to persistent chronic hyper-tyrosinemia. When overall caloric and protein ingestion does not meet the patient’s needs, disorders in body composition may occur.

Aim: To assess body composition and resting energy expenditure (REE) along time in patients with tyrosinemia type 1 undergoing treatment with NTBC, referred for specific nutritional support.

Methods: Body composition assessment using skinfold-thickness equations and bioimpedance analysis was performed. Lean body mass (LBM), fat body mass (FBM), total body water (TBW) and extracellular water (ECW) were expressed as percentage normal value (%). Body cell mass (BCM) was expressed as percentage LBM. Recommended caloric intake was estimated using REE measured by indirect calorimetry and physical activity level. Protein intake recommendations were made according to age and weight. Phe and Tyr intake was limited according to their plasmatic levels and special Phe-Tyr-free formula was prescribed to complete aminoacid requirements.

Results: Seven patients (4 male) were referred. Median age was 24 months (3–180). Median follow-up time was 10 months (1–25). In 5 patients, specific nutritional support was begun at the time of diagnosis. In 2 patients, nutritional follow-up was initiated at the age of 7 and 14 years, respectively. Patients with early monitoring showed good quantitative values of LBM (initial 98.2%N ± 14.5; final 96.3%N ± 8.5), with qualitative improvement throughout their follow-up (initial BCM 36.9% ± 3.93; final 43.76% ± 7.15). They also enhanced their FBM (initial 80.66% ± 61.77; final 97.37% ± 42.45), while TBW and ECW levels remained stable. In this group, initial REE was higher than that estimated by predictive equations (118.9% ± 26.36), showing a tendency to decrease along time. In the two patients who started monitoring later on, dietetic habits were hardly alterable. They both showed a tendency towards progressive increase in FBM, keeping steady levels of BCM. TBW also increased, but ECW values diminished throughout the evolution.

Conclusion: 1. When started in early stages, specific nutritional support and monitoring contributed to improve body composition.

2. REE was increased at diagnosis, probably related to a greater oxidative stress.

3. Patients who started monitoring later on showed progressive increase on their fat body mass.

Disclosure of Interest: None declared.

PO-N-397

FREQUENCY AND SIGNIFICANCE OF ERRORS RELATED TO PARENTERAL NUTRITION IN CHILDREN

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PO-N-398

LONG TERM EFFECTS OF LACTOSE RESTRICTED DIET AND PROBIOTICS IN CHRONIC ABDOMINAL PAIN IN CHILDREN: A RETROSPECTIVE STUDY

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Objectives and Study: The incidence of chronic abdominal pain in children in West Europe is 0.3–19%. Lactose malabsorption is present in many children with chronic abdominal pain, with a reported incidence of 2–24%. However, the role of lactose restriction in abdominal pain in children is controversial. In the literature positive short term effects of a lactose restricted diet have been reported, but convincing long term effects have not been found.

In this retrospective study we investigated the frequency of lactose intolerance and small intestine bacterial overgrowth (SIBO) in children with chronic abdominal pain and the effect of treatment (lactose restricted diet or probiotics) in short and long term follow up.

Methods: From April 2006 to January 2007 91 children between the age of 1 to 18 with chronic abdominal pain were evaluated. They underwent a lactose challenge breath hydrogen test. Children with a breath hydrogen concentration above 20 parts per million (ppm) on an empty stomach were considered to have SIBO. Children with an increase in breath hydrogen concentration of 20 ppm and abdominal pain after lactose challenge were considered to have lactose intolerance. Children with SIBO received 1 dose of probiotics for 8 weeks. Children with a positive lactose malabsorption test result were started on a lactose restricted diet. Complaints of abdominal pain were recorded 5 months and more than 1 year after the breath test.

Results: 37 children (41%) had an abnormal test result. 26 children (29%) were found to have lactose intolerance. 11 children had SIBO and 5 children had a combination of lactose intolerance and SIBO. 4 children had a primary lactase deficiency. The mean age was 8.4 years. 57% of the children was of Dutch origin. After 5 months 18 children with lactose intolerance (86%) had an improvement of their symptoms. After 5 months 18 children with lactose intolerance (86%) had an improvement of their symptoms. Only 11 children (52%) improved after 15 months.

Conclusion: In children with lactose intolerance, a lactose restricted diet and probiotics are associated with a decrease in abdominal pain after 5 months. These positive effects are maintained in only half the patients with continued exposure. A lactose restricted diet is just a short term solution in children with lactose intolerance.

Disclosure of Interest: None declared.

Table:

<table>
<thead>
<tr>
<th>Lactose tolerance test</th>
<th>Improvement 5 months</th>
<th>Improvement 15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIBO</td>
<td>11</td>
<td>7 (64%)</td>
</tr>
<tr>
<td>Lactose intolerant</td>
<td>21</td>
<td>18 (86%)</td>
</tr>
<tr>
<td>Lactose tolerant &amp; SIBO</td>
<td>5</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>29 (78%)</td>
</tr>
</tbody>
</table>

Long term effects lactose restriction and probiotics in abdominal pain *P < 0.005.

Conclusion: In children with lactose intolerance, a lactose restricted diet and probiotics are associated with a decrease in abdominal pain after 5 months. These positive effects are maintained in only half the patients with continued exposure. A lactose restricted diet is just a short term solution in children with lactose intolerance.

Disclosure of Interest: None declared.

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PO-N-399

COMPLICATIONS AND OUTCOME OF CHILDREN WITH INTESTINAL FAILURE IN A SPECIALIST CHILDREN’S HOSPITAL

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Objectives and Study: Children with severe intestinal failure (IF) who are dependent on intravenous feeding for more than 28 days are some of the sickest in-patients. Until recently many of these children would not have survived. They are at high risk of developing life-threatening complications. These include sepsis and intestinal failure associated liver disease (IFALD) that may develop in as many as 40–60% of cases. Risk factors include prematurity, lack of enteral intake, recurrent sepsis and components of the parenteral nutrition (PN) such as lipids.

Methods: The aim of this study was to retrospectively review the diagnoses that predispose children to IF and dependency on PN and review complications and outcome. Children receiving PN for >28 days at our specialist children’s hospital over a 2-year period were reviewed. Age, length of time PN was required, survival and outcome were recorded and analysed. We reviewed complications such as IFALD, the incidence and type of liver complications and additional risk factors including sepsis and prematurity.

Results: 143 children received PN for >28 days. 76 (53%) were male. The median age at start of PN was 1.2 years (range from birth–17 years). The median duration of PN was 60 days (range: 28–478) and median hospitalization was 98 days (range: 30–478). 22 (15%) children were preterm with a median gestational age of 27 weeks (range: 24–33). 75 (52%) had a primary non-digestive diagnosis and 68 (48%) a primary digestive diagnosis (PDD). 22 (15%) developed IFALD as a complication of PN. 14 (11%) developed IFALD type I, 6 (4%) type 2 and 2 (1.4%) developed IFALD type 3 (end stage liver disease) and died. IFALD was significantly more common in children with a surgical diagnosis (P = 0.045) independent of prematurity or sepsis. 98 (69%) children were weaned off PN. 21 (15%) patients had irreversible IF and were discharged home on PN and 23 (16%) children died. In 6 (4%) cases death was related to PN. 91 (64%) children developed sepsis whilst on PN with median episodes of 6/1000 catheter days (range: 0–90/1000).

Conclusion: Children in a specialist hospital with severe intestinal failure for >28 days have an 83% chance of survival. Two thirds or the majority of children are successfully weaned off PN. IFALD is almost always reversible. Death is almost always related to the underlying disease rather than PN. Children with a surgical diagnosis are at a significantly higher risk of developing liver disease. Sepsis with 64% incidence remains a frequent and severe complication.

Disclosure of Interest: None declared.

PO-N-400

COMPARISON OF LIVER FUNCTION TESTS AND SAFETY OF TWO NEW LIPID EMULSIONS SMOFA® AND LIPOFUNDIN® IN CHILDREN WITH INTESTINAL FAILURE

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Objectives and Study: A major complication of parenteral nutrition (PN) is liver disease. Liver damage appears to be multi-factorial in origin, the infusion of soybean emulsion as a lipid source is a major contributory factor. This emulsion is predominantly composed of W-6 fatty acids and has been shown to impair biliary secretion and generate inflammation. The high incidence of liver disease associated with soybean oil has led to the development of new lipid emulsions.

To compare the efficacy and safety of an emulsion incorporating soybean, coconut, olive and fish oils (SMOFA®) with an emulsion composed of medium and long chain triglycerides (LIPOFUNDIN®) in terms of biologic parameters.

Methods: A retrospective study was conducted in children with intestinal failure on treatment with PN when either SMOF or LIPOFUNDIN were introduced as the sole lipid source. Tolerance parameters including haematology and chemistry were assessed when either lipid was commenced and was weaned from PN. Metabolic measurements included serum levels of triglycerides and cholesterol. Clinical efficacy was assessed by reviewing duration of treatment and mortality.

Results: 106 children with median age 0.6 years (range 0–16) when commenced on either SMOF (50 cases, 66% male) or LIPOFUNDIN (56 cases, 59% male). Demographic characteristics and routine laboratory and clinical parameters were similar in both groups when the lipids were started. Both emulsions were well tolerated with no adverse events observed. There was a significant decrease in liver function tests in both groups during the treatment period. ALP fell from median 354 u/l when SMOF was commenced to 299 u/l (P = 0.08) when stopped and from 411 u/l to 340 u/l (P = 0.09) in patients on LIPOFUNDIN. ALT reduced from median of 98 u/l to 42 u/l (P = 0.015) with SMOF and from 110 u/l to 58 u/l (P = 0.001) on LIPOFUNDIN. g-GT reduced from 213 u/l to 105 u/l (P = 0.037) with SMOF and 211 u/l to 148 u/l (P = 0.329) with LIPOFUNDIN. Overall, hyperbilirubinaemia resolved in 30% of cases and bilirubin levels improved in 72% of children with either type of lipid. When PN was stopped, conjugated bilirubin level had significantly fallen to a median of 13 μmol/l (range: 2–231) with SMOF compared to 55 μmol/l (range: 2–548) P = 0.029 with LIPOFUNDIN. Concentrations of serum triglycerides and cholesterol were similar in both groups and within the normal range. Length of treatment with PN and outcome were similar in both groups.

Conclusion: SMOFA® and Lipofundin® are well tolerated in children. Pre-existing cholestasis significantly improves with both lipids, although SMOFA seems to be more effective in
improving hyperbilirubinaemia. SMOFá and Lipofundiná are both efficacious and safe substitutes for soybean emulsions.

Disclosure of Interest: None declared.

PO-N-401

C REACTIVE PROTEIN: A MARKER OF ADIPOSITY OR CARDIOMETABOLIC COMORBIDITIES OF PEDIATRIC OBESITY?

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Objectives and Study: Childhood obesity is a public health problem. The association between obesity and low-grade inflammation is well established. Our aim is to evaluate the association between C Reactive Protein (CRP) and cardiometabolic comorbidities in pediatric obesity.

Methods: Obese children/adolescents with nutritional obesity followed in our outpatient clinic (n=354) were included. Duration of disease (years), BMI Z-score (CDC), percentage of fat mass (DXA) and waist circumference were evaluated. Blood pressure, lipid profile and CRP were measured and HOMA IR was calculated.

Results: The mean chronological age was 10.1 years (SD 3.2; min =1.7; max =16.9) with no differences between gender.

Same data related to descriptive analyses can be observed in Table 1.

CRP was positive and significantly correlated with BMI Zsc (r = 0.271; P < 0.001), %fat mass (r = 0.366; P < 0.001) and waist circumference (r = 0.198; P < 0.001). A strong positive correlation was observed between CRP and fat mass, even for short duration of disease (< 2 years; r = 0.731; P < 0.001). No correlations were observed between CRP and lipid profile variables (total, HDL and LDL – cholesterol, apolipoproteins A1 and B and triglycerides), systolic and diastolic blood pressure and HOMA IR, independently of duration of disease.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 354)</th>
<th>Females (n = 182)</th>
<th>Males (n = 172)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI – Zsc</td>
<td>4.1 (1.7)</td>
<td>4.0 (1.7)</td>
<td>4.2 (1.8)</td>
<td>0.465</td>
</tr>
<tr>
<td>Waist (%/90thPc)</td>
<td>117.7 (12.4)</td>
<td>118.2 (15.9)</td>
<td>116.4 (11.4)</td>
<td>0.076</td>
</tr>
<tr>
<td>%fat mass – (DXA)</td>
<td>45.8 (6.1)</td>
<td>47.2 (5.7)</td>
<td>44.3 (6.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>CRP</td>
<td>0.31 (0.4)</td>
<td>0.32 (0.4)</td>
<td>0.31 (0.4)</td>
<td>0.581</td>
</tr>
</tbody>
</table>

Conclusion: Magnitude of obesity and adiposity as also intra-abdominal fat deposition are predictors of early expression of low grade inflammation. CRP seems not to be a sensitive/early marker of cardiometabolic comorbidity of pediatric obesity.

Disclosure of Interest: None declared.

PO-N-402

ASSOCIATION BETWEEN BREAKFAST CONSUMPTION, BMI AND WAIST/HEIGHT RATIO IN GREEK ADOLESCENTS

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Objectives and Study: To evaluate whether body mass index (BMI) and waist-height ratio (WHtR) are associated with frequency of breakfast consumption and type of breakfast in Greek adolescents.

Methods: This study involved 350 adolescents (162 boys and 188 girls) aged 15 - 18 years in northern Greece. Height, weight and waist circumference (WC) were measured and BMI and WHtR were calculated. Frequency of breakfast consumption and foods eaten for breakfast were recorded. Qualitative analysis of breakfast was based on the “Traffic Light” categories. Statistical analysis of the data was carried out using ANOVA followed by Student’s t-test.

Results: Based on BMI percentiles data, 29% of boys and 21.8% of girls were overweight; 12.3% of boys and 6.9% of girls were obese. WHtR ranged from 0.36 to 0.69 (0.485 ± 0.060, Boys, 0.48 ± 0.057; Girls, 0.49 ± 0.064). Breakfast was eaten 5–7 times/week by 56.2% of boys and 47.9% of girls, while 16.7% of boys and 18.7% of girls skip or rarely have breakfast (never and 1–3 times/week). Two-day breakfast records indicated that 6.8% boys and 5.9% girls eat nothing until 11:00 am, 30.9% of boys and 28.2% of girls eat ‘red’ foods, 47.5% of boys and 49.5% of girls eat ‘amber’ foods, while only 14.8% of boys and 16.5% of girls eat ‘green’ foods. Children who eat breakfast 5–7 times/week displayed statistically significant lower WHtR compared to those who tend to skip breakfast (P < 0.005 compared to never or 1–3 times/wk breakfast). Children consuming ‘amber’ foods displayed statistically significant lower WHtR compared to those eating nothing or eating red foods (P < 0.01 and P < 0.05 respectively (Table). There were no differences between sexes. BMI was similarly affected but only in boys the difference was statistically significant (P < 0.05). The same is the case for “traffic light” categories, displaying lower BMI values in children consuming amber foods.

Conclusion: Highest frequency of breakfast consumption and consumption of ‘amber’ foods are related to lower WHtR.
ratio in Greek adolescents. Further data need to be collected to obtain a nationally representative sample.

**Disclosure of Interest:** None declared.

**PO-N-403**

**SERUM ANGIOGENIC GROWTH FACTORS CONCENTRATIONS IN CHILDREN WITH ACUTE PANCREATITIS AND SEVERE MALNUTRITION TREATED WITH ENTERAL NUTRITION THERAPY**

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**Objectives and Study:** Enteral nutrition therapy is effective method of treatment in acute pancreatitis and malnutrition. Its mechanism of action is not only connected with improvement of the nutritional status of the patient but also with its anti-inflammatory activity and may be different in inflammatory diseases and malnutrition. Vascular endothelial growth factor (VEGF) and transforming growth factor beta 1 (TGF-beta 1) play an important role in the early stage of inflammation. The objective of our study was to assess the influence of the enteral nutrition therapy on serum VEGF and TGF-beta 1 concentrations in children with acute pancreatitis (AP) and severe malnutrition (M).

**Methods:** Twelve children with AP (5 boys, 7 girls, mean age: 13.0 yrs), 7 with M (3 boys, 4 girls, mean age: 8.5 yrs) and 15 healthy controls were enrolled into the study. Patients were treated with enteral nutrition therapy providing 100% of daily requirements, 24 hour a day for 4 weeks using semi-elemental diet. Serum VEGF and TGF-beta 1 concentrations were assessed at the baseline and after 2 and 4 weeks of enteral nutrition therapy using ELISA immunoassays.

**Results:** We found increased serum VEGF concentrations at the baseline in AP group (635.4 pg/ml, P < 0.05) and controls (169.9 and 165.2 pg/ml). Assessing serum TGF-beta 1 concentrations in AP group, we found them decreased at the baseline (18.8 ng/ml) compared to M group (31.3 ng/ml, P < 0.05) and controls (24.8 ng/ml; P < 0.05).

During enteral nutrition therapy we observed an increase of serum TGF-beta 1 concentration after 2 and 4 weeks (respectively: 26.6 and 27.5 ng/ml, P < 0.05) in AP group and a decrease in M group (respectively: 29.5 and 18.6 ng/ml, P < 0.05).

We found better improvement of nutritional status of the patients in M group compared to AP group after 4 weeks of the enteral nutrition therapy (respectively: weight gain: 5 vs 3%, body mass index: 1.2 vs 0.9).

**Conclusion:** Changes of serum VEGF and TGF-beta 1 concentrations during enteral nutrition therapy in children with AP and M may reflect different mechanisms of action of enteral nutrition therapy on the inflammatory process and malnutrition.

**Disclosure of Interest:** None declared.

**PO-N-404**

**BODY COMPOSITION IN CHILDHOOD INFLAMMATORY BOWEL DISEASE (IBD): RELATIONSHIP WITH DISEASE ACTIVITY**

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**Objectives and Study:** Nutritional impairment is common in childhood inflammatory bowel disease with poor weight gain, growth failure and pubertal delay. However, more detailed knowledge about body composition is poorly documented and is relevant to management, particularly nutritional care. The aim of this study is to describe the body composition of a consecutive cohort of children with IBD and describe any relationship with disease activity.

**Methods:** Children were recruited from the regional paediatric gastroenterology unit. All had confirmed inflammatory bowel disease. Height, weight, skinfold thicknesses and bioelectrical impedance analysis were performed using standard methodology. Disease activity was assessed; Paediatric Crohn’s disease Activity Index (PCDAI) for Crohn’s, and Simple Colitis Activity Index (SCAI) for Ulcerative Colitis.
(UC). Multiple regression analysis was used to describe relationships.

**Results:** 55 children were studied, 35 children were male. Median age was 13.7 years (range 6.5 – 17.7). 26 children were pre-pubertal, 9 mid way through puberty and 20 were post-pubertal. Median PCDAI was 10 (range 0–60), 22 (59%) had PCDAI >10. Median SCAI was 1.5 (range 0–12). Regression analysis accounting for age, height, gender and pubertal status assessed the effect of disease activity on weight, fat and lean mass. PCDAI had a significant negative effect on corrected lean mass (beta -0.20, p 0.005 CI -.17, -.03) but not fat mass while in UC disease activity measured by SCAI had no effect.

**Disclosure of Interest:** None declared.

**Table:**

<table>
<thead>
<tr>
<th>Group</th>
<th>Combined</th>
<th>Crohn’s</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>55</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>-0.30</td>
<td>-0.47</td>
<td>-0.23</td>
</tr>
<tr>
<td></td>
<td>(-0.97, 0.65)</td>
<td>(-1.18, 0.44)</td>
<td>(-0.45, 1.01)</td>
</tr>
<tr>
<td>Fat Free Mass</td>
<td>35.33</td>
<td>38.33</td>
<td>34.12</td>
</tr>
<tr>
<td>Mass (Kg)</td>
<td>(27.58, 43.75)</td>
<td>(27.88, 45.03)</td>
<td>(22.92, 40.93)</td>
</tr>
<tr>
<td>Fat Free Mass</td>
<td>14.82</td>
<td>15.04</td>
<td>14.44</td>
</tr>
<tr>
<td>Index (Kg/M2)</td>
<td>(13.81, 16.21)</td>
<td>(13.88, 16.36)</td>
<td>(13.38, 15.57)</td>
</tr>
<tr>
<td>Fat Mass (Kg)</td>
<td>7.52</td>
<td>7.52</td>
<td>6.58</td>
</tr>
<tr>
<td>Fat Mass Index (Kg/M2)</td>
<td>(4.33, 12.66)</td>
<td>(4.75, 11.84)</td>
<td>(3.92, 12.90)</td>
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<tr>
<td></td>
<td>(2.12, 4.86)</td>
<td>(1.96, 4.85)</td>
<td>(2.28, 4.87)</td>
</tr>
</tbody>
</table>

Figures are median (inter-quartile range).

**Conclusion:** Lean mass corrected for age, height, gender and pubertal status is significantly related to disease activity in children with Crohn’s disease but not those with UC.

**Disclosure of Interest:** None declared.

**PO-N-406**

**PREVALENCE OF NAFLD IN OVERWEIGHT AND OBESE SCHOOL CHILDREN**

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**Objectives and Study:** Obesity has been defined as excess of body fat mass. Obesity is a chronic illness whose prevalence increased in developed and developing countries, that affects gradually children as adults. Increase of obesity frequency is important because of accompanying with related problems such as metabolic, endocrine, structural, non-alcoholic fatty liver disease etc. Pediatric liver disease is a serious complication of childhood obesity.

The aim of this study is to determine the prevalence of overweight and obesity prevalence among children of age 6–18 years in Isparta and to determine the frequency of non-alcoholic fatty liver disease (NAFLD) in overweight and obese children.

**Methods:** In this study, children aged 6–18 years old was reached at 10 schools. Data of weight, height, age and gender were collected. Overweight and obesity using age and sex specific body mass index (BMI) cut-off points as defined. Ultrasonography (USG) was performed in overweight and obese children. Ultrasonographic findings were scored from 0 to 6 points.

**Results:** Total 5716 school children were surveyed (2449 girls, 3258 boys). Prevalence of overweight and obesity were 23.4% and 12.4%, respectively. According to gender, the prevalence of obesity in boys was 13.4% and overweight was 24.8%, while in girls, obesity was 11.1% and overweight was 21.5%. We evaluated 175 overweight and obese children with USG. Prevalence of NAFLD was 37%.

**Conclusion:** Obesity has emerged as a significant global health problem in children pediatric population. Pediatric liver disease is a serious complication of childhood obesity. Incidence of pediatric liver disease is rising as childhood obesity becomes increasingly prevalent.

**Disclosure of Interest:** This study is supported by Suleyman Demirel University Research found.

**PO-N-406**

**INTESTINAL PERMEABILITY IN TERM AND PRETERM INFANTS AND TYPE OF FEEDING: HUMAN MILK VERSUS FORMULA**

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**Objectives and Study:** Changes in intestinal permeability (IP) based on type of feeding may play a critical role in the development of gut maturation. Some studies in term infants have demonstrated lower IP in human milk (HM) fed infants compared to formula fed infants within the first postnatal week. The IP is higher in preterm infants than in term infants if measured within two days of birth, but not so clear after gut closure.

**Aim:** To analyze the effect of HM in IP after 7-day postnatal and under 4 months of age in preterm newborns (PN) and in healthy term infants (HTI).

**Methods:** PN inclusion criteria were: less than 35 weeks gestational age (GA), <1500 g birth weight and no significant intestinal or systemic disease. Feedings in HTI were either HM or infant formula (IF). Feeding type in PN was defined as fortified HM (FHM) or preterm formula (PF). A sugar permeability test with lactulose (L) (250 mg) and mannitol (M) (100 mg) per 5 ml water was performed by a single oral load method; 1 mL/Kg in PN and 5 ml in HTI. Urine was collected for 6 hours. Three urinary ratios were established: L/M (index of IP), L/creatinine (L/C) and M/creatinine (M/C).

**Results:** 57 HTI were collected, mean global age 72.5 ± 30.5 days, ranged 18–120 days (64.5 ± 31.6 days in HM group and 74.4 ± 30.3 days in IF group); 18 PN studied...
Table:

<table>
<thead>
<tr>
<th>Term Infants</th>
<th>L/M</th>
<th>L/C</th>
<th>M/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.31 ± 0.19</td>
<td>3.21 ± 2.80</td>
<td>11.62 ± 11.17</td>
<td></td>
</tr>
<tr>
<td>0.92 ± 0.93</td>
<td>11.67 ± 12.20</td>
<td>264.58 ± 972.49</td>
<td></td>
</tr>
<tr>
<td>P &lt; 0.01</td>
<td>P &lt; 0.001</td>
<td>ns</td>
<td></td>
</tr>
</tbody>
</table>

All figures are median (inter-quartile range).

**Conclusion:** Regarding IP, the L/M ratio is lower in full term infants than in preterm ones; the role of human milk appears to be more important in preterm infant than in term infant.

**Disclosure of Interest:** None declared.

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**PO-N-407**

**THE EFFECT OF DIET ON CHILDREN’S MENTAL PERFORMANCE – A QUALITATIVE STUDY OF PERCEPTIONS, ATTITUDES AND BELIEFS OF PARENTS IN FOUR EUROPEAN COUNTRIES**

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**Objectives and Study:** Nutrition is one of the many factors that influence a child’s cognitive development and mental performance. Understanding the relationship between nutrition and mental performance in children is important in terms of their attainment and productivity both in school and later life. Parents play a key role in the development of children’s food choices and dietary habits. To date, there is little published research on parent’s perceptions of the relationship between diet and mental performance of children. The present study aims to qualitatively examine parents’ perceptions and beliefs about this relationship.

**Methods:** The study was conducted in four European countries, England, Germany, Hungary and Spain. Participants were parents of children aged 4–10 years recruited through state elementary schools. A semi-structured interview schedule was used to conduct interviews with a total of 127 parents; it included questions on the effect of food on a child’s physical and mental wellbeing and development. Further questions were asked about short or long term effects of diet, the effects of specific foods, meals and supplements.

**Results:** Four main themes emerged from the interviews with a number of subthemes: “physical effects of diet”, “mental effects of diet”, “healthiness of diet” and “parenting (responsibility, food preferences, dietary habits)”. The mental effects of diet are perceived by parents to be on attention and concentration as well as on children’s mood and behaviour. Negative effects are associated with sugary and fatty foods while positive effects are associated more generally with a healthy balanced diet.

**Conclusion:** In all countries parents perceive attention and concentration to be negatively affected by sugary and fatty foods while a healthy balanced diet is believed to have a positive effect on mental outcomes. Based on the exploratory findings of this study, subsequent quantitative studies will need to further examine the prevalence of these perceptions in relation to socioeconomic factors. A detailed understanding of parents’ perceptions of the relationship between diet and mental performance can provide valuable input for better targeted and formulated communication with parents, including intervention programmes as well as claims related to specific food products.

**Disclosure of Interest:** None declared.

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**PO-N-408**

**ADIPONECtin, AFABP AND LEPTIN IN HUMAN BREAST MILK DURING TWELVE MONTHS OF LACTATION**

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**Objectives and Study:** Adiponectin, adipocyte fatty acid binding protein (AFABP) and leptin were previously shown to be present in human breast milk immediately after delivery. The aim of our study was to determine intra-individual changes of breast milk levels of these analytes during twelve months of lactation.

**Methods:** We collected breast milk from 72 healthy mothers after delivery (day 0) and after 1, 3, 6 and 12 months of lactation. We measured adiponectin, AFABP and leptin levels using high sensitive ELISA method. (Biovendor).

**Results:** Adiponectin levels in breast milk on day 0 (D0) were 22.8 ± 0.8 (mean ± S.E.M.), in 1 month (M1) 22.0 ± 0.6, in 3 months (M3) 20.5 ± 0.6, in 6 months (M6) 21.4 ± 0.8 ng/ml, and in 12 months (M12) 25.7 ± 1.4 ng/ml.

AFABP levels on D0 were 12.3 ± 2.0, in M1 6.2 ± 1.3, in M3 1.3 ± 0.2, in M6 2.5 ± 1.0 ng/ml, and in M12 4.6 ± 1.9 ng/ml.
Leptin levels on D0 were 0.3 ± 0.04, in M1 0.2 ± 0.03, in M3 0.1 ± 0.01, in M6 0.1 ± 0.02 ng/mL, and in M12 0.2 ± 0.04 ng/mL.

We found significantly higher levels of adiponectin in M12 in comparison to M3 and M6 (overall \( P = 0.0026 \), Kruskal-Wallis test), significantly higher levels of AFABP in D0 and M1 when compared to M3, M6 and M12 (\( P < 0.0001 \), Kruskal-Wallis test) and significantly higher levels of leptin in D0 than in M1, M3, M6 and M12 (\( P < 0.0001 \), Kruskal-Wallis test).

Conclusion: All hormones were detectable in breast milk up to 12 months of lactation with decreasing trend in levels until M3 and subsequent increase till M12. These hormones may play a role in nutritional programming of infants, probably during the whole lactation period. Higher levels in second half of lactation period may be caused by longer intervals between breastfeeding due to introduction of complementary food. The study was supported by research grant VZ MZO 64203/6903.

Disclosure of Interest: None declared.

PO-N-410

ANALYSIS OF NUTRITIONAL INTAKE AT 4 YEARS OF AGE IN A PROSPECTIVE COHORT: THE NUHEAL STUDY

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Objectives and Study: Seafood consumption during childhood may be beneficial for child neurodevelopment, perhaps via mechanisms involving docosahexanoic acid (DHA) and eicosapentaenoic acid (EPA), found at high concentrations in certain types of seafood, especially fatty fish. Our goal was to analyze data from three European countries to examine nutritional intake in 4 year old children, whose mothers participated in the NUHEAL Project. Study Design: 311 healthy pregnant women were recruited at three different European centres (Ludwig Maximilians University of Munich, Germany; University of Granada, Spain and University of Pécs, Hungary). They were randomly assigned to 4 groups and received daily from the 20th week of pregnancy until delivery either fish oil providing 500 mg DHA+150 mg EPA, 400 μg 5-MTHF, both or placebo, together with vitamins/minerals in amounts meeting the recommendations during pregnancy for European mothers.

Methods: At 4 years, dietary intake was assessed in 149 children using a food frequency questionnaire (FFQ) adapted for each country. Spanish food tables were used for nutrients and University of Granada data for fatty acids composition. Statistical Analysis: Kruskal Wallis Test was used for the comparison between centres. The statistical analysis was performed using SPSS version 16.0.

Results: The FFQ data showed no differences in dietary intake of energy and nutrients between treatment groups. However, there was evidence of differences between countries in Energy, Protein, Carbohydrates, total Lipids, Fatty acids, cholesterol and iron intake. The Spanish children showed a higher Energy, Protein, Carbohydrate and total
Lipids intake that those from Germany or Hungary (P=0.001). Saturated, monounsaturated and polyunsaturated fatty acids (PUFAs) as well as cholesterol and iron intake were higher in the Spanish children including DHA and EPA (P = 0.000). The German children had the lowest mean intake of Carbohydrate and PUFAs. Moreover, 7 of the Spanish children were overweight/obese (15%) and they showed total cholesterol intake 1.5 times higher than German and 1.7 higher than Hungarian children.

**Conclusion:** These results suggest that Spanish Andalusian children show a different pattern of dietary intake from German or Hungarian children, although they have a higher mean intake of DHA and EPA the rate of obesity and intake of cholesterol are higher than in the other European children studied.

**Disclosure of Interest:** "This work is a part of the 6th EU Framework Program Food quality and safety. EARNEST Project Contract n° 007036.

### PO-N-411

**QUANTITATIVE STUDY OF SPANISH PARENTS BELIEFS OF WHAT EFFECTS CHILDREN’S MENTAL PERFORMANCE**

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**Objectives and Study:** Parents have a direct influence on the food choices presented to children in the home. Thinking of what parents consider when choosing food for their children it is important to know what factors they perceive to influence a child’s cognitive development and mental performance. Parents play a very important role in the development of children food choices and eating habits which may in turn influence children’s future health positively or negatively. The present study aims to quantitatively examine parents’ understanding of the factors influencing children’s mental performance.

**Methods:** The study was conducted in Spain and participants were parents of children aged 4–10 years recruited through state elementary schools. A card sorting task was developed and used to conduct interviews with a total of 50 parents. Parents were asked about five different group of influencing factors: Biological, Educational, Social, Environmental and Psychological (18 factors in total), factors were based on evidence from scientific literature. Mental performance was defined in terms of Attention, Learning, Mood and Behavior. Parents were asked to rate the effect of each factor as strong, moderate or no effects on child’s mental development in relation to each of the chosen aspects of mental performance. Responses were recorded manually, coded and group analysed using Friedman test and Cronbach Alpha test with the SPSS version 15.0.

**Results:** The Friedman test for the general analysis show that factors that have a strong effect on mental performance for the participant were “School discipline”, “Parents education level”, “Class size”, “Regularity of meals” and “Nutrition as a baby” for the four groups of cards colors sorting. Although Mood is considered lower than Attention, Learning and Behavior, all were taking from the strong effects answers groups. The card sorting colors game was tested in the study. Using the Cronbach Alpha test the questions’ homogeneity, averaging all correlations between all items, were measured giving a mean value of 95.26/100.

**Conclusion:** Spanish data reveal that parents perceive the Environmental, Social and Educational group of factors as having most influence on children’s mental performance. Mood is valued by the Spanish parents with less responses regarding the strengths compared with Attention, Learning and Behavior, which appear more homogeneous in relation to which factors have an influence in mental performance.

**Disclosure of Interest:** "This study is part of the FP7 Project NUTRIMENTHE Grant agreement n°: 212652.

### PO-N-412

**FEEDING AND SWALLOWING PROBLEMS, GASTROINTESTINAL DYSFUNCTION, AND NUTRITIONAL STATUS IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY**

Y. Chen1, H. Shih, Y. Jong. Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

**Objectives and Study:** Duchenne muscular dystrophy (DMD) is a progressive X-linked myopathy arising from the complete absence of functional dystrophin at the myofiber plasma membrane and also results from mutations in the dystrophin gene. The progression of muscle degeneration affect motor functions, may compromise feeding and swallowing, gastrointestinal dysfunction, and nutritional status. We conduct a questionnaire survey for addressing the prevalence of and predictive factors for feeding and swallowing difficulties, gastrointestinal dysfunction, and malnutrition in DMD patients.

**Methods:** From January 2009 to November 2009, a dedicated questionnaire survey was conducted by a medical center in Kaohsiung, Taiwan, and 77 biopsied and/or genetically confirmed DMD patients participated. The questionnaire includes demographic data, current ambulatory status (walker, sitter, non-sitter), feeding and swallowing difficulties, gastrointestinal and respiratory dysfunctions. Malnutrition is defined as body weight Z score < -2.

**Results:** Sixty nine DMD patients met the inclusion criteria (mean age: 12.97 ± 5.47 years, range 4–32 years). The prevalence of feeding and swallowing difficulties in DMD is common (pre-oral phase 28/69, 40.6%; oral phase 25/69, 36.2%; pharyngeal phase 15/69, 21.7%; esophageal phase 14/69, 20.3%). The prevalence increases with age.

www.jpgn.org
Non-sitters have more feeding and swallowing problems than sitters. Sitters have more feeding and swallowing problems than walkers (pre-oral: $P < 0.001$, oral: $P = 0.02$, pharyngeal: $P = 0.014$, esophageal: $P = 0.002$). Patients with respiratory support have more feeding and swallowing problems than patients without respiratory support (pre-oral: $P = 0.048$, oral: $P = 0.015$, pharyngeal: $P = 0.002$, esophageal: $P = 0.001$). The prevalence of gastroesophageal reflux disease (GERD) in DMD is 4.3% (3/69). The patients with malnutrition have more recurrent pneumonia problems than patients with normal body weight ($P = 0.006$).

Conclusion: Feeding and swallowing difficulties, and gastrointestinal dysfunction are common in DMD. Age, ambulatory and respiratory status are predictive factors affect feeding and swallowing difficulties of DMD patients. Feeding, swallowing difficulties and gastrointestinal dysfunction may lead to malnutrition and compromise their respiratory status.

Disclosure of Interest: None declared.

PO-N-413

USE THE FAST AND EFFICIENCY MODEL TO EVALUATE BENEFICIAL OF LACTOBACILLI IN VITRO IMMUNODULATION IN INFAMED CAICO-2 CELLS AND MONOCYTES


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Objectives and Study: Lactobacilli have beneficial effect on intestinal inflammation in murine model or clinical trial. To evaluated this evidences efficiency and accurately is considered by in vitro. The mimicking local immune response is developed and utilized in the interactions among bacteria, enterocytes, and immune cells. Our objective is to determine the gene expression profiles of cytokines by anti-inflammatory ability of Lactobacilli in inflamed enterocytes cells and monocytes.

Methods: By using the transwell co-culture model, Salmonella lipopolysaccharide (LPS) was apically added to polarized Caco-2 cells co-cultured with peripheral blood mononuclear cells (PBMCs) in the basolateral compartment for 3 hours. Lactobacilli strains (Lactobacillus casei rhamnosus (Lcr35), L. rhamnosus GG (LGG), L. paracasei, or L. johnsonii) were added to Caco-2 cells in inflamed system for 1, 6, or 24 hours. Various cytokines (interleukin-6 (IL-6), IL-8, IL-10, TNF-alpha, TGF-beta1, interferon-gama and monocyte chemotactant protein-1 (MCP-1) were measured by quantitative RT-PCR. The IL-8 production was measured by ELISA.

Results: The IL-8 secretion in the apical and basolateral compartment was significantly inhibited after Lactobacilli inoculation at 24 hours. Lactobacilli except L. johnsonii significantly down-regulated gene expression of IL-8 in Caco-2 cells and PBMCs. With PBMCs and Caco-2 cells, Th3 cytokines (TGF-beta1 and IL-10) and Th1 cytokine (IFN-gama) were up-regulated but Th2 cytokine (IL-6) was down-regulated to Lcr35. In addition, various Lactobacilli were presented to strain-specific re-regulation or down-regulation of gene expression. They were noted to significantly differently from negative control.

Conclusion: Lactobacilli presented significantly anti-inflammatory effects by diminish IL-8 level and demonstrate immunomodulatory activity by up-regulated Th1 and Th3 type cytokines and down-regulated Th2 type cytokines gene expression. These cytokine profiles may help us to understand reasons through which Lactobacilli reduce excessive inflammation at a Caco-2/PBMCs co-culture model.

Disclosure of Interest: National Science Council, Grant Research Support.

Mackay Memorial Hospital, Grant Research Support.

PO-N-414

REINFORCING BARRIER EFFECTS OF COMMERCIAL LACTOBACILLI IN EPITHELIAL CELL CULTURE


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Objectives and Study: Probiotics are considered to reduce diarrhoea duration in clinical. Disruption of the epithelial barrier was affected by pathogens. We have previously shown that Lactobacilli provide anti-inflammation in vitro. The objective of this study was to investigate whether Lactobacilli may limit epithelial damage induced by lipopolysaccharide (LPS).

Methods: Salmonella enterica serotype typhimurium LPS was added to polarized Caco-2 cells for 3 hours. After removing LPS, L. rhamnosus GG (LGG) and L. paracasei were added on inflamed Caco-2 cells for 1, 6, or 24 hours. To identify the damage of Caco-2 cells monolayer was evaluated with epithelial permeability by transepithelial electrical resistance (TEER). The expression of tight junctional protein-1 was measured by immunofluorescence microscopy. The level of inflammatory cytokine interleukin-8 (IL-8) was measured by ELISA.

Results: Compared to LPS-pre-treated controls, TEER of the polarized Caco-2 cell monolayers co-cultured with LGG and L. paracasei was significantly increased after 24 hours. Tight junction in control cells without any supplementation...
PO-N-415

NUTRITIONAL STATUS, FEEDING BEHAVIOR AND INTESTINAL DISORDERS IN CHILDREN WITH PERVERSIVE DEVELOPMENTAL DISORDERS

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Objectives and Study: Pervasive developmental disorders (PDD), including autism, are characterized by disturbances in social interactions and communication, repetitive behaviors and limited range of interests and activities. Eating behavior disorders are recurrent in PDD children, leading to feeding difficulties and to potential nutritional deficiencies. Functional intestinal disorders are also frequent. These disorders lead to the emergence of exclusion diets, although they are not supported by Evidence Based Medicine. An observational study was therefore conducted in order to evaluate the feeding behavior, nutritional status and prevalence of gastrointestinal disorders in children with PDD.

Methods: This prospective, monocentric study was conducted from January 2007 to June 2008. It enrolled 34 children, aged 2 to 18 years, who where consulting for initial diagnostic assessment and evaluation of PDD, according to the standards of the Diseases International Classification. Anthropometric, clinical and biological data were collected as baseline data.

Results: 70.6% of PDD patients were selective eaters. 20.6% complained of abdominal pain more often than once per week, 23.5% had irregular transit and 7.4% of children over 4 years of age were constipated. Markers of celiac disease were not found in any of the patients. 33.3% had hypersensitivity (Elevated specific IgE) to cow’s milk proteins (CMP).

17.6% of children were on a gluten-free or on a CMP exclusion diet, without any improvement on autistic traits noted by parents. No association was found between intestinal disorders (abdominal pain or diarrhea) and hypersensitivity to CMP. The weight Z-score of children with PDD was 0.804 ± 1.49, the height Z-score was 0.29 ± 0.96 and the height to weight ratio was 100% ± 12%. 53% of the patients had a BMI of or greater than median value. No biological marker of undernourishment was identified. The phosphocalcic balance was normal, 45.8% of patients had abnormal low zinc blood levels.

Conclusion: Children with PDD mainly have eating behavior disorders characterized by a marked selectivity. This however does not affect their height and weight growth. Functional intestinal disorders were infrequent and common. The frequency of zinc deficiency should lead to systematic screening and perhaps to supplementation. Gluten and CMP exclusion from the diet did not seem to lead to any improvement on behavior or growth. A randomized controlled study would be necessary to precisely analyze the effects of such exclusion diets on the children’s growth, nutritional status and behavior.

Disclosure of Interest: None declared.

PO-N-416

OMEGA-3, BUT NOT OMEGA-6 POLYUNSATURATED FATTY ACIDS ARE POSITIVELY RELATED IN MATERNAL PLASMA AT BIRTH AND IN HUMAN MILK AT THE 6TH WEEK OF LACTATION

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Objectives and Study: While it is generally accepted that substantial portion of polyunsaturated fatty acids (PUFAs) in human milk (HM) originate from maternal stores and not directly from the maternal diet, the exact relationships are not fully understood.

Methods: We investigated fatty acid composition of maternal and infantile plasma phospholipids at birth and of human milk at the 6th week and 6th month of lactation in 61 mother-infant pairs.

Results: Neither at the 6th week, nor at the 6th month of lactation were n-6 PUFAs in HM related to maternal n-6 PUFAs at birth. In contrast, n-3 PUFAs in HM at the 6th week of lactation were significantly positively related to n-3 PUFAs in the mothers at birth (table). There were significant positive correlations between infantile C20:5n-3 values at birth and HM C20:5n-3 \((r = 0.45, P < 0.001)\), C22:5n-3 \((r = 0.33, P < 0.05)\) and C22:6n-3 \((r = 0.30, P < 0.05)\).

1.49, \(1.0 < r < 0.96, P < 0.001\), C22:5n-3 \((r = 0.30, P < 0.05)\) and C22:6n-3 \((r = 0.30, P < 0.05)\).

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at the 6th week of lactation. No correlations were seen in n-3 PUFAs between birth and the 6th month of lactation.

**Conclusion:** The observation that maternal n-3 PUFA status at birth is significantly and positively related to n-3 PUFA content of human milk at the 6th week of lactation calls further attention to optimal n-3 PUFA supply during pregnancy.

**Disclosure of Interest:** None declared.

**PO-N-417**

**INSULIN RESISTANCE, CLASSIC AND INFLAMMATORY CARDIOVASCULAR RISK FACTORS IN OBESE CHILDREN AND ADOLESCENTS**

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**Objectives and Study:** To analyse the association between classic cardiovascular risk factors, insulin resistance (IR) and adipokines in a sample of obese children and adolescents.

**Methods:** Obesity and overweight were defined according to Cole’s BMI cut off points for age and sex (1). 108 children and adolescent (ages 6–17 years) collected from 5 primary and 2 secondary schools were studied: 55 (40 boys) obese and 53 (33 boys) non-overweight controls selected in the same classroom than the obese students. Weight, height, and abdominal circumference (AC) were determined, and BMI was calculated. After a 12 hour fast, glucose, lipoproteins, high sensitivity CRP, adiponectin, leptin and insulin were determined. HOMA index was calculated afterwards. IR was defined as having a HOMA index value greater than 3.8. Statistical analysis: Chi-square and T-tests, Spearman and Pearson correlation coefficients and multiple logistic regression.

**Results:** 43% of the obese patients showed IR, compared to 8% in controls (P=0.001). Those with IR showed significantly higher leptin (24.1 vs 9.6; P=0.001), AC (84.8 vs 70.0; P=0.001), triglycerides and lower adiponectin (14.0 vs 18.4; P=0.021) and HDL values. HOMA index showed a statistical significant positive correlation with AC (r=0.6), BMI (r=0.6), leptin (r=0.57), CRP (r=0.33), and triglycerides (r=0.49), and a negative statistical significant correlation with adiponectin (r=-0.26), and HDL values (r=-0.34). Backwards multiple logistic regression analysis showed that AC was the only significant predictor for IR (OR: 1.1; 95% CI 1.05–1.17).

**Conclusion:** There is a strong relationship between IR and adipokines in children and adolescents, with multiple pathological implications in the overweight patient. The determination of AC could be an important marker for IR in the paediatric obese patient.

**Reference:**


**Disclosure of Interest:**

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**PO-N-418**

**PLASMA OCTANOYLATED GHRELIN LEVELS IN YOUNG CHILDREN WITH GASTROESOPHAGEAL REFUX DISEASE (GERD) AND FOOD REFUSAL**

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**Objectives and Study:** Ghrelin is an orexigenic peptide, mainly produced by the X/A like cells in the oxyntic mucosa of the stomach. Plasma ghrelin levels increase before the meal to regulate the frequency of the meals. Ghrelin octanoyltransferase octanoylates ghrelin to its active form which binds to the ghrelin receptor to stimulate food intake. The aim of this study was to determine total (octanoylated and non-octanoylated) and octanoylated ghrelin levels in young children with GERD and food refusal compared to normal controls.

**Methods:** A single centre, prospective observational study was performed in 9 patients aged between 0 and 5 years with GERD and food refusal (energy intake less than 80%). The median growth percentile is p10 in this patient group. The
control group consisted of 12 healthy children under 5 years of age with a normal growth and appetite. Their median growth percentile was 50.

Blood samples were taken after an overnight fast. Total and octanoylated plasma ghrelin levels were measured with radioimmunoassay. Statistical analysis was performed using the unpaired t-test. IRB approval was obtained for all subjects.

**Results:** Patients with GERD and food refusal have total plasma ghrelin levels of 957 ± 174 pg/ml. This was significantly ($P = 0.004$) lower than in the control group where ghrelin levels of 592±/−37 pg/ml were obtained. Octanoylated plasma ghrelin levels in the patient group were also elevated (98±/−27 pg/ml) in comparison with the control group (41±/−5 pg/ml) ($P = 0.014$).

**Conclusion:** Ghrelin is significantly higher in young children with GERD and food refusal. This can be explained as a result of their lower body weight. However, these children do not respond to this endogenous hunger stimulus possibly because of the pain due to pyrosis.

**Disclosure of Interest:** None declared.

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**PO-N-419**

**GROWTH TRENDS OF SCHOOL CHILDREN IN BURSA/TURKEY: RE-EVALUATION AFTER NINE YEARS**

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**Objectives and Study:** Nutrition has unique importance on growth, particularly during infancy and puberty. Nutritional insufficiency is a significant cause of morbidity and mortality, therefore assessment of nutritional status of children has a great importance on public health. In the present study anthropometric measurements of pediatric population in the same area was performed twice with nine years intervals (1998 and 2007) in order to compare the changes in children's growth trends.

**Methods:** The study was conducted in a big city, Bursa, which is located on the west part of Turkey and included 1671 schoolchildren (805 female, 866 male). The data of year 1998 formed Group I and year 2007 formed Group II. The selection of the two comparable pediatric populations was done according to Public Health Registry. Body weight, height, upper arm circumference, triceps skinfold and body mass index of the children were recorded. The statistical analysis was done using SPSS 16 TM.

**Results:** The study included 866(51.8%) boys and 805 (48.2%) girls between 6–14 years of age (mean 9.76 ± 2.22 years). Group I consisted of 569(51.4%) boys and 539 (48.6%) girls, mean ages were 9.40 ± 1.94 years and 9.29 ± 2.03 years, respectively. Group II included 297(52.8%) boys and 266 (47.2%) girls, mean ages were 10.64 ± 2.57 years and 10.49 ± 2.29 years, respectively. The comparisons of anthropometric measurements of Group I and Group II were done according to two separate age group: prepubertal (6–11 years) and pubertal (>11 years). While there was no statistical significance in pubertal ages, in prepubertal ages the measurements of both boys and girls in Group II showed statistically significant increase when compared to Group I. Moreover, it was remarkable that the increment in body weight was more than height.

**Conclusion:** The increases in body weight and height, similarly to far-east countries, are considered to be related to improvements in awareness of healthy nutrition in public. Currently prevalence of obesity is 1–40% in Turkey and is 18–54% in United States. Our results showed the increase of weight more than height in prepubertal age groups and this may indicate a risk of obesity for upcoming young generation. As a result of high consumption of fast-food, obesity is particularly a problem of developed countries, however, this problem does not seem so far for Turkey also.

**Disclosure of Interest:** None declared.

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**PO-N-420**

**THE INCIDENCE OF ANEMIA, HYPOPROTEINEMIA, AND EDEMA IN INFANTS AS PRESENTING SYMPTOMS OF CYSTIC FIBROSIS**


**Objectives and Study:** The association of hypoproteinemia/hypoalbuminemia, edema, and anemia is well recognized in infants with cystic fibrosis (CF). Hypoproteinemia is mainly related to malabsorption of dietary protein and excess faecal amino acid losses, secondary to pancreatic insufficiency. The anemia is related to vitamin E deficiency with increased peroxide hemolysis. It has been reported that 5-13% of infants with CF developed protein-energy malnutrition (PEM), which manifests as hypoproteinemia, edema, and anemia. The increased incidence of this symptom complex as first presenting manifestation of CF has been noticed in our region. The aim of this study was to evaluate the incidence of anemia, hypoproteinemia, and edema in infants as presenting symptoms of cystic fibrosis and possible risk factors for the developing of PEM.

**Methods:** Clinical and laboratory profiles (hemoglobin, red blood cells count, total serum protein, serum albumin and liver enzyme levels) and genotype data were analyzed in 120 newly diagnosed infants with CF, during the period from 1990 to 2009.

**Results:** The overall incidence of PEM in our infant CF population was 34% (n=41). A mail predominance was found in the group with PEM (73%). PEM was manifested usually within the first 5 months of life and in breast-fed infants. Mean hemoglobin, red blood cell count, total serum protein and serum albumin values in PEM subgroup were, respectively: 75.0 g/l, 2.4 mil/mm3, 38.2 g/l and 16.4 g/l. Clinically significant liver involvement was found in 22 (53.6%) patients with PEM. Concerning the molecular basis
of CF in these patients, PEM was always associated with DF508, G542X, N1303K and other “severe” mutations.

Conclusion: PEM is a common presenting manifestation of CF in infancy in our region. The predisposed factors for the development of PEM are early infant age, male gender, breast-feeding, impaired liver function and the presence of severe CFTR mutations with respect to pancreatic phenotype. Early diagnosis of CF with immediate initiation of pancreatic enzyme supplementation and nutritional rehabilitation, coupled with aggressive treatment of infections can improve the clinical outcome of CF complicated with PEM.

Disclosure of Interest: None declared.

PO-N-421

FATTY ACID COMPOSITION OF SERUM GLYCEROPHOSPHOLIPIDS IN CHILDREN

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Objectives and Study: Polyunsaturated fatty acids (PUFA) have important biochemical and physiological functions. An adequate PUFA availability is important for growth and development. Monitoring and therapeutic interventions are applied in children with impaired fatty acid (FA) intake, absorption or metabolism, e.g. with gastrointestinal, hepatic or metabolic diseases, which requires reliable assessment of FA status. FA composition of serum glycerophospholipids (GP) is a sensitive and reliable biomarker of the organism’s FA status. We aimed to establish reference values for children using a new and precise high-throughput methodology.

Methods: We analyzed the GP FA composition of 1326 serum samples obtained from a cohort of 951 children at 2 and 6 years participating in a prospective birth cohort study in Germany, the LISA study. FAs were determined from 100μl serum with a method as previously described (Glaser et al., 2010).

Results: We categorized the distribution of FAs in GPs by gender for both age groups (2 years: 412 boys, 325 girls; 6 years: 330 boys, 259 girls). Medians and interquartile ranges were similar for both genders. The two-sided Mann-Whitney rank test revealed no significant differences between boys and girls. GP FA composition from 375 children obtained at two different time points (2 years and 6 years) differed only slightly, with overlapping interquartile ranges. The FA distribution in GPs was similar to values in phospholipids for most of the analyzed FAs. GP FA composition is considered a valuable new biomarker that is very sensitive for PUFA and LC-PUFA status can be easily and fast assessed with high-throughput methodology.


Disclosure of Interest: None declared.

PO-N-422

EFFECTS ON THE IMMUNE SYSTEM OF YOUNG MICE FED WITH INFANT FORMULAS SUPPLEMENTED WITH POLYAMINES

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Objectives and Study: Polyamines are organic compounds present in the human milk. Besides their nutritional role, polyamines are known to play a key role in the development of infant immune system during lactation. In general, the amount of polyamines included in infant formulas (IF) is around ten-fold less than in breast milk. The aim of this study was to determine the impact on the development of the immune system of young mice fed with IF enriched with polyamines at different concentrations.

Methods: BALB/c mice pups of 14 and 18 days of age were orally administered with dam’s milk, physiological saline solution and different concentrations of polyamines, all given in similar volume of 100μl twice daily for four days. The pups were separated in seven experimental groups: A) Unweaned pups receiving milk by normal lactation; B) Unweaned pups receiving milk by normal lactation and saline solution; C) Early-weaned pups fed with mouse milk; D) Weaned pups fed on IF without polyamines; and the groups E), F) and G) fed on IF enriched with increasing amounts of polyamines. After the last day of administration, all the animals were euthanized and samples of blood, spleen, and the mesenteric lymph node were collected. The lymphocyte populations in all samples were analyzed by flow cytometry.
Results: Statistical differences were shown in the percentage of lymphocyte B population in spleen and blood between the group G (50.32 ± 7.50 %) and group D (30.25 ± 5.18 %). Statistical differences between group G and groups A, B and C were not detected. The levels of the CD4+ and CD8+ T cells were significantly higher group G. Statistical differences were not found in the mesenteric lymph node between any of the groups.

Conclusion: Our results suggest that the level of development of the immune cells in young mice receiving higher concentrations of polyamines in the IF is more similar to those receiving mother’s milk than in those receiving no polyamine supplementation in the IF. Findings from the present study appear to indicate that higher amounts of polyamines have a positive impact on the growth and maturation of the immune system of young mice.

Disclosure of Interest: None declared.

PO-N-423

THE PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE AND STEATOHEPATITIS IN TAIWANESE SCHOOLCHILDREN

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Objectives and Study: Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) are emerging clinical problems in both adults and children that may lead to cirrhosis and death. Subjects with NAFLD are found to have higher levels of triglyceride, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values when compared with the subjects without NAFLD. The aims of this study were to investigate the prevalence of NAFLD and metabolic parameters in schoolchildren with over weight and obesity. Moreover, the risks for NASH in obese children were estimated.

Methods: A total of 847 children aged 4 to 12 years with the male to female ratio 1.26 were enrolled. All participants were evaluated by anthropometric measurements including body height, weight and body mass index. The participants were categorized into three groups based on BMI: normal weight (BMI less than 85th%), overweight (BMI between 85th% and 95th%), and obesity (BMI more than 95th%). The serum glucose, AST, ALT, triglycerides and cholesterol levels were statistically different between groups.

Results: The prevalence of overweight and obesity in schoolchildren was 14.8% and 1.14%, respectively. The mean age and male-to-female ratio were significantly higher in children with obesity than those with normal weight (P = 0.001). The rates of abnormal AST and ALT were significantly higher in obese children than the other two groups (P < 0.001). Furthermore, the obese children had higher fasting triglyceride (P < 0.001) and glucose (P = 0.04) levels than those with normal weight. The cholesterol levels were not statistically different between groups.

Conclusion: Childhood obesity is closely related to the male gender, increase of age, fasting triglycerides, and glucose levels. Moreover, the obese children have significantly higher risks to develop NAFLD and NASH.

Disclosure of Interest: The authors guarantee that there are no financial relationships with any company and no conflicts of interest exist.

PO-N-424

THICKENED INFANT FORMULA, RHEOLOGICAL STUDY OF THE “IN VITRO” PROPERTIES

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Objectives and Study: Thickened infant formula, specially formulated to increase the viscosity, are commonly used in the treatment of regurgitation in the non-complicated gastrointestinal reflux. The aim is analyze viscosity and the rheological behaviour of different thickened formula from the Spanish market compared to an standard formula with or without the addition of 10 g/100 mL of gluten-free cereals.

Methods: Viscosity of the samples was evaluated in a Bohlin CS-10 controlled-stress rheometer and was performed at basal conditions (25°C, pH 7) and simulated gastric conditions for infants <6 months age (37°C, pH u and 10 g/100 ml of pepsine) at time 0, 30 and 60 minutes of incubation. Values were expressed as centipoises (1cp = 1/100cP).

Results: All formulas show a viscosity increase both in basal conditions and in gastric simulated conditions but the behaviour is very heterogeneous. Formulas containing bean gum (carob seed flour) with 2.9 g/100 mL and a protein ratio similar to cow’s milk (80 casein / 20 whey) show the highest viscosity (70 cp and 90 cp) and maintained, with significant differences with regard to the standard formula in all the measurements. When this thickener are in formulas with a protein ratio similar to breast milk (40 casein / 60 whey) the viscosity was lower and reached 50 cp only with the concentration of thickener of 4.7 g/100 mL, significant differences are reached versus standard formula. The formulas with thicker starches (rice, potatoes and corn) achieve a lower viscosity and less maintained, without a significant difference. The viscosity reached after the addition of cereals both in basal conditions and in gastric simulated conditions
was similar to that achieved with more effective ways of bean gum. Lipid concentration is not involved in viscosity and rheological behavior

**Conclusion:** The viscosity of the thickened infant formula depends on the agent used, concentration and ratio of this protein. Not all reach a viscosity of 50 cp, hypothetical value to get, since it would get double the viscosity of standard formula. It remains to be elucidated the ideal viscosity to be reached and the role of other components of the formula in the viscosity and rheological behavior.

**Disclosure of Interest:** None declared.

**PO-N-425**

**FEecal CALPROTECTIN IN AUTISTIC CHILDREN BEFORE AND AFTER THE USE OF ELEMENTAL DIET**

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**Objectives and Study:** Autism is a complexed neurodevelopmental-neurobiological disorder of behaviour, which is characterized from loss in three domains: social behaviour, status of contact-speech, interests. From the other hand, gastrointestinal problems like constipation, diarrhea or vomiting are often seen in autistic children, are very difficult to resolve and we don’t know if these are caused by the main disorder (are part of it) or are ‘side effects’. The aim of the study was the investigation of the degree of possible inflammation of the autistic children’s intestine mucosa by measurement of fecal calprotectin levels and observation of their changes after the introduction of elemental diet.

**Methods:** A total number of 65 children aged 2.5 to 8 years were checked(group A). All of them were diagnosed with pervasive developmental disorder (international criteria 1994). Further, the children were randomly divided in two groups, 32 of the children started elemental formula (containing free aminoacids-Neocate\(^{1}\)) diet with exclusion of all milk products or milk containing food(group B) and the rest 33 children continued their previous diet(group C). Also, fecal calprotectin levels were measured in samples of 22 healthy children(aged 2 to 8 years) having normal diet(group D). The count of the levels of calprotectin was done in fecal samples using Elisa method. Statistical analysis was performed using SPSS 14.0 statistical software and x2-test. The study was accepted by the hospital ethics committee.

**Results:** Statistical significant differences (\(P < 0.001\)) were found in fecal calprotectin levels between groups A and D. Also, after 4 months of observation, statistical significant differences (\(P < 0.001\)) were found in fecal calprotectin levels between groups B and C.

**Conclusion:** Children suffering from pervasive developmental disorder have increased levels of fecal calprotectin, but these levels are significantly reduced by the introduction of elemental diet. We have much more to investigate by measuring calprotectin plasma levels, examine the gastrointestinal tract by other methods and correlate the findings with the frequency of gastrointestinal symptoms of these children.

**Disclosure of Interest:** None declared.

**PO-N-426**

**FEEDING PRACTICES OF 12–23 MONTHS AGED CHILDREN IN TURKEY**

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**Objectives and Study:** Adequate nutrition during infancy and early childhood is essential to ensure the growth, health, and development of children to their full potential. Optimal feeding practice in the two years of life is crucial for the survival and health of infants, and has long-term consequences in later life. To determine the duration of breastfeeding and age of introduction of complementary feeding and to ascertain the social and demographic factors associated with them are the main objectives of this study.

**Methods:** A community-based, cross-sectional survey using a multistaged, weighted, cluster-selected sample was conducted in 3 NUTS regions with high, middle and low nutritional status (two cities in each region) of Turkey. As a total, 1729 children aged 12–23 months were enrolled. Mothers were interviewed to collect information on breastfeeding and amount and types of complementary foods introduced and potentially related factors by a questionnaire.

**Results:** In this survey, breast feeding rate of children was 99% at birth. Fifty six percent of mothers introduced yogurt-cheese, 32% cow’s milk, 41% formula and 40% cereals before the age of 6 months. Introduction of complementary foods such as meat-poultry-fish and eggs were late, and the given amounts of yogurt-cheese, meat-poultry-fish, fruits and vegetables were inadequate in the malnutrition high region, compared to other regions (\(P < 0.05\)). Higher educated and working mothers had better complementary feeding practices including both timing of introduction and the amount of complementary foods (\(P < 0.05\)).

**Conclusion:** Complementary feeding is introduced earlier than recommended. Early introduction of complementary feeding than recommended, rather than duration of breastfeeding is the main recognized problem in Turkey. Improvements in the nutrition of infants could be achieved by counselling on the correct timing of introduction and amount of complementary foods.

**Disclosure of Interest:** None declared.
PO-N-427

TGF BETA2 IN HUMAN MILK AND INFANT FORMULA RESISTS DIGESTION IN A SUCKLING RAT PUP MODEL

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Objectives and Study: TGFβ2 is present in human milk and in some powdered cow milk formulas and is believed to be important for IgA production and oral tolerance induction. We have shown earlier that TGFβ2 in human milk and formula can resist proteolytic degradation by pepsin and pancreatic enzymes in vitro. The purpose of this study was to investigate whether TGFβ2 in human milk and formula can resist proteolysis under conditions similar to those in the infant gut, using a suckling rat pup model that we have developed previously to study the proteolytic fate of human milk proteins.

Methods: Suckling rat pups (14 days old) were fasted 6 h prior to intubation with 0.5 ml human milk or infant formula using a ball-point needle. Pups were killed 4 h post-intubation and stomach and small intestine were removed and rinsed with ice-cold saline. TGFβ2 in original samples, stomach and intestinal contents was analyzed by enzyme-linked immunosorbent assay (ELISA). Alpha-lactalbumin (AL) was used as an easily digested marker protein and analyzed by Western blot. TGFβ2 signal through cell surface receptors with serine/threonine kinase activity to intracellular signaling components known as Smads, which in turn translocate to the nucleus leading to assembly of the transcriptional apparatus of target genes. The Smad2 Redistribution Assay utilizes the MDA-MB-468 cell line and TGFβ2-induced Smad2 translocation is monitored by translocation of a GFP-Smad2 fusion protein from the cytoplasm to the nucleus. The assay response is read using the Cellomics ArrayScan VTi HCS system.

Results: Concentrations of TGFβ2 in powdered cow’s milk infant formula varied and in some cases were higher than in human milk. Partially hydrolyzed infant formula contained 1454 pg/ml TGFβ2. Enfamil Lipil was found to contain 1454 pg/ml TGFβ2, with other intact cow’s milk formulas in the range of 733–1175 pg/ml. For all intact formulas in the cow’s milk formulas tested, 50–65% of TGFβ2 concen- trations were retained in stomach and small intestinal contents 4 h after intubation. No immunodetectable AL was found, demonstrating effective protein digestion.

Conclusion: TGFβ2 present in some infant formulas and human milk continues to be immunodetectable and retains activity 4 h after ingestion in our rat pup model, strongly suggesting that TGFβ2 can survive in the infant gut and exert its biological activities.

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PO-N-428

TWO QUANTITATIVE TRAIT LOCI INVOLVED IN PLASMA CHOLESTEROL LEVEL IN MICE OVEREXPRESSING INTESTINAL SCAVENGER RECEPTOR CLASS B TYPE I


Objectives and Study: The Scavenger Receptor class B type I (SR-BI) is one of the proteins involved in cholesterol transport through the apical membrane of enterocytes. We previously found a decrease by 50% of plasma total cholesterol (pTC) level in transgenic mouse overexpressing SR-BI specifically in the intestine as compared with wild type (WT) mouse1. However this decrease was absent in DBA/2 strains suggesting that the genetic background could modulate the consequences of intestinal SR-BI overexpression on the mechanisms of cholesterol homeostasis. The aim of this study is to determine genes and as a first approach, quantitative trait loci (QTL) associated with pTC levels in these two transgenic mouse strains.

Methods: We crossed one C57Bl/6 transgenic male (F0) with DBA/2 WT females, and selected F1 transgenic mice that were backcrossed with C57Bl/6 WT mice, generating a large number of recombinations. 226 of these transgenic mice (Bc2) were sacrificed at 8 weeks. All experiments were performed with the approval of Animal Ethics Committee.

Results: pTC levels were 0.27 ± 0.03 (F0, n = 33), 0.41 ± 0.02 (F1, n = 36) and 0.54 ± 0.01 g/l (Bc2, n = 226). According to variance analysis, genetic factors could explain up to 22% of pTC differences. We found 2 significant QTL, located on chromosome 8 at 32.9 cM, and on chromosome 4 at 83.7 cM, with LOD scores of 3.1 (P = 0.01) and 2.7 (P = 0.03) respectively. The QTL at chromosome 4 was associated with a lower pTC level in C57Bl/6 homozygote than in heterozygote, whereas it was the opposite for the chromosome 8 QTL. No significant QTL was found associated with plasma triglyceride levels. According to the literature, no gene or QTL involved in lipid metabolism is located near chromosome 4 QTL. On chromosome 8, some genes need further investigations.

Conclusion: In conclusion, we confirmed the difference in pTC levels between DBA/2 and C57Bl/6 intestinal SR-BI transgenic mice. Two significant QTL on chromosomes 4 and 8, are associated with this phenotype.

Reference:
Disclosure of Interest: E. Mas, Fondation pour la Recherche Médicale. X. Collet, INSERM, Grant Research Support. X. Collet, ANR (PNRA 2006), Grant Research Support.

PO-N-429

A NOVEL PREBIOTIC BLEND HAS A POSITIVE IMPACT ON INFANT STOOLING PATTERNS AND PROMOTES NORMAL GROWTH


Objectives and Study: Determine the safety, acceptance, and tolerance of an infant formula supplemented with galacto-oligosaccharide (GOS) and polydextrose (PDX) and its impact on growth, stool characteristics, fecal microbiota and sIgA.

Methods: In this multi-center, double-blind, parallel-designed study, 21 to 30-day old healthy term, vaginally delivered infants were randomized to receive Enfamil Lipil® (Control, Mead Johnson Nutrition) or Control + GOS and PDX (4 g/L, 1:1 ratio, GP) for 60 days. Formula intake, tolerance, and stool characteristics were collected daily using an electronic diary; biweekly mean values were analyzed by repeated measures analysis of variance. Anthropometric measurements and stool samples were obtained at baseline and after 30 and 60 days of feeding. Growth rates were analyzed by analysis of variance. Fecal microbiota was assessed by fluorescent in situ hybridization (FISH); fecal sIgA and parental product assessment (completed at end of study) were analyzed by Wilcoxon test. Dropouts and adverse events (AEs) were recorded.

Results: 159 infants completed the study (Control = 81, GP = 78). Infants in GP had significantly higher formula intake than in Control at 16–30 (29.3 ± 0.8 vs. 26.6 ± 0.8, P = 0.025), 31–45 (30.8 ± 0.9 vs. 27.9 ± 0.9, P = 0.016), and ≥46 days (33.2 ± 0.9 vs. 29.7 ± 0.9, P = 0.006). There were no differences between groups in gassiness, fussiness, and hours of crying per day. GP had softer stools than Control at all time points (see Table). Evaluation of the participants that were compliant with the feeding regimen showed no statistically significant differences in GP vs. Control in changes from baseline for bifidobacteria and sIgA. According to parent’s assessment, infants in GP were significantly more enthusiastic than infants fed the Control but there were no differences among those who received PG4 compared to Control and Control + GOS. No significant differences in growth, dropout rate, and AEs were observed between groups during the study.

Table: Mean Stool Consistency Score#

<table>
<thead>
<tr>
<th></th>
<th>1–15 days</th>
<th>16–30 days</th>
<th>31–45 days</th>
<th>≥46 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.9</td>
<td>3.0</td>
<td>3.0</td>
<td>3.1</td>
</tr>
<tr>
<td>GP</td>
<td>3.3*</td>
<td>3.4*</td>
<td>3.5*</td>
<td>3.4*</td>
</tr>
</tbody>
</table>

#1 = hard, 2 = formed, 3 = soft, 4 = loose, 5 = watery. *GP softer than Control, P < 0.001.

Conclusion: An infant formula with added GOS and PDX is well tolerated and promotes softer stools and growth similar to control formula in young infants.


PO-N-430

GROWTH AND TOLERANCE OF INFANTS FED FORMULA SUPPLEMENTED WITH POLYDEXTROSE (PDX) AND/OR GALACTOOLIGOSACCHARIDES (GOS)


Objectives and Study: Based on recent research that has further detailed the nutrient composition of breast milk, we designed a series of studies to optimize the carbohydrate, fat, and calcium content of infant formula. This study evaluated growth and tolerance in healthy infants who received one of two investigational cow milk-based formulas that differed from one another only in the addition of prebiotic supplements.

Methods: In this multi-center, double-blind, parallel-designed, gender-stratified prospective study 419 infants were randomized to receive a marketed routine cow milk-based infant formula (Enfamil Lipil®, Mead Johnson Nutrition, Evansville, IN; Control) (n = 142) or one of two investigational formulas from 14 to 120 days of age. Investigational formulas were supplemented with PG4 (PDX:GOS 50:50 blend, 4 g/L) (n = 139) or G4 (GOS, 4 g/L) (n = 138). Anthropometric measurements were taken at 14, 30, 60, 90, and 120 days of age. Daily recall of formula intake, tolerance, and stool characteristics was collected from study days 1 to 14 and 24-h recall was collected at 60, 90, and 120 days of age. Medically-confirmed adverse events were recorded throughout.

Results: There were no differences in growth rate from 14 to 120 days of age in infants fed the Control versus either investigational formula. Discontinuation rates were not significantly different among study groups. No differences in formula intake or infant fussiness were observed. During study days 1 to 14 and at 60 days of age infants fed investigational formulas had softer stools than those fed Control and stools remained softer at 120 days for investigational formulas. Discontinuation rates were not significantly different among study groups. No differences in formula intake or infant fussiness were observed. During study days 1 to 14 and at 60 days of age infants fed investigational formulas had softer stools than those fed Control and stools remained softer at 120 days for PG4 (all P < 0.005). Physician-confirmed diarrhea did not significantly differ among groups; nor did reported events of eczema or irritability. There were fewer adverse events related to Eyes, Ears, Nose, and Throat reported among those who received PG4 compared to Control and G4 (both P < 0.038). Interestingly, infants fed G4 had more spitting (P = 0.007) and PG4 less gas (P = 0.009) than infants fed the Control but there were no differences among those who received PG4 compared to Control and G4 (both P < 0.038). Interestingly, infants fed G4 had more spitting (P = 0.007) and PG4 less gas (P = 0.009) than infants fed the Control but there were no differences among those who received PG4 compared to Control and G4 (both P < 0.038). Interestingly, infants fed G4 had more spitting (P = 0.007) and PG4 less gas (P = 0.009) than infants fed the Control but there were no differences.
in gas or spitting between the two prebiotic-supplemented groups.

**Conclusion:** Investigational routine infant formula supplemented with 4 g/L of either a prebiotic blend of PDX/GOS or GOS alone was well-tolerated and supported normal growth. Compared to infants who received the unsupplemented control formula, infants who received prebiotic supplementation experienced softer, gentler stooling similar to that reported in breastfed infants.


**PO-N-431**

**STOOLEING PATTERNS OF YOUNG CHILDREN CONSUMING A FOLLOW-ON FORMULA SUPPLEMENTED WITH A NOVEL PREBIOTIC BLEND**

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**Objectives and Study:** Determine the effect of a prebiotic blend on growth, stool patterns (including constipation) and diarrhea in young children.

**Methods:** In this single-center, double-blind, parallel-designed, prospective study, 133 children 9–48 mo old attending a daycare were randomized to receive a follow-on formula (Enfagrow®), Mead Johnson Nutrition (Control) or the same formula with galactooligosaccharide (GOS) and polydextrose (PDX) (0.5 g of each/245 mL serving) (PG) 2 times a day for 108 days. Pediatricians assessed stool patterns, diarrheal disease (DD), formula consumption, adverse events (AEs), and growth. DD was defined as >3 liquid/semiliquid stools within a 24-h period with fever, vomiting and/or dehydration and compromised general status. A stool pattern of increased defecation (ID) was defined as >3 soft/loose stools/day without other symptoms. Chi-square was used to compare the incidence of DD and ID in the 2 groups. Cox’s Proportional Hazards was used to analyze duration of DD and ID events. Covariates were age (9–24 mo; 24–48 mo) and gender. Dropouts and AEs were recorded.

**Results:** Groups had similar baseline nutritional status. Median daily formula consumption was similar in both groups [372 (261–490) mL/d in Control and 362 (266–475) mL/d in PG; *P* = 0.597]. No significant differences between groups were observed in weight to length/height z-score and incidence of AEs during the study. When adjusted for covariates, PG had similar odds of DD and increased odds of ID compared to Control (see Table).

**PO-N-432**

**ANALYSIS OF HAIR TOXIC AND TRACE ELEMENTS IN KOREAN CHILDREN AND ADOLESCENTS**

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**Objectives and Study:** Hair tissue mineral analysis has been one of the best methods for detecting toxic elemental exposure in human for private or public purposes, because it’s storage of elements is cumulative and samples can be obtained via non-invasive way. It’s importance is increasing in the era of environmental crisis(1). However, there have been several limitations to make this method one of the routine clinical or research tools, such as lack of standardization in pre-treatment of samples, lack of inter-laboratory quality control and lack of normal references(2). It is important to get more information about normal references for the future research especially in children. To set the normal reference values in Korean children, we conducted an analysis of the pooled data obtained from laboratory performing hair mineral analysis.

**Methods:** Data obtained from TEI Korea, which has performed hair tissue mineral analysis for several years in Korea, was used. Data from total 16,103 children and adolescents, which had been collected from March 2003 to March 2009, was analyzed using statistical package, named STATA 10.1. All 36 elements, such as Ca,Mg,Na,K, Cu,Zn,P,Fe,Mn,Cr,Ni,Se,Hg, Cd,Pb,Al,As,Be,Ba,B,Co,Ge, Li,Mo,Sn,S,Sn,V, Zr,Pt,Ti,W,Bi,Rb,T1 and U were analyzed.

**Conclusion:** A follow-on formula with added GOS and PDX proved to be safe, well tolerated, and promoted softer and more frequent stools in young children. Thus, it is a dietary tool that may prevent constipation while promoting normal growth.

**Disclosure of Interest:** J Bean, none declared. PW Ferguson, Mead Johnson Nutrition, Employee. JC Khoury, none declared. SH Mitmesser, Mead Johnson Nutrition, Employee. HC Ribeiro, Mead Johnson Nutrition, research support. TCM Ribeiro, Mead Johnson Nutrition, research support. DMF Scalabrín, Mead Johnson Nutrition, Employee.
**Results:** Cases with very high level of toxic elements were rarely detected. Some outliers were notified, so it would be important to set the cut-off points for toxic heavy metals especially in Ca, Hg, Pb. Some nutritional and excretory elements (Ca, Mg, Na and K) showed striking differences according to the age and gender. Hair levels of Na and K were very high in infancy, but gradually decreased to the very low adult level inversely correlated to the incremental age. Levels of Ca and Mg were gradually increased according to the growth and were higher in girls than boys in all age groups.

**Conclusion:** These findings suggest that age-appropriate standard should be prepared to optimize the hair tissue mineral assay research in children, and our results may be useful for a reference. Many outliers of nutritional elements suggest diet or other nutritional parameters may be related with results.

**References:**

**Disclosure of Interest:** None declared.

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**PO-N-433**

**RESTING ENERGY EXPENDITURE IN DISORDERS OF AMINOACID METABOLISM**


**Objectives and Study:** Background: Nutritional support is the mainstay of the treatment of inborn errors of aminoacid metabolism (IEAM). Few data have been reported about actual energy requirements in these patients.

**Aims:** To assess resting energy expenditure (REE) in children with IEAM, and to know the level of agreement between indirect calorimetry and four predictive equations.

**Methods:** REE was determined by indirect calorimetry in patients with IEAM in stable condition, and in a group of healthy controls, matched by age and gender. REE per kilogram of lean body mass (REE/LBM) estimated by bioimpedance analysis was calculated. REE/LBM values were compared with those predicted by Schofield’s, WHO/FAO, Harris-Benedict’s and Fleisch’s equations. Differences between groups were analysed with Chi-square and non-paired t tests. Bland-Altman method was applied to evaluate the agreement between calorimetry and predictive equations.

**Results:** 22 patients (14 male) with urea cycle disorders (UCD) (n=9), organic acidurias (OA) (n=5), non-ketotic hyperglycinemia (NKH) (n=4) and type 1 glutaric aciduria (GA) (n=4) were assessed. Mean age: 4.37 ± 4.16 years (0.4–15.83). Time since diagnosis: 2.62 ± 3.02 years. Weight SDS: −0.38 ± 1.48. Height SDS: 0.09 ± 1.59. Mean REE/LBM was 65.47 ± 20.31 Kcal/Kg LBM, without differences between genders. In GA group, REE/LBM was significantly higher than in the other groups (P = 0.032) and in healthy controls (P = 0.02) (table 1). REE predicted was similar to calorimetry results in UCD and NKH patients. Equations over-estimated REE in OA and under-estimated it in GA. Correlation analysis performed in the largest group (UCD), showed that Schofield’s equation had the lowest mean difference with calorimetry (±0.4 ± 36.9 Kcal/Kg LBM).

**Table:**

<table>
<thead>
<tr>
<th>Groups</th>
<th>REE/LBM (patients)</th>
<th>REE/LBM (controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCD</td>
<td>61.17 ± 18.68</td>
<td>74.04 ± 15.89</td>
</tr>
<tr>
<td>OA</td>
<td>49.22 ± 19.43</td>
<td>45.31 ± 16.94</td>
</tr>
<tr>
<td>NKH</td>
<td>74.94 ± 37</td>
<td>68.92 ± 15.87</td>
</tr>
<tr>
<td>GA</td>
<td>93.68 ± 21.54*</td>
<td>60.29 ± 9.10</td>
</tr>
<tr>
<td>p</td>
<td>*0.032</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Patients with GA had significantly higher REE, compared with other IEAM and with healthy controls. Schofield’s equation showed the best agreement with calorimetry when estimating REE in patients with UCD.

**Disclosure of Interest:** None declared.

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**PO-N-434**

**TOTAL (TAA) AND FREE AMINO ACID (FAA) PROFILE IN TERM AND PRETERM HUMAN MILK (HM) THROUGH THE COURSE OF LACTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Objectives and Study:** Amino acid profile is a key aspect of HM protein quality. Herein, we report a systematic review and meta-analysis of FAA and TAA profiles in term and preterm HM derived from 13 and 19 countries, respectively.

**Methods:** More than 50 studies were critically reviewed for this analysis. Of these, 25 publications with a total of 3774 subjects were summarized for TAA profiles. For the FAA in HM, 22 studies with a total of 4747 subjects were reviewed. Analysis of Variance and Principle Components Analysis were used to analyze the effects of gestation period, lactation stage, and geographical region.

**Results:** Data on total nitrogen and TAA composition of HM revealed general inter-study consistency whereas FAA concentrations varied substantially between studies. All 18 individual FAA concentrations in HM steadily declined in the first two months of lactation and remained relatively unchanged until the study period of 18 months. In contrast, the levels of the FAA glutamic acid and glutamine peaked at 3–6 months and decreased thereafter. Interestingly, glutamic acid was present at ~50-fold higher level compared to other
FAA in HM. Statistically significant differences were observed for some of the TAA and FAA between preterm and term milk such as glutamine, leucine and taurine, as well as at a regional level, i.e. North America vs. Asia Pacific vs. Europe. It was striking to note the paucity of information on HM TAA and FAA from Africa.

Conclusion: This systematic review represents a useful data set for the nutritional quantification of human milk as well as for the evaluation of protein quality and quantity of breast milk substitutes for preterm and term infants. Its comprehensive nature may serve as a guide to support future efforts in the revision of a global and/or regional human milk amino acid standard throughout the first year of life.

A Adelman, Mead Johnson Nutrition, consultant.

PO-N-435
ESSENTIAL AMINO ACIDS PREVENT THE EXTRAUTERINE GROWTH RETARDATION IN VERY LOW BIRTH WEIGHT INFANTS.
PRELIMINARY DATA OF A DOUBLE BLIND RANDOMIZED CONTROLLED TRIAL

Objectives and Study: Extrashuterine growth restriction in very low birth weight (VLBW) infants, secondary to suboptimal nutrition, is a major problem in Neonatal Intensive Care Units (NICU) as VLBW infants are frequently discharged at weights less than the 10th percentile and significant nutrient deficiencies are often observed. Evidence is emerging that early growth deficits have long-term adverse effects, including short stature and poor neurodevelopmental outcomes. Despite aggressive nutrition (AN) with high intakes of amino acids (AA), it is impossible to reach levels of some essential amino acids (EAA) similar to those observed in human fetus during the second and third trimesters of pregnancy. We presumed that the lower concentrations of some EAA may limit protein accretion and growing performance of VLBW infants.

Aims: The effect on the body growth of supplementation with EAA as additional AA intake in VLBW infants, was evaluated.

Methods: In a double-blind, placebo-controlled, randomized controlled trial, VLBW infants received enteral EAA supplementation (0.8 g/kg/day) (EAA Group) or isonitrogenous placebo supplementation (Control Group) between days 3 of life and hospital discharge. The growth parameters, including body weight, length and head circumference, were evaluated according to growth curve of preterm newborns with their gestational age at birth and corrected gestational age on discharge. Growth retardation (GR) was defined as less than the 10th percentile of the expected value.

Results: Thirty patients were enrolled until now: 15 allocated in the EAA Group and 15 in the Control Group. The two Groups were comparable for main clinical and demographic characteristics (sex, gestational age at birth, anthropometric data at birth, % of birth weight <10th percentile, CRIB score, duration of mechanical ventilation, % of chronic lung disease, gestational age at discharge). Infants in the EAA Group went home with lower weight, length and head circumference z scores (mean ± 95% CI): −1.33 (−2.03; −0.64); −0.80 (−1.63; 0.03); 0.35 (−0.58; 1.27) respectively, compared with patients in the Control Group (mean ± 95% CI): −3.22 (−3.86; −2.58); −3.0 (−3.76; −2.24); −2.47 (−3.16; −1.77), respectively (P < 0.01). Percentage of GR at discharge was 85.1% in Control Group vs 50.0 % in EAA Group (P < 0.01).

Conclusion: The supplementation with EAA seems to reduce the postnatal growth restriction generally developed in VLBW infants. These preliminary data show the way to a more appropriate approach to the nutritional management of premature infants in order to obtain an optimal growth rate.

Disclosure of Interest: None declared.

PO-N-436
A RANDOMIZED, DOUBLE-BLEND, MULTICENTER, PROSPECTIVE STUDY TO EVALUATE THE SAFETY OF LACTOSE-FREE AND LACTOSE-CONTAINING FORMULA IN HEALTHY, TERM INFANTS
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Objectives and Study: Breast milk is the optimal food for infant growth and development. When breastfeeding is impossible, insufficient, or mother chooses not to breastfeed, infant formula is used during the infant’s first year. Lactose-free infant formulas have been commercially available for many years in developed countries.

Aim: To evaluate a new lactose-free infant formula (safety growth and behavior).

Methods: A controlled, randomized, prospective, double blind, multicenter, parallel 12 week trial was conducted on healthy, term infants, aged up to 16 days on enrollment. Infants were randomized to receive either Materna Stage 1 standard cow’s milk-based formula containing lactose (SF) or Materna Stage 1 Lactose-Free, cow’s milk-based infant formula (LF). Weight, length, and head circumference were measured at baseline and at 4, 8, 12 weeks of age in hospital or clinic. Questionnaires completed by parents during trial participation were used to assess formula acceptance and tolerance.
PO-N-437

BREAST MILK INSULIN-LIKE GROWTH FACTOR -1, LEPTIN, GRELIN AND ADIPONECTIN LEVEL AND ANTHROPOMETRIC INDICES OF INFANTS AND THEIR MOTHERS


Objectives and Study: Insulin-like growth factor -1 (IGF-1), leptin, grelin, and adiponectin play important role in energy homeostasis and appetite control in children and adults. However their physiological role in early infancy is not clear. In our previous study we observed enhanced level of IGF-1 and grelin in breast milk of mothers of infants with high growth rate during first three months of lactation. In this work we studied possible relation between IGF-1, grelin, leptin and adiponectin breast milk levels and anthropometric indices of infants and their mothers.

Methods: Body weight gain and length during each of first three months of life were studied in 71 breast-fed healthy infants. Body weight and height, body mass index (BMI) and breast milk content of IGF-1, grelin, leptin and adiponectin were studied in 71 infants’ mothers. All observed infants were divided into three groups varying in their monthly weight gain: with low (less than 500 g increase of body weight per month), normal (from 500 g to 1000 g increase) and high weight gain (more than 1000 g increase). Breast milk content of individual hormonal proteins was measured by ELISA. Correlation coefficients and their significance were calculated by SPSS 17.

Results: The breast milk adiponectin level positively correlated with the IGF-1 (r =0.5, P=0.001) and leptin level in it (r =0.6, P=0.008) and negatively with grelin level (r = -0.6, P=0.0001), IGF-1 level positively and significantly correlated with leptin level (r =0.8, P=0.0001). The leptin level in breast milk had high positive correlation with infants’ body weight in all three groups. But there were no correlation between leptin breast milk content and anthropometric indices of mothers. There was positive but small correlation between breast milk IGF-1 and growth rate of infants. The breast milk grelin and adiponectin level had very small or negative correlation with infants’ growth rate. Positive and significant correlation was found between breast milk grelin level and body weight (r =0.455, P=0.044) and BMI (r =0.444, P=0.05) of mothers of infants with high growth rate.

Conclusion: Possible association of breast milk level of hormonal proteins studied with infant body weight was found as a tendency only for IGF-1. It seems that the breast milk leptin does not play the role of negative energy homeostasis regulator in infancy as leptin does in adults. The functional role of all breast milk hormonal proteins needs further study.

Disclosure of Interest: None declared.

PO-N-438

LOW SERUM CONCENTRATIONS OF VITAMIN D IS ASSOCIATED WITH HIGH INSULIN CONCENTRATIONS IN HEALTHY NORMAL WEIGHT CHILDREN


Objectives and Study: The incidence of diabetes in children is increasing. Today there is strong evidence for an association between vitamin D and insulin sensitivity. Previous results have shown that about 20% of the children defined as being normal weight have high insulin concentrations, i.e. in the highest quartile (1). Several studies have also shown that the dietary intake of vitamin D is low. In a cross-sectional study of healthy 8-year old children 62% of the children had serum concentrations of vitamin D (25(OH)D) below 75 nmol/L, suggested for optimal health in adults. The objective of this study was to investigate if low serum concentrations of 25(OH)D was associated with higher insulin concentrations in healthy 8-year old children, forming a subgroup of children from a well educated urban Swedish community, who participated in a larger cross-sectional study on nutrition, body composition and bone mineralization.

Methods: Eighty-one healthy children of normal weight and their parents accepted participation after informed consent. Blood samples were taken after an overnight fast. Serum insulin concentrations were measured using Insulin Ultra-sensitive ELISA kit (Merckodia AB, Uppsala, Sweden) and 25(OH)D and blood glucose according to routine (Sahlgrenska University Hospital). Height and weight were measured and BMI and HOMA-index were calculated.
Results: There was no significant difference in serum concentrations of 25(OH)D or insulin between boys and girls, mean (SD) concentrations being 71.10 (28.56) nmol/L and 4.11 (2.28) mU/L, respectively. Serum concentrations of 25(OH)D was negatively correlated with the ln insulin concentration (r = -0.391, P < 0.001) and with the HOMA-IR index (r = -0.398, P < 0.001). Children with 25(OH)D levels below 50 and 75 nmol/L had significantly higher insulin concentrations than the children with higher levels, 5.45 (2.87) vs 3.66 (1.84) (P = 0.002) and 4.70 (2.44) vs 3.24 (1.64) mU/L (P = 0.004), respectively.

Conclusion: The inverse relationship between serum concentrations of 25(OH)D and insulin in children of normal weight may reflect an increased insulin resistance and thereby a risk for future development of diabetes. Prospective studies would be of great value but there is also a need for a consensus on appropriate concentrations of 25(OH)D in children. A re-evaluation on recommendations for supplementation would be desirable.

Reference:

Disclosure of Interest: None declared.

PO-N-439

EFFECTS OF N-3 LONG-CHAIN POLYUNSATURATED FATTY ACID SUPPLEMENTATION DURING PREGNANCY AND/OR LACTATION ON NEURODEVELOPMENT AND VISUAL ACUITY IN FULL TERM CHILDREN
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Objectives and Study: It is hypothesized that maternal supplementation with long-chain polyunsaturated fatty acids (PUFAs) during pregnancy and/or lactation is valuable for later infant neurodevelopment and better visual function. The objective of this study was to systematically evaluate the effect of PUFA supplementation of pregnant and/or breastfeeding women on the neurodevelopment and visual function of their term offspring.

Methods: Systematic review. We searched MEDLINE, EMBASE, the Cochrane Library, and the references in reviewed articles through May 2009 for randomized controlled trials (RCTs) comparing PUFA supplementation with placebo or no supplementation. No language restrictions were applied.

Results: Of 13 RCTs included for systematic review, 6 assessed outcome measures of PUFA supplementation during pregnancy, 4, exclusively during lactation and 3, during the period of pregnancy and lactation. Heterogeneity of the studies did not allow us to perform a meta-analysis. Supplementation during pregnancy significantly influenced eye and hand coordination in 30-month-old children assessed with the Griffiths Mental Development Scales (n = 29, MD: 6.0, 95% CI: 1.03, 10.9), with no influence either on the other outcomes of these scales or on the other tests performed in the same group of children. The other 2 studies did not reveal any effect of PUFA supplementation during pregnancy on child development. Supplementation during lactation significantly increased the Bailey Psychomotor Development Index in 30-month-old children (n = 133, MD: 8.4, 95% CI: 2.6, 14.2), with no influence on results of different tests performed either in the same group of children or in others. Supplementation with high doses of DHA during pregnancy and lactation did not affect child neurodevelopment assessed up to 7 y. Only supplementation during pregnancy significantly improved visual acuity in children assessed at 16 weeks with the Teller Acuity Card (MD: 0.30, 95% CI: 0.09, 0.51), with a statistically significant worsening of visual acuity at 32 weeks (MD: −1.2, 95% CI: −1.38, −1.02).

Conclusion: Evidence from RCTs does not demonstrate a clear and consistent benefit of maternal PUFA supplementation during pregnancy and/or lactation on child neurodevelopment and visual acuity.

Disclosure of Interest: None declared.

PO-N-440

INCREASED VISCERAL FAT MASS IS CORRELATED WITH IMPAIRED GLUCOSE HOMEOSTASIS IN OBESE ADOLESCENTS
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Objectives and Study: The prevalence of childhood obesity has increased rapidly over the past decades and is a strong risk factor for adult obesity and an important risk factor for adverse health outcomes in childhood and adulthood. Increased central and visceral fat, rather than a high body mass index (BMI) is linked to higher risks of development of obesity and metabolic and cardiovascular diseases in later life. Studies in adults have shown that increased abdominal fat mass, a measure of central and visceral fat, is associated with an increased risk of insulin resistance, dyslipidemia, hypertension and coronary heart disease and overall mortality rates. In the present study we investigated the influence of body fat distribution on glucose homeostasis in obese children with impaired glucose tolerance.

Methods: A total of twenty six Caucasian children aged between ten and twelve years, with a BMI above 25 showing moderate to severe impairment of glucose tolerance, were included in the study. Plasma glucose and insulin concentrations were measured at baseline and 30, 60, 90, and
E206

Objectives and Study: The main factor conditioning the development of the newborn's intestinal ecosystem is represented by the type of feeding. Beneficial effects of a microbiota dominated by bifidobacteria in breast-fed infants have been found as recently stressed by ESPGHAN (1). The bifidogenic effect of human milk has been ascribed to a low concentration of proteins, presence of lactoferrin, a-lactalbumin and nucleotides supplemented infant formula appear to mimic the effect of human milk selectively stimulating the growth of beneficial bacteria and inhibiting growth of potentially pathogenic bacteria.

Methods: Healthy full-term infants with age less than 10 days and weighing 2500 - 4200 g, were enrolled if they were being exclusively fed with either formula or breast milk. Formula fed group was randomized to control formula (CF) and supplemented formula (SF) group. At 15, 23, 42 and 87 days, fecal bacterial count was determined by plating and Bifidobacterium were determined by RT-PCR (2).

Results: A total of 66 infants completed the study. Of them, 34 were HM, 14 were CF and 18 were SF groups. In HM and SF groups, the level of colonization of bifidobacteria was not statistically different (P < 0.05) between different days neither between feeding groups (9.14, 9.38, 9.58 log10 UFC/g feces in HM group and 9.34, 9.07, 9.41 and 9.24 y SF group). Colonization levels of Bifidobacteria were lower than 100% at 8 days of age. SF fed infants were colonized by Bifidobacteria more quickly (100% at day 15) than CF group (100% at day 42).. During the study, statistically differences (P < 0.05) exist in Enterobacteria counts between SF and CF group being the counts lower in SF group (9.21, 8.95, 8.60 and 8.76 in CF group and 8.47, 8.66, 8.96 and 8.42 in SF group) than CF group. The counts of Enterobacteria showed a tendency to reduce with time in SF group and have a behaviour similar to HM group (8.61, 8.29, 8.25 and 7.96 in HM group).

Conclusion: This study demonstrates that α-lactalbumin and nucleotides supplemented infant formula appear to mimic the effect of human milk selectively stimulating the growth of beneficial bacteria and inhibiting growth of potentially pathogenic bacteria.

References:

R Martínez, Hero Spain S.A. Employee.
MC Martínez, University of Murcia, None declared.
P Peso, University of Murcia, None declared.
MJ Ballesta, Arrixaca Hospital, None declared.

PO-N-442

BREASTFEEDING IS NOT ASSOCIATED WITH THE INFLAMMATORY STATUS IN HEALTHY ADOLESCENTS: THE HELENA STUDY

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Objectives and Study: Breastfeeding (BF) has been suggested to be associated with a decreased risk of
cardiovascular disease (CVD) in adulthood. A low-grade inflammation is associated with an increased risk of CVD, even in apparently healthy children. The objective of this study was to assess the potential modulating effect of BF on the inflammatory status of healthy adolescents.

**Methods:** Information on BF (presence or absence as well as exclusive and duration of any BF) was obtained from parental records in 484 of the 1040 healthy European urban adolescents (56.4% females) participating to the HELENA study. Blood samples were drawn for analysis of inflammatory markers: ultra sensitive C-reactive protein, complement factors 3 and 4, ceruloplasmin, adhesion molecules (L-selectin and Se-selectin, soluble vascular cell adhesion molecule 1 and intercellular adhesion molecule 1), cytokines and Transforming Growth Factor beta-1. After univariate analysis, propensity score including all the potential confounding factors was performed to assess an association between BF and selected inflammatory markers. Written ethical committee approval was obtained from the 10 countries participating to the study.

**Results:** No significant association was found between BF and its duration and any of the inflammatory markers after adjustment by gender and propensity score including age, pubertal status, blood pressure, body mass index, waist circumference, physical fitness and physical activity, smoking status, socioeconomic level, oral contraception in girls, lipids levels, duration of gestation, and birth weight.

**Conclusion:** Our study found no association between breastfeeding in early infancy and low grade inflammatory status in healthy adolescents suggesting that the potential cardiovascular benefits of breastfeeding may be related to other mechanisms than modulation of inflammation.

**Disclosure of Interest:** None declared.

**PO-N-443**

**THE ALTERATIONS OF LIVER INFLAMMATORY CYTOKINES & RECEPTORS GENE EXPRESSION IN A RAT MODEL OF TOTAL PARENTERAL NUTRITION**

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**Objectives and Study:** The major side effect of total parenteral nutrition is liver injury leading to liver failure. This study was designed to identify the potential liver inflammatory cytokines & receptors gene, which may be either increased or decreased in expression during the administration of TPN, with a real time PCR array.

**Methods:** 12 male Sprague-Dawley rats were divided into two groups: The control group (N = 6) and the TPN group (N = 6). The TPN group received continuous TPN infusion through a silastic catheter inserted in the right jugular vein and the control group infusion of the normal saline by the same way. All animals were euthanized at 7 days. We used real time PCR array to analyze the differential expression of the cycle genes between the two groups.

**Results:** (1) Two groups were found to have gained weight on the last experimental day compared with the beginning of the experiment. The weights in the control group were higher than those in the TPN group. (2) The TPN group was found to have large lipid droplets with unclear margins in the peribular region and smaller lipid droplets in the centrilobular regions. Necrosis was found in one case. The control group did not show obvious change. (3) No liver change at the electron microscope was observed in the control group, but in the TPN group were found the distension of liver blood sinus and cholangiole, diluvium of microvillus, the color of mitochondrial matrix obviously deep, chromatin margination and several apoptotic bodies. (4) The up-regulated liver Inflammatory Cytokines & Receptors genes of the TPN group are CXCL11, CCL22, CCL24, IL17B, IL10, IL10Rα, IL11, IL13RA1, IL18, IL1H5, predicted, IL16, predicted, IL1R1, IL1R2, IL2Rb, IL2C, IL8, IL18, ITGAM, ITGB2, ITGB3, CX3C14, TGF-β1, TNF, Tnf1F1b, CD40LG. The down-regulated liver Inflammatory Cytokines & Receptors genes are CCR1, CCR2, CCR4, IL1b, IL6, IL6RA, IL6RB, MIF. 

**Conclusion:** TPN leads to significant alternations in the gene expressions of the inflammatory cytokines and receptors of the liver, which may give insight into the potential mechanism of total parenteral nutrition-associated liver disease.

**Disclosure of Interest:** None declared.

**PO-N-444**

**HIGH 2-PALMITATE AND OLIGOFRUCTOSE IN LOWER PROTEIN ALPHA-LACTALBUMIN-ENRICHED TERM INFANT FORMULA: EFFECTS ON STOOL CHARACTERISTICS AND STOOL COMPOSITION**

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**Objectives and Study:** Formula-fed infants have less frequent and harder stools than human milk (HM)-fed infants. A change in palmitate positional distribution in formula reduces stool soap formation and stool hardness. Oligosaccharides are associated with softer stools due to different mechanisms. The primary hypothesis was that an increase in proportion of palmitate in the sn-2 position in a lower protein (13 g/L), alpha-lactalbumin-enriched formula would result in reduced stool soaps and softer stools. We also sought to evaluate whether a combination of high sn-2 palmitate and oligofructose (OF) would lead to even softer stools closer to HM-fed infants without increased physician or parent reported problems.

**Methods:** Healthy term infants 7 to 14 days old were enrolled in an 8-week randomized, double-blind study.
Formula-fed infants (n = 300) were randomly assigned to 1 of 4 formulas: standard formula (control), formula containing 40% sn-2 palmitate (high sn-2) or a combination of high sn-2 with 3.0 g/L or 5.0 g/L OF. A HM-fed group (n = 75) was studied in parallel. The main outcome measure was stool volume and mineral contents at week 8. Secondary outcomes included stool characteristics via 3-day diary and gastrointestinal (GI) tolerance via physician reported study events and parent questionnaire.

Results: Of 375 enrolled infants, 369 completed the study. Infants receiving high sn-2 formula had 46% less stool palmitate soaps (P < 0.0001) and softer stools than did control group (78% vs. 65% mushy soft stool, P = 0.026; 15% vs. 29% formed stool, P = 0.003) at week 8 without increased stool frequency. GI event rates including constipation were low in both high sn-2 and control groups, and similar to HM-fed infants. Addition of OF resulted in even lower percentages of formed stools (10% for 3 g/L group; 6% for 5 g/L) compared to control group, more closely resembling that of HM-fed infants (2%) with higher OF dose (5 g/L vs. HM, P = 0.155). Addition of OF also led to a dose-dependent reduction in stool calcium (3 g/L vs. 5 g/L, P = 0.012) compared to control group (3 g/L vs. control, P = 0.029; 5 g/L vs. control, P < 0.0001). Based on parents’ report, incidence of watery stool or gassiness was not increased with addition of OF.

Conclusion: A lower protein alpha-lactalbumin-enriched formula with high sn-2 fat blend led to reduced stool soaps and softer stools. Addition of OF further improved stool consistency without physician or parent reported concerns. Dose-dependent reduction in stool calcium with OF in term infant formula and its effects on calcium absorption during infancy warrants further investigation.

Disclosure of Interest: R. Capeding was PI for Pfizer-sponsored study. Rest of the authors are Pfizer employees.

PO-N-445

USE OF AN ELECTRONIC HANDHELD DIARY TO VALIDATE A NEW PARENT QUESTIONNAIRE ASSESSING GASTROINTESTINAL TOLERANCE IN INFANTS

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Objectives and Study: Conventionally, infant nutrition studies use growth, safety and other clinical-endpoints as outcomes. To expand this area of research into patient reported outcomes, we developed a parent-reported measure of infant’s gastrointestinal (GI) tolerance called the Infant Gastrointestinal Symptom Questionnaire (IGSQ). The IGSQ assesses 5 types of symptoms associated with GI distress: stooling, vomiting, crying, fussiness, and flatulence. Items are rated by parents from 1 (not present) to 5 (extreme distress). The 13 item IGSQ has good internal reliability (Cronbach’s alpha = 0.72). The objective of the present study was to evaluate the validity of the IGSQ by comparing the results obtained on the IGSQ (7 day recall period) to data obtained from an electronic handheld diary during the same time period.

Methods: Healthy term infants 40 to 80 days old were enrolled in an observational stool composition study. Parents of these infants completed the IGSQ on day 1 (baseline). The parents then prospectively recorded infant GI experiences (stooling, vomiting, crying, fussiness, and flatulence) daily for 7 consecutive days using an electronic handheld diary. Stooling frequency, consistency, and degree of difficulty were recorded on the handheld device after every stooling episode. Questions related to the other GI symptoms were recorded every evening for the previous 24 hour period. Data were transmitted each evening to a central database to ensure high compliance with daily recording. The same parents completed the IGSQ again at the end of the study period.

Results: A total of 62 parents of healthy term infants completed both the IGSQ and electronic handheld diary information. The item level correlation from the IGSQ to electronic handheld diary ranged from 0.46 to 0.88 (P < 0.0001). The correlation between the IGSQ summary index score and the electronic diary summary score was 0.89 (P < 0.0001). There were no significant differences between IGSQ scores at baseline and at the end of the study period for individual items (12 out of 13 items) or for summary scores; daily recording of GI experiences using the electronic diary did not have an impact on parent’s responses to the IGSQ at the end of the study period.

Conclusion: The IGSQ is a valid tool to assess GI tolerance in healthy term infants. Future studies are planned to evaluate the performance of the IGSQ in infants with feeding intolerance.

Disclosure of Interest: M.J. Yao, J. Trabulsi, R. Northington and P.DeRusso are employees of Wyeth Nutritional Inc., a Pfizer company.

SP-G-013

IDENTIFICATION OF THE DISEASE-SPECIFIC COELIAC EPITOPE OF TRANSGLUTAMINASE 2 AND POSSIBLE ANTIBODY-BASED IMMUNOTHERAPY


Objectives and Study: Transglutaminase 2 (TG2) is the main autoantigen in coeliac disease (CD), but previous data on the binding epitopes of CD antibodies are controversial. We recently described two adjacent novel Ca2+ binding sites, S4 (amino acids 151–158) and S5 (433–438) where
mutations reduced the binding of CD antibodies and now we aimed to find the specific anchor points of the binding sites.

**Methods:** Serum IgA and IgG antibodies from 216 CD patients aged 0.9–78 years (including 56 IgA deficient and 11 latent cases), antibodies eluted from CD tissues, CD-derived monoclonal antibodies and various monoclonal mouse anti-TG2 antibodies were tested for their binding to wild-type and mutant TG2 proteins in conjunction with molecular modelling.

**Results:** Point mutants of the S4 and S5 sites revealed Glu153 as one important but alone not sufficient anchor point. Using further mutants each lacking one of the four functional domains of TG2, we found that amino acids also on the N-terminal domain and/or C-terminal domain are needed for the binding, and these are close to each other in the 3-dimensional structure of TG2. Serum and tissue-deposited CD antibodies showed uniformly reduced binding to double (6.6–28.8%) and triple mutants (13.4–22%) involving these anchor points, particularly Glu153 and Arg19 that remain unchanged and accessible both in the closed and open conformation of TG2. Antibodies from different CD patients competed with each other. This binding pattern was seen already in the latent phase of CD, remained dominant during long-standing active disease, but differed from that of TG2 antibodies in other disorders. Monoclonal mouse antibodies with partially overlapping epitope specificity competed with CD antibodies in vitro, released in vivo deposited antibodies from CD tissue sections and antagonised the harmful effects of CD antibodies in cell culture experiments.

**Conclusion:** CD antibodies bind to the same discontinuous conformational epitope formed by spatially close amino acids of adjacent domains. This finding has implications to design epitope-specific diagnostic tests that distinguish between anti-TG2 antibodies in coeliac condition and other diseases. Knowledge of this epitope and the possibility to find compounds that could interfere with the action of CD antibodies will facilitate the understanding of disease pathomechanism and could be exploited for antibody-based immunotherapy.

**Disclosure of Interest:** None declared.

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**SP-G-014**

**AT COELIAC DISEASE DIAGNOSIS DISTINCT TRANSGLUTAMINASE AUTOANTIBODY TARGET DOMAINS CHARACTERIZE ATYPICAL RESPECT TO TYPICAL AND SILENT COELIAC PATIENTS**

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**Objectives and Study:** Coeliac disease (CD) is an immunemediated gluten-sensitive enteropathy characterized, at disease diagnosis, by 3 different clinical pictures. Typical CD (T) is dominated by gastrointestinal symptoms, Atypical CD (A) show extraintestinal features, Silent CD (S) refers to patients without symptoms. The 3 CD forms are usually joined by the presence of coeliac-specific serum autoantibodies, in particular tissue transglutaminase autoantibodies (tTGAb). It was demonstrated that at CD diagnosis the tTGAb are directed against multiple epitopes of the protein and that the tTG autoreactive domains are age- and sex-dependent. To date, no information is available on the modulation of the tTG epitope immunoreactivity occurring in the 3 different CD forms. Aim to evaluate in T, A and S CD forms the epitope specific humoral immunoreactivity against various combinations of 3 human recombinant constructs of the tTG molecule (full-length aa.1–687, a.a.227–687 and a.a.473–687, respectively).

**Methods:** The sera of 256 CD patients at disease diagnosis (114 T, 69/45m, median 7.6 yrs; 71 A, 43/28m, median 9.5 yrs; 70 S, 44/26m, median 9.2 yrs) were analyzed by using three distinct fluid-phase radioimmunoprecipitation assays.

**Results:** As shown in the Table, all the CD patients were found full-length tTGAb+. The main target of immunoreactivity in T, A and S CD forms was the tTG(227–687) fragment [T: 100/114(87.7%); A: 59/71(83.1%); S: 58/70(82.9%)], in percentages not significantly different among the 3 CD forms. However, the analysis of the combined immunoreactivities of tTG(227–687) and tTG(473–687) constructs indicated that A CD patients were significant more frequently target of tTG(227–687)Ab+/tTG(473–687)Ab+ immunoreactivity in comparison to T and S CD patients. Conversely, A CD patients were significant less frequently target of tTG(227–687)Ab+/tTG(473–687)Ab-immunoreactivity relative to T and S CD patients.

**Conclusion:** Atypical CD patients at diagnosis are target of an increased anti-tTG C-terminal immunoreactivity compared to Typical and Silent CD patients. This is the first evidence of a distinct humoral immunoreactivity in the 3 CD forms.

**Disclosure of Interest:** None declared.

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**Table:**

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<tr>
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<td>34 (48.6 %)</td>
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*A P=0.034 vs T and P=0.004 vs S; **A P=0.003 vs T and P=0.003 vs S*
SP-G-070

DEFECTIVE ANTI-INFLAMMATORY CONTROL VIA IL-10 DEFINING A SUBGROUP OF PATIENTS WITH EARLY ONSET INFLAMMATORY COLITIS


Objectives and Study: Children with early-onset inflammatory bowel disease starting within the first year of life show most often an extremely severe disease course. The early onset of disease along with poor response to therapy might indicate a subgroup of patients with a distinct pathophysiology. Therefore, we aimed to test the hypothesis of a defective anti-inflammatory response in infants with severe colitis starting within the first year of life.

Methods: The production of and response to the anti-inflammatory cytokines TGFbeta and IL10 were studied in ten infants with early onset IBD. Activation of the stat3 pathway, cytokine production in response to bacterial motifs as well as IL10 receptor expression were studied on peripheral blood cells, after isolation via a FICOLL gradient. CD14+ cells were separated by MACS for detailed studies of monocytes. Ileal and colonic biopsies were analyzed by quantitative PCR.

Results: The anti-inflammatory potential of TGFbeta and IL10 were tested in a first step on monocyte-derived dendritic cells (MoDC), showing a normal suppressive response of TGFbeta in all patients. But one patient showed a normal suppressive effect of IL10 on LPS-induced IL8 production in MoDC and PMNC. Whereas, a normal phosphorylation of STAT3 was observed in those patients with a normal response to IL10 stimulation, the STAT3 pathway was not activated in this patient in response to IL10, albeit a normal phosphorylation in response to IL6 in CD3+, CD14+ and CD14+ cells. Receptor analyses by FACS showed a normal expression of the alpha but no signal for the beta chain of the IL10 receptor in this patient. Genetic analyses confirmed a mutation in exon 2 of the gene coding for the beta chain (cG421T). This mutation causes a stop codon and no protein expression. Within the intestinal tissue, a marked inflammatory reaction was observed in all patients, however, the patient with a defective response to IL10 displayed higher levels of IL6, IL22 and IL10 compared to the other patients with early onset IBD. Of note, the patient with a mutation in the beta chain of the IL10 receptor is issue of a consanguineous family, whereas no consanguinity was noted in the other families.

Conclusion: This work points out to the critical role of IL10 to the homeostasis of the intestinal mucosa. The finding of monogenetic defects affecting the IL10 pathway opens the view of causes of IBD and it also indicates new treatment options in form of hematopoetic stem cell transplantation, as recently suggested.

Disclosure of Interest: grant support from AFA and INSERM.

SP-G-071

LONG-TERM EFFICACY OF INFlixIMAB TREATMENT IN PEDIATRIC CROHN’S DISEASE IN THE NETHERLANDS

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Objectives and Study: Infliximab (IFX) is effective for induction and maintenance of remission in children with moderately to severely active Crohn’s disease (CD). Little is known about the efficacy of IFX after more than three years of treatment. The primary aim of this study was therefore to assess the long-term efficacy of IFX treatment in pediatric CD.

Methods: In this retrospective, multicenter study, all Dutch pediatric CD patients treated with IFX from October 1992 to October 2009 and with a minimal follow-up of three months since start of IFX, were studied. Patients, who didn’t receive a three-dose induction scheme at 0, 2 and 6 weeks and/or were treated episodically, were excluded from this study. Treatment outcome was considered successful when good clinical response was maintained minimally 90 days after IFX stopped or when repeated IFX infusions were needed to maintain clinical response (adjustments in treatment schedule were allowed).

Results: 154 CD patients (83 M/71 F) were treated with IFX by pediatric gastroenterologists in 13 hospitals. Mean age at start of IFX treatment was 14.5 years (range, 5.9 – 18.9 years) after a mean disease duration of 2.3 years (range, 0 – 10 years). A total of 2295 infusions was administered (mean, 14.9 infusions). Kaplan-Meier analysis showed that the likelihood of IFX treatment being successful after 1, 3 and 5 years was 84%, 65% and 56%, respectively. Adjustments in treatment schedule (dosage increase to 10 mg/kg and/or shortening of the interval between two infusions) at any time during follow-up were needed in 74/154 (48%) of the patients, with 22 of them eventually requiring both adjustments. Eighty-eight percent of the adjustments were made in the first two years of IFX treatment. In total, 47 patients were (eventually) unsuccessfully treated with IFX. The majority of these patients underwent surgery (53%), followed by treatment with adalimumab (43%), corticosteroids (13%) and/or restart of IFX (11%).

Conclusion: IFX is effective in refractory pediatric CD. However, the therapeutic effect decreases over time with lost response to IFX treatment in more than 40% of patients after five years. In addition, almost half of patients requires adjustment in treatment schedule in the first two years of treatment. These data emphasize the need for developing an effective, long-term treatment strategy for pediatric CD.

Disclosure of Interest: None declared.
SP-G-072

ENDOSCOPIC CLASSIFICATION OF GERD IN CHILDREN: IS IT CONVENIENT TO USE THE SCORING SYSTEMS DEVELOPED FOR ADULTS?

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Objectives and Study: Endoscopy is an important tool for assessing esophageal damage caused by gastroesophageal reflux disease (GERD) in all age groups. Multiple scoring systems have been developed for adult patients to make a more objective and reliable description of macroscopic lesions in esophagus. Although frequently used for the evaluation of childhood GERD, reliability or validity of these scoring systems was not interrogated methodologically. The aim of this study was to evaluate the reliability of three different endoscopic scoring systems by comparing them with the esophageal histopathology in children.

Methods: A total of 113 children aging between 5–17 years who underwent EGD because of symptoms suggestive of GERD were included into the study. Endoscopic appearance of esophagus was reevaluated from the detailed descriptive endoscopic reports and still images, and was assessed by the same investigator according to the Savary-Miller (SM), Hetzel-Dent (HD) and Los Angeles (LA) scoring systems. All esophageal biopsies obtained were reevaluated by the same pathologist by using the Vandenplas classification.

Results: The mean age of the study group was 10.8 ± 3.4 years. Endoscopic findings were normal in 93/113 (82.3%) children according to the SM and LA classifications whereas only 40/113 (35.4%) were defined as normal when HD classification was used. When we attempted to correlate the HD, SM and LA classification systems, a high degree of consistency was found between the SM and LA classifications only (kappa = 0.91). The frequency of histopathological esophagitis was 70.8% in the study group. When the correlation between each endoscopic scoring systems and the Vandenplas histological classification was assessed, a weak consistency was found between the HD assessment and the histopathology (kappa = 0.270). The sensitivity and specificity of the HD classification were 69.1% and 60.7%, respectively. However the other two endoscopic scoring systems were not correlated with esophageal histopathology.

Conclusion: Endoscopic findings of GERD are usually milder during childhood. However, even these mild endoscopic changes in esophageal mucosa are usually associated with various degrees of histopathological esophagitis in children. Hence it may be misleading to use the available endoscopic scoring systems in children. It would be wise to recommend taking esophageal biopsies in every children who have reflux symptoms until a more reliable endoscopic scoring system is developed particularly for children.

Disclosure of Interest: None declared.

SP-G-073

NON-ACID MORE THAN ACID GASTROESOPHAGEAL REFLUX (GOR) TRIGGERS GOR-INDUCED APNOEAS IN VERY PRETERM INFANTS


Objectives and Study: The relationship between apnoea of prematurity (AOP) and gastro-oesophageal reflux (GOR) has been frequently hypothesized. The widespread clinical perception that AOP can be related to GOR contributes to a GOR overtreatment. We aim to evaluate whether physical and/or chemical features of GOR influence the relationship between GOR and AOP.

Methods: Each premature infant with recurrent apnoeas underwent a simultaneous recording of polysomnography and combined impedance and pH monitoring (pH-MII). We analyze whether the correlation between GOR and AOP varies according to the acidity, duration and height of GOR episodes. All the episodes detected by MII with a concomitant decrease in pH to less than 4 are defined as acid MII-GOR (a-MII-GOR), while the episodes with a pH <4 are defined as non-acid MII-GOR (Na-MII-GOR). Acid GOR episodes recorded only by pH probe are defined as pH-GOR.

Results: Fifty-eight preterm newborns (20 male) with gestational age <33 weeks (range 25 - 33 ws) and mean birth weight 1170 g (range 750 - 1750 g) were studied. During 252 hours of registration, 1706 GOR episodes (20.3 ± 11.1 GOR/period [mean ± SD]) were identified by pH-MII: 657 (38.5%) of them were detected only by pH-monitoring, and therefore classified as pH-GOR. The remaining 1049 (61.5%) were detected by MII, and further divided into a-MII-GOR (n=239, 14%) and Na-MII-GOR (n=810, 47.5%). One-thousand-five-hundred-twenty-three apnoeas (18.1 ± 18.3 apnoeas/period [mean ± SD]) were detected by PS. The frequency of apnoeas detected in the 30” after pH-GOR (0.148/min) was higher than the frequency detected in the 30” before (0.085/min; p=.04); even more, the frequency of apnoeas detected in the 30” after non-acid MII-GOR (0.223/min) was significantly higher than the one detected in the 30” before (0.057/min; p=.000), whereas the frequency of apnoeas detected 30” before acid MII-GOR (0.029/min) did not differ (p=.137) from the one detected after (0.109/min). No difference in the mean height nor in the mean duration was found between GOR episodes inducing and those non-inducing an apnoea.

Conclusion: The analysis of physical and chemical features of GOR highlights that the most dramatic increase in the frequency of apnoeas after GOR is due to non-acid GOR episodes: this novel finding must be taken into consideration when a therapeutic strategy for this common problem is planned.

According to our data the use of drugs such as H2-blockers and proton pump inhibitors (PPIs) aiming to control gastric
acidity is probably not appropriate. Our preliminary data encourage to evaluate if there exists any possible effect on GOR-related apnoeas of a therapeutic strategy specifically designed for non-acid GOR.

Disclosure of Interest: None declared.

SP-G-115

A MODEL OF EOSINOPHILIC ESOPHAGITIS (EE) AND VILLUS ATROPHY (VA) AFTER CHALLENGE IN MICE SENSITIZED TO PEANUTS: IMPROVEMENT BY EPICUTANEOUS IMMUNOTHERAPY (EPIT)

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Objectives and Study: Food allergy may trigger EE and VA in humans. EPIT using a new epicutaneous delivery system (Viaskin(R)) has been described as a therapeutic method in food allergy (1). We developed a model of mice sensitized to peanut, exhibiting EE and VA after exclusive feeding with peanut protein extracts (PPE). This study was conducted in order to evaluate the efficacy of EPIT in such a model.

Methods: After oral sensitization with PPE and cholera toxin, 30 BALB/c mice were treated weekly during 8 weeks by PPE skin applications (EPIT), 20 mice were not treated (NT) and 10 mice constituted the control group (C). Mice were then exclusively fed with PPE. Specific IgE, IgG1 and IgG2a were monitored every 2 weeks. Esophageal and jejunal samples were taken for histology.

Results: sIgE increased after oral sensitization, respectively 0.207 ± 0.03 and 0.214 ± 0.04 μg/ml in EPIT and NT, with undetectable values in C. Following EPIT, sIgE decreased and sIgG2a increased, respectively 0.139 ± 0.01 vs 0.166 ± 0.01 μg/ml (EPIT vs NT, P < 0.05) and 14.96 ± 0.60 vs 4.73 ± 1.75 μg/ml (P < 0.05). Esophageal eosinophilic infiltration (measured in 6 high power fields) was higher in NT than in EPIT and C, respectively 1.6 ± 0.1 vs 2.3 ± 0.2 (P < 0.01) and 2.4 ± 0.1 (P < 0.001). Eosinophilic infiltration in jejunum was increased in NT compared to EPIT (P < 0.01) and C (P < 0.001).

Conclusion: EPIT seems efficient to prevent EE and VA induced by PPE exclusive feeding in previously sensitized mice.

Reference:

Disclosure of Interest: None declared.

SP-G-116

MATERNAL DIETARY POLYUNSATURATED FATTY ACIDS IN THE EARLY DEVELOPMENT OF THE IMMUNE SYSTEM


Objectives and Study: Polysaturated fatty acids (PUFAs) are important immune modulating elements. Prostaglandins and leukotrienes, which play an important role in the immune response, are derived from PUFAs. Furthermore, PUFAs can alter immune cell function via various mechanisms, including the activation of transcription factors. The development of the immune system occurs mostly perinatailly and since most PUFAs are acquired from the diet, the maternal diet may influence fetal and neonatal PUFA status. The last decades there is a significant increase in the prevalence of allergic disorders which coincides with a marked change in dietary fatty acid intake. Therefore, we investigated the effect of maternal dietary omega-3 and omega-6 PUFAs on the development of the immune system in the offspring.

Methods: Pregnant and/or lactating BALB/c mice were fed diets varying in C18:3omega-3/C18:2omega-6 ratio. After weaning, pups were transferred to a Western-style diet and the effects of maternal PUFA-diet were examined using the ovalbumin-induced allergic asthma model.

Results: Significant differences in the acute allergic skin response were observed between different diet groups and between different feeding periods; all PUFA-diets lowered the acute allergic skin response compared to control diet, but the high C18:3omega-3 diet was most effective when fed during lactation while the high C18:2omega-6 diet diminished the allergic skin response most when fed to pregnant dams.

Conclusion: Both the maternal omega-3 and omega-6 PUFA-diets lowered the allergic skin response in the adult offspring, indicating a long lasting effect of the maternal diet. Because each diet has the strongest effect when given in a different feeding period, the mechanism by which these PUFAs lower the allergic response might also differ.

Disclosure of Interest: None declared.

SP-G-119

ENTEROPATHOGENIC ESCHERICHIA COLI EFFECTOR PROTEIN NLEE SUPPRESSES NF-KB ACTIVATION AND IL-8 SECRETION BY HUMAN INTESTINAL EPITHELIAL CELLS IN VITRO

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Disclosure of Interest: PH Benhamou, DBV Technologies, CMO
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Objectives and Study: Enteropathogenic E. coli (EPEC) has previously been shown to suppress pro-inflammatory cytokine secretion during infection of intestinal epithelial cells. Down-regulation of the host innate immune response is dependent upon a function type three secretion system (T3SS), which translocates one or more bacterial effector proteins into host cells, resulting in the blockade of NF-κB and p38 MAPK signal transduction. The aim of this study was to identify the EPEC effector(s) involved.

Methods: Post-confluent, polarised Caco-2 cell cultures were inoculated with wild type EPEC strain E69, a T3SS deficient mutant (E69\Delta detector\beta) and a broad range of T3SS effector mutants. Infection was allowed to proceed for 4 hours, before bacteria were killed by antibiotic treatment. Caco-2 cells were then stimulated with the pro-inflammatory cytokine IL-1β. Controls included non-infected cells and non-infected cells treated with only IL-1β. 18 hours post IL-1β stimulation, IL-8 and β-defensin 2 (HBD-2) protein secretion was measured in supernatants using sandwich ELISA. Nuclear translocation of NF-κB was studied by immunostaining for p65 (an NF-κB subunit). Activation of the p38 MAPK pathway was examined by Western blotting for phosphorylation of p38.

Results: Relative to the T3SS deficient mutant E69\Delta detector\beta and IL-1β treatment alone, the wild type E69 strain suppressed IL-1β induced IL-8 and HBD-2 secretion (P = 0.001), NF-κB nuclear translocation and p38 activation. Deletion of the EPEC gene nleE, encoding an EPEC T3SS translocated protein, caused a diminution of IL-8 suppression (P = 0.001); complementation of the mutant with nleE restored inhibition (P = 0.001). Suppression of IL-8 production correlated with inhibition of NF-κB nuclear translocation and the reversal of suppression correlated with p65 nuclear localisation. In contrast, HBD-2 secretion and MAPK activation was still suppressed (P = 0.001) after infection with the nleE mutant.

Conclusion: Delivery of the EPEC T3SS effector NleE into host cells in vitro prevents nuclear translocation of the NF-κB subunit p65, leading to a diminished host cell IL-8 response. One or more, as yet unidentified, EPEC effector proteins are responsible for the blockade of NF-κB and HBD-2 secretion. NleE is responsible for EPEC suppression of host NF-κB activation and IL-8 secretion.

Disclosure of Interest: Supported by NIH grant RO1DK58957 to JBK.

SP-G-120

ORAL ZINC FOR THE TREATMENT OF ACUTE GASTROENTERITIS IN CHILDREN: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Disclosure of Interest: None declared.

SP-H-017

GOOD OUTCOME OF HEPATOCELLULAR CARCINOMA IN CHRONIC LIVER DISEASE OF CHILDHOOD

Objectives and Study: A number of randomized controlled trials, performed in developing countries, have shown that zinc supplementation is effective in reducing the duration and severity of diarrhea. Based on these findings, UNICEF/WHO currently recommends zinc supplementation as a universal treatment for all children with acute gastroenteritis (AGE). However, uncertainty exists regarding this treatment in children living in Europe, where zinc deficiency is rare (1). The objective of this study was to evaluate the efficacy and safety of zinc supplementation in the treatment of AGE in children in Poland.

Methods: Children aged 3–48 months with AGE were enrolled in a randomized, double-blind, placebo-controlled trial in which they received zinc sulfate (10 or 20 mg/d depending on the age) or placebo for 10 days.

Results: A total of 141 of 160 children recruited were available for intention-to-treat analysis. In the experimental group (n=69) compared to the control group (n=72), there was no significant difference in the primary outcome measure which was the duration of diarrhea (2.5 ± 1.8 vs. 2.4 ± 2.1 days, respectively, P > 0.05). Similarly, there was no significant difference between groups in stool frequency on days 1, 2, and 3, vomiting frequency, intravenous fluid intake, and the number of children with diarrhea lasting > 7 days.

Conclusion: Children living in a country where zinc deficiency is rare do not appear to benefit from the use of zinc in the treatment of AGE.


Disclosure of Interest: None declared.
liver disease (CLD) of infancy. It is not known whether the Milan criteria, adopted in the adult population, are good predictors of outcome in children. We therefore aimed to review the cohort of patients referred to our centre to evaluate the features and outcome of children with CLD in whom HCC has been discovered during the follow up or incidentally at explant pathology. We collected: demographic features, type of chronic liver disease, liver function tests including alpha foetoprotein (AFP), histological description, complications at transplantation (OLT), outcome. We reviewed the accuracy of the Milan criteria as predictors of poor outcome: single nodule >5 cm of size, multiple lesion (>3 nodules), angioinvasion, extrahepatic disease.

Results: Among 456 children transplanted at our centre in the last 15 years 10 (2%), 4 males, median age at diagnosis 1.8 years (range 0.5–7.2) had HCC on CLD and namely biliary atresia (3), low GGT PFIC (2), choledochal cyst (1), glycogen storage disease (1). No patient died from HCC without OLT. Median AST at diagnosis of HCC was 169 IU/L (43–541), ALT 83 IU/L (23–262), total bilirubin 48 umol/l (16–414), AFP 1166 (2–24196), INR 1.5 (1.0–2.0). In 4 patients the nodules were discovered incidentally at OLT whereas in 6 HCC was picked up at scheduled ultrasound scan (USS). Six patients had a single nodule whereas 4 had multiple lesions. Median nodule size was 1.5 cm (0.6–6 cm). No patient had extrahepatic spreading. Six patients did not fulfill the Milan criteria because of multiple nodules (4), nodule size (1) and angioinvasion (1), of whom 5 are alive and well. None died from tumour recurrence. Two patients died from graft primary non function and hepatic artery thrombosis, whereas 8 are alive and well with no evidence of disease after a median follow up of 3.7 years (0.3–11).

Conclusion: HCC occurs in 2% of children transplanted for another liver disease. Despite most of these patients do not fulfill the Milan criteria the outcome is good, with an overall survival of 80% and no tumour-related mortality. Such a benign prognosis is therefore probably due to a different biology of HCC in this setting along with an early discovery of the lesion by scheduled USS. The Milan criteria should not be applied to children with HCC in chronic liver disease.

Disclosure of Interest: None declared.

SP-H-018

IS REJECTION LESS COMMON IN CHILDREN UNDERGOING LIVER TRANSPLANTATION FOR HEPATOBlastoma?

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Objectives and Study: Hepatoblastoma is a rare malignant tumour, almost exclusive to childhood. Treatment consists of chemotherapy followed by either hepatic resection, where feasible, or liver transplantation. As this chemotherapy is immunosuppressive the incidence of rejection post transplantation may be reduced. This can have implications for future management as well as reducing potential side effects. The aim of this study was to compare the incidence of histological rejection in children undergoing liver transplantation for hepatoblastoma with those transplanted for biliary atresia in a single unit.

Methods: All 20 patients who underwent transplantation for hepatoblastoma were identified retrospectively. These were matched 1:3 for age, sex, year of transplant and type of immunosuppression to a control group transplanted for biliary atresia (n = 60). Exclusions were patients transplanted for other types of liver tumour and patients with biliary atresia-splenic malformation syndrome. Parameters recorded included the presence of acute and chronic histologically proven rejection, overall survival, renal function and immunosuppressive treatment and level achieved.

Results: Mean age at diagnosis of HCC was 169 IU/L (43–541), ALT 83 IU/L (23–262), total bilirubin 48 umol/l (16–414), AFP 1166 (2–24196), INR 1.5 (1.0–2.0). In 4 patients the nodules were discovered incidentally at OLT whereas in 6 HCC was picked up at scheduled ultrasound scan (USS). Six patients had a single nodule whereas 4 had multiple lesions. Median nodule size was 1.5 cm (0.6–6 cm). No patient had extrahepatic spreading. Six patients did not fulfill the Milan criteria because of multiple nodules (4), nodule size (1) and angioinvasion (1), of whom 5 are alive and well. None died from HCC without OLT. Median AST at diagnosis of HCC was 169 IU/L (43–541), ALT 83 IU/L (23–262), total bilirubin 48 umol/l (16–414), AFP 1166 (2–24196), INR 1.5 (1.0–2.0). In 4 patients the nodules were discovered incidentally at OLT whereas in 6 HCC was picked up at scheduled ultrasound scan (USS). Six patients had a single nodule whereas 4 had multiple lesions. Median nodule size was 1.5 cm (0.6–6 cm). No patient had extrahepatic spreading. Six patients did not fulfill the Milan criteria because of multiple nodules (4), nodule size (1) and angioinvasion (1), of whom 5 are alive and well. None died from tumour recurrence. Two patients died from graft primary non function and hepatic artery thrombosis, whereas 8 are alive and well with no evidence of disease after a median follow up of 3.7 years (0.3–11).

Conclusion: HCC occurs in 2% of children transplanted for another liver disease. Despite most of these patients do not fulfill the Milan criteria the outcome is good, with an overall survival of 80% and no tumour-related mortality. Such a benign prognosis is therefore probably due to a different biology of HCC in this setting along with an early discovery of the lesion by scheduled USS. The Milan criteria should not be applied to children with HCC in chronic liver disease.

Disclosure of Interest: None declared.

SP-H-117

STEPWISE APPROACH TO EXTRA HEPATIC PORTAL VEIN OBSTRUCTION IN CHILDREN

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Objectives and Study: Extrahepatic portal vein obstruction (EHPVO) in children causes portal hypertension (PH) without the complications of chronic liver disease. Children
with EHPVO can have severe bleeding episodes, hypersplenism and subclinical hepatic encephalopathy. The management of this condition is controversial. We report our experience of a stepwise approach to children with EHPVO based on severity of PH and feasibility of meso-portal bypass (M-Rex).

**Methods**: We reviewed the notes of patients with EHPVO referred to our institution in the last 10 years and we collected the following data: demographic features, neonatal history, presenting features, bleeding episodes, endoscopic procedures, retrograde portograms, shunting procedures, M-Rex procedure, complications and outcome. Children with clinical signs of PH underwent serial endoscopies and were started on propranolol when large varices were detected. Patients unresponsive to propranolol underwent endoscopic variceal treatment. M-Rex was considered for relapsing bleeders or severe hypersplenism. Shunt surgery was considered in relapsing bleeders with an obstructed Rex recessus.

**Results**: 56 children with EHPVO, M:F 33:23, median age 13.5 years (2.0–25.1), median age at diagnosis 4.0 years (0.2–17.7) to our unit during the studied period. 44 (78%) had a neonatal disease and 39 (70%) a umbilical vein catheterisation. 78% had at least one bleeding episode at a median age of 4.0 years (0.5–17.5). 86% were started on propranolol and 56% required endoscopic treatment of varices. Retrograde portogram was carried out in 27 (48%) patients and demonstrated a patent Rex recessus in 13/27 (48%). 26 (46%) patients underwent an operation including M-Rex (10), proximal spleno-renal (8), distal spleno-renal (2), meso-caval (4) and TIPSS (2). At the last follow up (median 9.4, range 3.4–18.6 years) 20/26 (77%) shunts are patent including 8/10 M-Rex. 54/56 (96%) patients are alive. Overall in 51 patients (91%) the bleeding is controlled.

**Conclusion**: Severe complications of EHPVO in children can be managed effectively with medical, endoscopic, radiological and surgical interventions. The overall success of surgery in this series is high with resolution of PH in 35% of all patients. In our experience the Rex recessus was patent in half of the studied cases allowing to restore a hepatopetal portal flow in about one third of the patients considered for surgery. Nevertheless the majority of patients are left with a compensatory portal hypertension. Further studies are required to evaluate the possible subtle complications of porto-systemic shunts and lifelong portal hypertension in children with EHPVO.

**Disclosure of Interest**: None declared.

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**SP-H-118**

**MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN WITH PORTAL VEIN THROMBOSIS**

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**Objectives and Study**: There are very few reports on the effect of pre-hepatic portal hypertension (PHPH) on mental ability in children. This matter is relevant since these patients are usually treated conservatively and grow and live with a condition that might impair their intellectual development. We aimed to investigate children with PHPH due to portal vein thrombosis to seek proofs of subclinical features consistent with minimal hepatic encephalopathy (MHE).

**Methods**: A consecutive sample of 13 children (age range 4–18 years, males 46%) with PHPH and no liver disease who had been referred to a single liver center (Group A) underwent a psychometric evaluation comprising of 26 tests exploring learning ability, abstract reasoning, phonemic and semantic fluency, selective attention, executive functions, short-term verbal and visual memory, long-term verbal memory, visuo-practic ability. Psychometric performance was stratified by age and education and evaluated according to norms for normal age-matched population. The same day the patients underwent fasting ammonia measurement and a digitalised electroencephalogram (EEG). Spectral analysis was performed on eye-closed EEG. Mean dominant frequency (MDF) and frequency bands were considered. The EEG of 14 age matched normal controls (Group B) was considered for comparison. Multiple regression analysis was performed to seek statistical significance between and within the two groups.

**Results**: Ten subjects of Group A (77%) had at least one altered psychometric test and two subjects had more than 5 abnormal tests. No subject had alterations concerning abstract reasoning, phonemic and semantic fluency. In contrast, selective attention, executive functions and short-term visual memory were the domains more frequently altered (50%) in keeping with MHE. Variability of EEG spectral parameters was predicted by age in both Group A and Group B as expected, with no difference between the two groups (ANCOVA). Ammonia plasma level was higher than the reference values of our laboratory (35 umol/L) in 5 subjects (48, 42–58 umol/L, median and range). Age (β=0.68±/0.19 P < 0.01) and ammonia (β=-0.44+/0.19 P < 0.05) were found to be independent predictors of the EEG MDF on multivariate regression. No relationship was found between ammonia levels and psychometric performance.

**Conclusion**: Cognitive impairment with a profile typical of MHE and mild hyperammonaemia were found to be common in children with portal vein thrombosis. Hyperammonaemia was found to be related to EEG slowing. These findings are in keeping with the existence of MHE in children with PHPH.

**Disclosure of Interest**: None declared.

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**SP-N-015**

**PRE AND POSTNATAL DETERMINANTS OF GENE EXPRESSION OF INFLAMMATORY MARKERS IN SUBCUTANEOUS ADIPOSE TISSUE**

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www.jpgn.org
Objectives and Study: Changes in both the pre and postnatal nutritional environment can have a long term impact on adipose tissue function in the offspring. This includes a resetting of inflammatory and related responses as a consequence of changes in gene expression. The aim of the present study was, therefore, to determine the extent to which exposure to a nutrient restricted diet in late gestation, with or without accelerated postnatal growth, determines gene expression of inflammatory markers in subcutaneous adipose tissue of young adult offspring.

Methods: Pregnant twin-bearing sheep were either fed to requirements (R; n=20) or nutrient restricted to 60% of this amount (N; n=20) from 110 days up to term (~147 days). Ten offspring in each group were then reared by their mother as singletons in order to promote postnatal growth (accelerated weight gain – A). Ten twin offspring from each group were reared by their mother together in order to restrict postnatal growth (standard weight gain – S). Offspring were humanely euthanased at 17 months of age, adipose tissue was sampled and stored at −80°C until analysis of mRNA abundance for the genes encoding adiponectin, interleukin-6 (IL-6), monocyte chemotactic protein (MCP)1, fat mass and obesity-associated (FTO) gene and glucose-responsive protein (GRP)78 using real-time PCR. Appropriate institutional animal ethics committee approval was obtained.

Results: Gene expression for adiponectin was increased with accelerated postnatal growth (X 1.5 and 1.9, P<0.05) whereas mRNA abundance for the FTO and IL-6 genes were both reduced by maternal nutrient restriction (R; 1.2 ± 0.8 vs 1.3 ± 0.1, (P<0.05)) whereas mRNA abundance for the FTO and IL-6 genes were both reduced by maternal nutrient restriction (R; 1.2 ± 0.8 vs 1.3 ± 0.1, (P<0.05)). Surprisingly, there were no changes in mRNA abundance for GRP-78 or MCP-1 with any of the interventions.

Conclusion: Subcutaneous adipose tissue exhibits limited changes in gene expression following manipulation of either the pre and postnatal nutritional environments. Even though fat mass quantity is similar between groups there are significant nutritionally programmed changes in gene expression. The main responses are related to increased postnatal growth and coincide with the period in which substantial amounts of subcutaneous adipose tissue are being deposited.

Disclosure of Interest: None declared.

IS THE COLON SUBMITTED TO NUTRITIONAL PROGRAMMING? DELAYED EFFECT OF A HIGH PROTEIN FORMULA ON COLONIC PHYSIOLOGY IN LOW BIRTH WEIGHT PIGLETS

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Objectives and Study: Numerous neonatal practices are likely to affect intestinal microbiota implantation. However, the intense period of interplay between colonic microbiota, epithelial and immune cells during the neonatal period is believed to shape their feature for the entire life. By increasing the colonic supply of non digested proteins and peptides, protein-enriched formulae could affect the intestinal microbiota, particularly in neonates suffering from intrauterine growth restriction who exhibit lower digestive capabilities. Using low birth weight piglets, we have therefore investigated whether a high protein formula would modify both the colonic microbiota implantation and the development of the immune and non-immune colonic barrier.

Methods: Low birth weight piglets were fed from day 2 to 28 either a normoproteic (NP) or a high protein (HP, +40% protein) formula and then the same diet for both groups until day 160. Immediate (d28) and delayed (d160) consequences on colonic microbiota (Q-PCR), ex vivo-permeability (Ussing chambers), cytokines profiles (RT-PCR) and immune cell density (IHC), and response to oxidative (0.1 mM NH2Cl in Ussing chambers) and inflammatory stresses (explants culture with 0 to 200 μg/mL of LPS) were evaluated.

Results: During the neonatal period (d28), the HP formula modified the colonic microbiota by increasing the percentages of Bacteroides (17 ± 1.8% vs 9.7 ± 0.5% (P<0.05)) and of bacteria from the Clostridium leptum cluster (1.8 ± 0.5 vs 0.3 ± 0.3%, P<0.05) compared to NP piglets. Permeability to macromolecules tended to be higher in HP compared to NP piglets (104.46 ± 17.7 ng/cm²/h, P<0.06). Moreover, IL-1β and TNFα mRNA levels were reduced (0.5 ± 0.2 vs 1.2 ± 0.1 and 2.3 ± 0.3 vs 3.8 ± 0.8, respectively, P<0.05) while T cells and myeloid cells densities were increased (X 1.5 and 1.9, P<0.05) in HP piglets.

Conclusion: The protein enrichment modified the postnatal development of colonic microbiota and immune and non-immune barrier. Later in life, in females, it was associated with some features which have been related to Crohn’s disease (reduced percentage of F. praustnitzii, higher sensitivity to oxidative and inflammatory stresses). This study clearly demonstrates for the first time the presence of long-term effect of neonatal nutrition on colonic physiology.

Disclosure of Interest: None declared.
immunological and probiotic elements vital to the health of preterm infants, and is not universal. UK guidelines exist for the routine pasteurisation of DEBM only. We examined the evidence for infection transmitted to preterm infants from HBM.

**Methods:** Medline, Cochrane and PubMed electronic searches (1950-September 27th 2009). MeSH Keywords: infant; preterm; human/maternal/breast/donor milk; sterilisation/pasteurisation/disinfection; milk banks; storage/freezing/refrigeration; and infection/sepsis/septicemia. Review articles were cross referenced. Entry criteria: preterm infants (<37 weeks) <28 d corrected gestational age, with microbiology and epidemiology confirming breast milk as the source of infection. SIGN guidelines for appraisal were employed (www.sign.ac.uk).

**Results:** 105196 articles cited, yielding 1081 abstracts. 15 articles relevant: two case-control studies were assigned EL (n = 14, all DEBM). Mean gestation: 28.7 weeks ± 2.75. Mean day of life on which milk-related sepsis first diagnosed: 21.9 ± 12.19. Milk storage methods: refrigeration (n = 12), freezing (n = 22), or NS (n = 11). Mothers were twice as likely to be asymptomatic (n = 12) as symptomatic (mastitis n = 4, mastitis and wound infection n = 1, or positive vaginal swab n = 1). Only 1 report tested expressing equipment for colonisation (n = 5 infants). Organisms included: Salmonella (n = 10), Klebsiella (n = 7), E. Coli O125 (n = 14), Group B Strep (n = 12) and MRSA (n = 2). Methods of detection: molecular techniques and conventional culture. 3 infants died.

**Conclusion:** The evidence for the transmission of infection to preterm infants from HBM is limited and the role of pasteurisation unclear. Future studies identifying milk as a source of infection should consider expressing and handling equipment. Only one study considered contamination from this source. The need for pasteurisation could be obviated by hygiene protocols, routine cultures and maternal screening questionnaires. HBM and handling equipment should be considered as a focus of late-onset, unusual or recurrent infection in preterm infants. Further studies are required to explore the effects of alternative methods of sterilisation.

**Disclosure of Interest:** None declared.

**SP-N-075**

**IRON DEFICIENCY OR ANAEMIA IN PRETERM INFANTS FED FORMULA OR HUMAN MILK OVER THE FIRST SIX MONTHS OF LIFE**

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**Objectives and Study:** To evaluate the effects of different iron intake with iron-fortified formula or human milk on iron status and red blood cell indices of preterm infants during the first six months of life.

**Methods:** Preterm infants <32 weeks gest. age and <1500 g. birth weight were fed formula (n = 92) or human milk (n = 46). Iron status and red blood cell parameters were measured at 0.3 and 6 m. corrected age.

**Results:** Mean RDW is significantly higher at 3 and 6 m. in infants fed human milk. Breast fed infants are 4 to 6 times more likely to develop iron deficiency (ferritin <10 ug/L) at 3 and 6 m. corr. age compared to formula fed infants.

**Conclusion:** Preterm infants fed human milk only after 0 m., without external iron supplementation, more frequently show signs of iron deficiency at 3 and 6 m. corr. age compared to formula fed infants.

**Disclosure of Interest:** E. A mesz, research fellow H.N. Lafeber, research professor M v.d. Lagemaat, student A.Schaafsma, Friesland Foods, Grant Research Support

### Table:

<table>
<thead>
<tr>
<th>Postnatal age of infants</th>
<th>0 m. corr. age formula - human milk</th>
<th>3 m. corr. age formula - human milk</th>
<th>6 m. corr. age formula - human milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe intake in mg/kg/d</td>
<td>3.1 ± 1.2 versus 1.5 ± 1.1</td>
<td>2.3 ± 1.3 versus 1.0 ± 0.8</td>
<td>1.2 ± 0.2 versus 0.1 ± 0.1</td>
</tr>
<tr>
<td>RDW &gt;14.5</td>
<td>- versus -</td>
<td>9.8 versus 26.1**</td>
<td>8.7 versus 28.3**</td>
</tr>
<tr>
<td>Ferritin &lt;10 (μg/L)</td>
<td>3.3 versus 6.5</td>
<td>4.3 versus 15.2*</td>
<td>3.3 versus 17.4**</td>
</tr>
<tr>
<td>Hb &lt;5.9 (mmol/l)</td>
<td>43.5 versus 50</td>
<td>1.1 versus 4.3</td>
<td>0.1 versus 2.2</td>
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<tr>
<td>Ht &lt;0.32 (l/l)</td>
<td>82.6 versus 80.4</td>
<td>6.5 versus 28.3**</td>
<td>4.3 versus 6.5</td>
</tr>
</tbody>
</table>

Iron deficiency and anaemia as %. (diff. = * P < 0.01, ** P < 0.005)