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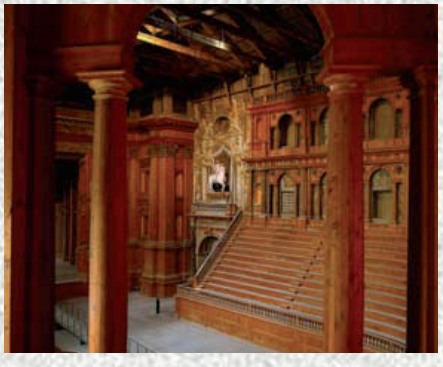

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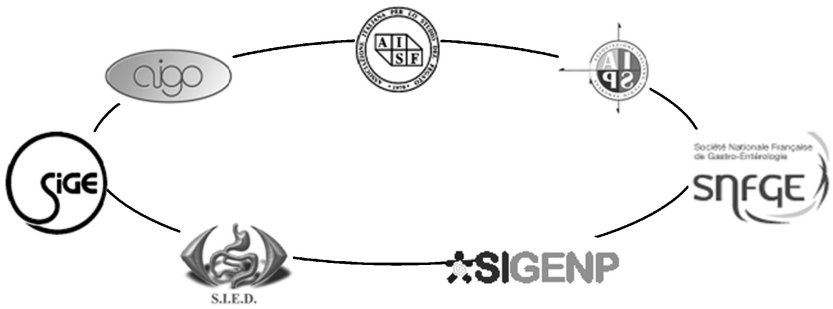

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Oral Communications

CO1
DISEASE COURSE AND OUTCOME OF MEDICAL THERAPY IN PEDIATRIC STRICTURING CROHN'S DISEASE

M. Aloi[1], G. D'Arcangelo[1], F. Civitelli[1], G. Di Nardo[1], E. Casciani[2], F. Nuti[1], G. Romano[1], F. Viola[1], S. Cucchiara[1]. *[1]Pediatric Gastroenterology And Liver Unit, Sapienza University of Rome, Rome, Italy; [2]Radiology DEA, Sapienza University of Rome, Rome, Italy*

Background and Aim: Stricturing is the most common complicated phenotype in children with Crohn's disease (CD), but only few studies have described its course and there are no data on the efficacy of medical treatment. The purpose of this study was to retrospectively describe in pediatric stricturing CD the course and assess clinical and radiological response to medical therapy.

Patients and Methods: 36 patients (pts) with stricturing CD (64% males, age range: 7.3–20.2 years, median 14.7), were identified by our department database. Records were reviewed for disease duration before detecting stenosis, location of strictures, type of medical treatment received, number of disease recurrences and hospitalizations. Pediatric Crohn's disease Activity Index (PCDAI), need to change medical treatment or surgery, magnetic resonance imaging or small intestine contrast ultrasonography were used as outcomes and evaluated at 6, 12, 18 and 24 months after diagnosis of stenosis.

Results: Strictures were ileal in 61% of pts, ileocolonic in 28% and colonic in 11%; 6 pts (17%) also had proximal jejunal stenosis. Thirteen pts (36%) had a stricturing disease at the time of CD diagnosis, while 64% developed it at the follow-up (2.48±4.12 years after CD diagnosis). Cumulative risk for developing stenosis was 22%, 27% and 28% at 12, 18 and 24 months, respectively. At baseline, 89% of pts underwent medical treatment, while 11% had surgical resection: in a multivariate analysis, only ileal stenosis and severe abdominal pain significantly differed between the two groups (p: 0.05 and p: 0.006, respectively). At 6, 12, 18, and 24 months, 53%, 50%, 42%, and 35% had a complete response to medical treatment, respectively; whereas 34%, 43%, 40%, and 34% had a partial response, defined as a radiological evidence of stenosis requiring a change of their medical therapy. Overall, 44% were unresponsive to medical therapy and required surgery during 24 months follow-up; responders and non-responders did not statistically differ for clinical variables such as duration of disease, location of stenosis, mean PCDAI at the beginning of the therapy and type of medical treatment.

Conclusions: A stricturing phenotype is not uncommon at the diagnosis of CD in children. Medical therapy seems to be poorly effective in avoiding intestinal resection and common clinical variables are not of value in discriminating between responder and non responders to medical therapy. Prospective studies are needed to define the optimal management strategy of stricturing CD and to identify predictive factors of medical treatment failure.

CO2
ULTRASONOGRAPHIC ASSESSMENT OF COLONIC WALL IN PEDIATRIC ULCERATIVE COLITIS: COMPARATIVE STUDY WITH ILEO-COLONOSCOPY

F. Civitelli[1], G. Di Nardo[1], S. Oliva[1], F. Nuti[1], M. Aloi[1], F. Ferrari[1], F. Viola[1], S. Cucchiara[1]. *[1]Pediatric Gastroenterology and Liver Unit, Sapienza University of Rome, Italy*

Background: Bowel ultrasonography (US) is a well established non-invasive tool in the evaluation of patients (pts) with inflammatory bowel disease, especially Crohn's disease. It is widely available, inexpensive, radiation-free and relatively easy to perform. However there are only few data on the role of US in Ulcerative Colitis (UC), particularly in paediatric age.

Aims: To evaluate the usefulness of bowel US in the assessment of pediatric pts with UC and compare US findings with clinical and endoscopic data.

Methods: 22 paediatric pts (median age 15 years; range 2–21) were prospectively enrolled. 7 pts had a clinical suspicion of UC, 15 pts had an already established diagnosis and showed a flare-up of disease. All pts underwent clinical evaluation, bowel US with Color-Doppler examination (Toshiba equipment, with 3.5 MHz convex and 7.5 MHz linear transducers) and ileo-colonoscopy. US and endoscopy were carried out by different operators, blind to the results of the other technique. For each patient Pediatric Ulcerative Colitis Activity Index (PUCAI) and Mayo endoscopic score were calculated. The US parameters assessed were Bowel Wall Thickness (BWT >3 mm), BW stratification, vascularity and presence of austrae: each parameter was assigned a value of 0 or 1 depending on the presence or absence of alteration.

Results: 20/22 pts were finally diagnosed as UC. Extension of disease according to Montreal Classification was: E2 (left-side colitis) in 9/20 (45%), E3 (extensive UC) in 11/20 (55%) pts. This extent was independently confirmed in 17/20 pts by US, that yielded a 97% concordance with endoscopic features concerning disease extension. Disease activity was mild (PUCAI 10–34) in 5 pts (25%), moderate (PUCAI 35–64) in 10 (50%) and severe (PUCAI >65) in 5 (25%.). The mean values of PUCAI, Mayo score and US score respectively were: 40.5±24.4, 2±1 and 2.8±1.4. The mean colonic BWT in UC children was 5±2 mm. The US score strongly correlated with PUCAI ($r = 0.85$, $p < 0.0001$) and Mayo index ($r = 0.90$, $p < 0.0001$). A positive correlation was also found between PUCAI and Mayo score ($r = 0.87$, $p < 0.05$). Multiple regression analysis considering Mayo endoscopic score as dependent variable showed a statistical significant correlation with BWT ($p < 0.007$) and vascularisation ($p < 0.038$).

Conclusions: Our preliminary data show a strong relationship between US and clinical and endoscopic findings, thus suggesting

that colonic US might represent a useful first line, non invasive tool in the evaluation of paediatric UC pts. In our experience it allows to assess in a relatively rapid manner the extension and activity of disease and helps to judge the severity of a flare-up in pts with an already established diagnosis, prior to further invasive tests.

CO3
ENDOSCOPIC TREATMENT OF ESOPHAGEAL VARICES

P. Perazzo[1], F. Fornaroli[1], A. Fugazza[1], E. Manzali[1], G. De Caro[1], S. Liatopolou[1], G.L. de'Angelis[1]. [1]*Complex Unit of Gastroenterology and Endoscopy, University of Parma, Italy*

Objectives: Esophageal varices are the major complication of portal hypertension. The major therapeutic strategy of esophageal varices consists of primary prevention, treatment for bleeding varices, and secondary prevention, which are provided by pharmacological, endoscopic, interventional and surgical treatments.
Evidence-based recommendations on endoscopic screening and prophylactic treatment in pediatric age are scarce. The purpose of this study is to consider endoscopic treatments by evaluating benefits, risks and effectiveness.
Methods: 27 children with portal hypertension (12 portal vein thrombosis, 6 autoimmune hepatitis, 7 cystic fibrosis and 2 congenital heart disease) aged from 4 months to 17 years were included in the study. The criteria for inclusion were: no previous variceal bleeding, the presence of varices grade II and III and their enlargement by at least I grade after 6 months of observation without endoscopic treatment or appearance of endoscopic signs of high bleeding risk. A Multi-Band Ligator was used, and 2 to 6 bands were fixed under general anesthesia during the procedure depending on the number and size of varices. Follow-up examinations were performed after 1 month and every 3 months for 1 year, repeating the procedure if necessary.
In endoscopic sclerosis, sclerosants are injected either intravariceally or paravariceally. This technique has been used in children less than 3 years and 15 kg.
Results: 20% of all children had esophageal varices classified grade III and 80% grade II.
8 patients underwent the treatment in emergency (3 patients with multi band ligator while 5 with sclerosis).
Of 18 children treated with multi band ligator, 13 patients, all with varices grade II, showed a regression after a single treatment, while 5 patients, with varices grade III and II, underwent multiple ligatures with totally regression after 1 year.
Of the 9 children who underwent sclerosis therapy, 3 had varices grade III and 6 grade II. They underwent more then one procedure with only reduction of varices to grade I.
No complications underwent in both groups. In the period of observation only one re-bleeding occurred in a patient treated urgently 6 months after first sclerosis.
Conclusions: This study confirms that endoscopic variceal ligation and sclerosis treatment are safe and highly effective procedures in children with portal hypertension, regardless of its etiology. Currently, the ligation of varices is the endoscopic treatment of choice for variceal bleeding in adults and it is proven to be safer, more efficient and requires less number of session then sclerosis.
Ligation of varices is the treatment for excellence also in pediatric age even if limited by the dimensions of the little patient.

CO4
EOSINOPHILIC OESOPHAGITIS: A NEW ICEBERG TO FIND OUT?

P. Soriani[1], F. Vincenzi[1], A. Fugazza[1], E. Manzali[1], F. Parmeggiani[1], A. Gnocchi[1], G.L. de'Angelis[1]. [1]*Complex Unit of Gastroenterology and Endoscopy, University of Parma, Italy*

Background: Eosinophilic oesophagitis is an emerging chronic inflammatory disorder, in particular in Western countries, characterized clinically by symptoms related to oesophageal dysfunction and histologically by eosinophils predominant infiltrate. It's more frequent in atopic males in the childhood. Clinical manifestations differ from the range of age: children tipically have feeding difficulties, failure to thrive, vomiting, dysphagia, abdominal pain, while adults present dysphagia, food impaction and are refractory to anti-GERD therapy; atopy is common in both groups.
Aim: To evaluate, prospectively, the epidemiology, the clinical manifestation and the endoscopic aspect of eosinophilic oesophagitis in our centre.
Patients and Method: This study considers new eosinophilic eosophagitis diagnosis between February 2011 and May 2012 in our centre. Age at diagnosis, sex, race, clinical presentation, endoscopic features, laboratoristic parameters (eosinophils count and ECP), allergy testing were recorded and other causes of gastrointestinal eosinophilia were ruled out (including PPI test).
Results: Between February 2011 and May 2012 we diagnosed 15 new cases of eosinophilic oesophagitis, with a prevalence in male versus female (13 M vs 2 F) and an age included between 1 and 17 years. Concerning racial groups, all patients were Caucasian; 7/15 patients presented dysphagia and difficult eating, 3/15 epigastric pain, 3/15 gastro-esophageal reflux symptoms and 2/15 failure to thrive. In 8/15 patients endoscopy showed a hyperaemic and weak mucosa at the oesophagus, whitish exudates in 2/15, trachealized aspect in 3/15 and a normal aspect in 2/15. Considering laboratoristic parameters, eosinophils counts were normal in all patients (n.v. 1–8% or 10–880/mmc), while ECP (n.v. <15 ug/l) was increased in 8/15 patients. Serum IgE and skin prick test were performed and resulted positive in 11/15 patients. Every patient non respond to PPI at all.
Conclusion: The incidence of eosinophilic oesophagitis is increasing from the past, also probably because of the crescent number of endoscopies and oesophageal biopsies. A significant number of patients, who initially presented only epigastric pain and not typical endoscopic feature, had diagnosis of eosinophilic oesophagitis and not completely respond to PPI treatment. So the debate is open: oesophageal biopsies are always necessary?

CO5
PNEUMATIC BALLOON DILATION IN PEDIATRIC ACHALASIA: EFFICACY, SAFETY AND FACTORS PREDICTING OUTCOME

S. Oliva[1], G. Di Nardo[1], F. Ferrari[1], P. Rossi[1], G. Pagliaro[1], S. Isoldi[1], L. Pierantoni[1], C. Ziparo[1], E. Barberini[1], C. Delli Colli[1], S. Cucchiara[1]. [1]*Pediatric Gastroenterology Endoscopy and Liver Unit, "Sapienza" University of Rome, Italy*

Background: Achalasia is a rare disease especially in children. Pneumatic dilation (PD) is well established in adults, however it is less commonly used in children.
Aims: To evaluate the short and medium-term efficacy of PD and to investigate predictive factors for treatment failure in pediatric achalasia.
Methods: Twenty-four patients (11 female; mean age 10 years; range: 4–17) with achalasia who were diagnosed and treated in our Unit from January 2004 to November 2009 were prospectively

included in this study. Patients were followed-up with the use of the Eckardt score, barium swallow contrast studies and esophageal manometry at baseline, 1, 3, 6 months after dilation, and every year thereafter. Patient outcome was evaluated according to the Eckardt score. Wilcoxon non parametric test was used to compare baseline characteristics between patients responding to the first PD and those needing to repeat treatment. PDs were performed under general anesthesia by using polyethylene balloon system.

Results: PD success rate was 67%. In 8 subjects there was a failure at first PD, but only 1 of them decided to undergo surgery for personal choice. Of the 7 patients who repeated the treatment 3 (43%) had a second failure. Overall only 3 patients out of 24 underwent surgery (overall success rate, after a maximum of 3 PDs, was 87%). Multivariate analysis showed that only older age was independently associated to a higher probability of the procedure success (HR 0.66; 95%CI: 0.45–0.97).

Conclusions: PD is a safe and effective technique in the management of pediatric achalasia. Young age is an independent negative predictive factor for successful clinical outcome.

CO6
GASTRIC XANTHOMATOSIS: A RARE FINDING IN THE PAEDIATRIC AGE

M. Gasparetto[1], G. Pennelli[2], M. Cananzi[1], F. Galuppini[2], M. Pescarin[1], G. Guariso[1]. *[1]University Hospital of Padova, Department of Paediatrics Unit of Gastroenterology, Digestive Endoscopy, Hepatology, and Care of the Child with Liver Transplantation, Italy ; [2]University Hospital of Padova, Department of Medicine DIMED Surgical Pathology and Cytopathology Unit, Italy*

Background: Gastric xanthoma are rare benign lesions most frequently found in the antrum. They can be associated with inflammation of the gastric mucosa, especially in patients with chronic gastritis, *Helicobacter pylori*, intestinal metaplasia, bile reflux. Their etiology is nevertheless not completely known as they are rarely described. Just a few number of adult cases aging >35 years has been reported [1], whereas to our knowledge only one previous paediatric case was described as yet [2].

Specific aim: We report a rare paediatric case of gastric xanthomatosis, whose endoscopic follow-up demonstrates the evolution of lesions and their correlation with Proton Pump Inhibitors (PPI) treatment administered.

Case Report: A 13 year old girl came to our attention for disphagia, chest burning, feeling of regurgitation and rumination after each meal. Neither abdominal pain, nor alteration in stool frequency were referred. The clinical assessment was normal, except for a mild decrease in body weight (from 25th to 10th percentile) with respect to the height (50th percentile). The general blood tests performed were all negative, gastro-panel included [3]. A first upper-GI tract endoscopy previously performed had identified two whitish kissing lesions with diameter of 0.3 cm surrounded by hyperhaemic mucosa, in the middle of the small gastric curve, and a mild hyperhaemic antral mucosa. The histologic examination demonstrated inactive chronic gastritis at the antrum as well as in the areas next to the two lesions; no *Helicobacter pylori* was detected. A therapeutic trial with PPI was suggested and performed for one month, with only partial remission of symptoms. Given a relapse of symptoms fifteen days after the suspension of the PPI treatment, we decided to perform at our Unit another upper-GI-tract endoscopy two months after the previous one, in order to evaluate the effect of the ongoing treatment on the gastric lesions. Six gastric lesions were found this time: they appeared as nodules and soft pseudo-polyps and measuring 0.5–1 cm, with a greyish-whitish top resembling a papilloma. The presence of bile reflux was observed. The histologic examination evidenced foamy histiocytes being compatible with gastric xanthoma.

Discussion: It is important not to misrecognize the nature of these lesions, since they may present at endoscopy an ulcer-like aspect, so that an anti-acidic treatment could be therefore inappropriately prescribed. Taking biopsies during upper GI-endoscopy is thus fundamental to diagnose gastric xanthoma as well as to exclude gastric tumors.

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CO7
S100 A8/A9 PROTEIN AS A MARKER FOR EARLY DIAGNOSIS OF NECROTIZING ENTEROCOLITIS IN NEONATES

G. Terrin[1], A. Passariello[2], S. Caoci[3], V. Cardi[3], M. De Curtis[3], F. Messina[4], R. Berni Canani[5]. *1. Department of Gynecology-Obstetrics and Perinatal Medicine, University "La Sapienza", Rome, Italy; 2. Neonatology Unit, AORN "Monaldi", Naples, Italy; 3. Department of Pediatrics, University "La Sapienza", Rome, Italy; 4. Department of Perinatal Medicine, Hospital "V. Betania", Naples, Italy; 5. Department of Pediatrics, University "Federico II", Naples, Italy*

Background and Aim: Innate immune inflammatory components have a central role in the pathogenesis of necrotizing enterocolitis (NEC). The potential diagnostic utility of these mediators remain largely uninvestigated in neonates with suspected NEC. Measurement of serum levels of S100 myeloid-related proteins A8/A9, one of the principal mediators of innate immune response, has been proposed as diagnostic marker for several inflammatory conditions. We evaluated the diagnostic accuracy of s-S100 A8/A9 in neonates with suspected NEC.

Methods: Prospective multicenter study enrolling neonates with gestational age (GA) <32 weeks with suspected NEC. Exclusion criteria were congenital defects, early onset sepsis, and critical conditions. Clinical details were collected at the enrollment, together with a blood sample to determine s-S100 A8/A9 concentrations using an ELISA kit. We evaluated if s-S100 A8/A9 is able to predict development of definite NEC (Bell stage $\geqslant$2) within 72 h from the enrolment.

Results: Out of 72 newborns with suspect of NEC (male 42; birth weight 1094 g, 95%CI 1047–1141; GA 28.9 w, 95%CI 28.4–29.4; postnatal age 12.2 d, 95%CI 12.3–14.2), 16 developed definite NEC (Bell stage $\geqslant$2), 11 culture-proven sepsis, 4 intestinal obstruction and 41 remain stable (Bell stage 1) or showed a resolution of symptoms and were considered as controls. Of the 16 neonates with definite NEC, 10 evolved in advanced disease (Bell stage 3) requiring surgery. The s-S100 A8/A9 level was significantly ($p < 0.001$) higher in newborns with NEC (4.04 mcg/ml; 95%CI 3.7–4.3) compared with those affected by sepsis (2.7 mcg/ml, 95%CI 2.5–2.8), intestinal obstruction (1.2 mcg/ml, 95%CI 0.81–1.59) and controls (0.68 mcg/ml; 95%CI 0.58–0.78). We calculated the accuracy of s-S100 A8/A9 (sensitivity 100%, 95%CI 79.4–100%; specificity

96.4%, 95%CI 87.6–99.6%; positive predictive value 88.9%, 95%CI 65.3–98.6%; negative predictive value 100%, 95%CI 93.4–100%; likelihood ratio for positive test 28, 95%CI 8–99) after definition of optimal cut-off value (3.0 mcg/ml) for diagnosis of NEC.
Conclusions: Results of this study are relevant because early and accurate diagnosis may change the prognosis of NEC. This is the first evidence for the utility of S100 A8/A9 protein in the diagnostic approach to a newborn with suspected NEC. The S100 A8/A9 protein could be considered a promising tool for early diagnosis of NEC.

CO8
A NEW SYNTHETIC BUTYRATE DERIVATE N-(1-CARBAMOYL-2-PHENYL-ETHYL) BUTYRAMIDE IS EFFECTIVE TO LIMIT INTESTINAL INFLAMMATION IN DEXTRAN SODIUM SULPHATE-INDUCED COLITIS ANIMAL MODEL

R. Meli[1], G. Mattace Raso[1], R. Russo[1], G. D'Agostino[1], R. Simeoli[1], A. Iacono[1], R. Berni Canani[2], A. Calignano[1]. *[1]Department of Experimental Pharmacology, Naples, Italy; [2]Department of Pediatrics and European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy*

Background and Aim: The short chain fatty acid butyrate has been proposed as potential therapeutic strategy for inflammatory bowel diseases. The low palatability and stability limit a wide therapeutic use of this substance. We have recently obtained a high palatable and stable synthetic butyrate derivate, N-(1-carbamoyl-2-phenylethyl) butyramide (BuBull). In this study we comparatively evaluated the effects of this new compound and of equimolecular doses of sodium butyrate (BuNa) in dextran sulfate sodium (DSS)-induced colitis animal model.
Methods: Young male ICR mice were used in all experiments. The oral treatment with BuNa (20 mg/kg/d, once daily) or BuBull (42.5 mg/kg/d, once daily), started 10 days before DSS challenge (2.5% for 5 d in drinking water) and continued for all experimental period (7 days). All mice were sacrificed 7 days after DSS challenge. Inflammatory markers in colonic tissue were analyzed.
Results: Both substances were able to significantly limit mucosal inflammation, a similar effect potency was observed even if BuBull showed a stronger effect on reducing COX-2 expression: iNOS 58.4% of inhibition for BuNa; 62.5% for BuBull, $p < 0.05$), COX-2 (20.1% of inhibition for BuNa; 50.5% for BuBull, $p < 0.05$), and TNFa (30.2% of inhibition for BuNa; 30.8% for BuBull, $p < 0.05$).
Conclusion: The new synthetic butyrate derivate, N-(1-carbamoyl-2-phenylethyl) butyramide (BuBull) is effective in inhibiting mucosal inflammation in an animal model of colitis. The effect open new therapeutic perspectives for this compound in the treatment of inflammatory bowel diseases.

CO9
GLYCOPROTEIN 2 ANTIBODIES IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: SIGNIFICANCE AND CORRELATIONS WITH THE PHENOTYPE

V. Romagnoli[1], S. Gatti[1], L. Marinelli[2], G. Ciarrocchi[1], C. Catassi[1]. *[1]Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy; [2]Clinical Analysis Laboratory, Ospedali Riuniti, Ancona, Italy*

Background: The zymogen granule membrane glycoprotein (GP2) has been recently recognized as the major antigenic target of Crohn's disease (CD) specific anti-pancreatic antibodies (PAB). Reactivity to anti-GP2 has been showed in 29% and 10% of adults patients with CD or ulcerative colitis (UC) respectively. Recent investigations revealed an association with distinct disease phenotypes in adults: anti GP2 are more prevalent in patients with a younger onset of CD, ileo-colonic location, stricturing tendency and perianal disease. The prevalence, the significance and association with clinical parameters has never been investigated in pediatric inflammatory bowel disease.
Objectives: To assess the prevalence of anti-GP2 and anti-Saccharomyces (ASCA) antibodies and their association with clinical parameters in a group of pediatric IBD patients.
Methods: Anti-GP2 IgG and IgA and ASCA IgG and IgA were determined by enzyme-linked immunosorbent assays (ELISA-GA Diagnostics-Germany) in sera of 28 pediatric IBD patients (10 CD, 17 UC and 1 indeterminate colitis IC patients), prospectively recruited from December 2010 to December 2011 at the Department of Pediatrics, Università Politecnica delle Marche. Data were compared with a control group of 25 healthy patients. Anti-GP2 antibodies were assessed in sera using an ELISA technique based on recombinant human GP2 as solid-phase antigen coating. According to previous studies a value >20 U/ml for both tests was considered positive.
Results: We found an overall IgG and/or IgA anti-GP2 positive result in 40% CD and in 0% UC patients, respectively. Among the CD cases with autoantibodies to GP2, 2 had IgG and 2 had both IgG and IgA reactivity. As far as ASCA we found positivity in 50% of CD and co-occurrence of IgG and/or IgA anti GP-2 in 33% of CD cases. Patients suffering from CD and anti GP2 positivity had most likely an ileo-colonic localization and a stricturing phenotype. Among the control group no IgG and/or IgA anti-GP2 antibody reactivity by ELISA was found. Diagnostic sensitivity for CD of anti GP-2 was 40% and specificity was 100%, while considering either ASCA and/or anti GP2 reactivity, sensitivity for CD raised to 70%.
Conclusions: Anti-GP2 antibodies are highly specific for CD also in pediatric patients and their testing could be of clinical value as their presence significantly relates to ileo-colonic involvement and stricturing disease. The test could be important also in cases of IC and at the onset of CD, to predict evolution toward a particular phenotype.

CO10
THALIDOMIDE AFTER INFLIXIMAB FAILURE IN CHILDREN AND YOUNG ADULTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS

M. Bramuzzo[1], M. Lazzerini[1], S. Martelossi[1], M.C. Pellegrin[1], M. Maschio[1], F. Marchetti[1], G. Magazzù[2], S. Pellegrino[2], C. Ruggeri[2], G. Scibilia[2], A. Barabino[3], A. Calvi[3], S. Arrigo[3], M. Fontana[4], P. Lionetti[5], F. Mangiantini[5], M. Lorusso[5], G. Palla[6], G. Maggiore[6], V. Villanacci[7], F. Bartoli[8], G. Decorti[8], S. De Iudicibus[8], L. Monasta[1], M. Montico[1], L. Ronfani[1], R. Paparazzo[1], A. Lora[9], A. Ventura[1]. *[1]Institute for Maternal and Child Health IRCCS Burlo Garofolo Trieste, Italy; [2]Unit of Cystic Fibrosis and Paediatric Gastroenterology, University Hospital G. Martino, Messina, Italy; [3]Gastroenterology and Endoscopy Unit, G. Gaslini Institute for Children, Genoa, Italy; [4]Paediatric Department, Children Hospital "V.Buzzi", Milan, Italy; [5]Department of sciences for Woman and Child's Health, University of Florence, Meyer Childrren's University Hospital, Florence, Italy; [6]Department of Pediatrics, University Hospital Santa Chiara, Pisa, Italy; [7]Department of Pathology, Spedali Civili di Brescia, Italy; [8]Department of Reproduction and Development, University of Trieste, Italy; [9]University of Trieste, Italy*

Objectives: Few therapeutic strategies are available for patients with refractory inflammatory bowel disease (IBD); it has been reported that thalidomide, an anti-TNF-alpha drug with immunomodulatory

properties, is an effective rescue therapy for Crohn's disease (CD) patients with previous failure to biologic drugs [1]. We evaluated the efficacy and the safety of thalidomide in young patients with active CD or ulcerative colitis (UC), refractory to conventional treatments, who failed to respond or experienced severe adverse events (AEs) to infliximab.

Methods: Within a polycentric trial, we prospectively examined patients with active CD or UC who failed infliximab therapy and subsequently received thalidomide at a dose of 1.5–2.5 mg/kg/die. Remission of disease was defined for CD as a Paediatric Crohn's Disease Activity Index (PCDAI) $\leqslant$10 and for UC, as a Paediatric Ulcerative Colitis Activity Index (PUCAI) $\leqslant$10. Patients who achieved remission or a 50% decrease from baseline values after 8 weeks of therapy were followed-up for maintenance of remission. Any clinical AE was registered; nerve conduction studies were regularly performed for the risk of developing peripheral neuropathy; all patients followed the Celgene Pregnancy Prevention Program and female patients with childbearing potential performed trimestral pregnancy tests.

Results: We recruited 27 patients (mean age 15.0 years, range 2–20 years); 19 have CD and 8 have UC. Fistulas complicated seven CD patients.

After 8 weeks, 15 patients achieved clinical remission (10 CD, 5 UC) and 4 patients (3 CD, 1 UC) had a clinical response; three of them subsequently achieved remission. Nineteen patients were followed-up: mean duration of remission was 140 weeks. Two UC patients required a short course of oral steroids because of a mild relapse during the follow-up period. Fistulae improved in 4 patients and completely close in 3 patients.

Six patients had to withdraw thalidomide: 3 patients (2 CD, 1 UC) because of a clinical relapse after a mean of 105 weeks, 4 (3 CD, 1 UC) patients because of an adverse event (3 peripheral neuropathy, 1 amenorrhea). Minor neurological, dermatological, gastrointestinal and haematological AEs not requiring discontinuation of thalidomide were reported in twelve patients.

Conclusions: Our study suggests that thalidomide may be an effective drug for inflammatory bowel diseases and that may be an effective rescue therapy after infliximab failure, both in patients with CD, as already reported in literature, and also in patients with UC. In our study, AEs, above all peripheral neuropathy, have been the main cause of thalidomide withdrawal.

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CO11
VITAMIN D STATUS AND BONE MINERAL DENSITY IN PEDIATRIC AND YOUNG ADULT PATIENTS AFFECTED BY INFLAMMATORY BOWEL DISEASES

C. Calzolari[1], B. Bizzarri[1], A. Ghiselli[1], A. Fugazza[1], E. Manzali[1], G. Nervi[1], G.L. de'Angelis[1]. *[1]Complex Unit of Gastroenterology and Endoscopy, University of Parma, Italy*

OBJECTIVES: Vitamin D (25OHD) is essential for normal bone mineralization. Studies report a high prevalence of vitamin D insufficiency (serum 25OHD concentration between 10 and 30 ng/mL) and deficiency (serum 25OHD concentration <10 ng/mL) among adults affected by inflammatory bowel diseases (IBD); however studies on children IBD populations are few. The aim of this study is to evaluate serum levels of 25OHD as well as factors predisposing to hypovitaminosis D in a population of IBD children. We also measured lumbar spine and hip bone mineral density (BMD) using dual energy x-ray absorptiometry (DXA).

METHODS: 28 pediatric IBD patients (15 Crohn's disease, 13 ulcerative colitis) aged less than 18 years were analyzed. For each patient serum 25OHD, PTH and calcium concentration, disease localization, c-reactive protein value (CRP) and biological therapy were recorded. Each patient was also submitted to a DXA for BMD calculation. If hypovitaminosis D was detected, patients assumed oral vitamin D supplementation at dose of 25000 IU/month if body weight was $\geqslant$40 kg or 12500 IU/month if body weight was <40 kg. After six months of treatment, a second serum 25OHD measurement was performed.

RESULTS: The prevalence of hypovitaminosis D was 86.67% in CD and 92.31% in UC, respectively, without a statistically significant difference between the two diseases. 25OHD insufficiency rate was 92.31% in CD and 100% in UC, while 25OHD deficiency was 7.69%. In pediatric CD and UC, BMD was normal in all patients. Supplementation of oral 25OHD for six months normalized serum 25OHD in 40% of CD patients and 60% of UC patients, respectively. A 100% compliance to supplementation therapy was demonstrated. None of the predisposing factors analyzed was statistically significantly associated to hypovitamonosis D, though we observed hypovitaminosis D in 100% of pediatric CD patients with CRP increased values. Ileal localization of disease was associated to hypovitaminosis D in 83.33% of patients but we did not found a statistically significant correlation between ileal disease and hypovitaminosis D.

CONCLUSIONS: Hypovitaminosis D is a highly prevalent condition in pediatric patients affected by IBD, generally not associated to BMD loss. Predisposing factors appear to be increased CRP values and ileal localization of disease. Oral 25OHD supplementation seemed to be quite effective to treat hypovitaminosis D.

CO12
PHENOTYPE AND CLINICAL CHARACTERISTICS OF EARLY COMPARED TO LATE-ONSET PEDIATRIC INFLAMMATORY BOWEL DISEASE

M. Aloi[1], P. Lionetti[2], A. Barabino[3], G. Guariso[4], S. Costa[5], M. Fontana[6], C. Romano[7], G. Lombardi[8], A. Staiano[9], P. Alvisi[10], P. Diaferia[11], M. Baldi[12], V. Romagnoli[13], M. Gasparetto[4], M. Di Paola[2], M. Muraca[3], S. Pellegrino[5], S. Cucchiara[1], S. Martelossi[14], on behalf of SIGENP IBD Group. *[1]Pediatric Gastroenterology And Liver Unit, Sapienza University of Rome, Italy; [2]Gastroenterology and Nutrition Unit, Meyer Pediatric Hospital, Florence, Italy; [3]Gastroenterology and Endoscopy Unit, G. Gaslini Institute for Children, Genoa, Italy; [4]Pediatric Gastroenterology, University of Padua, Italy; [5]Pediatric Gastroenterology, University of Messina, Italy; [6]Department of Pediatrics, University of Milan, Italy; [7]Pediatric Gastroenterology and Endoscopy, University of Messina, Italy; [8]Pediatric Gastroenterology and Endoscopy Unit, Spirito Santo Hospital, Pescara, Italy; [9]Department of Pediatrics, University of Naples Federico II, Naples, Italy; [10]Pediatric Department, Maggiore Hospital, Bologna, Italy; [11]Pediatric Department, Giovanni XXIII Hospital, Bari, Italy; [12]Pediatric Gastroenterology Unit, University of Turin, Italy; [13]Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy; [14]Department of Pediatrics, Institute of Child Health, IRCSS Burlo Garofalo, Trieste, Italy*

Background and Aim: Early-onset (EO) pediatric inflammatory bowel diseases (IBD) seem to be more severe and extensive than those with a later-onset. To test this hypothesis we examined the phenotype and clinical characteristics of patients (pts) with IBD diagnosis at 0–5 years (yrs), compared to the ranges 6–11 and 12–18 yrs.

Methods: Anatomic locations and behaviors were assessed in 505 consecutive IBD pediatric pts (54% males): 224 Crohn's Disease (CD), 245 Ulcerative Colitis (UC) and 37 IBD-unclassified (IBDU). Data were collected between January 2009 and April 2012 and stored in the Pediatric Gastroenterology, Hepatology and Nutrition Italian Society (SIGENP) IBD web-registry, recently developed.
Results: 11% of pts were in the range 0–5 yrs of age at the diagnosis, 39% in 6–11, and 50% in 12–18. UC was the most frequent diagnosis in EO-IBD and in 6–12 yrs old group, whereas CD was predominant in older children (p: 0.002). A classification as IBDU was more common in the range 0–5 yrs compared to the other groups (p: 0.005). EO-CD was characterized by a more frequent isolated colonic disease (p: 0.01). Seventy-nine % of the 0–5 yrs range pts had extensive UC, compared to 50% of 6–11 (p: 0.004) and 45% of 12–18 (p: 0.001) yrs range. A proctitis was diagnosed in 0.5% of 0–5 yrs age group, compared to 17% in 6–11 and 19% in 12–18 yrs ranges (p: 0.19). Most of younger pts received steroids and thiopurines at the diagnosis (58% and 55%, respectively), while use of steroids was reduced in older two age range pts (p: 0.001). Thirteen % of pts with EO-IBD underwent biological therapy within 1 year from the diagnosis (vs. 12% of 6–11 and 15% of 12–18 yrs range groups). There was no statistical difference for family history for IBD in the 3 age range groups.
Conclusions: EO-IBD exhibit an extensive disease phenotype and benefit from more aggressive treatment strategies. A family history for IBD is not common in younger children. Long prospective studies are needed to define the natural history of EO disease.

CO13
SPLANCHNIC AND CEREBRAL TISSUE OXYGENATION: EFFECTS OF BOLUS AND CONTINUOUS ENTERAL FEEDING EVALUATED BY NEAR INFRARED SPECTROSCOPY IN PRETERM INFANTS

L. Corvaglia[1], S. Martini[1], E. Legnani[1], B. Battistini[1], A. Aceti[1], G. Faldella[1]. *[1]U.O. Neonatologia e Terapia Intensiva Neonatale, Ospedale Sant'Orsola-Malpighi, Università di Bologna, Italy*

Background and Aims: Enteral nutrition is essential for the development and growth of the gastrointestinal tract in preterm infants. The acquisition of coordination between suction, swallowing and breathing is usually incomplete before 32–34 weeks of post-conceptional age; in the meantime, meals should be administered through a nasogastric or orogastric tube. Bolus and continuous feeding represent the enteral tube-feeding techniques most frequently used in preterm infants, but the best strategy is not yet established. Near-Infrared-Spectroscopy (NIRS) provides a noninvasive monitoring of splanchnic oxygenation, which may be influenced by feeding administration, playing moreover a role in the multifactorial pathophysiology of necrotizing enterocolitis (NEC).
The aim of this study was to evaluate and compare the changes in cerebral and splanchnic oxygenation occurring after bolus and continuous feeding in stable preterm infants with normal feeding tolerance.
Materials and Methods: Eighteen healthy preterms (GA 27–32 weeks), tolerating at least 100 ml/kg^{-1}/day^{-1} of fortified human milk or preterm formula, underwent a 6-hours simultaneous monitoring of cerebral and splanchnic oxygenation using NIRO-200 oximeter. Sensors were placed on frontal and sub-umbilical region. During the 6-hour monitoring, each baby was fed twice via a nasogastric tube: one feed was given as a 10 minute bolus, and the other one was given continuously over 3 hours. Recorded values of cerebral and splanchnic Tissue Oxygenation Index (TOI) were clustered in 5-minutes intervals and compared between different feeding techniques using Wilcoxon Signed Ranks Test. Statistical significance was set at $p \leqslant 0.05$.
Results: Splanchnic oxygenation during continuous feeding was significantly lower ($p < 0.05$) than after bolus feeding. A significant decrease was observed from 1.30′ hour after the beginning to the end of continuous feeding. On the contrary, no differences between the two techniques were found on cerebral oxygenation.
Conclusions: To the best of our knowledge, this is the first study comparing the effect of different feeding techniques on splanchnic and cerebral oxygenation in preterm infants. We found that splanchnic oxygenation detected during continuous feeding was significantly lower than that detected after bolus feeding for approximately 1/2 of the study period. No differences in cerebral oxygenation were found between the two techniques. As changes in splanchnic oxygenation may be involved in the development of NEC, our preliminary data deserve attention and require further investigation in larger studies.

CO14
POST-INFECTIOUS FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN: A MULTICENTER PROSPECTIVE STUDY

L. Pensabene[1], V. Talarico[1], F. Graziano[1], B.V. Palermo[1], E. Cozza[1], A. Campanozzi[2], A. Marseglia[2], T. Gentile[3], E. Gatta[3], V. Rutigliano[4], D. De Venuto[4], A. Ripepi[5], S. Salvatore[5], R. Turco[6], A. Staiano[6], C. Di Lorenzo[7], and on behalf of the Italian Society for Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). *[1]Dpt of Pediatrics, Univ. Magna Graecia, Catanzaro, Italy; [2]Dpt of Pediatrics, Univ. of Foggia, Foggia, Italy; [3]Dpt of Pediatrics, Univ. of l'Aquila, l'Aquila, Italy; [4]Dpt of Pediatrics, Univ. of Bari, Bari, Italy; [5]Dpt of Pediatrics, Univ. of Varese, Varese, Italy; [6]Dpt of Pediatrics, Univ. of Naples, Naples, Italy; [7]Dpt of Pediatrics, Nationwide Children's Hospital, Columbus, USA*

Objectives: (1) To investigate the occurrence of post-infectious functional gastrointestinal disorders (PI-FGIDs), diagnosed according to the Rome III criteria, in children with acute gastroenteritis (AGE) of infectious etiology. (2) To determine the proportion of proven cases of bacterial, viral or parasitic AGE that evolve into PI-FGIDs in children.
Study design: A prospective cohort multicenter study of children 4 to 17 years old with AGE and stool tests positive for bacterial, viral or parasitic infection.
Methods: Children presenting for AGE who tested positive for stool infection (2007–2010) were contacted within one month from the episode. Exposed children were matched with control subjects of similar age and sex presenting to the same hospitals for trauma or well-child visit within 4 weeks of the index case. Symptoms were evaluated using a validated questionnaire for all FGIDs (according to the Rome III criteria) at the time of enrollment in the study (within one month), after 3 months and 6 months after the positive stool tests.
Results: 64 patients (36 boys; mean age, 6.5 years; age range, 4–13 years) were recruited, 32 patients in each arm. Infections included rotavirus (56.8%), *Salmonella* (30%), adenovirus (6.6%), norovirus (3.3%), and *Giardia lamblia* (3.3%). Diagnosis of FGIDs was significantly higher in exposed patients compared to controls, within one month from AGE [40.6% vs. 12.5% ($p = 0.02$, RR = 1.9)], 3 months later [53% vs. 15.6% ($p = 0.003$, RR = 2.2)] and 6 months later [46.8% vs. 15.6% ($p = 0.01$, RR = 1.9)]. No correlation was found between different etiologies, age, or sex, and increased incidence of any specific type of FGIDs. At 6 months, FGIDs were diagnosed in 9/20 (45%) children with viral infections and in 6/11 (54.5%) of those with bacterial infections. Among exposed children, abdominal pain-

related FGIDs (AP-FGIDs) were diagnosed with increased frequency at subsequent control visit (18.7% at 1 months, 25% at 3 months, and 28.1% at 6 months), with statistically significant difference compared to controls only at 6 months ($p = 0.04$, $RR = 1.7$) [mostly functional abdominal pain (from 3.1% at 1 months to 12.5% at 6 months) and irritable bowel syndrome (from 9.4% to 12.5% at 6 months)]. At 6 months, AP-FGIDs were diagnosed in 6/21 (28.6%) children with viral infections and in 2/9 (22.2%) of those with bacterial infections.
Conclusion: This first prospective cohort multicenter study supports PI-FGIDs as a true entity in children. According to the Rome III criteria there is a significant increase in abdominal pain-related FGIDs after AGE in children, evaluated within one month, and 3 and 6 months later. However, no correlation was found between different etiologies and any type of PI-FGIDs.

CO15
DEMOGRAPHIC FEATURES OF CYCLIC VOMITING IN CHILDHOOD IN THE UK

V. Giorgio[1], O. Borrelli[1], J. Koeglmeier[2], P. Andrews[3], K. Lindley[1]. *[1]Neurogastroenterology, [b]Gastroenterology, Great Ormond Street Hospital for Children, [c]Physiology, St George's Hospital Medical School, London, United Kingdom*

Objective: To define the clinical characteristics of cyclic vomiting syndrome (CVS) in the UK.
Methods: A questionnaire was sent to members of the cyclic vomiting support association (UK) to identify disease associations with CVS. 204 questionnaires were sent out of which 99 were returned.
Results: Respondents comprised 68 (69%) females and 31 males (31%). 8 CVS sufferers (8.4%) had an affected mother and 3 (3%) had an affected maternal grandmother. 48/95 (50.5%) of mothers of affected respondents suffered from morning sickness in the first trimester of pregnancy whilst in 16/95 (16.8%) the mother suffered from nausea and sickness throughout pregnancy (hyperemesis gravidarum). The prevalence of morning sickness didn't differ significantly from that of the normal population. Assuming a prevalence of 1.5% for hyperemesis gravidarum in the general population then using a single proportion test $Z = 3.875$ $P < 0.0001$ supporting the hypothesis that the prevalence of HG is higher in the mothers of those suffering with CVS. Median age of onset was 48 months and was similar in boys and girls. 53 (53.5%) had another associated gastrointestinal condition (including 12 irritable bowel syndrome, 38 gastroesophageal reflux disease, 18 diarrhoea and 21 constipation). 38 (38.4%) suffered migraine, 27 (27.3% recurrent infections) and 17 (17.2%) balance problems. 8 (8.1%) had learning difficulties. 44 (44.4% suffered) from motion sickness. The prevalence of atopy was also high with 35 (35.4%) suffering from hayfever, 30 (30.3%) eczema and 21 (21.2%) asthma. 62% believed that infection was an emetic trigger. 74% believed that stress was a trigger. Other triggers included menstruation (44%), food (21%) and travel (26%). Stress 14%, exertion (physical/mental), travel 7%, late nights 8%, excitement 5%, and specific foods 5% were causitive. In 54% the time of onset was between 12 midnight and 8 am. During an episode 87% adopted a specific posture, the majority curling up and adopting the "fetal" position. 43% had between 5–10 vomits/hour during the most intense phase of the illness with the majority (62%) experiencing more than 30 vomits per episode.
Conclusion: These data show that intrauterine exposure to high concentrations of HCG (in hyperemesis) programs the emetic centre such that it predisposes to the development of CVS. They also highlight the important association of CVS with vestibular dysfunction, and coexistent gastrointestinal disease and confirm the observation of matrilineal inheritance in a high percentage of cases. These data will facilitate the development of a structured questionnaire to aid early diagnosis of CVS and provide a framework for the structured investigation of these individuals.

CO16
PREDICTING THE CLINICAL EFFECTIVENESS OF COLONIC STOMA FORMATION IN CHILDREN WITH SLOW TRANSIT CONSTIPATION AND COLONIC NEUROMUSCULAR ABNORMALITIES USING HIGH RESOLUTION MANOMETRY

V. Giorgio[1], N. Thapar[1], J. Koeglmeier[1], J. Curry[1], V. Smith[1], K.J. Lindley[1], O. Borrelli[1]. *[1]Gastroenterology, Motility Division, Great Ormond Street Hospital, London, United Kingdom*

Objective: Pediatric slow transit constipation (STC) is frequently associated with evidence of colonic neuromuscular abnormality. We have related high resolution colonic manometric (HRCM) abnormalities to neuromuscular histological phenotype and evaluated the role of HRCM in predicting outcome post stoma formation.
Methods: Prospective study of 17 children (8 males, mean age 9 years) with STC who underwent HRCM and subsequent Hartman's procedure and temporary colostomy formation. Resected colon was phenotyped histologically using a combination of standard histology and immunohistochemistry to identify abnormalities in the enteric nervous system, interstitial cells of Cajal (ICC), and smooth muscle. HRCM was performed according to a standardized protocol with a 20 channel catheter clipped in the caecum and measurements taken for at least 90 min before and after 2 instillations of bisacodyl (0.2 mg/kg). Variables analyzed included: number of high-amplitude propagating contractions (HAPC) and of low-amplitude propagating contractions (LAPC), presence of "common cavity", motility index (MI), Area Under the Curve (AUC) over 1 minute between 2 post-bisacodyl HAPC (1 min AUC). After colostomy was fashioned, children were reviewed every 3 months for a median period of 9 months (range 6–12) and evaluated clinically and reviewing a diary for: (a) number of stool productions per day after colostomy; (b) VAS score for abdominal pain.
Results: Neuromuscular abnormalities were prevalent (16/17, 90%). 12/16 (75%) had enteric neuronal abnormalities (group A), 3/16 (19%) had poorly formed ICC network (group B), 1/16 (6%) had a muscular abnormality (group C). Group A was manometrically characterized by a right colon 1 min AUC >125 mmHg. Group B and C were characterized by a right colon 1 min AUC <125 mmHg, with absent or confined to the ascending colon HAPC. All children underwent colostomy. Group A showed a good colostomy outcome and all children at 6 months follow up had a median of 1 stool production per day (range 1–3). At 9 months follow up 2/12 (17%) children of this group had less than 1 stool production per day and had to undergo ileostomy. Both children had ectopic neurons. All but one of Group B and the child of group C (3/4, 75%) had a bad colostomy outcome with less than 1 stool production per day at 6 months follow up, and underwent ileostomy.
Conclusion: HRCM is predictive of colonic neuromuscular phenotype in pediatric STC and is a discriminatory tool in predicting response to stoma formation. Measurement of segmental 1 min AUC within different regions of colon will facilitate decision making about the correct site of stoma formation.

CO17
FLUNARIZINE IN THE TREATMENT OF CYCLIC VOMITING SYNDROME (CVS)

R. Mallamace[1], D. Comito[1], S. Cardile[1], A. Chiaro[1], C. Romano[1].
[1]*Pediatric Department, University of Messina, Messina, Italy*

Background: CVS is characterized by recurrent, discrete, self-limited episodes of severe nausea and vomiting, interspersed with sign-free periods. Pediatric CVS was reported to exhibit a prevalence of 0.04–1.9% of children with an incidence of new cases at approximately 3 per 100,000 children/year. A diagnosis is based on a typical clinical presentation and by exclusion other possible causes with similar presentation. CVS is included in the International Classification of childhood periodic syndromes as abdominal migraine and benign paroxysmal vertigo. A family history of migraine is present in 67–82% of patients and a prediction analysis estimated that 75% of children with CVS would develop migraines by age 18 years. The management requires an individually tailored regimen and it is often a trial-and-error process. The prophylactic therapy to prevent subsequent episodes is recommended. Flunarizine is a non-selective calcium antagonist agent used successfully in migraine prophylaxis of both childhood and adult-onset. The aim of this study was to evaluate the efficacy of flunarazine as preventive agent in CVS in a small-cohort of patient.
Patients and Methods: A retrospective analysis has been done in 8 children, aged 4–8 years (mean age: 6.5 years) with CVS: flunarizine dose was 2.5–5 mg (mean dose: 5 mg/day) administered as once a day. The frequency of attacks was, before starting the treatment, average 4–6 episodes/year for every patients. The follow-up was continued for 3 years.
Results: In this group of patients there was a significative reduction of the frequency/year of attacks (from 4–6/year to 1–2/year, $p < 0.001$). No adverse events has been reported, none of the patients had to discontinue the therapy.
Conclusion: In this small cohort of children, the efficacy of flunarazina in the prophylaxis of CVS has been demonstrated. It is comparable to various prophylactic medications including amytriptiline and cyproheptadine, but with better tolerability and less side effects (sleepiness, weight gain). Larger prospective studies need to be done to confirm this observation.
Disclosure of Interest: None declared

CO18
PROSPECTIVE OBSERVATIONAL STUDY ON THE PREVALENCE OF SUBTYPES OF IRRITABLE BOWEL SYNDROME IN CHILDREN AT DIAGNOSIS AND CHANGES OF THESE SUBTYPES AT FOLLOW-UP

E. Giannetti[1], R. Turco[1], E. Miele[1], F.P. Giugliano[1], A. Alessandrella[1], A. Campanozzi[2], G.L. de'Angelis[3], L. Pensabene[4], S. Salvatore[5], A. Staiano[1]. [1]*Department of Pediatrics, University of Naples "Federico II", Italy;* [2]*Department of Medical Sciences, Pediatrics, University of Foggia, Italy;* [3]*Gastroenterology Unit, Hospital-University of Parma, Italy;* [4]*Department of Pediatrics, University "Magna Graecia" of Catanzaro, Italy;* [5]*Department of Pediatrics, University, University of Insubria, Varese, Italy*

Aims: Irritable bowel syndrome (IBS), as described by the Rome criteria, includes weekly symptoms of abdominal pain or discomfort accompanied by changes in bowel patterns: constipation (C-IBS), diarrhea (D-IBS) or alternating C and D (A-IBS). The importance of bowel habit heterogeneity has been highlighted by the partial response to medications that produce a major effect on bowel transit, either to decrease or increase it.
The aim of the present study was to evaluate the prevalence of IBS-subtypes (C-IBS, D-IBS or A-IBS) at diagnosis in children and any change at follow-up.
Methods: This is an observational, prospective, multicenter study. Consecutive patients with IBS as defined by the Rome III criteria, were enrolled within one year. Parents received a diary to record weekly stool frequency and consistency, the presence of specific behaviour during the evacuation and of any possible gastrointestinal symptom. A score of the stool consistency was then obtained, according to the Bristol Stool Form Scale. Children were prospectively evaluated at three time points. After 2 months from the enrolment children underwent clinical examination and all the weekly diares were collected. After 3 and 6 months from the enrolment, they and/or their parents were asked to complete again the IBS symptomatic questionnaire.
Results: We enrolled 90 children with diagnosis of IBS (*mean age: 9 yrs and 9 mths; range: 4 yrs and 5 mths to 17 yrs and 5 mths; F44/M46*). At time of enrollment (T0), C-IBS was the most prevalent subtype, presented in 45 out of 90 children (50%), with a prevalence of females of 64.4% (29/45; $p < 0.005$); D-IBS was reported in 20/90 (22.2%) children, with a prevalence of males of 75% (15/20; $p < 0.005$); A-IBS was described in 25 children (27.8%). The 18.7% had symptoms of IBS from 1–3 months, while 58.7% over 11 months; 40% of patients have difficulty falling asleep, 38.7% of patients reported absence from school and/or interruption of their activities. At two-month follow up (T1), 8 out of 83 (9.7%) patients presented changes in IBS subtypes: 3 from C-IBS to D-IBS, 2 from A-IBS to C-IBS and 3 from A-IBS to D-IBS.
At 3-month follow up (T2), 7 out of 76 (1.3%) patients presented changes in IBS subtypes: 3 from A-IBS to C-IBS, 2 from C-IBS to D-IBS and 2 from D-IBS to A-IBS.
At 6-month follow up (T3), 6 out of 58 patients (10.3%) presented changes in IBS subtypes: 2 from C-IBS to A-IBS, 3 from C-IBS to D-IBS and 1 from A-IBS to D-IBS.
Conclusions: This first survey on the prevalence of IBS subtypes in children shows that C-IBS is the most prevalent subtype, with a significant higher frequency in females. In contrast, in males D-IBS is the most common subtype. According to our preliminary results IBS-subtype changes at follow-up (25.3%), even though less frequently than in adults, in which, according to previous reports, such change is observed in about 70% of patients.

CO19
BLINDED COMPARATIVE STUDY OF MAGNETIC RESONANCE CHOLANGIOGRAPHY (MRC) VERSUS ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY (ERC) IN THE DIAGNOSIS OF SCLEROSING CHOLANGITIS (SC) IN CHILDREN

G. Rossi[2], M. Sciveres[1], L. Maruzzelli[3], G. Curcio[4], S. Riva[1], M. Traina[4], A. Luca[3], B. Gridelli[5], G. Maggiore[1,2]. [1]*Pediatric Hepatology and Liver Transplantation, ISMETT, Palermo, Italy;* [2]*Department of Maternal and Child Health, Second Pediatric Clinic, University of Pisa, Pisa, Italy;* [3]*Radiology,* [4]*Gastroenterology,* [5]*Surgery, ISMETT, Palermo, Italy*

Aims: MRC has been recently validated as comparable to ERC for diagnosis of sclerosing cholangitis (SC) in adult patients. Comparative studies have not been conducted yet in children and ERC remains the gold diagnostic standard even if MRC is widely used because of the lower rate of complications. Aims of this study were to determine diagnostic accuracy and interobserver agreement of ERC and MRC

for diagnosis of SC in children through a retrospective case-control study.

Patients and Methods: ERCs and MRCs of 7 children and adolescents (median age 9, range 7–20 years) with SC and 17 controls (median age 6, range 2 months to 29 years) with liver disease without macroscopic biliary abnormalities, were reviewed in a blinded, random and independent way. Only patients who underwent both examinations within a 6-months slot were included. One radiologist evaluated both ERCs and MRCs and one interventional endoscopist independently reviewed only ERCs. A common and previously validated classification system was used to score all records. Reviewers did not receive any demographic or clinical or laboratory information. Diagnosis of SC was established on the basis of history, laboratory data, radiologic examinations and clinical course and was used as gold standard to compare ERC and MRC diagnostic accuracy. Readers independently recorded: image quality, delineation of the first-, second-, third-, and fourth-order intrahepatic bile ducts, the extrahepatic bile duct, and the gallbladder (non depiction, fair for delineation of less than 90%, good for delineation of at least 90%, excellent for complete delineation); presence or absence of SC and their level of certainty for their diagnosis, recorded with the use of a 5-point rating system (definitely absent, probably absent, equivocal, probably present, definitely present); and they scored the bile duct images by using a classification system validated for PSC patients.

Results: Overall image quality was graded as very good in 57% of MRC cases and in 71% of ERC cases; difference was not statistically significant ($p = 0.24$) although the probability for MRC to be diagnostic increased with age of patient. Depiction of first, second and fourth order intrahepatic bile ducts was better in ERC ($p = 0.004$, 0.02 and 0.023 respectively), while depiction of extrahepatic bile ducts was comparable ($p = 0.052$) and depiction of gallbladder was even better in MRCs. Diagnostic accuracy of MRC and ERC resulted very high, without statistically significant difference ($p = 0.61$). Agreement between MRC and ERC defined as Kendall's tau-b value was considered good (0.65) even both interobserver readers of ERCs (0.61).

Conclusion: Despite an overall better depiction of biliary tree in ERC, especially in younger age, ERC and MRC are comparable for the diagnosis of SC in children. These data support MRC as the first imaging approach in children with suspected SC.

CO20
RAPAMYCINE AS IMMUNOSUPPRESSIVE TREATMENT IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS WITH POLYMORPHIC, POLYCLONAL, EBV-RELATED POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD)

M. Sciveres[1], F. Cirillo[1], S. Riva[1], P. Vitulo[2], M. Spada[3], A. Bertani[4], P. Grossi[5], A. Sonzogni[6], G. Maggiore[1,7], B. Gridelli[3]. *[1]Pediatric Hepatology and Liver Transplantation, [2]Pneumology, [3]Abdominal Surgery, [4]Thoracic Surgery, ISMETT, University of Pittsburgh Medical Center Italy, Palermo, Italy; [5]Infectious Diseases, Università dell'Insubria, Varese, Italy; [6]Pathology, Ospedali Riuniti, Bergamo, Italy; [7]Pediatric Gastroenterology and Hepatology, Università di Pisa, Italy*

Background: PTLD is a severe complication of transplantation, linked in most cases to EBV infection. Prevalence of monoclonal PTLD, in pediatric liver transplant (OLTx) recipients, is 5–7% and mortality is over 50%. Little is known about prevalence and natural history of early, polyclonal variants. However, since they are considered to be at risk of progression in more aggressive variants, treatment is mandatory and withdrawing/modulation of immunosuppressive treatment is usually the first line therapy. There is emerging evidence that mTOR inhibitors can have cytostatic effects that may be particularly relevant in the setting of EBV-associated PTLD. The aim of this study is to report on our experience with Rapamycine (Sirolimus) as first line therapy for polyclonal PTLDs in pediatric liver transplant recipients.

Methods: Among 130 liver transplant pediatric recipients 28 EBV-related PTLD (21%) were diagnosed in our Institution after a median time from OLTx of 4 years and 2 months (range 9 m to 12 y and 2 m). 16 of them were classified as "Early Lesions" and 12 as polymorphic polyclonal. 9 children with EBV-related, polymorphic PTLD, diagnosed in adenotonsillar and/or gastrointestinal-associated lymphoid tissue, were treated with the shift of immunosuppression from Tacrolimus to Rapamycine. 7 of them received Rapamycine in monotherapy while in 2 was associated with micofenolate mofetil. Target blood trough level was between 3 and 6 ng/ml. After a median time of 6 months (range 4–30) all patients underwent histological revaluation of affected tissues and liver biopsy.

Results: There were 5 males and 4 girls, median age at diagnosis of polymorphic PTLD was 6 years and 1 month (range 3 y 9 m to 15 y 8 m). Median age at OLTx was 1 year and 1 month (range 6 m to 11 y 3 m) and median time from OLTx was 4 years and 5 months (range 3 y 3 m to 6 y 1 m). Results of histological examination of adenotonsillar tissue and gastrointestinal-associated lymphoid tissue at diagnosis and after treatment with Rapamycine are summarized in table 1. Liver biopsy, performed after a median of 13 months (range 6–30 months) of rapamycin therapy did not show signs of rejection. After a median follow up of 20 months (range 13–35) all patients are alive and without signs of rejection or progression of PTLD.

Conclusions: The current standard first-line treatment of EBV related polyclonal variants of PTLD in liver transplanted children is reduction or even temporary withdrawal of immunosuppressive therapy. Although usually effective, this approach carries a high risk of acute and/or chronic rejection. Treatment with Rapamycine allowed a good control of PTLD with downgrade to "Early Lesions" in 6 out of 9 patients and complete remission in one, without exposing patients to risk of rejection.

Table 1

	Before treatment		After treatment		Duration of therapy
	Adenoids/ Tonsils	Gut	Adenoids/ Tonsils	Gut	
P1	PM	PM	–	PM	4 months
P2	PM	–	EL	EL	6 months
P3	PM	EL	EL	EL	6 months
P4	PM	EL	EL	EL	5 months
P5	PM	EL	NEG	NEG	12 months
P6	PM	PM	NEG	EL	6 months
P7	PM	PM	PM	EL	4 months
P8	PM	EL	EL	EL	12 months
P9	PM	EL	EL	EL	30 months

P: patient; PM: polymorphic PTLD; EL: "Early Lesions" PTLD; NEG: negative.

CO21
ADOPTIVE IMMUNOTHERAPY WITH EBV-SPECIFIC CYTOTOXIC T-LYMPHOCYTES (CTLs) IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS WITH LOW GRADE, EBV-RELATED POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD)

M. Sciveres[1], M. Miele[2], F. Cirillo[1], S. Riva[1], M. Di Bella[2], M. Spada[3], R. Liotta[4], A. Sonzogni[5], P. Grossi[6], G. Maggiore[1,7], P.G. Conaldi[2], B. Gridelli[3]. *[1]Pediatric Hepatology and Liver Transplantation, [2]Unit of Regenerative Medicine and Biomedical Technologies Pneumology, [3]Abdominal Surgery, [4]Pathology, ISMETT, University of Pittsburgh Medical Center Italy, Palermo, Italy; [5]Pathology, Ospedali Riuniti, Bergamo, Italy; [6]Infectious Diseases, Università dell'Insubria, Varese, Italy; [7]Pediatric Gastroenterology and Hepatology, Università di Pisa, Italy*

Background: PTLD is a severe complication of transplantation, linked in most cases to EBV infection. EBV infects naive B cells leading to immortalized lymphoblastoid cells which are normally destroyed by activated CD8+ T-lymphocytes. In immunosuppressed patients, the blasts can proliferate and eventually lead to PTLD. EBV-related PTLDs are particularly common in children who are more likely than adults to be EBV negative at the time of transplantation. One possible therapy, now clinically validated, is to infuse virus-specific lymphocytes expanded and activated *in vitro* in order to develop a cytotoxic response.

Patients and Methods: 5 (4 girls) liver transplanted children with a diagnosis of polyclonal EBV-related B-cell PTLD (2 polymorphic and 3 "Early Lesions") were treated with EBV-specific CTLs in our Institution. Median age at diagnosis was 5 years and 5 months (range: 4 y 6 m to 15 y 8 m) and median time from liver transplant (OLTx) was 3 years and 7 months (range: 3 y 4 m to 5 y 6 m). 4 patients were EBV-naive at the time of OLTx and early primary infection was documented from 1 to 3 months after OLTx. All patients showed adenotonsillar and gastrointestinal PTLD with positive EBER staining. At diagnosis they were symptomatic (nasal obstruction due to adenotonsillar hypertrophy) and the IFN-γ secreting EBV specific lymphocytes measurement at ELISPOT assay was low (median value 0.49 for μl of blood, range: 0–1.14, normal >2). They were previously treated with change of immunosuppression from Tacrolimus to Rapamycin. EBV-transformed B lymphoblastoid cells (LCLs) and EBV-CTL were generated from peripheral-blood mononuclear cells (PBMC). For CTLs, PBMC were stimulated with autologous irradiated LCL and expanded by rounds of restimulation with IL-2. EBV-CTLs, before infusion, were examined for immunophenotype, sterility, potency and EBV specificity. Treatment protocol consisted in one block of 3 monthly infusions at a median dose of 1.5×10^6/kg CTL cells followed by complete histological reassessment. In case of persistence of PTLD a second block of 3 infusions was administered at the same dose. 3 patients received 6 infusions while 2 patients to date completed only the first block.

Results: Infusions were well tolerated and no adverse reactions were recorded. A check of aminotranspherases activity, performed one week after each dose of CTL showed no abnormalities. Results of histological assessment before treatment and after 3 and 6 infusions are summarized in table. EBER staining after CTL treatment showed an improved picture with no or very few positive cells.

Conclusions: Adoptive immunotherapy with EBV specific CTL cells is feasible and safe in liver transplanted children with EBV related B-cell PTLD. Although it is known that infected B-cells in low grade PTLD have low proliferation rate and are slightly immunogenic we documented downgrading of polymorphic PTLD to "Early Lesions" in one patient and a generalized decrease in EBER positive lymphocytes. Even if these preliminary results are encouraging more experience is needed to draw any conclusion. The major benefits are expected in the long term since some CTLs could persists as memory cells and grant a durable, increased immunization against EBV-infected B-cells.

Table. Histological assessment before treatment and after 3 and 6 infusions

	A0	A3	A6	G0	G3	G6
Pt1	PM	NA	EL	PM	EL	EL
Pt2	EL	EL	NA	EL	EL	Neg
Pt3	PM	EL	EL	EL	EL	EL
Pt4	EL	Neg		EL	EL	
Pt5	EL	PM		EL	EL	

A0, A3, A6: adenoids/tonsils at diagnosis, after 3 infusions and after 6 infusions; G1, G3, G6: gut at diagnosis, after 3 infusions and after 6 infusions; PM: polymorphic PTLD; EL: "Early Lesions" PTLD; Neg: negative; NA: not available.

CO22
INSIDE AND OUTSIDE THE LIVER: HEPATITIS-ASSOCIATED APLASTIC ANAEMIA (HAAA) IN THREE PAEDIATRIC CASES

M. Gasparetto[1], M. Pillon[2], M. Cananzi[1], C. Messina[2], G. Guariso[1]. *[1]Unit of Gastroenterology, Digestive Endoscopy, Hepatology, and Care of the Child with Liver Transplantation, Italy; [2]Unit of Haematology and Oncology, Department of Paediatrics, University Hospital of Padova, Italy*

Background: Hepatitis-associated aplastic anemia (HAAA) is a variant of aplastic anemia (AA) in which pancytopenia appears two to three months after an acute hepatitis [1]. The etiology of this syndrome is still uncompletely clarified: a role of various hepatitis and non hepatitis viruses (i.e. CMV, EBV and Parvovirus B19) has been detected; genetic predisposition and immune-mediated mechanisms (including imbalance of the T cell immune system and the response to immunosuppressive therapy) are also considered to have a pivotal role.

Specific aim: We report three paediatric cases with HAAA who where successfully treated with haematopoietic stem cell transplantation (HSCT) or with administration of anti-lymphocyte globulins.

Case serie: (1) A formerly healthy 9 year old boy was admitted to our Unit of Paediatric Gastroenterology and Hepatology for detection of elevated transaminases and GGT at blood tests prescribed for sudden appearance of hecchymoses and petechiae at his limbs, feet and face. No trauma had occurred. In the previous two months, asthenia had been referred. Blood tests showed pancytopenia and repeated transfusions of immunoglobulines and platelets were required. CRP-DNA for Parvovirus B19 was positive both on blood and on bone marrow aspirate. Bone marrow aspirate and bone biopsy confirmed AA. Given the absence of any recovery of the medullar function within one month of follow-up, a HSCT was successfully performed thank to the HLA compatibility of one sibling. (2) A 12 year old boy was evaluated at our Unit for jaundice with acute onset. A diagnosis of Type 1 Autoimmune Hepatitis (AIH 1) was based on both serologic profile and liver biopsy. The genetic screening for thiopurine methyltransferase excluded mutations, so a treatment with azathioprine was began to withdrawal corticosteroids. Pancytopenia was detected after two weeks of therapy. The CRP-DNA for Parvovirus B19, initially negative at the time of AIH 1 diagnosis, turned out to be positive on both peripheral blood

and bone marrow. Pancytopenia persisted with a worsening trend until the appearance of clinical signs (major epistaxis, ecchymoses) and repeated administrations of immunoglobulins, platelets and erythrocytes were needed. A bone biopsy evidenced AA. HSCT was finally required, and the existence of a HLA compatible twin made it feasible. (3) A 3 year old boy was admitted at our Unit for acute jaundice and detection of leucopenia, thrombocytopenia and elevated transaminases. Infusions of platelets and erythrocytes were required, given a progressive worsening of the bone marrow function. A bone biopsy evidenced AA. An immunosuppressive treatment with anti-lymphocyte globulins, cyclosporine, methylprednisolone was administered, together with G-CSF. No infective causes were detected. The bone marrow and liver function increased significantly until a final recovery, so that no bone marrow transplantation was needed.

Discussion: Diagnosis of HAAA includes clinical manifestations, blood profiling, viral testing, immune functioning and bone marrow examination. Patients presenting the features of HAAA are mostly treated with HSCT from HLA matched donor. Immunosuppressive therapy has a minor efficacy, as far as it is currently demonstrated.

Table

Pts	Clinical onset	AST/ ALT (U/L)	GGT (U/L)	Parvovirus B19 DNA PCR on blood and bone marrow	Ig adm. and blood component transfusions	Anti-lymphocyte globulins and/or G-CSF Adm.	Allogeneic HSCT	Follow-up since diagnosis	Current clinical and haemat. outcome
Pt 1	Hecchymoses and petechiae at limbs, feet and face Asthenia	1284/ 2949	111	Positive	Yes	No	Yes	1 year	Good
Pt 2	Jaundice major epistaxis ecchymoses at limbs	540/ 780	94	Positive	Yes	No	Yes	5 months	Good
Pt 3	Jaundice	1357/ 2322	230	No	Yes	Yes	No	10 years	Good

Pt: Patient, Adm.: Administration, Ig: Immunoglobulines, Transpl: Transplantation, Haemat.: Haematological, HSCT: Haematopoietic Stem Cell Transplantation.

Reference(s)

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CO23
SYSTEMATIC REVIEW AND META-ANALYSIS OF THE ASSOCIATION CELIAC DISEASE–LIVER DISEASES IN THE PEDIATRIC AGE

G. Paolella[1], G. Giordano[2], C. Veropalumbo[3], S. Maddaluno[3], P. Vajro[1,4]. *[1]Chair of Pediatrics-School of Medicine, University of Salerno, Italy; [2]Department of Economics & Statistical Science, University of Salerno, Italy; [3]Department of Pediatrics, University of Naples "Federico II", Italy; [4]ELFID-European Laboratory for Food Induced Diseases, Naples, Italy*

Objectives and Study: Meta-analytical data of the reported association celiac disease (CD)–liver diseases are still unavailable in pediatrics. Therefore we performed a systematic review and meta-analysis to evaluate the prevalence of CD in children with either cryptogenic serum hypertransaminasemia (HTS) or autoimmune hepatitis (AIH), and vice-versa.

Methods: PUBMED was checked up to May 2012. Literature search included the following free terms: transaminases OR hypertransaminasemia OR cryptogenic hypertransaminasemia OR autoimmune hepatitis OR liver disease AND celiac disease OR gluten sensitive entheropathy AND children OR pediatric patients. Suitable case-control studies and case series of children (n = 58) with either CD and HTS or AIH were examined. Two reviewers (PV and GP) independently screened the abstracts and the full-text articles matching the inclusion criteria. Only diagnoses of CD obtained by duodenal biopsy and/or serological tests (AGA, EMA, t-TGAse) and exclusion of known causes of liver abnormalities other than CD were accepted. Pooled prevalences with 95% confidence intervals (CI), chi square (χ^2) and odds ratios were calculated.

Results: The nine qualified studies (ten series with 2046 patients) with appropriate methodology were chosen. Pooled prevalences of CD in children with cryptogenic HTS and vice versa were 12.0% (95% CI 4.17–29.96), (χ^2 26.91), and 36.0% (95% CI 32.15–40.11), (χ^2 494.95), respectively.

A gluten-free diet normalized serum transaminase levels in 77–100% of patients within 4–8 months. Pooled prevalences of CD in children with AIH and vice-versa were 6.3% (95% CI 3.87–11.73), (χ^2 36.43) and 1.4% (95% CI 0.84–2.15), (χ^2 619.34), respectively. The odds ratios of HTS in children with CD versus the general population, and of CD in children with HTS were 9.76 and 13.04, respectively. The corresponding odds ratios of AIH in children with CD ranged between 1368.746 and 80.502. The odds ratio of CD in children with autoimmune hepatitis was 6.44.

In Caprai's study, 2 autoimmune cholangitis and 2 AIH/cholangitis overlap syndrome were also reported.

Conclusions: Celiac disease frequently presents HTS in newly diagnosed children. In up to 1/3 of cases it refers to a gluten dependent mild non specific hepatitis, but a CD related autoimmune hepatopaty is observed only in a minority of cases. Celiac disease-related AIH may be overlooked in rare true serum-negative cases or in cases with still poorly investigated autoantibodies (e.g. anti Liver Cytosol 1 Antibodies).

CO24
AUTOIMMUNE HEPATITIS TYPE 2 (AIH2): LONG-TERM PROGNOSIS FROM CHILDHOOD TO ADULTHOOD

S. Nastasio[1], M. Sciveres[2], S. Ghione[1], F. Cirillo[2], S. Riva[2], G. Rossi[1], G. Maggiore[1,2]. *[1]Pediatric Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy; [2]Pediatric Hepatology and Pediatric Liver Transplantation, UPMC Ismett, Palermo, Italy*

Background and Aims: AIH2 is a recognized entity since 1986, identified by the presence of anti-liver-kidney microsome type 1 (aLKM1) and/or anti-liver cytosol type 1 (aLC1) autoantibodies, but the long-term prognosis is scarcely known. This study aimed to describe the presenting features and the long-term follow-up of a cohort of patients diagnosed in pediatric age.

Patients and Methods: Retrospective analysis of 21 patients (18 females; median age at diagnosis 6.3 yrs, range 1–16.1).

Results: Presenting features were: acute hepatitis (7), asymptomatic abnormal liver enzymes (13) and hepatosplenomegaly (1). Family history for autoimmune disorders was present in 9; 4 patients had a previously diagnosed autoimmune disorder and 1 patient was newly diagnosed with celiac disease. Median time from symptoms and/or abnormal laboratory findings to diagnosis was 2.5 mo (range 1–36). Clinical findings included jaundice (7), hepatomegaly (16) and splenomegaly (3). 5 had no clinical evidence of liver disease. Baseline laboratory features included (median; range): total bilirubin in the 7 patients with acute hepatitis (4.2 mg/dL; 1.3–6.4), AST (12 × N; 1.9–55), ALT (13 × N; 3.3–73), IgG (1760 mg/dl; 656–2970). Prothrombin activity was <60% in 5. aLKM1 were present in 20 (titers 1:160 to 1:1280) and aLC1 in 8 (isolated in 1). Liver biopsy performed at baseline in 20 patients showed moderate to severe

inflammatory activity and fibrosis. No biliary lesions were recorded. IAIH score was consistent in all with definite AIH.
All were administered immunosuppressive drugs: prednisone (PDN) and/or azathioprine (AZA) in 13, cyclosporin (CSA) in 7, CSA and AZA in 1. First remission was achieved in a median period of 8 weeks (range 2–16). 19 patients underwent a programmed discontinuation of therapy: 10 reducing the dosage and 9 safely shifting to a monotherapy (AZA [7], PDN [1], CSA [1]); 6 relapsed. At the end of follow-up (median 74 mo; range 4–264) all patients are alive with native liver; therapy was tentatively stopped in 3 after 252, 144 and 94 months: 2 relapsed within 11 months. 2 patients, aged 24 and 30, stopped therapy for 55 and 10 mo, respectively. 19 are still treated: 8 with 1 drug, 10 with 2 drugs and 1 with 3 drugs. Quality of life was considered good to excellent in all except 2. A young lady on AZA monotherapy gave birth to a normal baby girl. Severe adverse effects were recorded in 3 (short stature, vertebral collapse, cataracts, and severe obesity) and correlated to steroid treatment.
Conclusions: Diagnosis of AIH2 can be suggested by a family history of autoimmune disorder and by the concurrence of a specific autoimmune disease, and can be diagnosed even in absence of clinical evidence of liver disease. AIH2 promptly responds to immunosuppressive treatment, however, therapy must be prolonged in most patients for the long-term and can be definitively stopped in a few. Tailored treatment is associated with long-term survival with native liver and good quality of life.

CO25
EFFICACY OF THE COW MILK PROTEINS FREE DIET IN CHILDREN SUFFERING FROM ROLANDIC EPILEPSY

S. Lucarelli[1], T. Frediani[2], G. Lastrucci[1], G. Viscido[1], T. Federici[1], A. Spalice[3], D. Rossetti[1], S. Cucchiara[1]. *[1]Pediatric Gastroenterology and Liver Unit, Sapienza University of Rome, Italy; [2]Pediatric Allergology Unit, Sapienza University of Rome, Italy; [3]Pediatric Neurologic Unit, Sapienza University of Rome, Italy*

Background and Objective: Rolandic epilepsy is the best known and best described form of idiopathic epilepsy and unquestionably the one with the best prognosis. Given the partial nature of the fits as well as the low level of frequency and danger registered in the literature, it is preferred in most cases to limit the pharmacological treatment of this disorder. When such treatment does prove necessary, sodium valproate (VPA) or carbamazepine (CBZ) are nearly always used. Various references have been made in the literature over the last hundred years to the possibility that certain foods or allergens might bring about seizures in adult patients. It has nevertheless proved impossible to demonstrate a strict correlation between allergy and epilepsy, and most of the reports are anedoctal and open to any every aetiological hypothesis. One exception is the study carried out by Crayton with a double-blind provocative test on a single patient whose epileptic fits were both triggered and increased in frequency by food sensitivity. Interest in food allergy as a cause or aggravating factor of epilepsy was reawakened by Egger, whose studies on children suffering from migraine and/or hyperactive syndrome reported an improvement in the convulsive symptomatology subsequent to an oligoantigenic diet. It has been suggested that one of the mechanisms involved may be central hypoperfusion, a disorder common to both migraine and hyperactive syndrome. The aim of this study was to assess the efficacy of a cow milk (CM) proteins free diet in 56 children suffering from rolandic epilepsy.
Materials and Methods: All the patients underwent a diagnostic procedure to ascertain CM allergy by means of prick test and level of IgE specific for CM proteins, while total IgE were within the norm and specific IgE were present. A 1-month diet without CM led to the disappearance of the neurological symptoms as well as the EEG anomalies. The diagnosis of CM allergy was verified after 4 weeks of diet by means of orally administered double-blind placebo-controlled food challenge (DBPFC). 17/20 children underwent a seizure analogous to those previously experienced with reappearance of paroxysmal electroencephalographic anomalies. Non-allergic subjects (39/56) underwent a pharmacological treatment with sodium valproate or carbamazepine. The allergic subjects, positive to DBPFC (17/20 cases), were treated with a CM free diet.
Results: The CM free diet made it possible to obtain complete clinical and EEG remission in 17/20 (85%) cases of the allergic group versus 29/39 (74%) cases of non-allergic group.
Conclusion: The study suggests that while CBZ an VPA are effective drugs with comparatively few undesired effects, an allergen-free diet makes it possible to obtain complete clinical and electroencephalographic remission with no side effects as well as a behavioral improvement in cases where there is valid evidence of hypersensitivity.

CO26
^{1}H NMR-BASED METABOLOMICS ON HUMAN MATURE MILK REVEALS THE EFFECTS OF ORAL VSL#3 PROBIOTIC SUPPLEMENTATION TO MOTHERS

M.E. Baldassarre[1], A. Tomassini[2], P. Mastromarino[3], G. Capuani[2], M. Delfini[2], F. Urbano[1], N. Laforgia[1], A. Miccheli[2]. *[1]Department of Gynecology, Obstetrics and Neonatology, Section of Neonatology and NICU, University of Bari, Italy; [2]Department of Chemistry, Sapienza University of Rome, Italy; [3]Public Health and Infectious Diseases, Sapienza University of Rome, Italy*

Background: Perinatal manipulation of maternal gut microflora has been recently proposed as a possible dietary strategy to reduce the risk of disease in the infant. However, how a modulation of gut microbiota can affect the host physiology, the breast milk composition, and finally the infant physiology is still unclear.
We applied a metabolomics approach, based on ^{1}H NMR spectroscopy and multivariate analysis, to characterize the mature breast milk metabolome. Furthermore, we evaluated the possibility of identifying changes occurring in the breast milk composition as induced by oral supplementation with the probiotic VSL#3.
Materials and Methods: Pregnant women have been administered perinatally either oral VSL#3 or placebo. Breast milk was collected one month after delivery, extracted into polar and organic phases and analysed by ^{1}H NMR spectroscopy. The metabolic profiles were defined by applying statistical multivariate methods on the collected spectra. Immunological assays were performed on the same milk samples to determine the interleukin levels.
Results: ^{1}H NMR spectra allowed to classify the milk samples on the basis of Lewis epitopes.
VSL#3 supplementation to mothers induced a different milk metabolome characterized by a significant decrease in the levels of some fucosyl-oligosaccharides and citrate levels, and an increase in MUFA, phosphatidylglycerols, and succinate levels. Milks from probiotic supplemented mothers showed a significant increase in TGF-β and IL-10 levels compared to the placebo group.
Conclusions: ^{1}H-NMR-based global metabolic profiling is a powerful analytical approach to investigate the subtle changes on human milk induced by a dietary intervention may induce in human milk. Our results can have important implications give a good insight to understand how the modulation of mother gut microbiota may affects the breast milk composition, and thence the infant health.

CO27
HYPOVITAMINOSIS D AND NOCTURNAL HYPERTENSION IN OBESE CHILDREN: AN INTERESTING LINK

C. Banzato[1], C. Maffeis[1], E. Maines[1], P. Cavarzere[1], R. Gaudino[1], C. Fava[2], P. Minuz[2], A. Boner[1], F. Antoniazzi[1]. [1]*Department of Life and Reproduction Sciences, Section of Pediatrics, University of Verona, Verona, Italy;* [2]*Department of Medicine, University of Verona, Verona, Italy*

Context: Hypovitaminosis D is an independent risk factor for cardiovascular morbidity. In adults, low levels of vitamin D are associated with hypertension. The prevalence of hypertension is increasing in childhood especially in obese children.
Objective: The aim of this study was to evaluate the relationship between 24-hour blood pressure patterns and vitamin D levels in obese children.
Subjects and Methods: We recorded anthropometric parameters, took blood samples for 25-hydroxyvitamin D measurements and monitored ambulatory blood pressure (ABP) in 32 obese children (M/F: 21/11, age 7–16 years).
Results: Hypovitaminosis D was diagnosed in 84.4% of the study group children. Subjects in the lower tertiles had higher $HOMA_{IR}$, nighttime systolic and diastolic ABP, nighttime systolic and diastolic ABP load, 24-h ABP index and nighttime systolic and diastolic ABP index than those in the higher tertile. Vitamin D correlated negatively with 24-hour and nighttime systolic ABP, 24-h systolic ABP load, nighttime systolic and diastolic ABP load, 24-h systolic ABP index and nighttime systolic ABP index.
The percentage of subjects with pathological 24-h SBP load, nighttime SBP load, nighttime DBP load, nighttime SBP index and nighttime DBP index increased progressively as the vitamin deficiency categories increased (χ^2 10.26, $p < 0.05$; χ^2 16.34, $p < 0.01$; χ^2 10.23, $p < 0.05$; χ^2 10.38, $p < 0.01$; χ^2 10.06, $p < 0.01$).
Conclusions: Low levels of vitamin D in obese children were associated with a higher BP burden, especially at night. Prospective studies and vitamin D supplementation trials could confirm a cause-effect relationship between vitamin D and BP also in children/adolescents.

CO28
VSL#3 PROBIOTIC MATERNAL SUPPLEMENTATION AFFECTS BREAST MILK COMPOSITION AND NEWBORN FAECES MICROBIOTA

M.E. Baldassarre[1], F. Cacciotti[2], A. Miccheli[3], F. Urbano[1], N. Laforgia[1], P. Mastromarino[2]. [1]*Department of Gynecology, Obstetrics and Neonatology, Section of Neonatology and NICU, University of Bari, Italy;* [2]*Department of Public Health and Infectious Diseases and* [c]*Chemistry, Sapienza University of Rome, Italy*

Aim of study: Microbiological and immunological investigations were performed in order to evaluate the changes induced by VSL#3 probiotic maternal supplementation on breast milk and newborn faeces. Maternal milk was analyzed for factors known to modulate immunological characteristics and the developing microbiota within the gastrointestinal tract (probiotic bacteria, cytokines and immunoglobulins). The functional effects of maternal probiotic intervention on the newborn health were assessed evaluating stool composition in terms of lactobacilli and bifidobacteria contents.
Materials and Methods: This pilot double-blind, randomized, placebo-controlled clinical trial enrolled 35 healthy pregnant women four weeks before expected delivery. Participants received daily oral probiotic or placebo supplementation starting from the enrolment until four weeks after delivery. At 3 (T0) and 30 (T30) days after birth, infant stools and milk samples were collected.
Results: The amount of lactobacilli and bifidobacteria in breast milk of probiotic treated group was higher compared to controls. However due to the high individual variability of bacterial concentration, this increase did not result statistically significant. Noteworthy, the concentration of lactobacilli tended to be higher in the colostrum of the mothers in the probiotic group as compared with those on placebo ($p = 0.099$). At birth the amount of lactobacilli in faeces of neonates from VSL#3-supplemented mothers was significantly higher than in control group ($p < 0.05$). In these samples, the concentration of bifidobacteria tended to be higher as compared with those on placebo. No differences in the presence of VSL#3 *Lactobacillus* and *Bifidobacterium* species were observed between groups in both milk and faecal samples. TGF-β values were significantly higher in colostrum from probiotic group in comparison to the control group and increased significantly at T30 only in the probiotic group. IL10 levels were significantly higher in the mature milk from probiotic treated group and IgA levels were significantly higher in colostrum and mature milk from probiotic group.
Conclusions: Our microbiological results exclude a direct colonization of the VSL#3 probiotic strains in the mammary gland through a suggested migration from the intestine to the lactating mammary gland.
Cytokines evaluations suggest that VSL#3 could represent a good supplementation in the diet of pregnant women.

CO29
A COMPARISON OF TODDLERS MILK: ARE ALL THE SAME?

M. Sangermano[1], R. D'Aniello[1], G. Paolella[1], C. Veropalumbo[2], S. Maddaluno[2], P. Vajro[1,3]. [1]*Chair of Pediatrics, University of Salerno, Italy;* [2]*Department of Pediatrics, University of Naples "Federico II", Italy;* [3]*ELFID – European Laboratory for Food Induced Diseases, Naples, Italy*

Background and Aims: Breast milk is the most appropriate food during the first six months of life (WHO). When breastfeeding is not possible, one should consider suitably modified cow's milk formulas: type 1 (newborns up to 4–6 mos), type 2 (>4–6 mos), type 3 (or toddlers milk >12th mo). While for 1 and 2 formulas clear limitations on the concentration of each nutrient have been defined (ESPGHAN), for toddler milks there are still uncertainties, especially with regard to the protein content (Agostoni 2011). The aim of our study was therefore to assess the formulation of several (n = 6) toddlers milk formulas present on the Italian market, and revise the international literature.
Methods: We consulted the databases of PubMed, Google Scholar and Google using the keywords: infant, follow-on, toddler, milk, formula, nutrition. Qualitative and quantitative compositions related to proteins, carbohydrates, lipids, vitamins, minerals and fibers of 6 toddlers formulas and cow's milk were compared versus the nutritional needs in children after 1 year of life (Allen 2006).
Results: Overall, the toddlers formulas examined have comparable compositions, except for the levels of the protein content. We selected and analyzed 7 relevant studies. All suggested introducing cow's milk not before the 12th month of life. Several supplements taken into account by the literature (e.g. probiotics, enzymes, growth factors) are still under evaluation (Koletzko 2005), while others (e.g. poly-unsaturated long chain fatty acids, LC PUFA) are already widely accepted due to proven safety and benefits. Two studies were relevant to the possible link between excessive protein intake and epidemic of overweight/obesity. Both regard high-protein load during the first

year of life, while there are no data concerning high-protein formulas during the subsequent 12 months (Koletzko 2009). The randomized clinical trial CHOP (Socha 2011) shows that the intake of milk with high protein content in the 1st year of life, stimulates the GH-IGF-1 axis and, therefore, a weight gain. Subsequent monitoring up to 24 months, however, shows an obesogenic effect limited to this type of feeding given during the first 6 months of life.

Conclusions: Toddlers milks have compositions which are substantially equivalent. After 12 months of age and up to 3 years a toddler milk is preferable to standard cow's milk, as it presents qualitative and quantitative characteristics (vitamins, minerals, dietary fiber, ω3/ω6 ratios) potentially advantageous for bone growth, decreased risk of iron deficiency and prevention of cardiovascular disease. Their protein content, at times variable, does not seem to have clear obesogenic implications. Hitherto, obesogenic implications have been demonstrated only for type 1 and type 2 higher-protein formulas fed during the first six (-twelve) months of life and not later for toddlers milks.

CO30
LONG-TERM IMPACT OF FEEDING FORMULA ON INTESTINAL ADAPTATION OF INFANTILE SHORT BOWEL SYNDROME

F. Panetta[1], A. Diamanti[1], D. Elia[1], A. Tentolini[1], M. Candusso[1], P. Bagolan[1], M.S. Basso[1], M. Grisoni[1], R.E. Papa[1], G. Torre[1].
[1] "Bambino Gesù" Children's Hospital, Rome, Italy

Objectives: Short bowel syndrome (SBS) generally follows a resection of the small bowel (SB), that determines a malabsorption. Today the majority of neonates with SBS survives, and through the process of adaptation become independent from parenteral nutrition (PN). Intestinal adaptation refers to a process wherein the intestine undergoes various structural and functional alterations to compensate for loss of intestinal function because of injury or resection. Enteral nutrition (EN) plays an important role here: the intraluminal nutrients have a stimulatory effect on the epithelial cells and the production of trophic hormones. There is no consensus regarding the optimal feeding formula to improve the adaptation in SBS infants and the practice in individual centers depends more on personal experience than on research. The hypothesis of this study was that the formula feeding employed in the first six months of life, after a bowel resection, may influence the outcome of the bowel adaptation. Therefore our main objective was to compare the time required to wean off PN and to establish full enteral feeds, in SBS patients receiving hydrolyzed whey (HW), hydrolyzed casein (HC) and amino-acid based (AA) formulas, during the first six months of the life, after an extensive SB resection.

Materials and Methods: From 1984 to 2012, 86 SBS patients with extensive neonatal SB resection were followed at the Gastroenterology, Hepathology and Nutrition Unit of "Bambino Gesù" Children's Hospital in Rome. Seventy-two of them, for whom enough information was available, are described here. In our Institution, in the absence of breast milk, we have employed HW since 1984 to 1992; AA since 1993 to 1997; HW since 1998 to 2002 and HW and HC since 2003 up to now, based on their presence in our hospital. Therefore the employ of the three formulas (AA, HC and HW based formulas) has been blinded for the anatomical and the clinical conditions of the SBS patients.

Results: Four patients in our series died while they were on PN: two of them have been listed for SB and liver transplantation, and both died due to the worsening of the liver failure; the remaining two dead patients, both affected by liver disease, died for a severe CVC-related sepsis. We did not find any differences regarding the anatomic characteristics among the three groups. The PN duration in adapted and not adapted SBS patients was significantly reduced in patients HC feed, than in patients HW and AA feed. We did not find significant differences, in terms of PN duration, between the HW and AA group. The tendency of the weaning off PN was different among the three groups: after 12 month of observation indeed, 30% of the HC, 50% of the AA and 60% of the HW feed patients remained dependent on PN.

Conclusions: The results of our study suggest that the use of HC formula seems to improve the trend of bowel adaptation in infants with infantile short bowel syndrome.

CO31
GLUTEN SENSITIVITY IN CHILDREN: CLINICAL, SEROLOGICAL, GENETIC AND HISTOLOGICAL DESCRIPTION OF THE FIRST PAEDIATRIC SERIES

L. Mastrototaro[1], S. Castellaneta[2], A. Gentile[1], C. Fontana[1], E. Tandoi[3], S. Dellatte[3], V. Romagnoli[4], C. Catassi[4], R. Francavilla[1].
[1] Dipartimento Interdisciplinare di Medicina, Università di Bari, Italy; [2] Clinica Pediatrica, Ospedale San Paolo, Bari, Italy; [3] Mulini e Pastifici Tandoi, Bari, Italy; [4] Dipartimento di Pediatira, Clinica Pediatrica, Università di Ancona, Italy

Background and Aim: At present no data is available on the clinical/genetic/serologic presentation of Gluten Sensitivity (GS) in children although it might have been diagnosed as non-IgE-mediated adverse reactions to wheat; the aim of the present study is to describe the first paediatric series of children with GS and to compare it with celiac and healthy gluten-tolerant children trying to understand the similarities and differences between these two gluten-associated disorders.

Materials and Methods: The population of the present study is composed by 36 children: 12 (F: 4; mean age: 8.7±5.0) with GS diagnosed on the bases of a clear association between wheat consumption and appraisal of symptoms after ingestion which relapsed after the open gluten challenge who tested repeatedly negative for celiac disease serology and wheat allergy; 12 children (F: 8; mean age: 8.8±3.6) with active celiac disease (CD) diagnosed according to the ESPGHAN criteria and 12 control children (F: 6; mean age 8.6±2.8) enrolled from children followed in our out-patient clinic for functional disorders. The following tests were done performed: (a) CD serological panel including AGA-IgG and IgA, tTG-IgA, and -IgG and EmA-IgA; (b) hematological parameters including Hb, serum iron, ferritin, GOT, ESR, HLA and small intestinal biopsy.

Results: Clinical presentation of GS: abdominal pain was the most complained symptom (83%), followed by chronic diarrhoea (66%), tiredness (42%), bloating, vomiting, headache (25%), failure to thrive and limb pain (17%). The most common presentation was a combination of abdominal pain and chronic diarrhoea (50%). Females with GS were older than males ($p < 0.03$). AGA-IgG positivity was the most frequent antibody found in GS children (50%) as compared to CD (67%) and controls (8%). AGA-IgA and TTG-IgG were found in only one GS child as compared to 7 in CD patients ($p < 0.002$). No difference was found in the determination of nutritional, biochemical and inflammatory markers between GD and controls. Children with CD had significantly lower level of ferritin and higher levels of liver enzymes. HLA typing showed the presence of DQ2 in all celiac and in 5 of GS children (42%). Histology revealed a normal to mildly inflamed mucosa (Marsh 0–1) in GS patients, while all CD patients showed subtotal/total villous atrophy..

Conclusion: The present study represents the first attempt to describe a series of pediatric cases of gluten sensitivity that support the

existence of this condition in children across all ages with clinical, serological, genetic and histological features similar to those reported in adults although in children the classical gastrointestinal symptoms are more frequent.

CO32
TUMOR NECROSIS FACTOR ALPHA (TNFa) PROMOTER HAPLOTYPE CONCURS WITH HLA-DQA1–DQB1 IN DETERMINING COELIAC DISEASE (CD) RISK

G. Guariso[1], E. Rossi[2], C.F. Zambon[2], F. Navaglia[2], E. Greco[2], D. Bozzato[2], M. Pelloso[2], A. Padoan[2], A. Aita[2], M. Gasparetto[1], P. Fogar[2], M. Pescarin[1], S. Moz[2], M. Cananzi[1], A. Tessari[2], E. Gnatta[2], D. Basso[2], M. Plebani[2]. *[1]Departments of Paediatrics, Unit of Gastroenterology, Digestive Endoscopy, [2]Department of Laboratory Medicine, University of Padova, Italy*

Background: The rare A alleles at −308 and −238 positions of the TNFa gene have been associated with CD. Although they may be candidate disease susceptibility factors, it is likely that they act as part of TNFa haplotypes resulting from the combination of more SNPs of the promoter.

Aim: To ascertain whether five SNPs in the TNFa promoter (−1031T>C, −857C>T, −376G>A, −308G>A, −238G>A) are associated singly or as haplotypes with CD and whether their effect is HLA-DQA1/-DQB1 dependent or independent.

Methods and Results: 527 children (250 CD, 277 controls) were studied. TNFa gene polymorphisms and HLA-DQA1 and -DQB1 alleles were analysed by RT-PCR. The TNFa-1031C (OR = 2.540, 95% CI: 1.157–5.575), −857T (OR = 0.421, 95% CI: 0.282–0.627), −376A (OR = 2.037, 95% CI: 1.109–3.741) and −308A (OR = 4.486, 95% CI: 3.076–6.541), but not −238 alleles, were significantly CD-associated, this finding being confirmed by a multivariate logistic regression analysis. The possible haplotypes derived from the combination of these four SNPs were estimated using the Arlequin statistical software. Six haplotypes were obtained: two (CCGG, TTGG) were more frequent in controls; three (CCAG, TCGA, CCGA) were more frequent in CD; one (TCGG) was equally found in controls and CD. TNFa promoter genotypes inferred from haplotypes were classified in six categories: (1) CD-associated/CD-associated; (2) CD-associated/TCGG; (3) CD-associated/control-associated; (4) control-associated/TCGG; (5) TCGG/TTG; (6) control associated/control-associated. A strong correlation was found between the first two categories and CD and between the last category and controls not only considering all cases, but also considering only those bearing HLA-DQA1/-DQB1 risk alleles. Binary logistic regression analysis performed by including among predictors TNFa promoter genotypes and HLA-DQ haplotype, documented a strong association between CD and homozygous HLA-DQ2 (OR = 481; 95%CI: 112–2068), heterozygous HLA-DQ2 (OR = 73; 95%CI: 26–208) or HLA-DQ8 (OR = 14; 95%CI: 5–45), but also an HLA-independent correlation with CD-associated TNFa promoter homozygous (OR = 7; 95% CI: 1.48–34.31) or heterozygous (OR = 5; 95%CI: 1.56–16.59) genotypes.

Conclusion: TNFa promoter haplotypes CCAG, TCGA and CCGA was shown to increase CD risk independently from HLA-DQ alleles suggesting the pivotal role of TNFa in the disease pathogenesis.

CO33
BOTH GLIADIN PEPTIDE P31–43 AND TOLL-LIKE RECEPTOR 7 LIGAND, LOXORIBINE, ARE ABLE TO INDUCE IFN-ALPHA PATHWAY, INCREASING MXA EXPRESSION

M. Sarno[1], M. Nanayakkara[1], G. Lania[1], M. Maglio[1], A. Gaito[1], K. Ferrara[1], M. Cuomo[1], D. Ponticelli[1], R. Aitoro[1], V. Discepolo[1,2], B. Jabri[2], R. Troncone[1], S. Auricchio[1], M.V. Barone[1]. *[1]Department of Pediatrics and ELFID, University of Naples Federico II, Naples, Italy; [2]Department of Medicine, Pathology and Pediatrics, University of Chicago, Chicago, IL, USA*

Objectives: Mucosal damage in Celiac Disease (CD), is the result of an intestinal stress/innate immune response to certain gliadin peptides (e.g., A-gliadin P31–43) in association with an adaptive immune response to other gliadin peptides (e.g., A-gliadin P57–68). P31–43 can alter trafficking of endocytic vesicles through interference with localization of HRS (Hepatocyte growth factor Regulated tyrosine kinase Substrate), a regulator of endocytic maturation and trafficking. Gliadin peptides (e.g. P31–43) can induce epithelial innate immune response interacting with epithelial cells and altering vesicular trafficking, similarly to viral ligands. In this paper we test the hypothesis that P31–43 and a viral ligand can act on partially overlapping pathways, to induce and/or sustain innate immune response in the intestinal epithelial cells.

Materials and Methods: We studied MXA, IFN-alpha effector during viral infections, by western blot (WB) both in CaCo2 cells stimulated with P31–43 (100 micrograms/ml) and Loxoribine (Lox, 1 mM), a ligand for Toll-like receptor 7 that mimic viral response, and in biopsies from CD patients in the active phase of the disease and controls treated with P31–43. Sub-cellular localization of MXA was studied by immunofluorescence.

Results: MXA protein is increased in CaCo2 cells treated for 24 h with P31–43 (3 times) and Lox (7 times). Limiting concentrations of P31–43 (20 migrograms/ml) and Lox (0.25 mM) have reduced effect when used singularly, but together can increase 7 times MXA expression, showing a sinergic effect. Lox and P31–43 induce the same sub-cellular spots-like MXA distribution, and MXA shows co-localization with actin cytoskeleton. In biopsies from CD patients, MXA is increased in the active phase of the disease respect to controls. When they are cultivated with P31–43 for 24 h they show increase of MXA protein (3–5 times), no effects in controls.

Conclusions: In intestinal epithelial cells and CD biopsies, gliadin peptide P31–43 is sensed in the same way as a viral ligand. This together with sinergic effects of Lox and P31–43 indicates that gliadin and viral infections act on overlapping pathways, to induce innate immune response.

CO34
INTESTINAL ANTI-TISSUE TRANSGLUTAMINASE2 IN POTENTIAL CELIAC DISEASE

D. Ponticelli[1], A. Tosco[1,2], R. Aitoro[1], E. Miele[1], R. Auricchio[1,2], R. Troncone[1,2], M. Maglio[2]. *[1]Department of Pediatrics University Federico II, Naples, Italy; [2]European Laboratory for the Investigation of Food Induced Diseases (ELFID), University Federico II, Naples, Italy*

Objectives: Anti-tissue transglutaminase2 (anti-TG2) antibodies are present in the serum of the great majority of untreated celiac (CD) patients. They are produced in the small intestinal mucosa and deposited here. Potential CD patients present serum positivity for anti-TG2 antibodies, but a normal duodenal mucosa where sometimes mucosal deposits of anti-TG2 are not detectable. Aim of our work was to investigate the production of anti-TG2 intestinal antibodies in

patients with potential CD, and to identify the most suitable test. For this purpose we compared two assays: the search of intestinal deposits of IgA anti-TG2 and the measurement of the same antibodies in the supernatants after organ culture of duodenal biopsies.

Material and Methods: Twelve active CD patients, 28 potential CD patients and 30 non-CD controls were enrolled. Biopsy fragments from all patients were analyzed by double immunofluorescence to detect mucosal deposits of anti-TG2 antibodies. Fragments from the same subjects were also cultured for 24 h with medium in presence or absence of gliadin peptides. Anti-TG2 autoantibodies secreted into supernatants were measured by ELISA.

Results: All active CD, 19/28 (68%) of potential CD patients and 6/30 (20%) of non-CD controls showed mucosal deposits of IgA anti-TG2; at the same time 12/12 (100%), 27/28 (96.4)% and 3/30 (10%) of active CD, potential CD and non-CD control patients, respectively, secreted these antibodies to culture supernatants. In active CD very high titers (>100 U/ml) of anti-TG2 into culture supernatants were secreted unlike potential CD with secreted variable titers of the same antibodies (range 9.45–100 U/ml). Supernatants anti-TG2 titers correlated with serum anti-TG2 titers (Pearson's $r = 0.8$ $p < 0.0001$). After culture with gliadin peptides, active CD and non-controls patients did not show increase of both mucosal deposits and secreted anti-TG2 IgA. Moreover, the number of potential patients with intestinal deposits before culture was reduced after culture with medium alone, 15/20 vs 12/20, when we compared the presence of mucosal deposits in medium vs P3143/PTG cultured fragments we observed significant increase of it [12/20 (60%) vs 18/20 (90%) $p = 0.02$].

Conclusion: Our data showed that to detect intestinal anti-TG2 antibodies, the measurement of antibodies secreted into culture supernatants seems to have a higher sensitivity and specificity (97.5% and 92.3% respectively) than the detection of mucosal deposits (77% and 80% respectively). This test may prove useful in clinical practice to predict evolution to mucosal atrophy in potential celiac patients and to identify patients with gluten sensitivity.

CO35
SPONTANEOUS NORMALIZATION OF ANTI-TISSUE TRANSGLUTAMINASE ANTIBODY LEVELS IS COMMON IN CHILDREN WITH TYPE 1 DIABETES MELLITUS: A TEN YEARS EXPERIENCE

S. Castellaneta[1], E. Piccinno[2], E. Frezza[2], M. Oliva[3], C. Fontana[3], F. Indrio[3], T. Capriari[3], L. Cavallo[3], R. Francavilla[3]. *[1]Clinica Pediatrica, Ospedale San Paolo, Bari, Italy; [2]Endocrinologia Pediatrica, Giovanni XXIII, Bari, Italy; [3]Dipartimento Interdisciplinare di Medicina, Università di Bari, Italy*

Background and Aim: This study was prompted by the observation that elevated levels of anti-TTG antibody in children with T1DM may spontaneously normalize, despite continued consumption of gluten. The objectives of this study were: to investigate the prevalence and extent of spontaneous normalization of TTG-IgA antibody levels in patients with T1DM and to characterize this population and identify possible factors predictive of seronegativization of celiac serology.

Materials and Methods: All 419 children with T1DM children diagnosed from 2002 and 2011 prospectively screened for CD were enrolled. Out of these, 361 (86%) were persistently negative for CD serology (T1DM), 31 (7.4%) and were diagnosed with CD (T1DM-CD) and 27 (6.5%) had spontaneous decline/negativity of CD serology (T1DM-CDneg). Demographic, clinical, genetic and serological data prospectively recorded and analysed to identify possible factors predictive for celiac serology negativization.

Results: The mean time of follow-up was similar in the three groups (5.7 ± 2.8 vs. 5.3 ± 2.6 vs. 5.5 ± 3; p = NS). Females were more represented in the T1DM-CD as compered to T1DM group ($p < 0.03$). No differences were found for mode of delivery, duration of breast-feeding (2, 4 or 6 months), history of infections in the first year. Overall, the prevalence of celiac serology negativization in children with T1DM is 5.7% (95%CI: 3.2–7.5). The age at first anti-TTGA positivity was significantly lower in T1DM-CD as compared to T1DM-CDneg (5.5 ± 3.7 vs. 8.6 ± 3.6; $p < 0.006$) while no difference was found for age at diabetic onset (5.6 ± 3.4 vs. 6.3 ± 3.7; p = NS). Serum anti-TTG-IgA antibody levels were significantly higher in T1DM-CD as compared to T1DM-CDneg children at the time of first TTG-A positivity ($p < 0.0001$). In all T1DM-CDneg children, anti-TTG-IgA titre showed a progressive reduction and normalized in 15 (26%) while 3 (5%) became subsequently positive. The median time to normalization of for anti-TTG antibody was 1.3 ± 1.1 years (95%CI: 0.8–1.8 years).

Conclusion: Our study in a large cohort of children with T1DM shows that children with T1DM have fluctuations in serum anti-TTG antibody levels and that the titre of serological tests spontaneously decrease/normalize in 45% of the cases and became persistently negative in at least 20% while on a gluten-containing diet. This finding suggests that in diabetic children it may be possible a state of temporary positivity of celiac serology and therefore in absence of clinical symptoms or sign of CD, the histological confirmation of the disease and the gluten free diet should be postponed to avoid unnecessary procedures and further dietetic limitations.

CO36
INTESTINAL IgA ANTI-TISSUE TRANSGLUTAMINASE DEPOSITS IN PEDIATRIC CELIAC DISEASE

V. Romagnoli[1], S. Gatti[1], M. Rossi[1], C. Giorgetti[1], V. Albano[1], A. Mandolesi[2], C. Catassi[1]. *[1]Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy; [2]Department of Pathology, Università Politecnica delle Marche, Ancona, Italy*

Background: In patients presenting with an early-stage CD with a low-grade enteropathy or a morphologically normal mucosa, more sensitive, specific and supportive diagnostic aids are needed for a proper diagnosis of CD.

Aim: To establish the diagnostic value of intestinal deposits of anti-TG2 IgA for celiac disease in a paediatric cohort, to assess the degree of concordance with serum anti-TG2 and eventually to provide a pattern and staining intensity classification of anti-TG2 IgA mucosal deposits.

Materials and Methods: Sixty children who underwent small intestinal biopsy for suspected CD were prospectively recruited in this study from June 2010 to June 2012 at the Department of Pediatrics, Università Politecnica delle Marche. Control group consisted of twenty children with other gastrointestinal disease. At the time of intestinal biopsy, serum samples from all patients were collected to evaluate serum levels of anti-tissue transglutaminase IgA antibodies (values $\geqslant 10$ U/ml were considered positive). From all patients five duodenal fragments were obtained by upper endoscopy, four of which were fixed in formalin and processed for histological and morphometric analysis. The last one was frozen and stored in liquid nitrogen and investigated for the presence of intestinal deposits of anti-TG2 IgA antibodies using double immunofluorescence. The evaluation of anti-TG2 IgA mucosal deposits was performed by studying the pattern and the intensity of the staining.

Results: Results are currently available for thirty-five patients. Mean age (±SD) at diagnosis was 7.8 ± 3.9 years, M/F ratio was 1.1/5 and mean length of disease was 926.6 days (±1062.9, median 376.0).

Serum anti-TG2 IgA resulted positive in 82.9% of subjects, 45.7% with high titres (>10 times ULN) and 37.2% with low titres, while 11.4% were negative and 5.7% presented serum IgA deficiency. Double immunofluorescence showed specific anti-TG2 IgA deposits, appearing as a yellow-orange staining due to the colocalization of IgA with TG2, in all 35 samples. Normal villous morphology (Marsh 0–1) was noted in nine patients, and among these five subjects were positive for serum anti-TG2 IgA and four presented normal levels of serum anti-TG2, one of which associated with IgA deficiency. The other 3 patients with normal levels of serum anti-TG2 were: one anti-TG2, anti-endomisium and anti-gliadin negative patient with dyspepsia and recurrent oral aphtous lesions, one patient with a previous anti TG-2 positivity subsequently not confirmed and the last one was an 8-year-old child with isolated positivity of anti-gliadin IgA. We observed that all children with potential CD showed mucosal deposits characterized by localization around mucosal vessels and basement membrane.

Conclusions: These preliminary results evidenced the high diagnostic sensitivity of mucosal anti TG2 IgA deposits in pediatric CD. This tool seems to be much more useful in patients with so called potential CD, since it could be considered an early marker of mucosal involvement in presence of normal villous morphology. It is interesting that anti-TG2 deposits have been detected even in low or negative serum anti TG2 IgA titres, as well as in patients with IgA deficiency. However these preliminary data await confirmation from further prospective studies and the sensitivity of the test needs to be evaluated in a larger control group.

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Posters

PO1
TWO CASES OF ATYPIC PANCREATITIS TREATED WITH IMMUNOSUPPRESSIVE THERAPY

M. Cinquetti[1], C. Voltolina[1], E. Battisti[1], A. Grezzani[1], Y. Suzuki[1], F. Fornasa[2]. *[1]Pediatric department, G. Fracastoro Hospital, ULSS 20, Verona, Italy; [2]Radiologic department, G. Fracastoro Hospital, ULSS 20, Verona, Italy*

We report the case of two Indian girls (16 and 14 years old) from the same ethnic group, who referred with fever, abdominal pain and elevation of serum levels of both lipase (534 and 1834 U/L) and amylase (350 and 653 U/L, two thirds of which of pancreatic origin). In one girl vomiting and sialorrhea, in the other cervical lymphoadenopathy concurred.

Serological tests for both bacteria and viruses, indexes of inflammation and of autoimmune disease were negative in both girls. Except for a transient enlargement of the pancreatic head observed in one girl, both ultrasound and MR examinations of the pancreas were normal. However, on the hypothesis of acute pancreatitis, fasting, parenteral nutrition and omeprazole were administered.

General conditions impaired in both girls, with persisting fever in one girl, and onset of neurological symptoms in the other case, in which at brain MR examination, edema of the cortical sulci was observed.

Ig serum were administered without resolution of the symptoms. High dose corticosteroid therapy (methylprednisolone) was therefore intravenously administered, achieving a quick improvement of both abdominal and neurological symptoms and normalization of serum lipase ad amylase levels.

Therefore, we hypothesized autoimmune pancreatitis (associated in one case with neurological signs) without significant anatomical alterations of the pancreas and without serologic markers of autoimmune disease.

PO2
INFLAMMATORY BOWEL DISEASE ASSOCIATED WITH INFLAMMATORY CHOLANGITIS HAD A DISTINCT PHENOTYPE IN CHILDREN

S. Ghione[1], S. Riva[2], F. Cirillo[2], G. Palla[1], M. Segreto[1], M. Sciveres[2], G. Maggiore[1,2]. *[1]Pediatric Division University of Pisa, Pediatric Gastroenterology and Hepatology Unit, University Hospital Santa Chiara, Pisa and [2]Pediatric Hepatology and Liver Transplantation, ISMETT, University of Pittsburgh Medical Center Italy, Palermo, Italy*

Background and Aims: An inflammatory bowel disease (IBD) mostly with the features of chronic ulcerative cholitis (CUC) is frequently associated in patients with immune mediated inflammatory bile duct disease. The existence of a specific phenotype of the IBD associated to immune mediated biliary disorders (Biliary-IBD; B-IBD) is strongly suggested in adults.

The purpose of this study was to describe the features of the IBD associated in a group of patients followed at Pediatric Clinic of University of Pisa (PCUP) and at Pediatric Hepatology, ISMETT, Palermo, and to compare the characteristic of this group of patients with a group of pediatric patients with CUC without evidence of liver disease followed at Pediatric Clinic of University of Pisa.

Patients and Methods: Medical records of 27 patients (mean age 16.9; 5–29 yrs) with a B-IBD (IBD confirmed endoscopically and histologically and inflammatory biliary disease diagnosed on histologic and imaging criteria) with at least a follow-up period of 5 years were reviewed. The control group consisted of 20 CUC patients without clinical, biochemical and imaging evidence of liver disease, evaluated at the PCUP from 1998.

Results: According to the sex distribution there were no differences between case group B-IBD and control CUC. Among the 27 patients with B-IBD: all of them (100%) had liver biopsy characteristic of sclerosing cholangitis (SC); on imaging all patient, except for 4, (85%) showed typical cholangiographic features of SC. After a mean period of 5 years 2 of them repeated a cholangioRMN and showed bile ducts alteration. In 12/27 patients (45%) we found characteristics of overlap syndrome (evidence of autoimmunity and histologic features of interface hepatitis).

Patients with B-IBD were younger, although not statistically significant, at the time of diagnosis of IBD compared to the control CUC group (9.1 yr, vs 11.6 yr, ns). Of 27 patients with B-IBD, 17 (63%) were diagnosed as CUC and 10 (37%) as indeterminate colitis (IC); none was diagnosed as Crohn's disease. Prevalence of pancolitis, ileitis and endoscopical (but not istological) rectal sparing was higher, although not significantly, in B-IBD patients compared to control group (74% vs 60%, 30% vs 0% and 50% vs 33% ns). Concerning the severity of IBD, based on the number of symptoms and endoscopic disease activity, patients with B-IBD had milder clinical course (<1 symptom and normal/loss of vascular pattern/erythematous mucosa) compared with the control group (37% vs 20% patients with degree 1 of the disease).

Conclusions: A mild-asymptomatic pancolitis with rectal sparing and many times with ileitis is the most common IBD profile in pediatric patients with B-IBD patients suggesting the existence of a specific IBD phenotype in pediatris patients as suggested in adults.

PO3
OUTCOME OF BILIARY ATRESIA AFTER KASAI PORTOENTEROSTOMY AT A SINGLE ITALIAN CENTER (UNIVERSITY OF PADOVA, 1990–2011)

M. Cananzi[1], P. Betalli[2], M. Gasparetto[1], E. La Pergola[2], P.G. Gamba[2], F. Zanon[2], U. Cillo[3], L. Zancan[1], G. Guariso[1].
[1]Department of Paediatrics, Unit of Gastroenterology, Digestive Endoscopy, Hepatology, and Care of the Child with Liver Transplantation, University Hospital of Padova, Italy; [2]Pediatric Surgery, University of Padova, Italy; [3]Department of Surgical Oncological and Gastroenterological Sciences, DiSCOG, Hepatobiliary and Liver Transplant Unit, University Hospital of Padova, Italy

Background: Biliary Atresia (BA) is worldwide the leading cause of end-stage liver disease in children and the most common indication for pediatric liver transplantation (LT). National studies from several European, Asiatic and North American countries report a 48% median success rate (range 30–61%) of Kasai Portoenterostomy (KPE) and a median survival with native liver (SNL) of 37.9% (range 31–53) at 10 years after KPE. Young age at diagnosis (<45 days) and center experience (>5 cases/year) are the main prognostic factors associated to KPE success. No published data are available concerning BA epidemiology and outcome in Italy.
Objective: The aim of this study is to describe the outcome of children with BA treated at a single University Center of Pediatric Hepatology and LT in Italy.
Methods: Health records of all cases of BA diagnosed at the Department of Pediatrics of the University of Padova between January 1990 and December 2011 were retrospectively reviewed.
Results: A total of 52 children were diagnosed with BA during the study period (mean 2.5/year) of which 20 in the last 5 years (mean 4/year). 51 patients underwent KPE at a median age of 66 days (range 19–115); a significant difference ($p < 0.001$, unpaired t test) was observed concerning the mean age at KPE between children diagnosed during the 1990s (mean 49±5 days) and after 2000 (mean 72±3 days). Median age at last follow up was 5.6 years (0.7–22 years). KPE success (i.e. total bilirubin <20 umol/L at 6 months after KPE) was 31%. Among patients with unsuccessful KPE (n = 34): 64% underwent LT at a median age of 1.8 years (main indications consisted in end-stage liver disease, hepato-pulmonary syndrome/HPS, hepatocellular carcinoma); 8% died on the waiting list for transplant at a median age of 10 months (all due to uncontrolled variceal bleeding); 14.7% have compensated cirrhosis and are still on follow up; one patient is on the waiting list for liver transplantation and one was lost at follow up. Among children with successful KPE (n = 15): 4 have no clinical or biochemical signs of liver disease; 4 have signs of portal hypertension; 4 show signs of compensated chronic liver disease; 1 was transplanted for HPS at 9.5 years of age; 1 died for reasons unrelated to BA; one was lost at follow up. Data of two patients were untraceable. Overall the rate of NLS at 10 years after KPE was 38%.
Conclusions: Despite advanced age at KPE and relatively low numbers of new cases per year, both the success rate of KPE and the 10 years SNL after this intervention are comparable with current international standards. As demonstrated in other countries, centralization of surgical care and the launch of a screening program to anticipate age at referral have the potential to further improve the outcome of children after KPE. The time to begin an Italian National Program for the management of BA has definitely come.

PO4
EPSTEIN–BARR VIRUS INFECTION IN A PATIENT WITH ULCERATIVE COLITIS

M.T. Illiceto[1], M. Filippone[1], G. Lisi[2], C. D'Amario[3], G. Lombardi[1].
[1]Unit of Pediatric Gastroenterology and Digestive Endoscopy, Department of Pediatrics, Pescara, Italy; [2]Unit of Pediatric Surgery, University "G. D'Annunzio" of Chieti, Pescara, Italy; [3]Unit of Pathology, Hospital of Atri (TE), Italy

Background and Objectives: The Inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the gastro-intestinal tract and by an immunosuppressive status, directly related to the disease, but also secondary to immunosuppressive therapies which are often subject patients. Epstein–Barr virus (EBV) infection is associated with increased disease severity in therapeutically immunosuppressed IBD patients. The role of EBV infection in patients with IBD who are unresponsive to medical therapy is unclear. We report a case of a child with steroid-dependent ulcerative colitis who developed EBV infection associated with acute exacerbation of intestinal disease.
Material and Methods: M, female 6 years old, had an onset of ulcerative colitis (UC) with severe pancolitis. We induced remission with steroids and mesalazine, and after 1 month we started immunosuppressive therapy with azathioprine. Reducing the steroid, we observed recurrent moderate-severe relapses of UC, despite the increased dosage of azathioprine (2.5 mg/kg). Was configured a state of steroid-dependent and azathioprine resistance UC. So, we decided to start the biological therapy with anti-TNF (infliximab), and to submit the child to the various investigations of screening, before the infusion. EBV-DNA copy numbers were measured by real-time PCR in peripheral blood mononuclear cells, showing a high copy number. Clinical, endoscopic and blood-test follow-up, showed that the reactivation of EBV-infection corresponded to a worsening of colonic inflammation and to an increased use of steroids. Based on the known relationship between EBV infection, immunosuppression and carcinogenesis, we have discontinued azathioprine, and we have not considered appropriate to start additional immunosuppressive therapy with infliximab. We were faced with a dilemma: given an antiviral drug (with the hope that it was the EBV infection to cause a relapse of intestinal disease) or increase the dose of steroid and possibly make use of cyclosporine as a drug-bridge to surgery. We have opted for the anti-viral strategy.
Results: Administering the antiviral drug, it was possible to manage UC with progressively lower doses of steroid, associated with oral and topical mesalazine. We are seeing a gradual reduction in the number of copies of replicating EBV. The perspective for this child is to start therapy with infliximab, as soon we reach the negativity of PCR EBV-DNA. Of course, the monitoring during biological therapy should be continued and careful, with periodic assessment of the absence of viral replication prior to infusion.
Conclusions: EBV replication in IBD patients is often associated with severe disease and mucosal inflammation. The immunomodulatory effects of EBV could delay the resolution of the IBD associated inflammation, thus contributing to disease progression. As in other cases described in the literature, the outcome in our patient indicate that anti-viral therapeutic strategy may be useful for the resolution of IBD.

PO5
GIARDIASIS IN SUSPECTED CELIAC DISEASE

M.T. Illiceto[1], M. Filippone[1], G. Lisi[2], C. D'Amario[3], G. Lombardi[1]. *[1]Unit of Pediatric Gastroenterology and Digestive Endoscopy, Department of Pediatrics, Pescara, Italy; [2]Unit of Pediatric Surgery, University "G. D'Annunzio" of Chieti, Pescara, Italy; [3]Unit of Pathology, Hospital of Atri (TE), Italy*

Background and Objectives: Celiac disease (CD) is an immune-mediated enteropathy induced by gluten ingestion in a genetically susceptible patient. *Giardia lamblia* is the most common human parasite with a worldwide distribution and fecal-oral way of transmission. *Giardia lamblia* has a cosmopolitan distribution. Infected children may have acute or chronic diarrhea, crampy abdominal pain, anorexia, malasorption and poor weight gain and may be misdiagnosed as celiac disease. Diagnosis is usually made by finding the characteristic cysts in stool specimens or by duodenal aspiration. In most cases histology reveals a dense accumulation of the parasites on the surface of the duodenal mucosa with no or only slight inflammation. In rare cases, a dense inflammatory infiltrate with severe mucosal atrophy and increased count of intraepithelial lymphocytes may be seen. If in such cases the amount of parasites is low, the histological picture may mimic celiac disease. We report the case of a child 2 years old who presented poor growth, recurrent aphtous stomatitis, abdominal pain and recurrent diarrhea. No family history of CD.
Material and Methods: In suspected CD, were assayed the IgA anti-endomysium antibodies (EmA-IgA) that resulted doubt and the IgA anti-tissue transglutaminase antibodies (TgA-IgA) that were found weakly positive (17.50 UA; normal value <9 UA; borderline 9–16 UA; positive >16 UA). He was referred to our hospital for further diagnostic. We performed the search for genetic susceptibility of CD; the antibodies assay was repeated after 3 months. These investigations documented the presence of HLA-DQ2, positivity of EmA-IgA and an increase value of TgA-IgA (20.70 UA). In the meantime symptoms worsened, so we proceeded performing the esophagogastroduodenoscopy and duodenal biopsies. The macroscopic appearance of duodenal mucosa was of villous atrophy, but microscopic examination showed a parasitic duodenitis, with the presence of microorganisms like *Giardia lamblia*. Then was started medical therapy with metronidazole per os for 10 days, and the child continued to eat gluten.
Results: Abdominal pain and diarrhea disappeared gradually but rapidly; the parasitological examination was negative on 3 consecutive samples (at 3 weeks after eradication therapy); EmA-IgA and TgA-IgA were negative at 1 month after eradication. The follow up to 1 year had confirmed that the increase in IgA was secondary to giardiasis, and that the symptoms were due to the histological damage of the parasite.
Conclusions: When investigating a patient with suspected celiac disease (CD), several other conditions must be considered, including potential infection with *Giardia lamblia*. In doubtful cases like our patient, are of fundamental support an accurate assessment and appropriate follow up.

PO6
LYMPHOCYTIC COLITIS IN A YOUNG GIRL

M.T. Illiceto[1], M. Filippone[1], G. Lisi[2], C. D'Amario[3], G. Lombardi[1]. *[1]Unit of Pediatric Gastroenterology and Digestive Endoscopy, Department of Pediatrics, Pescara, Italy; [2]Unit of Pediatric Surgery, University "G. D'Annunzio" of Chieti, Pescara, Italy; [3]Unit of Pathology, Hospital of Atri (TE), Italy*

Background and Objectives: Microscopic colitis (M.C.) includes lymphocytic colitis and collagenous colitis. The entity of M.C. is considered an important cause for unknow chronic diarrhea, is a well established clinicopathological diagnosis (triad of watery diarrhea, normal results on endoscopy and characteristic microscopic findings) and is being diagnosed with increasing frequency. M.C. is mainly a condition of the elderly, rare in children, and pediatric data are scarce. The etiology of MC remains enigmatic and is multifactorial with different elements being more influential in different individuals.
Material and Methods: We describe the case of B.B., a girl 13 years old, with a history of allergy to grass and familial hypercholesterolemia, that came to our attention for the appearance for several months of abdominal pain (on one occasion so violent as to cause fainting), diarrhea, weight loss, anorexia and progressive weakness. The girl was subjected to blood tests, ultrasound of the abdomen, esophagogastroduodenoscopy and colonoscopy.
Results: Blood test showed: normality of the indices of inflammation and intestinal absorption, sensitization to some food allergens (wheat, tomato and apple), negativity of the anti-saccaromyces cerevisiae antibodies (ASCA), the anti-neutrophil cytoplasmic antibodies (ANCA), the IgA anti-tissue transglutaminase antibodies (TgA-IgA) and the IgA anti-endomysium antibodies (EmA-IgA). The finding of endoscopic hyperemic proctosigmoiditis and duodenitis, and colonic lymphoid nodular hyperplasia, led us to perform multiple biopsies. The histopathological evidence of chronic atrophic gastritis, and immunomorphological findings compatible with a diagnosis of lymphocytic colitis, in the context of the clinical and instrumental findings, have allowed a diagnosis. Considering therapies indicated for pediatric lymphocytic colitis, as first step therapy the patient was started on oral mesalazine. To follow up there was the gradual disappearance of diarrhea and remission of abdominal pain and asthenia, with return of appetite and ponderal increase.
Conclusions: M.C. has a symptomatyc overlap with irritable bowel syndrome, inflammatory bowel disease and functional diarrhea. It is reasonable to obtain multiple biopsies in patients with chronic diarrhea even if the mucosa is substantially normal at colonoscopy. We don't know how long the anti-inflammatory therapy is appropriate. Large multicenter pediatric trials with long-term follow up are needed to allow investigators to have a better understanding of this rare condition in children.

PO7
RESPONSE TO NUTRITIONAL THERAPY IN CHILDHOOD: ANOTHER PREDICTOR OF THE DISEASE COURSE?

F. Bracci[1], B. Papadatou[2], D. Knafelz[1], R.E. Papa[3], A. Diamanti[1], F. Ferretti[1], F. Panetta[1], G. Torre[1]. *[1]Epato-gastroenterology and Nutrition Unit. Ospedale Pediatrico Bambino Gesù, Roma, Italy; [2]Epatometabolic Disease Unit. Ospedale Pediatrico Bambino Gesù, Roma, Italy; [3]Clinica Pediatrica Università La Sapienza, Roma, Italy*

The incidence of Crohn Disease (CD) in children has increased in the last years. Children with CD often present growth impairment with nutritional complications already at the time of diagnosis.
Steroids, usually used as first line therapy also in children, can reduce bone mineral density and worsen linear growth. Exclusive nutritional therapy (NT) is often indicated as a useful alternative to steroids.
The aim of this study was to evaluate efficacy of NT to induce and maintain remission after discontinuation in a series of CD pediatric patients.
We included in the study 25 pts (11m; 14f; mean age = 13.7±5.2 yrs) at the onset of moderate inflammatory CD, all with ileal involvement. All patients assumed polymeric formula as exclusive nutritional intake for a period of 8 weeks. All patients were asked to refer about their feeling of wellbeing during the observational period. Fecal calprotectin was evaluated at the beginning of NT and after 1, 3

and 6 months (6 mo). PCDAI was calculated at the beginning and at 6 months. Statistical analysis was performed using Student's t test and the value of $p < 0.05$ was considered statistically significant. Calprotectin mean value was 1296.4±1203.8 mcg/ml at the onset, 645.9±623.8 at 1 month ($p < 0.05$); 633.6±722.5 ($p < 0.05$) at 3 months; 642.89±532.00 ($p < 0.05$) at 6 months. PCDAI of all patients was 20.00±4.5 at the beginning of NT, 14.8±5.5 at 6 mo ($p < 0.05$), that indicates reduction of values, but not complete clinical remission (PCDAI <10). Patients were then divided in two groups on the basis of their personal feeling about wellbeing. Twelve patients (48%) referred clinical improvement (group 1), while 13 did not (group 2). In group 1 PCDAI was 19.5±4.4 pre-treatment and 10.4±2.9 at 6 mo ($p = 0.0004$). In group 2 PCDAI was 20.5±4.6 pretreatment and 18.5±4.4 at 6 mo (p = n.s.). No difference in PCDAI values was observed at the beginning of the treatment between the two groups (p = n.s.). PCDAI values at 6 mo were significantly different between the two groups ($p = 0.000$). NT demonstrated to be effective in inducing significant clinical improvement in half of patients in our series. When after years of follow-up we revaluated our data on the basis of the disease evolution, we noted that 3 patients (23%) of the group 2 presented a severe inflammatory form, 31% developed a penetrating disease and 46% a stricturing form. Only one patient (8%) of the group 1 developed a complicated form (penetrating).
Our data confirm that NT can be useful to induce and maintain clinical remission in moderated CD pediatric patients. The fact that we observed that most of non responders developed a complicated form of disease suggests that the absence of response to NT could be associated to a more complicated course of CD.

PO8
OATS IN THE DIET OF CHILDREN WITH CELIAC DISEASE: PRELIMINARY RESULTS OF A RANDOMIZED, DOUBLE-BLIND, MULTICENTER ITALIAN STUDY

E. Lionetti[1], S. Gatti[2], N. Caporelli[2], M. Grilli[2], T. Galeazzi[2], R. Francavilla[3], C. Fontana[3], B. Malamisura[4], T. Passaro[4], M. Barbato[5], C. Di Camillo[5], I. Celletti[5], S. Leoni[5], R. Panceri[6], A. Lazzerotti[6], P. Roggero[6], G. Iacono[7], M.L. Lospalluti[7], W. Kleon[8], M. La Rosa[1], S. Tomarchio[1], I. Brusca[9], P. Restani[10], E. Peñas[10], A. Budelli[11], S. Manferdelli[11], A. Grinzato[11], R. Gesuita[12], F. Carle[12], C. Catassi[2,13]. *[1]Department of Pediatrics, University of Catania, Catania, Italy; [2]Department of Pediatrics, Polytechnic University of Marche, Ancona, Italy; [3]Department of Biomedicina dell'età evolutiva, University of Bari, Bari, Italy; [4]Department of Pediatrics, Cava de' Tirreni Hospital (SA), Italy; [5]Department of Pediatrics, "Sapienza" University of Rome, Rome, Italy; [6]Department of Pediatrics, Monza, University of Milan, Milan, Italy; [7]Department of Pediatrics, Bolzano's Hospital, Bolzano, Italy; [8]Department of Pediatrics, University of Palermo, Palermo, Italy; [9]"Buccheri La Ferla", Hospital of Palermo, Palermo, Italy; [10]Pharmacological Sciences, University of Milan; Milan, Italy; [11]R&D Heinz Italia S.p.A., Italy; [12]Department of Epidemiology, Biostatistics and Medical Information Technology, Polytechnic University of Marche, Ancona, Italy; [13]Center For Celiac Research, University of Maryland School of Medicine, Baltimore, USA*

Objectives: To determine the safety and the acceptance of selected oats varieties in the treatment of Italian children with celiac disease (CD).
Methods: Children with CD were enrolled in a 15 months, randomized, double-blind controlled multicenter trial. Participants were randomized in 2 groups following either A-B treatment (6 months of diet "A", 3 months of standard GFD, 6 months of diet "B"), or B-A treatment (6 months of diet "B", 3 months of standard GFD, 6 months of diet "A") (crossover with washout design). A and B diets included GF products (flour, pasta, biscuits, cakes and crisp toasts) with either purified oats or placebo, given in a double blind fashion. The oat varieties used to manufacture experimental gluten-free products were selected in vitro, in a previous study, for their low amount of gluten-like proteins. Clinical data (GSRS score, growth data) and intestinal permeability test (IPT) by measurement of urinary lactulose/mannitol (L/M) ratio were monitored at 0, 3, 6, 9, 12 and 15 months. Serological (IgA-TTG, IgG-DGP, anti-avenin and anti-zonulin antibodies) and biochemical data were measured at 0, 6, 9, and 15 months.
Results: During the period September 2008–September 2011, 247 children were enrolled. 137 children have received at least 6 months of treatment and 85 completed the protocol. No significant differences were found in GSRS score, BMI and urinary L/M ratio between 0 to 6 months in each group and between the 2 groups after 6 six months of treatment.
Conclusions: These preliminary results show that addition of selected varieties of non-contaminated oats in the treatment of children with CD does not determine changes in intestinal permeability. No gastrointestinal disturbances were associated with either product A or B consumption. The final results will clarify the safety, tolerability and acceptance of oats containing products in the GFD of Italian children with CD.

PO9
TOXIC EPIDERMAL NECROLYSIS ASSOCIATED WITH MESALAMINE IN A CHILD WITH ULCERATIVE COLITIS

V. Romagnoli[1], S. Gatti[1], C. Proietti Pannunzi[1], M.L. Palazzi[1], M. Gabrielli[1], E. Franceschini[1], M. Rossi[1], V. Albano[1], C. Catassi[1]. *[1]Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy*

Background: Toxic epidermal necrolysis (TEN), also known as Lyell syndrome, is a rare (incidence 1–2/1,000,000/year) form of drug-induced skin reaction, characterized by epidermal detachment in >30% of total body surface area. Drugs at higher risk of inducing TEN are anti-infectives agents such as cotrimoxazole and sulfonamides, allopurinol, carbamazepine, phenytoin, phenobarbital and non-steroidal anti-inflammatory drugs. TEN is considered a medical emergency as it may be potentially fatal and carries a high mortality rate (more than 40%).
Case Presentation: A 13-years-old boy affected by Ulcerative Colitis (UC) was admitted to our department with maculo-papular and pruritic exanthema, spread to the entire body surface, including palmoplantar regions, without other associated symptoms. UC had been diagnosed 2 months before based on clinical picture (abdominal pain, tenesmus, hematochezia), on laboratory (persistent high values of fecal calprotectin, positivity of p-ANCA) and endoscopic findings. Therapy with 50 mg/kg/day oral mesalazine and 60 mg/day oral deflazacort (starting dose: 72 mg/day) was prescribed 67 days before. Forty-eight hours after admission erythematous macules evolved into vesicles and flaccid bullae, associated with fever, malaise and burning pain. Drug history suggested clinical diagnosis of mesalazine-related TEN. Treatment consisted of intravenous immunoglobulins (2 g/kg/day for 3 days) and steroid administration (methylprednisolone 60 mg/die), associated with supportive care (fluid resuscitation, parenteral nutrition, analgesic therapy, systemic antibiotic and local treatment). Mesalazine was promptly discontinued. Skin biopsy resulted compatible with erythema multiforme. Skin lesions fully recovered after 14 days with persistence of a partial onycholysis.
Conclusions: Despite its rare occurence, toxic epidermal necrolysis is a condition with a high incidence of complications and mortality.

Patients with severe conditions affecting a large degree of the skin surface area should be considered and promptly treated as burned patients. Recently three case of sulfasalazine and one case of mesalazine-related TEN have been reported. For patients with TEN, immediate withdrawal of the offending medication should be done when blisters or erosions appear in the course of a drug eruption, as this may improve the prognosis.

PO10
INTESTINAL PERMEABILITY IN CELIAC DISEASE: CORRELATIONS WITH GLUTEN FREE DIET

S. Gatti[1], V. Romagnoli[1], T. Galeazzi[1], C. Catassi[1]. [1]*Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy*

Aims: To evaluate the intestinal barrier function with the double sugar test during treatment of celiac disease, and to correlate this function with the persistence of symptoms and duration of diet.
Materials and Methods: Fifty-five children with previously diagnosed celiac disease (CD) on a gluten free diet (GFD) from at least two years were prospectively recruited in this study from September 2008 to March 2011 at the Department of Pediatrics, Università Politecnica delle Marche. Intestinal permeability test (IPT) by measurement of urinary lactulose (L%), mannitol (M%) and lactulose/mannitol ratio (L/M%) and serological test (IgA-TTG) were performed in patients as well as in 50 healthy controls. The Gastrointestinal Symptom Rating Scale (GSRS) was also evaluated in celiac children on a gluten-free diet and in controls.
Results: Mean age (±SD) was 9.1±3 years in patients and 8.4±2.9 years in controls. F/M ratio was 2.6/2 and 2.3/1 in the celiac and the control group, respectively. All children were of Italian origin. The celiac patients were on a gluten free diet from 4.7±2.7 years, and all of them were strictly adherent to the diet. The GSRS score in the celiac group was significantly higher than in control subjects (mean ± SD: 5.35±3.43 vs 3.31±2.60 – $p < 0.05$). No significant differences were found in L/M%, L% and M% between celiac patients and controls, however all the parameters were higher in the celiac group and lactulose excretion was more affected than mannitol excretion (L%: 0.73 vs 0.39%, M%: 34.59 vs 30.55%). No correlation was found between duration of GFD, GSRS score and the results of IPT.
Conclusions: In our cohort no significant differences were found in intestinal permeability between healthy subjects and pediatric celiac patients strictly adherent to gluten free diet, despite the higher values of urinary excretion of lactulose and mannitol in the celiac group. No correlations were found between intestinal permeability, length of GFD and intensity of gastrointestinal symptoms in the celiac group.

PO11
PREGNANCY OUTCOME AND BREASTFEEDING: INFLUENCE ON AGE OF THE ONSET OF COELIAC DISEASE AND SEROLOGICAL REGRESSION AFTER GFD

D. De Venuto[1], M.P. Natale[1], A. Di Mauro[1], S. Tafuri[1], C. De Venuto[1], S. Russo[1], V. Rutigliano[1]. [1]*Department of Medicine, University of Bari "Aldo Moro", Bari, Italy*

Aim: Assess whether the delivery and the breast-feeding are able to influence the early onset of celiac disease, the degree of intestinal injury and the time required for serological negativity, once started a gluten-free diet (GDF).
Methods: In the period from January 2007 to December 2011 were included in the study 400 patients with biopsy proved coeliac disease, who had HLA DQ2/DQ8, EMA and htTG positive. For each of the children sex, age at diagnosis, delivery mode, time of breast-feeding, histological grading according to Marsh and time of serological negativity after GDF were recorded. To evaluate the role of each of the investigated factors on the timing of negativity univariate analysis and a multivariate logistic regression model were performed. For all tests used, p value <0.05 was considered significant.
Results: The study sample includes 400 children, of whom 61% were female. 37% had an age at diagnosis between 23 and 36 months, 30% between 37 and 72 months and the remaining 33% are aged between 73 and 180 months. 83% of those sampled had been breastfed and in particular 50% had been breastfed for more than 4 months. 42% had been given birth by caesarean section. The time for serological negativity was reached in six months by 18% of the subjects studied, between 7 and 12 months by 43%, and more than 12 months by the remaining 39%. Univariate analysis showed that a negative serology (htTG and EMA) within six months of started GFD was associated with age at diagnosis between 23 and 36 months (OR = 3.38, 95% CI = 1.17–9.72, z = 2.26, P = 0.024), breastfeeding for more than 4 months (OR = 3.16, 95% CI = 1.03–9.68, z = 2.02, P = 0.044), birth by caesarean section (OR = 6.75, 95% CI = 2.03–22.43; z = 3.12, p = 0.002), while the histological grading and breastfeeding duration of less than 4 months do not seem to be associated with an early decreasing of htTG. The multivariate analysis showed that the serological negativity within 6 months of GFD was only associated with the birth by caesarean section (OR = 7.9, 95% CI = 1.9–33.3, z = 2.81, P = 0.005).
Conclusions: In the last 10 years some works on coeliac disease concluded in a contradictory manner for perinatal factors, such as caesarean section, in the development of coeliac disease and ascribed a protective role to breastfeeding. In our cohort the serological negativity of htTG within 6 months of GFD was only associated with caesarean section born patients, suggesting a pivotal role of socio-economical factors in the compliance of GFD.

PO12
CAN A SIMPLE LABORATORY TEST RECOGNIZE QUICKLY THE MOST COMMON CAUSE OF INFLAMMATORY DIARRHEA?

G.P. Piras[1], C. Clemente[2]. [1]*Ambulatorio Pediatrico Privato Iglesias, Italy;* [2]*U.O. Pediatrica P.O. "S.Barbara" Iglesias, Italy*

Background: Acute diarrhea (AD) is a clinical syndrome that's commonly understood to be infective gastroenteritis. However AD may be a symptom of other intra abdominal or systemic illnesses. Careful history, laboratory evaluation are necessary to exclude these conditions. Clinical features are useful but inadequate in differentiating the infectious gastroenteritis into inflammatory diarrhea (ID), caused by invasive agents such as *Salmonella*, *Shigella*, *Campylobacter*, and non inflammatory diarrhea (NID), caused by viruses, parasites as Giardia and enterotoxigenic bacteria. Inflammatory diarrheas involve presence of polymorphonuclear leukocites in stool specimens. The presence of visible blood in feces is a highly specific clinical feature of ID, but suffers from low sensitivity. Among the major clinical features, fever was most often seen in diarrhea due to *Salmonella*; vomiting was mostly associated with rotavirus infection. Nevertheless that symptoms have law specificity and law sensitivity. Therefore a lab test immediately available could be helpful. This may have implications for prevention measures management: *Salmonella* infections, very common in our country, are acquired from domestic sources, such as poultry and infected eggs. This study aimed to explore the association of ESR levels (erythrocyte sedimentation rate in a period of 1 hour) with the ID.
Methods: We reviewed a cohort of hospitalized (between January 2006 and June 2008) children (140 males, 123 females) affected by

acute diarrhea. The initial clinical evaluation of the patients should focus on identifying likely causes on the basis of history and clinical findings. Blood routine analyses were performed upon admission in the hospital. Stool samples were obtained from all the children affected by gastroenteritis. All the specimens were tested for the presence of rotavirus antigens using validated ELISA test. Rectal swabs were cultured for *Salmonella*, *Campylobacter* and *Shigella*. We used Bayes' theorem to establish ESR threshold level that could distinguish the two group of different causative agents of acute diarrhea.

Results: *Salmonella* spp. grew in 27 samples, Rotavirus antigens were detected in 31 specimens. All the Children were culture-negative for *Shigella* and *Campylobacter*. 53% of patients with ID had ESR levels greater than mm. 29, 46% had levels lower. Only 5% of patients with NID had ESR values greater than mm 29. Using Bayes' theorem, if ESR level is greater than mm 29, the probability that a patient with acute diarrhea has salmonellosis is 0.88.

Conclusions: In our country the children admitted in hospital for AD with ESR levels higher than mm 29 have likely contracted salmonellosis.

PO13
SHALL WE CARE ABOUT ANTIBIOTIC ASSOCIATED DIARRHEA IN CHILDREN?

E. Bargozzi[1], M. Gaiazzi[1], I. D'Amico[1], F. Meneghin[2], F. Penagini[2], C. Mantegazza[2], S. Cardile[3], G.V. Zuccotti[2], S. Salvatore[1]. *[1]Pediatric Department, Ospedale "F. Del Ponte", University of Insubria, Varese, Italy; [2]Pediatric Department, Ospedale Sacco, Milano, Italy; [3]Pediatric Department, Messina, Italy*

Antibiotic associated diarrhea (AAD) has been reported in 5–39% of children, largely depending on drug and host factors and definition of AAD. Data on the use of probiotics in the prevention of AAD in children are limited and prescription of probiotics during antibiotic treatment is controversial for both scientific and economical reasons.

The aims of this study were to assess the incidence of AAD in children and the effect of concomitant probiotic administration.

Methods: All children discharged from Emergency Department with an antibiotic prescription since January 2012 were enrolled. A phone interview was made after 1 month. Age, site of infection, antibiotic treatment, probiotic supplementation, occurrence, duration and severity of diarrhea were considered. AAD was defined as the presence of diarrhea (at least 3 liquid stools in 24 hours) within 2 weeks of discharge without signs of a new infection.

Results: 322 (mean age±SD 54±42 months, median age 43 months, 177 male) completed the follow-up so far. AAD was reported overall in 42/322 (13%) children (median age 21 months), and in 25/92 (27%) subjects younger than 24 months. No case of hospital admission for AAD occurred. Duration of AAD was 1–15 days with 3–15 stools per day. Amoxicillin-clavulanate was the most frequent prescribed antibiotic (171/322 children, 53%) and AAD occurred in 27 (16%) of these patients. AAD was reported in 31/217 (14%) children with probiotic compared to 11/105 (11%) without probiotic supplementation. The most frequent probiotic strains used were: Lactobacillus GG (n = 114), Lactobacillus reuteri (n = 55) and Bacillus clausii (n = 27). No significant difference on AAD was present among different probiotic supplementation.

Conclusion: AAD occurred in 1:8 children and in 1:4 children younger than 2 years but with mild severity not requiring hospital admission. In our population probiotic supplementation was commonly used but without a protective effect on AAD.

PO14
FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS AND NEONATAL PERIOD: WHICH CORRELATION?

E. Dattoli[1], F. Tandoi[2], M. Agosti[2], C. Luini[1], F. Meneghin[3], D. Dilillo[3], G.V. Zuccotti[3], S. Salvatore[1]. *[1]Pediatric Department, University of Insubria, Varese, Italy; [2]Neonatology Department, Hospital "F. Del Ponte", Varese, Italy; [3]Pediatric Department, Ospedale Sacco, Milano, Italy*

Functional gastrointestinal disorders (FGIDs) are a common condition in children. Different predisposing factors, including infections, microflora disturbance, genetic predisposition and early stressful events have been considered but not fully explored. Data on the prevalence of FGIDs in infants are limited, especially for preterm newborns.

Aims: To evaluate the prevalence and influence of neonatal period on FGIDs occurring in the first year of life. Primary endpoint: To assess whether preterm delivery or other neonatal complications increase the incidence of FGIDs in the first year of life. Secondary endpoint: To detect possible protective factors for FGIDs in infants.

Material and Methods: The study has a multicenter design with a retrospective and a prospective phase, including both preterm and at term newborns. In all subjects a detailed medical history evaluated gestational age, kind of delivery, complications, diet, probiotic treatment and family history for allergy and FGIDs. Retrospective data of newborns born in 2011 were recorded through a phone interview and medical charts of hospital and out-patient clinic admissions. Since May 2012 newborns were prospectively enrolled in the first week of life and the recall at 3, 6, 9 and 12 months is scheduled. Exclusion criteria included: malformations, neurological impairment, surgery, metabolic or cardiac or renal diseases, immunodeficiency, and cystic fibrosis. The presence and classification of FGIDs were considered according to Rome III criteria.

Results: Up to now, we have analysed data on 80 subjects (40 severe preterm and 40 healthy at term newborns) born in 2011. In the preterm group (gestational age 26–33 weeks, weight at birth 720–1490 grams) FGIDs occurred in 36/40 (90%) subjects, and in 13/16 (81%) of preterrms with hospital staying less than 1 month. In the at term group (gestational age 38–41 weeks, weight at birth 3000–3400 grams) FGIDs were reported in 20/40 (50%). Colic and regurgitation were significantly ($p < 0.03$) more present in the preterm group (60% vs. 35% and 45% vs. 18%, respectively). Dyschezia was reported in 13 (33%) preterms compared to 5 (13%) at term newborns, whereas constipation in 6 (15%) compared to 5 (13%) newborns. No case of chronic diarrhea occurred. Caesarean section was present in 95% preterm compared to 8% of at terms babies. Exclusive breast milk was reported in 15% preterm compared to 53% of at term newborns. Antibiotic was used in all preterms and in none at terms newborns.

Conclusion: FGIDs are common disorders in infants. Severe preterms babies reported a significant increased incidence of FGIDs, mostly colic and regurgitation, compared to healthy newborns. The influence of neonatal complications, different gestational age, antibiotic use and feeding regimen on FGIDs in infants is still unclear and is the matter of ongoing research.

PO15
ANTI-TNF ALPHA THERAPY AND MUCOSAL HEALING: THE KEY TO CHANGE THE STORY OF PEDIATRIC CROHN'S DISEASE?

F. Nuti[1], C. Alessandri[1], A. Dilillo[1], F. Civitelli[1], M. Aloi[1], G. Di Nardo[1], S. Cucchiara[1], F. Viola[1]. [1]*Pediatric Gastroenterology and Hepatology Unit, Sapienza University, Rome, Italy*

Background: Efforts have been made to optimize the use of available therapies to improve the outcome of patients with Crohn's disease (CD), but up to now nothing seems capable to change the natural history of the disease. Mucosal healing (MH) is arising as a therapeutic goal able to predict sustained clinical remission. Of the available therapies biological therapy with anti-TNF alpha antibodies, infliximab (IFX) in particular, have been proven effective in achieving MH with a more potent and rapid effect compared to immumomodulants (IMM).

No specific studies evaluating MH as a therapeutic goal are available for pediatric CD.

Aims: Aim of our study is to assess the efficacy of IFX in obtaining MH in a pediatric CD cohort. Secondary aim is to evaluate differences in response in children with early (<1 year) or late (>1 year) disease.

Methods: Patients (pts) with an established diagnosis of CD, between 6 and 18 years of age, starting IFX from January 2009 were prospectively enrolled. All pts were naïve to biological therapies but could have been previously treated with corticosteroids, IMM and aminosalycilates.

At baseline the following pts' characteristics have been collected: age at diagnosis, indication for IFX treatment, age at first infusion, duration of disease, disease location and concomitant medications. An endoscopic procedure to evaluate macroscopic and histological mucosal aspects was performed before starting IFX and after 9 to12 months to evaluate MH.

Disease activity was assessed by Pediatric Crohn's Disease Activity Index (PCDAI) at time 0 (T0) and at the time of endoscopic follow-up (FU) to assess correlation between clinical and endoscopic appearance. Endoscopic activity was scored using the Simple Endoscopic Score (SES-CD).

Patients underwent IFX therapy with appropriate induction and maintenance therapeutic schemes. Concomitant IMM were allowed and recorded.

Results: Twenty pts were enrolled, 14 males. At enrollment mean age was 11.8±2.9 years and mean disease duration was 16.5±17.4 months. Six pts were in the early disease group, 14 in the late disease group. At T0 11 pts (55%) of pts were on IMM, of these 7 were still on IMM at FU. Mean values of PCDAI and SES CD at T0 and FU are in table 1. The values of both PCDAI and SES CD were significantly reduced at FU ($p < 0.005$). Good correlation between the indexes was found both at T0 (r 0.34) and at FU (r 0.55). Dividing patients on the basis of disease duration prior to IFX introduction SES CD values in early disease patients decreased significantly at FU ($p < 0.005$), whilst in late disease pts it decreased but not significantly (p 0.08).

Table 1

	T0	FU
SES CD	17.55±9.2	7.7±8.3
PCDAI	31±18	14.75±13.4

Conclusions: In our cohort biological therapy wih IFX appears effective in achieving mucosal healing, probably in a more efficacious way if introduced early in the course of the disease.

A longer follow up together with larger studies will highlight the effect of MH on disease evolution.

PO16
CYCLOSPORINE AS RESCUE THERAPY FOR ACUTE ULCERATIVE COLITIS IN CHILDREN: A SINGLE ITALIAN CENTRE EXPERIENCE

S. Arrigo[1], M. Vannati[1], M. Bertamino[1], S. Vignola[1], P. Gandullia[1], A. Calvi[1], A. Barabino[1]. [1]*Gastroenterology Unit G. Gaslini Institute, IRCCS, Genoa, Italy*

Objective: In comparison to adult-onset disease, severe ulcerative colitis (UC) is more frequent in childhood and more likely associated to steroid failure. In such cases Cyclosporin A (CyA) is an alternative option to infliximab. We describe our experience in the management of severe steroid-refractory UC with CyA as second-line rescue therapy.

Materials and Methods: We carried out a retrospective review of inpatients with acute steroid-refractory UC treated with either intravenous or oral CyA in our Unit between May 1997 and March 2012. The data collected included patient demographics, colitis severity, dose and route of administration of CyA, therapeutic range, adverse effects, timing and rate of clinical remission and CyA failure with need for early colectomy. PUCAI score was used to define the severity of the disease and the response to CyA. A follow-up of responder patients was assessed to evaluate the rate and time of colectomy in the long term.

Results: A total of 43 episodes treated with CyA in 42 children were analysed (median age 9.7 ys, range 2.6–17.4; male 20/42). The median PUCAI at onset of acute colitis was 65 (45–85). A total of 32 pts underwent full colonscopy without any complication; 27 pts presented pancolitis while the others left colitis. In 28 episodes steroids were started as first line therapy and CyA commenced after a median of 6 days (range 3–22), with a median PUCAI of 70. In the others 15 cases CyA was started on admission because history of steroid dependence or severe side effects. Most cases (79%) received CyA orally at a mean starting dose of 3.8 mg/kg daily (range 2–5.5); then doses were adjusted with a serum range of 101–167 ng/ml. The other pts (21%) received iv CyA at 1.5–4 mg/kg and then shifted to oral CyA 3 days after. Six side effects occurred in 6 patients (14%), including 3 headache, treated with dose reduction; 1 urticaria, 1 hepatoxicity/hypertriglyceridemia and 1 seizure, all treated with CyA discontinuation. The latter occurred in oral CyA, few days after i.v. administration, with a serum level of 100 ng/ml. Typical RMi cerebral features were detected, spontaneously resolved without any sequelae.

30/43 (69.8%) cases resolved the acute attack (median PUCAI 5) after a median of 6 days (range 2–11) and all discharged on CyA for 3 months. The others (30.2%) underwent urgent colectomy after a median of 4 days (range 3–22). During the follow-up after discharge, 10/30 pts required colectomy (33.3%) after a mean time of 0.8 ys (range 0.2–2.3) while 19/30 (63.3%) maintain the colon at a mean of 3.5 ys (range 0.2–9.8 ys). One patient was lost to follow-up.

Conclusions: Our experience in the use of CyA shows a rate of colon savage in the short- and long-term of 69.8% and 63.3% respectively. In the era of biologics, CyA remains an effective second-line therapeutic option in steroid-refractory acute UC in children, with a good tolerability and safety.

PO17
RECURRENT ABDOMINAL PAIN (RAP) APPARENTLY PSYCHOSOMATIC

A. Macaluso[2], F. Cavataio[1], E. Difrancisca[1], M.L. Lospalluti[1], F. Miciotto[2], C. Scalici[1], F. Varia[1], M. Varvarà[1], G. Iacono[1]. *[2]Dipartimento Materno Infantile, Università degli Studi di Palermo, Italy; [1]U.O. I Pediatria-Gastroenterologia; Ospedale G. Di Cristina A.R.N.A.S. Palermo, Italy*

Introduction: Recurrent abdominal pain is in most of case a functional disease. It has been consistently found that only 5 to 10% of children with RAP have an underlying organic process that contributes to their pain. A careful analysis of components of the clinical history, meticulous examination and laboratory findings are mandatory in order to minimize the diagnostic error, saving invasive procedures, without underestimating the continuous pain.

Case report: A 10-year-old female, previously well, was admitted in hospital because of fever, vomiting and epigastric periumbilical abdominal pain. Pain was unresponsiveness to H2 receptor antagonist. She was 60 kg, in good general condition, no pain during abdomen palpation. During hospitalitation laboratory exams (fecal occult blood, and calprotectin, count blood cell, test for celiac disease) and instrumental examination (abdomen XR and ultrasound) were performed and they were negative.

Because of persistent abdominal pain and constipation has performed psychosomatic counseling and started methyl bromide and diazepam therapy with improvement. After one month she turned back to hospital because of vomiting and abdominal pain. She was 47 kg, clinical examination was negative. Laboratory findings showed leucocytosis, and acute renal failure due to dehydration. Despite fluid resuscitation she had vomiting and persistent low potassium level. Abdomen XR was negative, but the patient refused to take the barium contrast medium for XR. For the suspicion of organic cause of anorexia she made cranial CT scan that was negative. Upper GI endoscopy revealed in the gastric cavity abundant secretions with bile and food residues, in the bulb and second duodenal portion a dystrophic whitish mucosa like a maceration; at the third duodenal portion accumulation of greenish liquid secretions likely substenosis of the distal intestinal tract. Finally, the abdominal CT shows gastrectasia, duodenum like corkscrew around the mesenteric vessels, hypervascular appearance of the mesentery, which argue for intestinal malrotation confirmed by radiographs obtained with barium administered. She subsequently underwent surgery.

Conclusions: Malrotation may be manifested also in older children and adults (5,20–22). The clinical manifestations in older patients often are much less straightforward than are those in neonates and may include a wide variety of signs and symptoms like vomiting, constipation, failure to thrive, abdominal pain. They need surgical intervention.

PO18
JUST NOT HYPERTROPHIC PILORY STENOSIS

A. Macaluso[2], F. Cavataio[1], E. Difrancisca[1], M.L. Lospalluti[1], F. Miciotto[2], C. Scalici[1], F. Varia[1], M. Varvarà[1], G. Iacono[1]. *[2]Dipartimento Materno Infantile, Università degli Studi di Palermo, Italy; [1]U.O. I Pediatria-Gastroenterologia; Ospedale G. Di Cristina A.R.N.A.S. Palermo, Italy*

Introduction: Hypertrophic pilory stenosis (HPS) is one of the most common diseases during early infancy. HPS occurs secondary to hypertrophy and hyperplasia of the muscular layers of the pylorus, which cause a functional gastric outlet obstruction. The cause is unknown, however, various environmental and hereditary factors have been implicated. Babies with this condition usually present in the first weeks to months of life progressively worsening vomiting and develop marked hypochloremic alcalosis.

Case report: Patient was born at term by spontaneous vaginal delivery, the perinatal course had been unremarkable. Birth weight was 3000 gr, after average loses he regained the wieght slowly. At 12 days of life he was admitted in UTIC where it was detected a "Hyperarousal syndrome type 1A and ventricular septal defect". At 44 days because of poor weight gain and projectile vomiting, an abdomen ultrasound exam showed hypertrophic pylorus and baby underwent to pyloromyotomy. Despite successful surgery, he developed a progressive anemia and he was admitted in NICU. His weight was 2686 gr (3º centile), patient was hypotonic, hyporeactive, dehydratated, with a murmur 2–3/6L. For an episode of melena he was fed by total parenteral nutrition with gradual recovery enteral nutrition, no more episodes of vomiting and a trend of growth uphill. After 20 days showed a weight of 3170 (3–10 centile), normal physical examination and therefore was discharged with an infant formula 1. After a few days of well-being appeared projectile vomiting all feedings, for which he was admitted in gastroenterology. On entering the weight was reduced (2920 g), poor general condition, pale skin. He performed first-level examinations with evidence of mild anemia and neutrophilic leukocytosis, abdominal echo normal, then skin prick and RAST for cow's milk proteins both negative. It was decided to split the feedings and to monitor the weight, which remained constant during first days. For the persistence of the vomiting began a gradually increased mixture of amino acids: disappeared vomiting and gained regular weight.

Results: After 6 weeks baby performed oral provocation test that had positive result. After one month baby is well and weighs over 4000 g.

Conclusions: Although HPS has been recognized and treated, however, has masked the underlying non-immune-mediated intolerance to cow's milk protein, which was responsible for malnutrition and emaciation of the patient. The association between the two diseases should always be considered.

PO19
FREQUENCY OF COELIAC DISEASE (CD) IN HIGH RISK YOUNG CHILDREN FROM FAMILIES WITH CD: THE PREVENT CD COHORT

R. Auricchio[1], M.G. Limongelli[2], V. Bruno[1], E. Piccolo[1], P. Stellato[1], A. Smarrazzo[1], B. Malmisura[3], L. Greco[1], R. Troncone[1], on behalf of the Prevent CD Study Group. *[1]Department of Pediatrics, University Federico II, Naples, Italy; [2]Ospedale Fatebenefratelli, Benevento, Italy; [3]Ospedale S. Maria dell'Olmo, Cava de' Tirreni, Salerno, Italy*

Objectivies: To evaluate the frequency of CD in the first 3 years of life, in a prospective cohort of high risk children from families with CD.

Subjects and Methods: In the context of the EU-funded PreventCD project (www.preventcd.com) 1326 infants belonging to families with a first degree relative with CD were recruited. 952 of them, who were HLADQ2 and/or DQ8 positive, were prospectively followed-up for the development of CD. Biopsies to confirm the diagnosis were performed if symptoms appeared and/or if two or three consecutive samples were positive for anti-tissue transglutaminase (a-tTG) or anti-gliadin (a-gli) antibodies, respectively.

Preliminary results: As of the 1st of May 2011, 938, 790, 560, 177 and 28 infants were older than 12, 24, 36, 48 and 60 months respectively. Sixty-six biopsies were performed and 49 diagnosis (74%) of CD diagnosis had made (CD group). Higher titer of anti-tTG have been demonstrated in the CD group rather than in the

non-CD group. Otherwise, no significant differences have been noted about symptoms, birth weight and duration of breast-feeding. The cumulative incidence of CD is about 5.6%, 2.5% and 0.25% at 3, 2 and 1 years of age respectively.

Conclusions: These preliminary observations suggest a high incidence of CD in at-risk infants, at quite an early age. All had major damage (villous atrophy) involving the intestinal mucosa. a-tTG antibodies showed a high predictive value.

PO20
BENIGN PANCREATIC HYPERENZYMEMIA, A CONDITION YET TO BE STUDIED

P. Stellato[1], A. Smarrazzo[1], M. Proto[1], D. Del Buono[1], E. Piccolo[1], R. Auricchio[1]. *[1]Department of Pediatrics, University of Naples "Federico II", Italy*

Background: Benign Pancreatic Hyperenzymemia (BPH) is a newly recognised syndrome characterized by serum pancreatic enzyme elevation in absence of pancreatic disease. Usually pancreatic enzymes show a remarkable variability, even a temporary normalization. BPH may occur either as a sporadic or a familial condition but there is no evidence of a relationship between a known gene mutation related to pancreatitis (SPINK1, PRSS1, CFTR) and BPH.

Case report: We describe a case of a familial benign pancreatic hyperenzymemia with recurrent vomiting episodes. Laboratory tests showed hyperamylasemia (114 U/L), normal lipase values (15 U/L) as reported in 5–10% of BPH patients, mild increase of amylasuria (438 U/24 h) and pancreatic amylase (42 U/L) and no other alteration. The ultrasonography couldn't reveal pancreatic abnormalities neither liver or biliary tract damages, all of these findings are compatible with BPH. A second grade (Hetzel-Dent) gastroesophageal reflux disease was diagnosed by endoscopy as the cause of vomiting.

Conclusion: A correct diagnosis of this form of hyperenzymemia is important because there is a small risk (1–2%) of a pancreatic tumor. The planned follow-up was a "wait and see" strategy, assuming a real but non-pathological biochemical alteration. Further studies will be necessary to define the prognosis of this disease.

PO21
THE IMPACT OF A NEW HYPOTONIC SUPER ORS IN GEL FORMULATION ON THE APPLICABILITY OF GUIDELINES FOR MANAGING ACUTE GASTROENTERITIS IN PEDIATRIC CLINICAL PRACTICE

A. Passariello[1], G. De Marco[1], G. Cecere[1], M. Micillo[1], V. Pezzella[1], L. Cosenza[1], G. Terrin[2], R. Berni Canani[1]. *[1]Department of Pediatrics, University of Naples "Federico II", Naples, Italy; [2]Department of Ginecology-Obstetrics and Perinatal Medicine, University of Rome "La Sapienza", Rome, Italy*

Background and Aim: Oral rehydration solution (ORS) is the key treatment for the management of children with acute gastroenteritis (AGE), as suggested by the recent ESPID/ESPGHAN recommendations, but it is largely underused. Refusing to drink ORS is a major factor limiting the applicability of these recommendations. We investigated if a new hypotonic super-ORS, administered in a gel formulation, could improve the adherence to these recommendations.

Methods: We enrolled ambulatory children (aged 3–36 m) consecutively observed by family pediatricians, from January to May 2012, because AGE. Patients were randomly assigned to: Group 1, standard hypotonic ORS (Na^+ 60 mmol/L); or to Group 2, new hypotonic (Na^+ 45 mmol/L) super (Zn^{2+} 1 mmol/L) ORS administered in gel (Vitagel Minerali, DMF, Limbiate, Italy). Main outcome measure was the rate of children adherent to recommendations regarding oral rehydration. The use of additional medications was also evaluated.

Results: We evaluated 78 children with AGE (50 male, age 21±11 m, body weight 12±2 kg, vomiting 37.7%), 38 in Group 1 and 40 in Group 2. Baseline main demographic and clinical characteristics of the two study groups were similar. Children adequately rehydrated by oral route, according to the recommendations, were 3 out of 38 in Group 1 (7.9%) and 27 out of 40 in Group 2 (67.5%) ($p < 0.001$). Additional medications use was higher in Group 1 (26.3%) if compared with Group 2 (5.0%, $p = 0.009$).

Conclusion: The new hypotonic super ORS in gel formulation is effective to optimize the management of AGE according to the recent ESPID/ESPGHAN recommendations.

PO22
RENAL SIDE EFFECTS IN CHILDREN TREATED WITH MESALAZINE FOR INFLAMMATORY BOWEL DISEASE

D. De Venuto[1], A. Di Mauro[1], M.P. Natale[1], M. Monteduro[1], C. De Venuto[1], G. Lassandro[1], V. Rutigliano[1]. *[1]Department of Medicine, University of Bari "Aldo Moro", Italy*

Aim: The first line therapy for Inflammatory bowel diseases (IBD) to induce remission, consists in 5-aminosalicylate (5-ASA) at higher dosage in combination with corticosteroids. 5-ASA are characterized by adequate efficacy and safety but adverse effects can occur in a small cohort of patients. Although mesalazine is generally well-tolerated, adverse effects from hypersentitivity and intolerance can occur and have impairment of renal function in patients with IBD, especially where not early recognized.

Method: We report two different renal side effects occurring during therapy with mesalazine in young patients affected by IBD. The simultaneous therapy with prednisone masked mesalazine idiosyncratic reaction. A 14-year-old girl affected by ulcerative colitis (UC) and an 18-year-old boy affected by ileocolonic Crohn Disease (CD) were treated with mesalazine (50 mg/kg/die) in association with prednisone (2 mg/kg/die). They showed an initial clinical improvement but 15 day after, when steroid therapy has been reduced up to the suspension, they revealed a sudden worsening of symptoms. For this reason the patients were admitted to the hospital. Laboratory data revealed raised creatinine: 1.6 mg/dl in the girl and 0.76 mg/dl in the boy. Moreover the boy presented back pain. A renal scintigraphy showed an interstitial nephropathy in the girl. A diagnosis of nephrolitiasis was performed in the boy after both renal echography and X-ray. Both patients withdrawal the 5-ASA. In few days occurred normalization of blood creatinine and resolution of back pain.

Results: We confirm the mesalazine intolerance through *ex-adiuvantibus criteria*: stop mesalazine therapy recovered the nephrotoxic side effects. In both cases, the initial concurrent steroid therapy had masked the mesalazine intolerance, which became apparent as steroids were tapered.

Conclusion: Although mesalazine is frequently used in children, it may induce nephrotoxicity. The timing and the grading of the renal impairment differs significantly up to an irreversible renal disease if not early recognized and not recovered with discontinuation of mesalazine. In contrast to an abundant literature regarding efficacy and safety of mesalazine in adult IBD patients, few double blind placebo controlled trials have been reported in children. Further studies are needed to optimize its use in management of IBD and to prevent renal side effects. Seriated follow up of serum creatinine and renal echography may be an easy and low expensive way to prevent detrimental side effects.

PO23
PROTEOMIC AND IMMUNOASSAY CHARACTERIZATION OF A NEW FOOD ALLERGEN FROM HAZELNUT (*CORYLUS AVELLANA*)

C. Nitride[1], G. Mamone[2], G. Picariello[2], R. Nocerino[3], R. Troncone[3], R. Berni Canani[3], P. Ferranti[1,2]. *[1]Department of Food Science, University of Naples "Federico II", Portici (Naples), Italy; [2]Institute of Food Sciences, CNR, Avellino, Italy; [3]Department of Pediatrics and European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy*

Background and Aim: Hazelnut (*Corylus avellana*) is a common cause of lifetime lasting IgE-mediated food allergy. Symptoms range from mild oral allergy syndrome to severe life-threatening anaphylaxis. We aimed to identify allergenic determinants in children living in the Campania region (Italy) with hazelnut allergy.
Methods: Otherwise healthy children with oral food challenge confirmed hazelnut allergy were prospectively evaluated. Crude protein extracts were obtained from 5 hazelnut varieties, including autochthon, Northern Italy and Oregon (USA) cultivars, with phosphate saline buffer, pH 7.2. The immunoreactive protein components were identified by SDS-PAGE electrophoresis and Western immunoblotting, using patients sera as source of specific IgE. The IgE-binding protein bands were characterized by advanced proteomic strategies and tandem mass spectrometry (MS)-based *de novo* peptide sequencing.
Results: Four subjects were evaluated (2 male, 50%; mean age 39 m). Symptoms were: urticaria (2), angioedema (3), anaphylaxis (2). No significant differences were observed considering the main demographic and clinical characteristics at diagnosis. All children's sera were immunoreactive to a protein, not previously annotated in database, occurring in hazelnut regardless the variety. The allergen was isolated by combined chromatographic strategies. Only one patient exhibited an additional reactivity to the vicilin-like 7S 48 kDa glycoprotein (Cor a 11). The MS-based characterization provided evidence of a high homology degree between the IgE-binding protein subunit and 11S globulin-like storage proteins expressed in other seeds. The new allergen shares structural traits with the hazelnut 11S globulin-like proteins (Cor a 9) such as the disulfide linkage of two subunits, an acidic (~35 kDa) and an alkaline (~21 kDa) one. Interestingly, only the alkaline subunit exhibits antigenic properties.
Conclusions: A previously unrecognized hazelnut allergen was identified. Except for a faint IgE reactivity of Cor a 11 recorded in a single case, the new allergen was the unique IgE-binding protein in our patients. Future studies are warranted to better define possible prognostic and immunotherapeutic implications.

PO24
BENEFIT OF ATOPY PATCH TEST IN DECIDING WHEN TO REINTRODUCE COW'S MILK IN NON-IgE-MEDIATED ALLERGIC CHILDREN WITH GASTROINTESTINAL SYMPTOMS

R. Nocerino[1], V. Granata[1], V. Pezzella[1], L. Leone[1], M. Di Costanzo[1], A. Passariello[1,3], G. Terrin[1,4], R. Troncone[1,2], R. Berni Canani[1,2]. *[1]Department of Pediatrics, University of Naples "Federico II", Naples, Italy; [2]European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy; [3]Monaldi Hospital, Naples, Italy; [4]Department of Woman's Health and Territorial Medicine, University of Rome "La Sapienza", Rome, Italy*

Background and Aim: Oral food challenge (OFC) is required to establish the persistence or resolution of cow's milk allergy (CMA). Atopy patch test (APTs) are useful in the initial diagnostic approach in children with non-IgE-mediated CMA. We aim to investigate the benefit of APTs in predicting a reaction to the OFC in children with non-IgE-mediated CMA.
Methods: We enrolled consecutively children with CMA admitted for OFC to reassess their allergy. The APTs were performed using a drop (20 μl) of fresh cow's milk (CM) containing 3.5% fat placed on filter paper and applied with adhesive tape to the unaffected skin of the child's back using a 12-mm aluminum cup. Isotonic saline solution was used as negative control to exclude false positive reactions. The occlusion time was 48 h, and the results were read 20 min and 24 h after removal of the cups. Antihistamines and anti-inflammatory agents were discontinued at least 7 days before the test. All tests were performed by the same nursing staff, and the results were read by two expert pediatric allergists blind to the outcome of OFC. Skin findings were recorded on a standardized form. Reactions were judged to be either negative or positive. Positive skin reactions on the APTs site were classified mild (erythema and slight infiltration, +), moderate (erythema plus papules, ++), or severe (erythema plus vesicles, +++). The OFC was performed after 12 months of exclusion diet. Accuracy of APTs and their correlation (Spearman's Test) with OFC results were calculated.
Results: 172 children (97 boys, 56.4%; age 6.37 months, range 2–12 months) with CMA-related gastrointestinal symptoms were evaluated. Gastrointestinal symptoms at presentation were vomiting (72, 41.9%), chronic diarrhea (117, 68%), abdominal pain (45, 26.2%). At diagnosis 113/172 (65.7%) children had positive APTs to cow's milk proteins (CMP). After 12 months of exclusion diet 94 children outgrown CMA. The APTs performed immediately before OFC at 12 months showed a sensitivity of 67.95% (95%CI 56.42–78.07), specificity of 88.3% (95% CI 80.03–94.01), PPV of 82.81% (95%CI 71.32–91.1), NPV of 76.85% (95%CI 67.75–84.43) and a LR of 5.80 (95%CI 3.35–10.38). APTs were significantly correlated ($p < 0.001$) with OFC outcomes (r 0.579).
Conclusion: The APTs could be a valuable tool in the follow-up of pediatric patients with non-IgE-mediated CMA by contributing in determining when to introduce CM.

PO25
GASTROINTESTINAL SYMPTOMS AND FABRY DISEASE

L. Pensabene[1], S. Sestito[1], A. Nicoletti[1], F. Graziano[1], P. Strisciuglio[2], D. Concolino[1]. *[1]Department of Pediatrics, University "Magna Graecia", Catanzaro, Italy; [2]Department of Pediatrics, University "Federico II", Naples, Italy*

Aims: Gastrointestinal (GI) symptoms, mostly diarrhoea and abdominal pain, are one of the earliest reported signs of Fabry disease (FD), a rare X-linked deficiency of α-galactosidase A. It has been reported that GI symptoms occur in approximately 60% of hemizygous males and between 30% and 60% of heterozygous females. Many FD patients had a previous diagnosis of diarrhea-predominant irritable bowel syndrome (IBS), a functional gastrointestinal disorder (FGID). Aims of this study were to characterize GI symptoms in paediatric and adult patients with FD, to evaluate if GI symptoms in FD mimic a FGID, diagnosed according to Rome III criteria and to evaluate if this can be used as a diagnosis tool to recognize the FD patients.
Methods: 42 patients with FD (6 M; range: 9–70 y; 35 adults, 7 children) were recruited for the study. Two validated questionnaires, one on paediatric and the other on adult GI symptoms, were used to diagnose FGIDs, according to Rome III criteria, respectively in those children and adults with FD who had GI symptoms. The pattern of GI manifestations was analyzed separately in the two age subgroups.

Results: 29/42 (69%) patients with FD [25/35 adults (71.4%), 4/7 children (57.1%)] reported GI symptoms, without subsequent improvement for those who were in enzyme replacement therapy. According to the Rome III criteria, 16/25 (64%) adults and 2/4 (50%) children presented GI symptoms, mimicking FGIDs. In the adult subgroup, we found: Unspecified Functional Bowel Disorder (n = 9), Functional Bloating (n = 7), IBS (n = 5), Functional Dyspepsia (n = 4), Functional Constipation (n = 4), Functional Dysphagia (n = 3), Globus (n = 3), Postprandial Distress Syndrome (n = 3), Aerophagia (n = 3), Unspecified Excessive Belching (n = 3), Proctalgia Fugax (n = 3), Functional Chest Pain of Presumed Esophageal Origin (n = 2), Cyclic Vomiting Syndrome (n = 2), Chronic Idiopathic Nausea (n = 1), Functional Diarrhoea (n = 1), Functional Fecal Incontinence (n = 1). Among the 2 children with FGIDs, one was diagnosed with Abdominal Migraine, the other with IBS. Among the 25 adults, 14 reported full felling after a regular-size meal (8/14 at least 2–3 days/month), 13 reported fewer than 3 defecations per week (11/13 only sometimes) and/or hard stools, 12 complained abdominal bloating or distension (8/12 at least 2–3 days/month). All children with GI symptoms (4/4) complained low abdominal pain associated with a change in form of stool or improvement with defecation.
Conclusion: The prevalence of GI symptoms in our patients with FD was high in both age subgroups. The most frequent pattern of FGID in our adults was Unspecified Functional Bowel Disorder; therefore according to Rome III criteria GI symptoms didn't mimic diarrhea-predominant IBS as previously described. However the most frequent GI symptom in our children was IBS-like abdominal pain, while in adults were full feeling after a regular-size meal and abdominal bloating/distension, followed by constipation-like symptoms.

PO26
REFRACTORY IRON DEFICIENCY ANEMIA: THE ROLE OF *HELICOBACTER PYLORI* INFECTION

D. Dilillo[1], F. Penagini[1], C. Mantegazza[1], F. Meneghin[1], V. Giacomet[1], C. Mameli[1], E. Galli[1], G.V. Zuccotti[1]. [1]*Department of Pediatrics, Luigi Sacco University Hospital, Milan, Italy*

Helicobacter pylori (*H. pylori*) infection is associated with gastric and extra-gastric disorders including iron deficiency anemia, usually unresponsive to iron replacement therapy. *H. pylori* induces mucosal abnormalities such as atrophic and nodular gastritis that may impair iron absorption. A possible competition for iron between the bacteria and the host has also been suggested. The report below describes the case of a 10-year-old adopted Chilean boy who was accepted to our Pediatric Department with a 6 year history of severe microcitic anemia. Clinical documentation from Chile was scanty; from the reports at our disposal the child had experienced severe iron deficiency anemia, with minimum hemoglobin (Hb) levels of 3 g/dl, since the age of four. In Chile, serology for celiac disease, fecal occult blood test, bone marrow aspiration and Technetium-99m scan for Meckel's diverticulum were negative. Esophagogastroduodenoscopy (EGDS) had also been performed and evidenced chronic antral gastritis but no biopsies were available. Oral iron supplementation had been given throughout childhood without complete normalization of hemoglobin levels. At arrival to our Department the child presented good general conditions except for pallor and a cardiac murmur. Blood tests revealed severe hypochromic microcitic anemia: Hb 5.6 g/dl, MCV 65.6 fl, MCH 18 pg. His iron profile showed low iron values (serum iron 13 μg/dl, transferrin 3.6 g/L and ferritin 1 μg/L). Hemoglobin electrophoresis and glucose-6-phosphate dehydrogenase levels were normal. Fecal occult blood test was negative and abdominal ultrasound unremarkable. EGDS showed nodular gastritis, predominantly in the antrum. On antral biopsies rapid urease test was positive, light microscopy showed moderate chronic active gastritis with lymphoid follicles in lamina propria and identified organisms consistent with *H. pylori*. Thus, an *H. pylori* eradication regimen was started with clarithromycin 20 mg/kg/day, amoxicillin 50 mg/kg/day and omeprazole 1 mg/kg/day, all drugs for 14 days. Oral iron replacement therapy as well as folate and vitamin B12 were implemented. Four weeks after completion of antibiotic treatment, C13-urea breath test confirmed eradication of *H. pylori* a, blood tests showed an increase of Hb to 10.3 g/dL and iron status remained steady. Iron deficiency anemia is a known complication of *H. pylori* infection. It can occur in the absence of any gastrointestinal symptom and is usually refractory to iron therapy. Evidence of iron deficiency anemia of unknown cause presenting in children and adolescents should prompt the clinician for a gastroenterology referral for consideration of endoscopy to exclude *H. pylori* infection and gastritis.

PO27
A CASE OF MONOCLONAL GAMMOPATHY IN PEDIATRIC CROHN'S DISEASE

D. Dilillo[1], E. Galli[1], F. Meneghin[1], F. Penagini[1], C. Mantegazza[1], A. Dolci[2], I. Infusino[2], M. Panteghini[2], G.V. Zuccotti[1]. [1]*Department of Pediatrics and* [2]*Clinical Biochemistry Laboratory, Luigi Sacco University Hospital, Milan, Italy*

Monoclonal gammopathies are characterized by proliferation of a single clone of plasma cells. They can denote the presence of a malignant process, but they have also been described in patients with non-neoplastic disease and in healthy individuals. Inflammatory bowel disease (IBD) may predispose to monoclonal gammopathy through chronic stimulation of B lymphocyte. Here we describe the case of a 12 years-old boy affected by Crohn's disease, in which three monoclonal components were detected in serum. Diagnosis of ileocolonic Crohn's disease was made in May 2010, after the boy had experienced abdominal pain, bloody diarrhea, fever and weight loss. At diagnosis, serum protein electrophoresis (SPE) showed a single monoclonal peak of 3.3 g/L in the gamma-globulin region (no previously SPE was available for comparison). Hemoglobin in blood was 10.1 g/dL, white blood cell count was 15,850/mm^{3}with significant neutrophilia, while concentrations of serum calcium and clinically relevant enzymes were in the physiological range. There was no evidence of infections and chest X-ray was normal. Induction of remission was obtained with prednisolone; contemporaneously, azathioprine (AZT) was started obtaining good clinical response. In February 2011 the boy presented a relapse of disease, during which AZT was withdrawn and, after having excluded the progression of monoclonal gammopathy, infliximab (IFX) was started, achieving initial remission of clinical symptoms. After three doses of IFX, the patient relapsed again, so that the biological therapy was switched to adalimumab (ADA) obtaining disease remission. Five months later the patient presented a severe relapse, his general conditions being deteriorated. During hospitalization, hemoglobin was 9.3 g/dL, white cell count was 12,270/mm^{3}without any alteration of differential. SPE showed three monoclonal peaks of 3.7 g/L, 2.8 g/L and 3.8 g/L in the gamma globulin region. High concentrations of kappa and lambda free light chains were detected in serum, but with a normal kappa/lambda ratio. Immunofixation assay allowed to qualify the three monoclonal peaks as kappa IgA, kappa IgM, and lambda IgG, respectively. Monoclonal free kappa light chains, i.e. Bence Jones protein, were detected in patient's urine. Bone marrow aspiration was performed revealing adequate representation of hematopoietic series and the presence of 5–6% of plasma cell, indicating a reactive state. The patient was treated with corticosteroids in combination

with ADA at increased dosage, achieving remission of disease until today. Monoclonal gammopathies are rarely detected in children. In patients with IBD, both chronic inflammation and immunosuppressive therapy may be risk factors for progression to neoplastic disease. Therefore, SPE request for screening and follow-up of these patients is fundamental for early detection of monoclonal components and for monitoring progression to lymphoid/myeloid malignancy.

PO28
CELIAC DISEASE AND NOONAN SYNDROME: CASE REPORT

C. Caloisi[1], D. Maiorani[1], T. Gentile[1]. [1]*Pediatric Department, L'Aquila University, Italy*

We describe a patient referred to our query 5 years and 4 months old for diarrhea, abdominal pain, weight and height loss from the first months of life. Family history: paternal grandfather died from unknown heart disease and maternal grandfather from leukemia. At birth the child was diagnosed with right cryptorchidism. At the age of 3 months he underwent surgery for bilateral inguinal hernia. Physical examination at first observation showed: height 104.5 cm (18ºC), weight: 17.5 kg BMI: 16 kg/m^2 (50ºC). Target height was 175 cm (52ºC). Lab tests, which were positive for anti-transglutaminase and anti-gliadin deamidata antibodies. Celiac disease (CD) was confirmed by intestinal biopsy and gluten-free diet was administered. At the age of 10 years and 4 months, become more evident the typical features of Noonan Syndrome (NS) as: inverted triangle face shape, wide forehead and pointed chin; hypertelorism and slight ptosis; short and broad nose with a depressed root; low-set and/or posteriorly rotated ears with an oval shape and thickening of the helix; sparse, thin, slow growing hair with low posterior hairline; short and webbed neck with pterygium colli; pectus carinatum superiorly and excavatum inferiorly; scoliosis; separated nipples; cubitus valgus; transparent and thin skin, delay of the pubertal growth spurt. At the same observation a 2–3/6 systolic murmur was found. NS was suspected on the basis of the clinical findings (3–4 major signs, Table 1), however, further investigations are in progress to ascertain this diagnosis.

Table 1. Scoring system for Noonan syndrome (NS)[a]

Feature	A = Major	B = Minor
1 Facial	Typical face dysmorphology	Suggestive face dysmorphology
2 Cardiac	Pulmonary valve stenosis, HOCM and/or ECG typical of NS	Other defect
3 Height	<P3*	<P10*
4 Chest wall	Pectus carinatum/excavatum	Broad thorax
5 Family history	First degree relative with definite NS	
6 Other	Mental retardation, cryptorchidism and lymphatic dysplasia	One of mental retardation, cryptorchidism, lymphatic dysplasia

[a] Adapted from [2].
HOCM: hypertrophic obstructive cardiomyopathy.
*P3 and P10 refer to percentile lines for height according to age, with the normal range of variation defined as P3–P97 inclusive.
Definitive NS: I "A" plus one other major sign or two minor signs; I "B" plus two major signs or three minor signs

NS is a congenital genetic disorder, autosomal dominant with a high percentage of sporadic cases caused by de novo mutations. The incidence of NS is estimated at 1 in 1000–2500 births. Heterozygous mutations in nine genes (PTPN11, SOS1, KRAS, NRAS, RAF1, BRAF, SHOC2, MEK1 and CBL) have been documented to underlie this disorder that encode for proteins participating in the RAS-mitogen-activated protein kinases (MAPK) signal transduction pathway. The association of RASopathies [NS and N-related S] and autoimmune disorders has been reported sporadically. Have been described only two or three cases of CD in patients with NS. Quaio CR et al. (2012) analyzed the clinical and laboratory features in 42 RASopathy patients with evidence of numerous autoantibodies including anti-endomysial. Moreover, NS used to be referred to as the male version of Turner's syndrome (TS), and is still sometimes described in this way. Since the last decade, an increasing number of studies have demonstrated a higher prevalence of CD among females with TS when compared with the general population (5–9% compared with 0.5–1.0% in the general population) one might suppose a common pathogenetic mechanism. Until a final conclusion of the real incidence of CD in NS is drawn, the physicians should be alerted to the possibility of this association and the need for a serological screning in patients with NS.

PO29
COELIAC SALIVARY SCREENING: L'AQUILA EXPERIENCE

C. Caloisi[1], M. De Stefano[1], R. Nenna[2], M. Bavastrelli[2], L. Petrarca[2], G. Mastrogiorgio[2], C. Tiberti[2], M. Bonamico[2], T. Gentile[1]. [1]*L'Aquila University, Italy;* [2]*Sapienza University, Rome, Italy*

In previous studies anti-tissue transglutaminase autoantibodies (tTGAb) were detected in saliva with a sensitive fluid-phase radioimmunoassay (RIA). The aim of our study was to identify, by salivary test, coeliac disease (CD) in 6- to 8-year-old children for a timely diagnosis, start gluten-free diet (GFD) in compliant subjects, achieve the growth target, and prevent CD complications.
924 school-children were invited to participate in the study. 752 saliva samples (420 M and 332 F, aged between 5.3–9.8 years) were tested for RIA anti-tTG IgA. Positive children were tested for serum RIA tTGAb, ELISA tTG IgA, and anti-endomysium IgA. Children positive by serum assays underwent endoscopy with multiple duodenal biopsies and GFD was started.

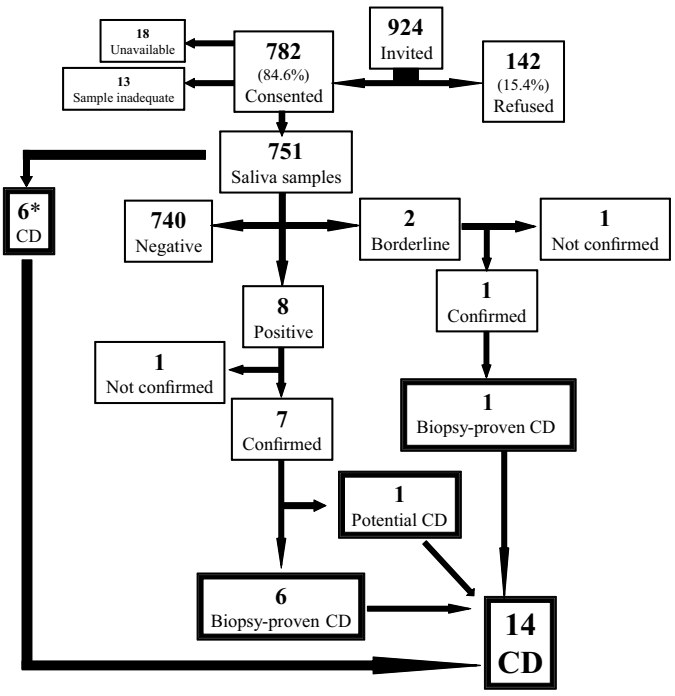

Figure 1: flow chart of the study. *CD previously diagnosed.

Consent for the screening was obtained from 782 parents (84.6%) and adequate saliva samples were collected from 752 (96.2%) children.

10 children (6 M, 4 F) of 752 (1.3%) were found to be salivary tTG IgA positive (2 borderline). 8 children (1 borderline) have been confirmed in a second determination of saliva and serum tTG IgA. 7 children showed villous atrophy when undergoing intestinal biopsy, whereas 1 had Marsh 1 lesions. In the group of children enrolled, 6 had previously received the diagnosis of CD (0.8%). On the whole, CD prevalence in the population studied (including 6 CD cases known) was 1.86%. The ratio between symptomatic (atypical) and asymptomatic patients was 1:1.7. In the sample of children screened there was a slight predominance of males (54.5%), while in the group of celiac M:F ratio were 1:1. In the group of celiac 30.8% had at least one first-degree celiac patient, while in non-celiac the percentage drops to 7.3%. 672 children in the study population (89.4%) had both Italian parents, 22 (2.9%) at least one Italian parent, 58 (7.7%) two foreign parents (mostly Romanian, Albanian and Macedonian).
This study demonstrates that it is possible to detect salivary tTG-Abs in CD with a non-invasive, simple to perform, reproducible and sensitive method. The prevalence of CD found (1.8%) was higher than expected than the prevalence reported in other studies.

PO30
FOOD PROTEIN INDUCED ENTEROCOLITIS SYNDROME (FPIES): DATA OF SIGENP EMILIA-ROMAGNA GROUP

P. Alvisi[1], P. Bottau[2], D. Dal Pozzo[2], S. Amarri[3], M. Mainetti[4], S. Brusa[2]. *[1]Unità Operativa Pediatria, Ospedale Maggiore, Bologna, Italy; [2]Unità Operativa Complessa di Pediatria e Neonatologia Ospedale S. Maria della Scaletta, Imola (BO), Italy; [3]Unità Operativa Complessa Pediatria, Ospedale S. Maria Nuova, Reggio Emilia, Italy; [4]Unità Operativa Complessa Pediatria, Ospedale S. Maria delle Croci, Ravenna, Italy*

Food protein-induced enterocolitis syndrome (FPIES) is a severe, non IgE mediated, food hypersensitivity, characterised by gastrointestinal symptoms, that typically appear within few hours from the introduction of food proteins. Clinically it can cause a severe pathology, and induce hypovolemic shock. Diagnosis is clinic and based on the presence of repetitive vomiting and diarrhea without other causes, after exposition to incriminated food proteins, with negative skin prick tests (SPT).

Aims of the study:

1. evaluate FPIES incidence among the SIGENP Centres of Emilia Romagna region
2. evaluate the delay in diagnosis since the onset of symptoms
3. compare therapy/exclusion diet in the different Centres.

Materials and Methods: An easy survey was sent to the 11 SIGENP centres of our region, with questions about clinical presentation (onset symptoms, delay within first episode and diagnosis, incriminated food); results of blood tests (complete blood count, venous emogasanalysis); allergologic tests (SPT, atopy patch tests); therapy/diet (in the acute phase, exclusion diet, oral food challenge (OFC)).

Results: 7/11 SIGENP centres answered to our survey; 4 of them had some cases of FPIES, the total number of patients with this diagnosis were 10: 6 males and 4 females. The age at clinical onset of symptoms varied from 7 days to 11 months (mean 4.10 months; median 5 months). Onset symptoms were purely gastrointestinal (vomiting, diarrhoea, hypovolemic shock) in 10/10 patients, 2/10 presented also with cough. The mean delay in diagnosis was 40 days (median 9 days), with a mean of 1.5 episodes to formalise a clinical diagnosis. Only 2/10 children underwent OFC at diagnosis, and both were positive. 4/10 children presented elevated neutrophil count and acidosis. 10/10 children underwent allergologic evaluation: 1/10 had positive SPT to cow milk, egg, beef, wheat; 6/10 had normal total IgE count; atopy patch tests were not performed (0/10). Incriminated food proteins were: cow milk (4/10), cow milk and rice (1/10); potato and lamb (1/10); corn and tapioca (1/10); banana 1/10; corn (1/10); cheese (1/10). Acute phase therapy consisted in rehydration, whereas exclusion diet is still going on in 8/10 children (mean: 14.5 months, median 13 months). 6/10 children had an OFC during follow up, after a range between 6 and 20 months since diagnosis. 2/10 children reintroduced cow milk after 15 and 20 months.

Discussion: Emilia Romagna data were collected in collaboration with the Allergology Centres. Infact FPIES diagnosis and follow up is often a prerogative of Pediatric Allergists, less frequently of Gastroenterologists. This could be the reason of a leakage in data, which is not desirable in such a rare condition.
Our brief survey observed that the delay from the first onset of symptoms and diagnosis is relatively short, compared with literature and also that an OFC at diagnosis is quite difficult to perform since the severity of symptoms at diagnosis.
8/10 of our patients (80%) does still not have enough follow up to introduce the incriminated food, which, according to literature, is more frequently (4/10 – 40%) cow's milk.
According to our experience we hope that strict cooperation with Pediatric Allergist will help to collect data as to know better and better treat these patients.

PO31
WORRIES AND NEEDS IN CHILDREN AND ADOLESCENTS WITH CELIAC DISEASE. ADHERENCE TO GLUTEN-FREE DIET. IMPLICATIONS FOR CLINICAL PRACTICE

S. Battistutta[1], S. Martelossi[2], C. Cervesi[1], M. Montico[3], M. Bin[4], S. Dal Bo[1], A. Ventura[1]. *[1]Institute for Maternal and Child Health, IRCCS "Burlo Garofolo" and University of Trieste, Department of Pediatrics, Trieste, Italy; [2]Institute for Maternal and Child Health, IRCCS "Burlo Garofolo", Department of Pediatrics, Trieste, Italy; [3]Institute for Maternal and Child Health, IRCCS "Burlo Garofolo", Epidemiology and Biostatistics Unit, Trieste, Italy; [4]Institute for Maternal and Child Health, IRCCS "Burlo Garofolo", Child Neurology and Psychiatry Ward, Department of Paediatrics, Trieste, Italy*

Aims: Being diagnosed with celiac disease (CD) is a critical event for children, adolescents and their families, who must adapt to the changes that the diagnosis and treatment of CD require. Disease-related psychological features add to other age-related issues influencing the adherence to gluten-free (G-F) diet. Patients and their families often autonomously adapt to CD though sometimes a psychological support or psycho-educational information to patients/parents are needed.
The aims of the study were:

1. To study the psychological issues of children and adolescents with CD;
2. To compare the patients' point of view with the one of their parents;
3. To analyze the implications for clinical practice.

Methods: Patients visiting IRCCS Burlo Garofolo between August-December 2011 were enrolled in the study. A questionnaire was filled in only by parents for patients aged 0–8 yrs ($n=24$), while for patients aged 8–18 yrs ($n=36$) it was filled in both by patients and parents. Overall 96 questionnaires were administered. The questionnaire focused on health worries, needs and adherence to G-F diet. Statistical analysis was performed considering the influence of some variables (sex, age, age at diagnosis, CD duration, symptomatic/not-symptomatic onset) and the degree of agreement between the patients' and parents' answers.

Moreover patients were informed by the doctor about the availability of a psychological support and to date 13 patients asked or accepted to meet the psychologist. Data emerged from the visits was scheduled and qualitatively analysed.

Results: Sixty patients took part in the study (response rate 88.2%). The participants were mainly female patients (70%); 40% of the patients were younger then 8-years-old, 25% were aged between 8–10, 35% between 11–18. CD was more frequently diagnosed before the child turned 5 years-old (55%). Among the worries, the most frequent reports were: "I'm bothered by abdicating some foods" (33.3% patients, 31.5% parents). For 11/19 questions the Patients–Parents Agreement was lower than 70%. As far as needs are concerned, participants more frequently referred "I need more information about my future health conditions" (33.3% patients, 25.4% parents). Scarce adherence to diet, most common in adolescence (no transgressions referred only by 76.2%), is mainly due to the limitations it imposes in daily life.

Among the 13 patients that asked for or accepted to meet the psychologist (84.6% female; mean age: 10 years 7 months), 54% needed psychological support to adapt to the G-F diet, 15% had previous psychological problems or difficult context and in 38% of cases parents needed information or psycho-educative support.

Conclusions: Health caregivers must be aware of and ask for patients' and parents' opinions. More information about future conditions is required. Moreover doctors should realize their patients' difficulties with diet (eg. suggesting alternative foods). Parents' strengths and fragilities must be kept in consideration to prevent problematic situations.

PO32
EFFICACY OF A NEW PARTIALLY HYDROLYZED WHEY FORMULA ON INFANT COLIC: A RANDOMIZED CONTROLLED TRIAL

R. Nocerino[1], G. De Marco[1], L. Cosenza[1], V. Pezzella[1], A. Passariello[1,3], G. Terrin[4], R. Berni Canani[1,2]. *[1]Department of Pediatrics, University of Naples "Federico II", Naples, Italy; [2]European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy; [3]Monaldi Hospital, Naples, Italy; 4. Department of Women Health and Territorial Medicine, University "La Sapienza", Rome, Italy*

Background and Aim: Colic is a common functional gastrointestinal disorder in healthy infants and it's a frequent cause of formula milk changing. Several new formulas are on the market for the treatment of this condition, but evidences on its clinical efficacy are still scarce. The aim of our study was to evaluate the efficacy on infant colic of a new partially hydrolyzed whey formula.

Methods: Randomized controlled clinical trial on formula fed-infants (aged $\leqslant$3 months), born at term, with body weight adequate for gestational age, with regular weight gain and normal physical examination, consecutively observed by 4 family pediatricians because of suspect of infant colic were considered eligible for the study. Subjects with a confirmed diagnosis of infant colic (Rome III criteria) were randomly allocated in two groups. Group 1 received nonanalgesic, non-nutritive soothing maneuvers and continued the standard formula, Group 2 received the same recommendations plus a new partially hydrolyzed whey formula (Humana DG, Humana Milan, Italy) containing oligosaccharides (0.5 g/100 ml) and β-palmitic acid (55%), low content of lactose (3.3 g/100 ml) and low osmolarity (213 mOsm). Infants were clinically reevaluated after 21 d from the enrollment. A questionnaire was given to parents to evaluate the daily number of colic episodes, bowel movements, and of regurgitation episodes during 21 days of study.

Results: Fifty-two infants completed the study (26 male; age 1.9 m, 95%CI 1.7–2.1; body weight 5.3 kg, 95%CI 5.1–5.6): 25 in Group 1, and 27 in Group 2. Baseline clinical and demographic characteristics were similar among the 2 Groups. During the 21 d of the study period, infants of Group 2 had less colic episodes compared to infants of Group 1 (77.8% vs 88% at 7 d; 44.4% vs 80% at 14 d, $p = 0.008$; 7.4% vs 76% at 21 d, $p < 0.001$). Comparing Group 1 vs. Group 2, daily regurgitation episodes/patient (6.1 ± 2.4 vs 0.8 ± 1.4, $p < 0.001$) and daily bowel movements/patient (1.5 ± 0.9 vs 4.9 ± 0.8, $p < 0.001$) were significantly different after 21 d. No adverse events were reported.

Conclusion: The use of this new partially hydrolyzed whey formula, with low osmolarity and lactose content, efficiently reduces the number of colic episodes. Milk formula changing because colic should be based on the results of controlled clinical trials.

PO33
EOSINOPHILIC ESOPHAGITIS: DOUBTS AND CERTAINTIES

C. Pierobon[1], S. Martelossi[1], A. Ventura[1]. *[1]Institute for Maternal and Child Health, IRCCS Burlo Garofolo and University of Trieste, Trieste, Italy*

Objectives: Define clinical features and diagnostic-therapeutic problems that characterize Eosinophilic Esophagitis (EoE) and underline elements for the drafting of guidelines useful to paediatricians.

Materials and Methods: This is a retrospective study on 21 pediatric patients with EoE followed at the Pediatric Clinic of the IRCCS Burlo Garofolo in Trieste. Clinical history, allergy tests, endoscopic and histological evolution from diagnosis to last follow-up were evaluated according to the therapeutic program used. In all cases first-line therapy was topical corticosteroid (Fluticasone), Montelukast was chosen as maintenance therapy in 15 cases. Four patients were also treated with elimination diet. Systemic corticosteroid (Prednisone) was administered only to five patients, those with more severe disease.

Results: Eighty percent of participants were male and median age at presentation for diagnosis was 10 years. The most frequent symptoms were dysphagia (81%) and food bolus impactions (57%). There was correlation between EoE and atopy (67%), two patients also had celiac disease. The endoscopic features, localized in the middle and upper esophagus, consisted mostly whitish papules (81%) and trachealization (43%). Biopsies revealed >15 eosinophils per high power field (hpf) in all children, 14% of whom presented >40 eos/hpf.

Fluticasone caused disappearance or improvement of symptoms. Diet was highly divergent. Montelukast was found to yield good clinical effects however doubts endoscopic and histological findings. Four patients responded to the PPI-Fluticasone combination therapy.

Conclusions: EoE is rare but present in our region. Typical symptoms are dysphagia for solid food and food impactions. A small proportion of cases are associated with reflux. We found a good response to Fluticasone in acute phase and Montelukast helps in controlling symptoms.

Clinical progression is dissociated from endoscopic and histological findings. We believe further study is needed to determine if the treatment goal should be histological healing in addition to clinic.

PO34
PRESENTING FEATURES AND DISEASE COURSE OF PEDIATRIC ONSET ULCERATIVE COLITIS

M. Aloi[1], G. D'Arcangelo[1], G. Di Nardo[1], F. Vassallo[1], V. Rizzo[1], F. Pofi[1], A. Dilillo[1], F. Nuti[1], S. Cucchiara[1]. *[1]Pediatric Gastroenterology And Liver Unit, Sapienza University of Rome, Italy*

Background and Aim: The clinical variables and disease course of pediatric ulcerative colitis (UC) have been poorly reported and characterized. The aim of this study was to retrospectively describe the phenotype and disease course of pediatric onset UC diagnosed at a tertiary referral Center for Pediatric Gastroenterology.
Patiens and Methods: 110 patients (pts) (43% males) with a diagnosis of UC were identified at our department database (age range: 1.2–22.5 years, mean 10.3±4.8). Records were reviewed for disease location and behavior (i.e., rectal sparing, skip lesions) at the diagnosis, family history for inflammatory bowel disease and other immune-related disorders, changes of the pattern at the follow-up, need for surgery and cumulative risk for colectomy.
Results: Median follow-up was 29 months (range: 11–60); 17% of pts had an early-onset (EO) disease (0–5 years). At the diagnosis, 22% of pts had a proctitis, 29% a left-sided colitis, and 49% an extensive colitis. Six % of pts presented with a rectal sparing, while a patchy colonic inflammation was reported in 8%. There was no statistically significant difference for disease location and behavior at the diagnosis between pts with early and late-onset disease. Disease extension at the follow up was reported in 13% of pts. No clinical variables at the initial diagnosis were related to the subsequent extension of the disease. Ten % of pts needed surgery. The cumulative rate of colectomy was 9% at 1 year and 13% at 2 years. The presence of extensive disease at the diagnosis was associated with an increased risk of colectomy (Odds Ratio (OR) = 6.0 (1.18–30.3). Among pts with limited disease at the diagnosis, the risk of colectomy was higher in those who experienced disease extension than in those who did not (Hazard ratio (HR) = 12.3 (1.7–101.7).
Conclusions: Pediatric UC is characterized by a widespread location at diagnosis. Intriguingly, EO-UC does not seem to be more severe than the late-onset entity, in terms of both disease location and risk of surgery. The colectomy rate was related to location of the disease at the diagnosis and influenced by disease extension during the follow-up.

PO35
CELIAC DISEASE AND TYPE 1 DIABETES MELLITUS ASSOCIATION: A RETROSPECTIVE ANALYSIS OF PEDIATRIC CASES IN ROME

F. Valitutti[1], M. Barbato[1], M. Massoud[2], F. Costantino[1], G. Di Nardo[1], D. Iorfida[1], C.M. Trovato[1], L. Di Iorio[2], A. Pierantonozzi[2], M.L. Manca Bitti[2], F.M. Paone[2], S. Cucchiara[1]. *[1]Department of Pediatrics, "Sapienza", University of Rome, Rome, Italy; [2]Department of Pediatrics, Tor Vergata University, Rome, Italy*

Background and Aims: A clinical association between celiac disease (CD) and type 1 diabetes mellitus (DM1) has largely been recognized. The risk of developing CD in diabetic patients seems to be strongly correlated to the presence of HLA-DQ2 haplotypes; moreover, experimental and clinical data have recently addressed the possible role of gluten in promoting DM1. According to several studies, the mean onset of DM1 is 8–9 years, while the age of CD diagnosis may be highly variable. Therefore, we wanted to assess the epidemiological features of pediatric patients affected both by CD and DM1 referred to two university hospitals of Rome (Sapienza and Tor Vergata universities), from 1980 to 2010.
Materials and Methods: We retrospectively collected data (age at diagnosis, gender) from 1894 CD patients on a gluten-free diet and 971 DM1 patients referred to these hospitals, in order to elucidate specific patterns of disease onset.
Data from CD patients with known poor compliance were not considered in the study design.
On purpose, we analyzed data from the CD-DM1 cohort through logistic regression models.
Results: Among these 1894 CD patients (mean age at CD diagnosis: 7.9; SD: ±4.8), only 3, diagnosed with CD in the adolescence, afterward developed DM1; nevertheless, 80% of CD cohort (1515 patients) had been diagnosed with CD before ten years of age.
Contrarily, among 971 DM1 children, CD had been then identified in 99 (10.1%) (mean age at CD diagnosis: 14.1; DS: ±6.9); only 28 of them, anyhow, had been diagnosed under ten years, while 49 and 22 received the diagnosis of CD between 10 and 20 and after 20 years of age, respectively.
In the cohort of 99 children affected both by DM1 and CD, the male/female ratio was mostly 1:1 (51 F/48 M).
Patients whose DM1 onset registered under two years of age had a risk of developing CD 5.79-fold increased (IC 95%: 1.16–28.79; $p = 0.032$) compared to the overall DM1 group.
The median interval of diagnosing CD following the onset of DM1 was 1.6 years (interquartile range: 3.1 years).
Conclusions: As previously reported, in our study we described a CD prevalence of 10% among DM1 patients, with a male/female ratio of 1:1. On the other hand, we only detected 3 cases of DM1 among 1894 children previously diagnosed with CD; moreover, the age at CD diagnosis in non-DM1 children was significant lower than in the group of CD-DM1 children ($p < 0.001$). Thus, according to these two data, we could speculate that an early gluten avoidance in celiac patients might prevent the onset of DM1.
Furthermore, as the early presentation of DM1 seems to increase the risk of CD, we strongly recommend a strict follow up for CD in this subpopulation and we call for upcoming studies investigating this specific issue.

PO36
CHARACTERIZATION OF MUCOSA-ASSOCIATED AND FECAL MICROBIOTA OF CHILDREN WITH AUSTISM SPECTRUM DISORDER

M. Barbato[1], S. Schippa[2], F. Valitutti[1], V. Iebba[2], F. Santangelo[2], C.M. Trovato[1], S. Leoni[1], S. Gatti[1], M. Marazzato[2], M.P. Conte[2], V. Leuzzi[1], S. Cucchiara[1]. *[1]Department of Pediatrics, Sapienza University of Rome, Italy; [2]Department of Public Health and Infectious Disease, Sapienza University of Rome, Italy*

Background and Aims: It has often been suggested that there might be an intriguing relation between the gut microbiota and ASD (Autism Spectrum Disorder), and some authors have previously addressed the existence of a possible disbiosis in gut microbiota of autistic children.
Our aim was to evaluate duodenal mucosa-associated and fecal microbiota of autistic children compared to age-matched controls.
Patients and Methods: 11 autistic patients and 8 controls underwent upper GI endoscopy and stool collection. All upper GI endoscopies were performed because of alarm symptoms (unexplained iron-deficiency anaemia; food impaction; weight loss; vomiting; chronic diarrhoea).
Samples of total DNA were extracted both from duodenal biopsies' and stools. "Temperal Temperature Gel Electrophoresis" (TTGE) was employed to analyze the composition of dominant intestinal

microbiota. In particular, the primers GCclamp-U968 (5′GCclamp-GAA CGC GAAGAACCT TAC) and L1401 (5′GCG TGT GTA CAA GAC CC) were used to amplify the V6 to V8 regions of bacterial 16S rRNA. TTGE profiles were then analyzed through multivariate analysis.

Results: Preliminary results showed a significant ($p = 0.000$) partition of fecal TTGE profiles from autistic patients and fecal TTGE profiles of control group; contrarily, no significant difference was disclosed as regard to mucosa-associated TTGE profiles.

Conclusions: Our result might be interpreted as a possible disbiotic event in the intestinal microbiota of autistic patients and warrants further investigations.

PO37
REPORT OF EXACERBATION OF COLITIC SYMPTOMS DUE TO A MESALAZINE INTOLERANCE IN CHILDREN DIAGNOSED WITH ULCERATIVE COLITIS

D. De Venuto[1], A. Di Mauro[1], F. Di Mauro[1], F. Nicastro[1], C. De Venuto[1], V. Rutigliano[1]. [1]*Department of Pediatrics, University of Bari, Bari, Italy*

Aim: Therapy for inflammatory bowel disease (IBD) in children is designed for induction of remission of disease activity, maintenance of remission, prevention of relapse and finally support of a normal growth and pubertal development. Aminosalicylates are the first line therapy for IBD. They can be administered as sulfasalazine (5-ASA + sulfapyridine) or as mesalazine (5-ASA + resins). The recent trend in inducing and maintaining remission in mild to moderately active IBD prefers mesalazine to sulfasalazine due to its less frequent adverse effects. Although mesalazine is generally well tolerated, adverse effects from hypersensitivity and intolerance can occur and mimic symptoms of active IBD.

Method: We report a case of a 13-year-old boy with anemia, bloody diarrhoea and weight loss. He was diagnosed with ulcerative colitis (UC) by total colonoscopy and histology. He began oral mesalazine to induce remission. Despite therapy, the patient worsened: he had nausea and vomit, abdominal cramps, bloody diarrhoea, skin rush and fever. He was admitted to the hospital. On admission, physical examination, laboratory data and abdominal radiographs were performed. His blood tests revealed a white blood cell count of 13.5×10^3/ul with neutrophils 79.8%, an erythrocyte sedimentation rate of 109 mm/h haemoglobin of 8.0 g/dl, albumin concentration of 2.3 g/dl. Stool tests for bacterial pathogens, Cytomegalovirus and *Clostridium difficile* toxin, and ova and parasites were negative. A magnetic resonance imaging showed colonic distension, significant symmetrical bowel wall thickening and adjacent mesenteric inflammatory changes extending from the descending colon to the rectum. Mesalazine was discontinued and treatment with prednisone, complete bowel rest and total parental nutrition was started. He responded well: within the next few days, the bloody diarrhoea dramatically subsided, and the abdominal pain and nausea disappeared. The patient was discharged after 7 days and gradually weaned over the next 3 months from prednisone.

Result: To confirm the intolerance, a mesalazine challenge test was performed during a quiescent phase of the disease after informed consent. Bloody diarrhoea, fever and abdominal pain were noted at 800 mg/die. These symptoms disappeared only after mesalazine withdrawal. We concluded for an exacerbation of ulcerative colitis due to mesalazine intolerance.

Conclusion: Although mesalazine is frequently used in children with mild disease, mainly due to its perceived lack of side effects, side gastrointestinal effects are described in up to 8% of patients. Reports of exacerbation of colitic symptoms caused by intolerance to mesalazine are infrequent but have been described in adult patients. In contrast to the abundant literature regarding efficacy and safety of mesalazine in adult IBD patients, a few double-blind, placebo-controlled trials have been reported in children. Further studies are needed to optimize the use of 5-ASA in management of IBD.

PO38
PROLONGED *CLOSTRIDIUM DIFFICILE* DIARRHOEA AMONG CHILDREN IN A TERTIARY CARE HOSPITAL: A 10 YEAR RETROSPECTIVE STUDY

E. Borali, C. Moretti, E. Stacul, R. Lipreri, C. De Giacomo. *Pediatrics Division, Niguarda Ca' Granda Hospital, Milan, Italy*

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

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

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

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

PO39
EFFICACY OF THE ELEMENTAL DIET IN A SEVERE PEDIATRIC CASE OF PRIMARY EOSINOPHILIC GASTROINTESTINAL DISEASE

S. Lucarelli[1], G. Lastrucci[1], G. Di Nardo[1], T. Frediani[2], T. Federici[1], C. Santarelli[1], S. Frediani[3], S. Cucchiara[1]. [1]*Pediatric Gastroenterology and Liver Unit, Sapienza University of Rome, Italy;* [2]*Allergology Unit, Sapienza University of Rome, Italy;* [3]*Pediatric Surgery Unit, Sapienza University of Rome, Italy*

Background and Objective: Primary eosinophilic gastrointestinal diseases (EGIDs) are very rare in pediatric age. The mean feature is the gastrointestinal (GI) inflammation rich in eosinophils, leading to a wide spectrum of non-specific clinical presentations depending on the affected segment. Diagnosis requires the bioptic demonstration of eosinophilic infiltration in any segment of GI tract and the exclusion of other known causes of GI eosinophilia. Etiology is still unknown, however both the presence of atopy in 75% patients and the efficacy of steroids suggest an ipersensitivity mechanism. The mainstay treatment are topic steroids but a relapse is often observed at suspension of therapy. Elimination or elemental diets may be helpful in patients with mucosal disease or identified allergic response to foods. Our aim was to assess the efficacy of an exclusive elemental diet in a severe presentation of pediatric EGIDs, with the objective to spare steroid therapy.
Materials and Methods: A 6 years-old girl referred to our Pediatric Gastroenterology Unit for a history of abdominal pain, vomiting, diarrhoea and weight loss associated to high peripheral eosinophilia, fever and artralgies. At admission to our unit, a wide laboratory and allergologic evaluation were performed. The patient underwent complete radiologic study of GI tract, abdominal MR, upper and lower GI enteroscopy with multiple biopsies. Osteomedullary biopsy with assessment of FIP1LI-PDGFRA rearrangement was also performed. Once the diagnosis of EGIDs was confirmed, the patient started an exclusive enteral nutrition with amino acid based formula.
Results: Laboratory tests showed leucocitosis (14900/μl), eosinophilia (42.1%), and increased total IgE value (319 kU/L). Prick tests, atopy patch test, and specific IgE for foods were negative. Endoscopy confirmed duodenal, ileal and colonic inflammation mimicking Crohn's disease. Histology showed a deep infiltration of eosinophils (40–60/HPF) in all mucosal layers of each biopsy specimen. Abdominal imaging showed a diffuse involvement of small bowel with mild ascitis. Hypereosinophilic syndromes, infections, inflammatory bowel diseases, celiac disease, connective tissue disorders, vasculitis, neoplasia, responses to immunologic injury, were excluded. After a 3 months period of elemental diet the girl had a complete resolution of symptomatology and peripheral eosinophilia, and the follow-up endoscopy confirmed the remission of the disease. Long term follow-up showed a good prognosis with an oligoantigenic diet for 1 year and subsequent gradual reintroduction of foods in a 2 years period.
Conclusions: EGIDs in pediatric age should always be suspected in case of severe GI manifestations, especially whether associated to peripheral eosinophilia. In our case, the elemental diet was effective despite negativity of allergological assessment. The remission seemed to be associated with a good long term prognosis, avoiding the problem of steroid dependence.

PO40
INFLIXIMAB THERAPY IN MANAGING PEDIATRIC IBD

S. Accomando[1], C. Albino[1], A. Di Fiore[1], F. Ferraro[1], V. Maniscalchi[1], G. Corsello[1]. [1]*Department of Pediatrics; University of Palermo, Italy*

Background: Treatment of IBD is complex and based on different drugs. The biological treatments act on different stages of immuno-physiopathological processes of the disease to change the evolution or natural history. At present the most studied and used biological drug is a chimerical monoclonal antibody to TNF alpha known as infliximab.
Aims: We describe evolution and clinical response to infliximab in pediatric patients with IBD diagnosed and followed at our centre. We also evaluated the mucosal healing and the growth pattern.
Patients and Methods: In the last five years, in our centre, 7 patients, 3 males and 4 females, with mean age of about 12 years, affected by pediatric IBD, were treated with infliximab. Six were suffering from Crohn's disease, while only one female is affected by UC with skin manifestation of pyoderma gangrenosum as onset sign. They are patients who were steroid resistant or dependant or who did not respond to other forms of traditional therapy. According to the ACCENT 1 study, all our patients underwent to periodic infusions at a dose of 5 mg/kg (at weeks 0, 2, 6 and then every 8 weeks). Infliximab was administered by intravenous infusion. The infusions had a duration of 2–3 hours. Paediatric Crohn's Disease Activity Index, nutritional status and disease activity serum variables, associated to ileocolonscopy (with histology) were evaluated before and 54 weeks after the beginning of therapy. Weight and height Z scores were measured before starting the baseline infusion programme and after 6 months. All our patients had simultaneous intake of immunosuppressants (azathioprine) in order to reduce the risk of immunological side effects and of lacking the response to biological drug due to production of antibodies to infliximab (ATI).
Results: All patients showed a good clinical response, a gradual reduction of the PCDAI score, while nutritional status and disease activity serum variables improve, as well as endoscopic and histological scores. Five patients had a clinical remission (PCDAI <10), 6 patients had inflammatory remission (decrease in both endoscopic and histological scores for >50% as compared to baseline values). In all patients corticosteroids were stopped within 4 weeks after beginning infliximab therapy. A significant increase in both weight and heigt Z scores was observed 6 months after beginning of the baseline infusion programme. None of our patients had neither immediate nor late adverse reactions. At the moment only one patient with fistulising Crohn's disease has presented a disease flare and needs to switch infliximab therapy at dosage of 10 mg/kg.
Conclusions: Our pediatric experience with infliximab is positive and confirmed the great potential of the drug in improving the treatment of IBD. However, it remains to be determined which is the long term tolerability of the drug and to examine whether its effectiveness is not reduced by the continuation of its administration.

PO41
ENTERAL FEEDING FOR GERD-RELATED ALTE: A THERAPEUTIC OPTION?

P. Orizio[1], L. Tonegatti[1], L. Righetti[1], F. Torri[1], D. Alberti[1]. [1]*U.O. di Chirurgia Pediatrica, Spedali Civili, Brescia, Italy*

Objective: We report two cases of apparent life threatening events (ALTE) associated to gastro-esophageal reflux disease (GERD) refractory to medical therapy and successfully treated with prolonged enteral feeding.

Case report 1: A previously healthy 1-month-old baby was referred for ALTE episode; history, physical examination and basic blood test were unremarkable. GERD was diagnosed by abnormal pH-MII (multichannel intraluminal impedance) and upper GI series. Others common causes of ALTE were excluded.
Medical treatment was started (esomeprazol 2 mg/kg/die, Domperidone 1 mg/kg/die, Gaviscon 1 cc/kg/die), but recurrence was observed few days after, and cardiopulmonary resuscitation needed. Antireflux surgery was offered but refused by parents. In order to limit GER we started a continuous enteral feeding by naso-gastric tube. There was no ALTE recurrence in inpatient observation for five days. The infant was than discharged with home monitoring. Continuous enteral feeding was gradually shifted to nocturnal, with a limited amount of milk permitted daily by mouth. Weaning was uneventful. Nocturnal enteral feeding was gradually reduced and finally discontinued at 10 months of age; in the same time oral feeding was progressively unrestricted. Medical therapy was stopped at 12 months. After three months of follow up the patient is asymptomatic.
Case report 2: A 2-month-old infant had three episodes of ALTE, two on antireflux therapy. History, diagnostic work up, treatment and outcome were similar to the case reported previously. Also in this case antireflux surgery was refused. Enteral feeding was discontinued at 5 months of age, and medical treatment at 11 months. After four months of follow up she is asymptomatic.
Discussion: The problem of ALTE is faced frequently by frontline clinicians, with an estimate incidence of up to 6% of all infants.
Although the issue of causality between ALTE and GERD is challenging, widely discussed in literature and not clearly established, many Authors reported the benefits of antireflux therapies.
Treatment includes feeding management (i.e. postural therapy), medical management (H-2 antagonist, proton pump inhibitors) and surgical intervention. The last option is often offered for recurrent ALTE in patients on medical therapy or as first line treatment in more severe cases.
Enteral feeding has never been reported in literature to the best of our knowledge.
We offered this solution as medical therapy was ineffective and surgical therapy was refused.
Enteral feeding permitted an adequate caloric intake reducing gastric distension and GER as physiologically in bolus feeding.
It was well tolerated; troubles were limited to naso-gastric tube dislodgment.
Conclusions: Enteral feeding may be considered a therapeutic option for patients with GERD-related ALTE unresponsive to medical therapy when surgical procedures are unfeasible.
A larger experience is needed to confirm this preliminary data.

PO42
COLONIC PERFORATION IN A CHILD WITH CROHN'S DISEASE: SUCCESSFUL MEDICAL TREATMENT CAN RESCUE FROM COLECTOMY

M. Gasparetto[1], B. Giorgi[2], F. Albunni[2], W. Kleon[3], M. Cananzi[1], G. Guariso[1]. *[1]University Hospital of Padova, Department of Paediatrics Unit of Gastroenterology, Digestive Endoscopy, Hepatology, and Care of the Child with Liver Transplantation, Italy; [2]University Hospital of Padova, Department of Medical Diagnostic Sciences and Special Therapies Institute of Radiology, Italy; [3]Hospital of Bolzano, Unit of Paediatrics, Italy*

Background: The challenging treatment of penetrating paediatric Crohn's disease (CD) involves pharmacological and surgical approaches [1–2]. Despite a proved efficacy of anti-TNF agents for treatment of complex fistula, a large number of patients cannot achieve a complete healing and relapses during the follow-up [3].
Specific aim: We report a paediatric case with CD and colonic perforation who was successfully treated with medical therapy only, including anti-TNFα.
Case Report: During a colonoscopy performed on a 9 year old girl with CD, a perforation occurred in correspondence of the splenic flexure. A laparoscopic suture of the colonic wall was required. The formation of a peri-splenic and retro-colonic collection was then detected (US, enteric-CT), with concomitant appearance of fever and severe increase in the inflammation markers. Images also demonstrated a fistula connecting the colon to the collection. The girl was kept fasting and treated with total parenteral nutrition and antibiotic therapy. The dimensions of the collection decreased progressively at control images within two months. Treatment with infliximab was started according to the standard schedule, and after the third dose a US control showed disappearance of the collection and complete healing of the enteric fistula. Parenteral nutrition was progressively substituted with enteral feeding and no surgical treatments have been needed as yet. The girl is gaining weight and is maintaining good general conditions.
Discussion: In pubertal children with CD, the option of an efficacious medical treatment to avoid a major surgical approach on the bowel (colectomy, ileostomy) is to be aimed for growth improvement. This approach requires a strictly monitored long-term follow-up.

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PO43
GASTRIC FINDINGS IN COELIAC CHILDREN AND ADULTS

L. Petrarca[1], R. Nenna[1], R.P.L. Luparia[1], G. Mastrogiorgio[1], M. Mennini[1], S. Pontone[2], N. Pietropaoli[1], M. Brighi[1], M. Florio[1], F.M. Magliocca[3], M. Bonamico[1]. *[1]Department of Paediatrics, of [b]Surgical Sciences and of [c]Experimental Medicine and Pathology, "Sapienza" University of Rome, Rome, Italy*

Objectives and Study: Gastric involvement has been described in coeliac disease (CD). A possible relationship between *Helicobacter pylori* (Hp) infection and CD is controversial. Hp is the main cause of gastritis. The aim of our study was to evaluate the differences in terms of endoscopic and histologic gastric findings and prevalence of Hp in CD children as compared to adults.
Methods: Sixty-one (38 Females; age ranged from 1 to 16.8 years; median age: 7.1 years) children (Group 1) and sixty (43 Females; age ranged from 18 to 74 years; median age: 35.5 years) adults (Group 2) with CD were evaluated. Gastric biopsies were performed for histological evaluation (hematoxylin and eosin, Giemsa) and for Rapid Urease Test (RUT). Diagnosis of Hp infection was based on positivity to histology and RUT. Gastritis was classified and scored according to the Updated Sydney System; duodenal biopsies were evaluated according to Marsh classification modified by Oberhuber.
Results: Chronic Superficial Gastritis (CSG) was diagnosed in 20 (32.8%) Group 1 patients and in 17 (28.3%) Group 2 patients.

Lymphocytic gastritis (LG) was diagnosed in one (1.6%) child and in three (5%) adults. Hp infection was diagnosed in two (3.3%) Group 1 patients and in eleven (nine with CSG, one with interstitial gastritis and one an atrophic gastritis) (18.3%) Group 2 patients ($p < 0.02$). The two Hp positive CD children had a typical CD form without epigastralgia and severe duodenal lesions (3c type). Among Hp positive CD adults, six had a typical CD form (one with epigastralgia), two atypical and three a silent form; eight patients showed 3c and three patients 3b lesions of the duodenum.

Conclusion: CSG is the most frequent gastric lesion in CD patients and it is sometimes Hp related. The prevalence of Hp infection in coeliac patients is quite similar to the general population both in children and in adults. LG is more common in CD adults and it seems not related to Hp infection.

PO44
JOINT INVOLVEMENT IN COELIAC CHILDREN: AN ULTRASONOGRAPHIC STUDY

G. Mastrogiorgio[1], R. Nenna[1], R.P.L. Luparia[1], M. Mennini[1], L. Petrarca[1], I. Rutigliano[2], F. Ceccarelli[2], N. Pietropaoli[1], M. Montuori[1], A. Iagnocco[2], M. Bonamico[1]. *[1]Department of Paediatrics, "Sapienza" University of Rome, Rome, Italy; [2]Internal Medicine and Medical Specialties, "Sapienza" University of Rome, Rome, Italy*

Objectives and Study: Coeliac disease (CD) is a gluten-dependent enteropathy characterized by a wide spectrum of clinical manifestations. Some reports have highlighted the association between rheumatic disorders and CD, with an improvement when the patients are on a gluten-free diet (GFD). Studies focusing on imaging evaluation of joint involvement in children affected by CD are not available. The aim of our study was to evaluate the prevalence and severity of joint involvement in paediatric CD patients using ultrasonography (US).

Methods: We enrolled 37 consecutively children (11 males; mean age 6.9±4.4 SD) on a free diet at CD diagnosis. All children were evaluated to assess tender or swollen joints. US evaluation of hip, knee and ankle bilaterally was performed, in order to detect the presence of joint effusion, synovial proliferation, power Doppler signal, bone profile irregularities, according with published definitions. The examination was performed by a rheumatologist experienced in US, blinded to clinical conditions of children.

Results: US evaluation demonstrated the presence of at least one modification in 18 children (48.6%). The most involved joint was the knee: alterations involving at least one knee, were detected in 14/37 (37.8%) children, 22/74 (35.2%) of the knees showed modifications. Regarding hip evaluation, 5/37 (13.5%) children (7/74 joints) showed US modifications. Only 3 children showed effusion involving the ankle (8.1%). Six over 37 CD children, (16.2%) showed arthralgias at different joint levels, all of them showed US abnormalities. None of the children showed bone profile irregularities.

Conclusion: By using US, our study confirmed the frequent joint involvement in children affected by CD. In our children, the most frequently involved joint was the knee, and the modification most frequently detected was joint effusion. Only one child showed the presence of synovitis, with positive power Doppler signal demonstrating active inflammation, suggesting that generally joint involvement was mild. Finally, we confirm the higher sensitivity of US assessment respect to clinical evaluation.

PO45
COELIAC DISEASE AND HEADACHE: A POSSIBLE CORRELATION EXPLORED IN A LARGE COHORT OF CHILDREN AND ADOLESCENTS

M. Mennini[1], R. Nenna[1], R.P.L. Luparia[1], G. Mastrogiorgio[1], N. Pietropaoli[1], L. Petrarca[1], M. Brighi[1], M. Florio[1], P. Verdecchia[1], M. Bonamico[1]. *[1]Department of Paediatrics, "Sapienza" University of Rome, Rome, Italy*

Objectives and Study: Among the extra-intestinal gluten-dependent disorders ataxia and peripheral neuropathy have been described. Growing evidence reports headache as atypical manifestation of coeliac disease (CD). The aim of our study was to establish the prevalence of coeliac disease in children affected by headache.

Methods: In our retrospective study we have revised data from 883 children (480 females; age ranged from 3 to 19 years; median: 9.9 years) attending the Centre for Paediatric Headache over the period 2000–2011. They were screened for CD using anti-transglutaminase autoantibodies and EMA. Positive patients were referred to our Operative Unit on Coeliac disease, where they were submitted to a further serological evaluation. Confirmed positive children underwent upper endoscopy with multiple duodenal biopsies. Histological lesions were evaluated according to Marsh classification, as modified by Oberhuber. Coeliac children started the gluten-free diet.

Results: 16 children (10 females; age ranged from 5.7 to 14 years) were diagnosed to be coeliacs. Ten of them were diagnosed through the CD screening performed at the Centre for Paediatric Headache, while 6 CD children had already been diagnosed when occurred to the neurological evaluation. Moreover, two patients were tTG Ab and/or EMA positive but the upper endoscopy was not performed. The prevalence of CD in children and adolescents affected by headache is 1.8% that could reach 2%, by considering coeliac also the two Ab-positive patients.

Conclusion: Our study demonstrates, on a large cohort, that CD prevalence is quite doubled in patients with headache. Screening for CD could be advised as part of the diagnostic flow-chart in these paediatric patients. In fact, a timely diagnosis and the prompt gluten-free diet, in otherwise asymptomatic patients, could improve symptom as well as drugs' absorption.

PO46
COMPLIANCE TO GLUTEN FREE DIET AND AWARENESS OF THE DISEASE IN ADULTS AND CHILDREN WITH CELIAC DISEASE

C. Zanchi[1], N. Orzes[2], S. Martelossi[1], T. Not[1], A. Ventura[1], in collaboration with Italian Celiac Disease Association (ICA). *[1]IRCCS Burlo Garofolo and University of Trieste, Italy; [2]Department of Gastroenterology and Digestive Endoscopy, Civil Hospital of Gorizia, Italy*

Background: Gluten-free diet (GFD) has a considerable impact on daily living of patients with celiac disease (CD). The aim of our study was to investigate the compliance to GFD and to understand the factors associated with a poor compliance.

Methods: 248 biopsy-proven CD patients (189 F, 59 M, median age 34±18 yrs) on GFD for at least 1 year were examined. A questionnaire was designed to assess compliance to GFD as well as awareness about CD.

Results: 128 (52%) celiacs used to eat outside everyday, but 13% of subjects admitted to be afraid of eating out and 45.8% reported having fear of the contaminations. 80% of celiacs who used to eat outside revealed their disease to the waiter. 37% of celiacs answered that all drugs are safe, 30% that drugs could contain gluten and 33%

didn't know the answer. 50% of subjects said that gluten inhalation is dangerous, 20% didn't know the answer. 54% of interviewees didn't know if homeopathic products are safe for celiacs and 30% didn't know if beauty creams and lipsticks are dangerous. 74% of celiacs answered that gluten-free foods contain less than 20 parts per million and 23% didn't answer. 13% admitted transgressions to the GFD. 89% of subjects stated they receive a better information from AIC and 67% usually use the ICA-vademecum.

Conclusion: Patients declared to be afraid of eating outside for the risk of contaminations, but many of them admitted GFD transgressions. Celiacs need more information about the safety of GFD.

PO47

INTRAPARTUM ANTIBIOTIC PROPHYLAXIS IN MOTHERS GBS-POSITIVE: EFFECTS ON NEWBORN MICROBIOTA

L. Corvaglia[1], E. Legnani[1], S. Martini[1], D. Di Gioa[2], I. Aloisio[2], M. Oss[1], B. Biavati[2], G. Faldella[1]. [1]*U.O. Neonatologia e Terapia Intensiva Neonatale, Ospedale Sant'Orsola-Malpighi, Università di Bologna, Italy;* [2]*Dipartimento di Scienze e Tecnologie Agroambientali, Area di Microbiologia, Università di Bologna, Italy*

Background and Aims: Group B *Streptococcus* (GBS) early-onset bacterial sepsis is an important cause of neonatal morbidity and mortality. In the last decade, after the introduction of intrapartum antibiotic prophylaxis in pregnant women during labor and delivery, the sepsis-associated death rates have declined. However, in current literature there are no information on the effect that the antibiotic treatment may have on the early colonization of bacteria in the newborn gut, which is known to be highly influenced by maternal microorganisms. The aim of this study is to evaluate the effects of antibiotic treatment of pregnant women GBS-positive on early colonization of bacteria in the newborn gut, which is known to be related to immunity development.

Materials and Methods: Thirty-four vaginal breastfed newborns were enrolled; 17 had mothers GBS-positive treated with 2 g of ampicillin and 17 had mothers GBS-negative (control group). Further inclusion criteria were: infants aged between 6–7 days, with a regular birth weight. Only infants born by natural delivery and breastfed were enrolled in order to reduce variability in the intestinal microbiota consequent to diet and delivery.

Two-hundred milligrams faeces were collected for each subject and processed for DNA extraction, performed with QIAamp DNA Stool Mini Kit [Qiagen, Cat. No. 51504]. To analyse the effects of the maternal antibiotic treatment against *Streptococcus* infection on the intestinal microbiota of the newborns, the quantification of the principal groups of the newborn gut microbiota was carried out. *Lactobacillus* spp., *Bidobacterium* spp., *Bacteroides fragilis* group, *C. difficile* and *E. coli* quantification was obtained with real-time PCR. Data of microbial counts were subjected to one-way variance analysis in order to evidence significant differences between treated and control group of newborns.

Results: No variation in the number of *Lactobacillus* spp., *C. difficile* and *E. coli* was observed in association to the treatment; on the contrary antibiotic therapy reduced the intestinal colonization of *Bifidobacterium*: 5.51 Log(CFU/g) in treated samples against 7.07 Log(CFU/g) in control samples ($p < 0.05$).

Conclusions: Preliminary results showed a decrease of early Bifidobacterium count in the microbiota of newborns; the clinical meaning or the effect on newborn immunity need to be investigated with larger studies.

PO48

FOCUS ON *AVENA IRINA*

M. Maglio[1], D. Ponticelli[2], M. Nanayakkara[1], C. Gianfrani[3], R. Aitoro[2], K. Ferrara[2], M. Sarno[2], L. Cuomo[2], M.V. Barone[1,2], R. Troncone[1,2]. [1]*European Laboratory for the Investigation of Food Induced Diseases (ELFID), University Federico II, Naples, Italy;* [2]*Department of Pediatrics University Federico II, Naples, Italy;* [3]*Italian National Council of Research, Institute of Food Sciences, Avellino, Italy*

Objectives: The search for cereals suitable for celiac patients is a real need both to render more acceptable the gluten-free diet and to improve its nutritional quality. Alternative cereals to be introduced into CD diet should be tested for their effects on both adaptative and innate/proliferative response. The aim of this study was to investigate the toxicity of prolamins derived from oat variety *Avena Irina* using assays to investigate both the proliferative/innate and adaptive immunity activation.

Materials and Methods: We evaluated crypt epithelial cell proliferation, in small intestinal biopsies from 4 active CD patients cultured for 24 h with medium alone or 0.5 mg/ml of a peptic-tryptic (PT) digest from *Avena Irina* or PT digest from bread wheat (*T aestivum Sagittario*), by immunofluorescence detection of BrdU incorporation. ERK2 phosphorylation was analyzed by Western blot in CaCo2 cells after 30 min stimulation with the same cereals. Finally, to study adaptive immunity activation, we detected γIFN production after stimulation with PT-digest from *Avena Irina* of specific T cell lines from 5 CD patients.

Results: PT digest from *Avena Irina* (PT-Avena Irina) did not induce significant increase of crypt epithelial cell proliferation in small intestinal biopsies after 24 h of incubation (10.3±3.9%) unlike PT gliadin (29.0±5.8%) respect to medium alone (13.47±2.4%). Oat PT digest did not induce increase of ERK2 phosphorylation in Caco2 cells after 30 min incubation; finally gliadin specific T cell lines did not produce γIFN after PT-Avena Irina stimulation.

Conclusions: All in-vitro bio-assays used to investigate proliferative/innate and adaptive immunity responses of Avena irina, show that this oat variety is not toxic for celiac mucosa. The toxicity for celiac patients of Avena irina should now be tested in vivo.

PO49

IN POTENTIAL COELIAC DISEASE PATIENTS INTESTINAL CD4+CD25+FOXP3+ REGULATORY T CELLS ARE INCREASED AND FUNCTIONALLY ACTIVE

K. Ferrara[1], S. Santagata[1], M. Cuomo[1], M. Agnese[1], M. Maglio[1], M. Borrelli[1], G. Mazzarella[2], R. Auricchio[1], E. Miele[1], M. Sarno[1], D. Ponticelli[1], R. Troncone[1], D. Zanzi[1]. [1]*Department of Pediatrics, ELFID, University Federico II, Naples, Italy;* [2]*Immunobiology, Institute of Food Science, CNR, Avellino, Italy*

Objectives and Study: Celiac disease can be seen as the result of a break of tolerance in which the immune response to dietary gliadin might be altered. Several T regulatory cells (Treg) subsets are involved in immune tolerance. These subsets include natural Treg cells expressing the Foxp3 transcription factor. We previously demonstrated an increase of the percentage of CD4+CD25+Foxp3+ cells in intestinal mucosa of untreated CD. We investigated the presence and the suppressive function of Treg cells in the intestinal mucosa of potential CD patients.

Methods: We studied by flow cytometric analysis 9 patients with untreated CD, 12 potential CD (4 Marsh 0 (M0); 8 Marsh 1 (M1)) and 9 controls. Cells were isolated from duodenal biopsies and intracytoplasmatic staining for Foxp3 was performed. By immunohistochemistry we analysed biopsies from 6 untreated CD,

10 potential CD (5 M0 and 5 M1) and 6 control patients looking for Foxp3 staining. Furthermore, we analyzed the suppressive function of Treg cells, isolated from potential CD biopsies, on autologous peripheral blood responder CD4+CD25− Tcells, in the presence of a polyclonal stimulus and with or without IL15.

Results: In potential CD the percentage of CD4+CD25+Foxp3+ cells was significantly increased if compared to control patients. Interestingly, it was significantly increased in M1 potential CD if compared to controls (mean%±SD: potential CD = 9.86±3.2; M1 = 10.91±3.1; controls = 6.5±3.1; M1 vs controls $p < 0.05$). Immunohistochemical analysis confirmed a significant increase of the density of Foxp3+ cells in the lamina propria (LP) of untreated and potential CD if compared to control patients (mean of cells/mm^2 LP: active CD = 181.0±84.8; potential CD: M0 = 19.0±4.0; M1 = 44.6±12.9; controls = 11.7±5.6. M0 vs controls: $p < 0.05$; M1 vs controls $p < 0.0001$). In vitro coculture assay, intestinal Treg cells from potential CD exerted significantly suppressive effects on T responder cells proliferation ($p < 0.05$), whereas IL15 was not able to counteract their suppressive activity.

Conclusions: In the small intestinal mucosa of potential CD, the percentage and the density of Foxp3+ Treg cells are increased if compared to control patients. These cells are functionally active as they inhibit T responder cells proliferation but their suppressive activity is not altered by IL15 on the contrary of CD patients. These data suggest that Treg might contribute to downregulate inflammation in the early stage of celiac disease and let us to hypothesize that IL15 does not exerts a fundamental role in the early stage of CD.

PO50
THE EFFICACY OF MAGNESIUM ALGINATE PLUS SIMETHICONE (GASTROTUSS) FOR THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN

C. Tolone[1], V. Pellino[1], M. Piccirillo[1], I. Belfiore[1], F. Rinaldi[1].
[1]*Department of Pediatrics, Second University of Naples, Italy*

Background: Over the last few years the use of Ranitidine and Protonic pump inhibitors (PPI) has significantly increased for the treatment of gastroesophageal reflux disease (GERD) in pediatric patients. However, these drugs have significant side effects.

The aim of our study is to evaluate whether a Magnesium Alginate plus Simethicone therapy (Gastrotuss baby) could be effective to relieve GERD symptoms without using other drugs (Ranitidine-PPI).

Method: One-hundred and ten children came to the Department of Pediatric Gastroenterology suffering from GERD-related symptoms. They were evaluated by means of an "I-GERQ-R" questionnaire adjusted for patient age. In children up to 1 year of age we investigated reflux/vomiting, inappetence, insufficient weight gain, crying, snappiness, belching, hiccup, cough, pneumonia infections, arching (hyperextension) of the torso, head rotation, cyanosisapnoea, convulsive crisis. In older children we evaluated regurgitation/vomiting, pirosis, acid regurgitation, retrosternal burning, epigastric pain, recurrent abdominal pain, dysphagia, irritability, cough, pneumonia infections, sleep disturbances, hematemesismelena. Symptoms were scored from 1 to 3 depending on severity. Thirty children underwent esophageal pH-impedance and/or upper endoscopy. The remaining were only evaluated clinically. We administered non-pharmacological treatment (food advice, elevation of the head of the bed) and a Magnesium Alginate plus Simethicone therapy (1–1.5 ml/kg/die bid or tid). The same examiner re-evaluated children after 4 and 8 weeks of therapy. Questionnaire was repeated at 8-week follow-up.

Results: Ninety-two children (50 male), median age 12 years (range 1 month to 15 years), completed the follow-up. The drug was suspended in one patient for exanthema and in another for diarrhea onset (regressing in 48–72 hours).

Patients were classified in 3 groups by comparing questionnaire scores at enrollment and after 8 weeks: Resolution = disappearance of symptoms; Improvement = $\geqslant$50% reduction; Unchanged symptoms = $\leqslant$50% reduction. Data are summarized in Table 1.

Conclusion: Magnesium Alginate plus Simethicone proved to be useful for GERD treatment with symptoms resolutions in 54% and improvement in 31% of patients. Symptoms were unchanged in 13/92 children (14%).

Table 1. Results of therapy with Magnesium Alginate plus Simethicone after 8 weeks

	Age >1 year (n = 80)	Age <1 year (n = 12)	Total
Resolution	5 (42%)	45 (56%)	50 (54%)
Improvement	3 (25%)	26 (32%)	29 (31%)
Unchanged symptoms	4 (33%)	9 (12%)	13 (14%)

PO51
ACUTE PANCREATITIS IN CHILDREN: A PEDIATRIC EXPERIENCE

C. Campagna[1], R. Bergamaschi[1], F. Bedetti[2], F. Bernardi[1]. [1]*U.O. di Pediatria d'Urgenza, Pronto Soccorso Pediatrico e Osservazione Breve Intensiva, Azienda Ospedaliero-Universitaria Policlinico S. Orsola Malpighi Bologna, Italy;* [2]*Scuola di Specializzazione in Pediatria. Università degli Studi di Bologna, Italy*

Objectives: The aim of this paper is to report our experience of acute pancreatitis in our Department of Pediatric from April 2010 to February 2012.

Material and Methods: Clinical data were extracted by medical records. Sistematic review of MEDLINE in the last three years on acute pancreatitis in children, as well as, consultation of relevant references on the texts obtained.

Results: From April 2010 to February 2012 in our Department were hospitalized five children with acute pancreatitis. They were on average 9 years old (range: 4–12 years), three males and two females.

All patients had abdominal pain at the presentation. In three of them the pain was localized in epigastrium with radiation to the back. Fever is present in three case and vomit in two case.

Three of them had an infection (one case Epstein–Barr virus, one case Influenza A virus, one case *Salmonella* Typhi). One of them had a traumatic event.

Laboratory investigation showed in all pazients elevation in serum amylase and serum lipase. In two of them we found elevation of white cell counts and C reactive protein level.

Ultrasonography showed in three cases hypoechogenicity associated in one case to peripancreatic fluid collection without morphological alterations.

One of them had a relapsing of acute pancreatitis (twice) and biliary disease with transaminase elevation (once). In this patient genetic mutation study of Cystic Fibrosis was negative.

Colangiopancreatography RM (CPRM performed in this case) showed a dilatation of ventral pancreatic duct (Wirsung) joined to common bile duct in preampollar site, as anomalous arrangement of pancreaticobiliary ductal system. Three of them restarted enteral

feeding after three days of total fasting, only one needed parenteral nutrition (for 6 days).
Three patients were treated with octreotide acetato and antibiotic therapy.
Conclusions: Acute pancreatitis in children has received growing attention in recent years, and an increase in the number of cases has been reported in several studies. There are many differences between children and adults about etiology, diagnosis and outcome. The main etiologies in children involved biliary disease, medications, idiopathic form, systemic disease and trauma, followed by infectious, metabolic and hereditary.
The clinical definition of acute pancreatitis generally accepted, consider at least two of three following criteria: (1) typical abdominal pain, (2) elevation in serum amylase and serum lipase three time more to high level of normal (even if we don't have a standardized level in children). (3) typical imaging of pancreas. Ultrasound is the most useful investigation. Computed Tomography should be performed in particular cases.
Management include intravenous hydration, pain control and specific nutrition therapy.
The pancreaticobiliary ductal system disease may be considered in different diagnosis of relapsing acute pancreatitis in children. Cholangio-pancreatography RM (CPRM) is the gold-standard in diagnostic approach in these children because less invasive and with the same diagnostic definition of endoscopic retrograde cholangio-pancreatography (ERCP).
Our patient, during the follow-up, treated with medical therapy (ursodeoxycholic acid) and then monitored through regular controls (clinic, blood tests and US) in order to consider the right timing for any possible surgical approach. All our patients had a good outcome. The early diagnosis and the appropriate handling can contribute to a better outcome in children with acute pancreatitis and to prevent the complications related to the disease.

PO52
BLOODY DIARRHEA: IT'S NOT ALWAYS INFLAMMATORY BOWEL DISEASE (IBD)!

P. Alvisi[1], A. Lambertini[1], P. Billi[2], A. Salerno[3], E. Mengozzi[4].
[1]Pediatrics Unit, [2]Gastroenterology Unit, [3]Pathology Unit, [4]Radiology Unit, Ospedale Maggiore, Bologna, Italy

The diagnosis of IBD is often difficult and many diseases, as bacterial or viral infections, may mimic Crohn's disease and Ulcerative Colitis.
Case report 1: Alessandro, Male, 13 years old. Family history: mother with rheumatoid arthritis; pathological history: fever and bloody diarrhea during from the last 3 months; weight loss of about 5%. He was hospitalized because of worsening of fever, bloody diarrhea and abdominal pain. Blood examination showed: neutrophilic leukocytosis (WB 11350/mmc, N 10060/mmc) and elevated CRP value. A colonoscopy was performed and showed deep serpiginous ulcers, expecially localized in left colon and the rectum. We suspected an IBD but waited for the results of fecal culture before starting therapy. Fecal coltures documented a group B *Salmonella* infection. Histology confirmed the diagnosis of infectious colitis. We made a long follow up and a control of colonoscopy that was normal. After this infection Alessandro has always been healthy.
Case report 2: Francesco, Male, 12 years old. Family history: no history of chronic diseases; pathological history: deep asthenia and some episodic bloody diarrhea and abdominal pain. He also suffered for constipation. Blood and stool examinations showed: deep microcitic anemia (Hb 7.5 g/dl), CRP value and blood sedimentation were normal; fecal occult blood test was positive in many samples; fecal calprotectin was positive (250 mg/g). Colonoscopy was performed and found an ulceration occuring on the anterior wall of the rectum at 6 cm from the anal verge. The histological features were fibro muscolar obliteration of lamina propria, presence of collagen infiltration of the lamina propria and distortion and hyperplasia of mucosal crypts. The histologyc pattern was typical and allowed the diagnosis of solitary rectal ulcer (SRUS) [1]. Treatment was intermittent use of laxatives, and topical therapy.
Discussion: Both pathological histories may mimic IBD. In the first case symptoms were similar to those of IBD as well as colonoscopy features; the second case had a typical endoscopic feature but above all histopathological examination is diagnostic of SRUS. The correct diagnosis of SRUS in the pediatric experience is delayed of approximately 5 to 7 years [2].
It's important for a pediatric gastroenterologist, in presence of typical signs and symptoms of IBD, to be able to exclude some simple diseases, as infections, but also rare ones, as SRUS.
Infact there are some conditions, as SRUS, usually unrecognized or misdiagnosed in pediatric age that has to be kept in mind of pediatric gastroenterologist.

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PO53
EPIDEMIOLOGICAL FACTORS AND FOOD: WHICH IS THE ROLE IN *HELICOBACTER PYLORI* RE-INFECTION IN PEDIATRIC AGE?

T. Sabbi[1]. *[1]Pediatric Unit, Belcolle Hospital Viterbo, Italy*

Background: *Helicobacter pylori* (Hp) infection has been recognized as a cause of chronic gastritis, peptic ulcer, atrophic gastritis and gastric cancer. Its acquisition is related with poor socioeconomic conditions while the relationship of nutrition and Hp is still a question.
Aim: To analyzed if socioeconomic factors and dietary contribute to Hp re-infection in pediatric age.
Patients and Methods: 150 patients (92 males; age range 5–16 years) with Hp infection treated and eradicated in the past. 55 patients with Hp re-infection and 95 patients not re-infected.
We interviewed the children with questionnaire about socioeconomics factors, hygiene, living conditions and their dietary habits.
Results: A lower frequency of fermented dairy food, fruits and vegetable consumption was registred among children with Hp re-infection as compared to not been re-infected.
Among persons with Hp re-infection were noted low socio-economic markers such as croweded living conditions, a large number of siblings and unclean water.
Conclusions: Might decrease the risk of Hp re-infection the use of probiotic, vitamin C, antioxidants contained in fruit and vegetables.
Risk factors for Hp re-infection are low socioeconomics factors, hygiene and living conditions.

PO54
NSP4 PRODUCED BY ROTAVIRUS INDUCES CHLORIDE SECRETION WITH AN OXIDATIVE DEPENDENT MECHANISM WHICH IS INHIBITED BY *LACTOBACILLUS CASEI RHAMNOSUS* STRAIN GG

V. Buccigrossi[1], M. Sofia[1], M.A. Verrone[1], R. Amatruda[1], L. Bracale[1], F. Basile[1], E. Nicastro[1], A. Guarino[1]. [1]*Department of Pediatrics, University of Naples Federico II, Naples, Italy*

Background/Aim: Rotavirus (RV) is the most severe agent of gastroenteritis and induces a sequence of enterotoxic and cytotoxic effects in enterocytes [1]. The former is linked to the presence of NSP4. The aim of this study was to investigate the mechanisms linked to the RV-induced chloride secretion, namely the oxidative stress is implicated in this effect. Because *Lactobacillus casei rhamnosus* strain GG (LGG) has been proposed as first line therapy in addition to ORS for RV diarrhea, we study the effect of LGG in our in-vitro model.

Methods: Caco-2 cell monolayers were infected with RV strain SA11 [1]. The ion transport was studied by the intensity of most circuit (Isc) in Ussing Chambers. Reactive oxygen species (ROS) and reduced (GSH)/oxidated (GSSG) glutathione ratio were assessed using respectively dichlorofluorescein (DCF) and a colorimetric assay. DCF was also used to evaluate ROS increase by fluorescence microscope. We also tested the effects by the antioxidant N-acetylcysteine (NAC) and LGG.

Results: RV induced a significant increase in intracellular ROS level (223 ± 76 vs 25 ± 19 DCF fluorescence units, $p < 0.05$) and a reduction of GSH/GSSG ratio compared to controls (4.48 vs 0.08, $p < 0.05$) with a peak within 2 hours. The addition of NAC to Caco-2 cells completely inhibited RV-induced ROS increase, GSH/HSSH unbalance ($p < 0.05$) and reduced the RV-induced chloride secretion by 68.9% ($p < 0.05$). LGG prevented the RV-induced ion secretion by 75.3% ($p < 0.05$). In addition, LGG counteracted RV-induced oxidative stress, reducing ROS increase by 42.8% and restoring GSH/GSSH ratio to the control level ($p < 0.05$). Microscopic evaluation confirmed the protective role of LGG in RV-induced oxidative stress.

Conclusions: Dehydration induced by RV is the result of NSP4-induced chloride secretion and the oxidative stress is directly implicated in the RV enterotoxic damage. LGG prevents ion secretion induced by RV counteracting the oxidative stress induced by the viral infection. These data provide a new mechanism for the high efficacy of LGG against childhood diarrhea observed in clinical trials.

Reference(s)

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PO55
SCREENING FOR NUTRITIONAL RISK IN A POPULATION OF HOSPITALIZED CHILDREN

M.I. Spagnuolo[1], I. Liguoro[1], F. Chiatto[1], B. Aceto[1], D. Mambretti[1], A. Guarino[1]. [1]*Department of Pediatrics, University Federico II, Naples, Italy*

Objectives: The risk to develop malnutrition is high in patients admitted to hospitals, especially in those with chronic diseases. Malnutrition was reported in 6 to 19% of patients hospitalized in European countries including UK, France, Germany and Neetherlands. Different from adults, there is no validated instrument to specifically evaluate the nutritional status of hospitalized children. Aim of this study was to investigate the applicability and efficacy of a new tool, the STRONGkids (Screening Tool for Risk Of Impaired Nutritional status and Growth [1]), to estimate the risk of malnutrition in hospitalized children.

Methods: A prospective observational multi-centre study was performed in 12 hospitals in Campania region (including one University hospital). Children from 1 to 18 years of age admitted for any disease in the hospitals were enrolled. The STRONGkids consists of 4 items (clinical assessment, high risk disease, nutritional intake, weight loss) and categorizes patients into three classes for malnutrition (low, moderate, high risk). The questionnaires were administered by nurses or by dieticians. Anthropometric measurements were taken. The risk score (scale 0–5) was compared with the actual nutritional status on admission expressed as BMI SD-score. SD-scores <–2 for BMI and height-for-age (HFA) were considered hallmarks of acute and chronic malnutrition, respectively. For each patient, the nutritional status was then linked to the STRONGkids score (scale 0 to5) and the data were analyzed with multiple regression analysis, taking into consideration a set of clinical factors such as age, chronic conditions and the reason for admission as variables.

Results: A total of 144 children (71 males, mean age 6.6 ± 4.6 years) were enrolled. Sixty patients were admitted in an academic hospital, while the other 84 were enrolled in regional hospitals. Overall 49/144 (34%) of the hospitalized children suffered from an underlying disease, including 30/60 (50%) admitted to the University and 19/84 (23%) in the general hospitals ($p = 0.0008$). 50/144 (35%) of children were at low risk, 73/144 (50.5%) at medium risk and 21/144 (14.5%) at high risk to develop malnutrition. Children at high risk had significantly lower SD-scores for HFA (mean SD score –1.22; $p = 0.0203$) in comparison to other groups, but the scores were not related to the incidence of acute or chronic malnutrition in the three categories of risk of the STRONGkids.

Conclusions: The STRONGkids screening tool is easy to administer. However it is highly sensitive and not specific. However its systematic use in hospitalized children may lead to the early detection of children at high nutritional risk, thereby promoting timely and effective interventions to restore their nutritional health.

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PO56
SURVEY ON THE ASSESSMENT OF VITAMIN D STATUS IN PATIENTS WITH CHRONIC GASTROENTEROLOGIC DISEASE IN EMILIA ROMAGNA GASTROENTEROLOGIC PEDIATRIC CENTERS (ERPGC)

M.R. Govoni[1], G. Turlà[2], E. Fabbri[2], C. Malaventura[1], P. Alvisi[3], A. Lambertini[3], S. Amarri[4], S. Brusa[5], R. Fornaro[6], R. Pini[7], L. Viola[7], C. Zanacca[8], G. Biasucci[9], L. D'Amato[9], S. Alessandrini[10]. [1]*Ferrara University Pediatric Gastroenterologic Unit, Italy;* [2]*Ferrara University Pediatrics Specialization School, Italy;* [3]*Bologna Maggiore Hospital Pediatric Gastroenterologic Unit, Italy;* [4]*Reggio Emilia Hospital Pediatric Gastroenterologic Unit, Italy;* [5]*Imola Hospital Pediatric Gastroenterologic Unit, Italy;* [6]*Forlì Hospital Pediatric Gastroenterologic Unit, Italy;* [7]*Rimini Hospital Pediatric Gastroenterologic Unit, Italy;* [8]*Sassuolo Hospital Pediatric Gastroenterologic Unit, Italy;* [9]*Piacenza Hospital Pediatric Gastroenterologic Unit, Italy;* [10]*San Marino Hospital Pediatric Gastroenterologic Unit, San Marino*

Aims: Vitamin D (vitD) is known for its role in calcium and phosphorus metabolism and in maintaining bone trophism. In recent

years it has been recognized to reduce the risk of chronic diseases such as autoimmune diseases, cancer, cardiovascular diseases. VitD is produced in the skin after exposure to sunlight and introduced by the diet. It is absorbed in the small intestine, incorporated in chylomicrons, and subsequently metabolized in the liver and kidney. Patients with gastrointestinal diseases are prone to develop vitD deficiency for many reasons: poor introduction, malabsorption of fat, reduced absorptive surface (post-surgical), increased permeability of the wall, impaired hepatic or biliary function. There is no agreement to date about the optimal plasma level of vitD and the most appropriate treatment in adults and children, particularly in patients with chronic gastrointestinal diseases. The aim of our study was to evaluate the diagnostic and therapeutic approach towards the vit.D status in patients with chronic gastroenterologic diseases, in the ERPGC, by sending a brief questionnaire:

Materials and Methods: We developed a questionnaire, structured into nine questions, and we sent it to the referents of ERPGC.

Do you dose vit.D in your center?	Yes	No
If not, in which center do you send the exam?		
_____		
In which patients do you check the level of vitD?		
_____		
Coeliac disease	Yes	No
Chronic inflammatory bowel diseases	Yes	No
Chronic liver diseases	Yes	No
Other: _____		
If the patient has insufficiency/deficiency of vitD, which formulation do you use?		
Trade name ____ drops __ ampoules __		
Do you obtain a dosage of vitD before prescribing it?	Yes	No
Which other exams do you perform before starting supplementation?		
Calcium Phosphorus Alkaline Phosphatase Renal function Urine calcium Urine creatinine Others		
How long do you maintain the supplementation?	___	
Which exams during the follow-up?		
_____		
When? Every 3 mo. Every 6 mo. Every 12 mo. Never		

Results: 9 of 15 Emilia Romagna (ER) canters answered. Analysis of questionnaires showed that the dosage of vitD is always performed in patients with chronic gastreonterologic disease. All centers agree in taking the supplements only with laboratory data support. The mean time of supplementation was 6 months, with exams every 6 months. Cholecalciferol and calcifediol were the most used formulations. Every center has different follow up with a different attention to the renal function.

Conclusions: Our survey shows a particular attention to the vitD status in patients at risk followed by ERPGC. We found differences in management relative to the formulation, the dosage, the time of vitD supplementation and its follow up. These data may be an interesting starting point and suggest the need of shared guidelines.

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PO57
ACTIVE SEVERE ULCERATIVE COLITIS (UC): WHICH SECOND-LINE OR RESCUE THERAPY?

D. Comito[1], A. Chiaro[1], R. Mallamace[1], S. Cardile[1], C. Romano[1].
[1]*Pediatric Department, University of Messina, Italy*

Background: Pediatric ulcerative colitis (UC) has a more severe phenotype, reflected by more extensive disease and a higher rate of acute severe exacerbations. Data suggest that the Pediatric UC Activity Index (PUCAI), determined at day 3 should be used to screen for patients likely to fail corticosteroids (>45 points), and at day 5 to dictate the introduction of second-line or rescue therapy (>65–70 points). In case series was reported the effectiveness of cyclosporine (CyA) as a salvage therapy in steroid-refractory children with UC with a pooled short-term success rate (i.e. lack of colectomy). In CyA-treated patients there was significant adverse events including nephrotoxicity, serious infections, seizures and anaphylaxis. We report the data of our experience of cyclosporine (CyA) versus infliximab (IFX) as second-line of rescue therapy.

Materials and Methods: In this retrospective and observational single study, we reviewed, from July 2005 and January 2012, the charts of 10 children (mean aged 9.3 yrs) with severe acute UC. In according to consensus for managing severe acute colitis (SAC) in children (Dan Turner, 2011), indication to start second-line of rescue therapy (IFX or CyA) was ASC not steroids iv responding at day 3–5 (Pediatric Ulcerative Colitis Activity Index PUCAI score >45 or PUCAI >65 at day 5). Group 1 (4 pts) started oral CyA at 5–8 mg/kg/day with subsequent dose adjustments based on drug levels (150–200 ng/ml). Group 2 (6 pts) started infusion with IFX iv at 5 mg/kg and next scheduled therapy (after 2 and 6 weeks for the induction).

Results: In Group 1, only in 1 pts was induced remission after 11 days of the therapy, 2 pts discontinued treatment for side effects and 1 pts underwent emergency colectomy after 3 days. In Group 2, in 5 pts, IFX has proved efficacy in short and long-term success rate (1 yr) without necessity of colectomy. 2 pts have short-term success (3 months) with subsequent relapse of disease and necessity of the colectomy. No side effects were reported after IFX therapy.

Conclusions: ASC is frequent condition in pediatric CU in comparision to adult-onset disease. In retrospective studies, 40% developed at least one severe attacks during childhood. The steroids failure rates is from 9% to 47%. Introduction of second-line therapy should ideally be based on early recognition of patients likely to fail steroids therapy. Although second-line of therapy is usually preferred in children, colectomy should always be seriously considered. In our small retrospective study, IFX is more efficacy and safe versus CyA therapy both in short and long-term success. Randomized comparision between CyA, IFX and tacrolimus must be started.

PO58
PULMONARY INVOLVEMENT OF CROHN'S DISEASE: A CASE REPORT

A. Chiaro[1], S. Riva[2], M. Sciveres[2], I. Loddo[1], C. Romano[1].
[1]*Pediatric Department, University of Messina, Messina, Italy;*
[2]*Ismett Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione, Palermo, Italy*

Background: Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) often presenting with extra-intestinal manifestations (EIM) that may include rheumatologic, ocular, dermatologic, biliary and pulmonary involvements. The most common pulmonary manifestations of IBD are drug-induced lung disease. Other manifestations include parenchymal disease, pleuritis and overlap syndromes. Pulmonary localization of CD is quite rare.
Case report: An 18-year-old girl was diagnosed with ileo-cecal CD at 10 years of age. After 1 year, was performed ileal and colonic resection for stenosis and post-operative relapse of CD was treated with steroids and biological therapy. At the age of 18 years, onset a symptomatology characterized by persistent fever with non-productive cough without gastrointestinal symptoms (CDAI <100). Fever was persistent for 3 months. Infections were excluded. CT scan of the chest showed multiple pulmonary nodules. Ultrasound-guided fine-needle aspiration biopsy of pulmonary nodule was preformed and histologic examination showed the presence of noncaseating granulomatous inflammation with multinucleated giant cells. She started corticosteroid therapy with benefits. Control CT-scan of the chest was performed 3 months later showing almost complete regression of pulmonary nodules.
Conclusions: The lung involvement of IBD is considered to be a rare extraintestinal manifestations. The true prevalence seems to be much higher due to a subclinical course. The most clinical reported manifestations was cryptogenic organizing pneumonia (COP), known as bronchiolitis obliterans, with organizing pneumonia (BOOP). Only Gill and Mahadevan (2002) described 1 adult case with CD and pulmonary noncaseating granuloma which have resolved after infliximab therapy. In conclusion, we report a second unusual case of diagnosed pulmonary CD in young adult.
Disclosure of Interest: None Declared

PO59
IDIOPATHIC PANCREATITIS IN INFLAMMATORY BOWEL DISEASE: CAUSATIVE OR PATHOGENETIC RELATIONSHIP?

S. Cardile[1], D. Comito[1], A. Chiaro[1], R. Mallamace[1], C. Romano[1].
[1]*Pediatric Department, University of Messina, Italy*

Background: In IBD patients there are a increased risk for developing both acute and chronic pancreatitis (AP and CP) and recently there is indication about a rarer variant as autoimmune pancreatitis. Most of studies suggest that pancreatitis can related to course of IBD and could be mainly a silent disease. In most cases pancreatitis associated with IBD can be caused by drugs, biliary lithiasis or duodenal involvement. There are only few reports, mainly in adults, about demographic, clinical, laboratory data and natural history of idiopathic AP (IAP) in children with IBD. In many cases has been reported that IAP precedes the appearance of IBD and it is more frequent in colonic Crohn's Disease (CD).
Patients and Methods: We retrospectively identified all patients with IBD in whom AP was diagnosed. Data was collected from January 2001 to December 2011 in 93 children (age 6–16 years) with IBD (n. 36 with Ulcerative Colitis, CU, n. 57 with CD). The diagnosis of IBD was done on the basis of the endoscopic and histological criteria. AP was diagnosed by the occurrence of at least 2 of the following findings: acute onset epigastric pain, elevated serum amylase and/or lipase >3 times the upper level of normal and characteristic radiological changes.
Results: We identified 8 patients (8%, mean age: 8 yrs) with diagnosis of AP (5 with CD and 3 with CU). In only 1 case, the diagnosis of AP preceded the diagnosis of IBD. Epigastric pain was the dominant clinical characteristic in 7 pts (87%), vomiting in 4 pts (50%). The mean serum amylase level was 800.8±111 (median 798) and mean lipase blood level was found to be 918 (median 821). Median time between onset of first episode of AP in relation to onset of IBD was variable (1–3 yrs). All the patients underwent imaging with ultrasound scan, 3 of the 8 (37%) pts also at computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) scans. An enlarged of the head of pancreas was found in only 3 pts (37%) and no patients has been documented anatomic alterations of biliary and pancreatic duct. In only one (12%) patient, AP was diagnosed after start therapy with AZA. The course was benign in every patients without complications (infected pancreatic necrosis). In all patients, the episode of AP was isolated, except in 1 pts that presented 2 episodes.
Conclusions: Our study, retrospective and with a small group of patients, is the first to investigate incidence of IAP in pediatric IBD. This condition has distinctive pattern from secondary (drugs, hepatobiliary) pancreatitis. In contrast to adults, IAP is more frequent in colonic CD. The clinical course is mild not correlated with IBD activity, the symptoms resolve without complications. In our study IAP is associated with young age. We believe that there is autoimmune connection between IB and IAP also if specific attention be paid to other susceptibility factors as familiy history and sierological markers.
Disclosure of Interest: None Declared

PO60
CLINICAL EVALUATION OF CHILDREN AND ADOLESCENTS WITH GASTRO-ESOPHAGEAL REFLUX DISEASE: IS THERE A RELATIONSHIP BETWEEN SYMPTOMS AND ESOPHAGEAL MUCOSAL BREAKS?

P. Quitadamo[1], E. Sciorio[1], V. Mancusi[1], F. de Seta[1], G. Bruscino[1], A. Staiano[1]. [1]*Department of Pediatrics, University of Naples "Federico II", Italy*

Aims: Currently, no questionnaire for the pediatric assessment of symptoms suggestive of gastro-esophageal reflux disease (GERD), compared with the esophageal mucosal lesions, has been validated for children aged between 8 and 17 years of age. The aims of the study were to develop and validate a questionnaire to evaluate children with symptoms suggestive of GERD and to assess the relationship between the symptomatic score and the histological esophagitis score.
Methods: Children aged between 8 and 17 years who underwent endoscopy with multiple esophageal biopsies because of symptoms suggestive of GERD, such as regurgitation, vomiting, weight loss, ruminative behavior, heartburn or chest pain, hematemesis, dysphagia, odynophagia, wheezing, stridor, cough and hoarseness, were enrolled from January 2012 to May 2012. Each enrolled child was asked to complete a questionnaire investigating the presence, frequency and severity of the main symptoms of GERD during the previous 60 days. A total symptomatic score, resulting as the sum of frequency per severity of each investigated symptom, was calculated for each children (maximum possible value: 54). Esophageal biopsies were analyzed and scored according to the Yerian-Fiocca classification from 0 (normal mucosa) to 4 (severe esophagitis). Symptomatic scores and histological esophagitis scores were then analyzed and a possible relationship was searched.

Results: Thirty children (14 boys and 16 girls) fulfilled the criteria for enrollment and were included in the study. The mean age of the study population was 122.8 months (range 84–180). The mean reflux symptomatic score was 11.93 (range 4–21). The mean esophagitis score was 0.86 (range 0–4). A positive association between symptomatic score and esophagitis score was found, although not significant (p: 0.658).
Conclusions: According to our preliminary data, there is a directly proportional relationship between hystological and symptomatic scores of esophagitis. More data are needed to establish the strenght of this relationship.

PO61
CLOSTRIDIUM DIFFICILE AND INFLAMMATORY BOWEL DISEASE: DATA FROM A PROSPECTIVE, COMPARATIVE, MULTICENTER, EUROPEAN PAEDIATRIC STUDY

M. Martinelli[1], F.P. Giugliano[1], F. Javier Martin Carpi[2], S. Cucchiara[3], A. Levine[4], A. Mocic[5], A. Paerregard[6], D. Turner[7], G. Veres[8], A. Staiano[1], on behalf of Porto Group. *[1]Department of Paediatrics, University of Naples "Federico II", Italy; [2]Department of Paediatric Gastroenterology, Hepatology and Nutrition, Hospital San Joan De Deu, Barcelona, Spain; [3]Department of Paediatrics, University of Rome "La Sapienza", Italy; [4]Wolfson Medical Center, Tel Aviv University; Israel; [5]Clinical Hospital Center "Sister of mercy", Zagreb, Croatia; [6]Department of Paediatrics, Hvidovre Hospital, Denmark; [7]Shaare Zedek Medical Center, The Hebrew University of Jerusalem, Israel; [8]Semmelweis University, Budapest, Hungary*

Aims: Recent changes in the epidemiology of *Clostridium difficile* (Cl.d) infection include the identification of patients with inflammatory bowel disease (IBD) as a group at risk in comparison to the general population. Cl.d seems to associate with the disease course of IBD in several ways, including triggering disease flares, sustaining activity, and in some cases, acting as an "innocent" bystander. The aims of this study were to determine the occurrence of Cl.d in paediatric quiescent and active IBD patients and to compare these findings with children with coeliac disease.
Methods: In this prospective, comparative, multicenter study, paediatric IBD patients with quiescent or active disease were tested for the presence of Cl.d toxins A and B in their stools from October 2010 to October 2011. During the same study period, stool specimens for Cl.d toxins analysis were collected from a group of coeliac children. Demographic information, diagnosis, disease location, symptoms, disease activity, recent hospitalization, IBD therapy, antibiotic and PPI exposures were also recorded.
Results: 292 patients were enrolled, of whom 191 affected by IBD (Ulcerative Colitis: 85; Crohn's Disease: 106; Mean age: 13.08±3.2 years; range 2 to 18 years) and 101 by Coeliac disease (Mean age: 11.1±4.9 years; range 2 to 18 years). Cl.d was detected significantly more often in patients affected by IBD compared with coeliac patients (14/191 (7.3%) vs 1/100 (1%); $p = 0.02$; OR=7.91; 95% confidence interval 1.02 to 61). We did not identify a specific type of IBD predisposing to CD infection ($p = 0.3$). The presence of Cl.d toxins was associated with active disease in 9 out of 14 (64.2%) IBD patients ($p = 0.08$). In particular, Cl.d infection was found in 11.7% of all IBD patients in relapse (9/77). Five IBD patients (35.8%) with positive Cl.d toxins were totally asymptomatic. Antibiotics, PPI and IBD therapies did not predispose patients to Cl.d infection ($p = 0.5$; $p = 1$; $p = 0.4$). Previous hospitalizations were registered significantly more frequently in IBD patients without Cl.d infection than in IBD patients with Cl.d infection ($p = 0.05$).
Conclusions: Our findings confirm that paediatric IBD is associated with an increased Cl.d detection. The infection was mainly community acquired. Although the presence of Cl.d toxins in the stools often correlated with an active disease, confirming the importance of testing Cl.d during IBD flares, we found a considerable number of IBD patients showing an asymptomatic carriage. The role of Cl.d carriage in subsequent Cl.d associated disease or in IBD relapse needs to be further elucidated.

PO62
ESOPHAGEAL MOTILITY ABNORMALITIES IN CHILDREN WITH SECONDARY ESOPHAGEAL DISORDERS

R. Turco[1], R. Buonavolontà[1], M. Russo[1], F. de Seta[1], M. Andreozzi[1], E. Miele[1], A. Staiano[1]. *[1]Department of Pediatrics, University "Federico II", Naples, Italy*

Aims: Esophageal high-resolution manometry (EHRM) provides advantages over conventional techniques for the assessment of oesophageal function. To evaluate the esophageal motility in neurologically impaired children (NIC) and in children treated for esophageal atresia (EA) in order to assess the applicability and clinical utility of EHRM.
Methods: Thirty-eight pediatric patients (mean age + SD: 92.3 + 40.2 months, range 8–215 months; M/F: 25/13) underwent unsedated EHRM. They were divided in three groups: group A included 10 patients with EA; group B included 14 NIC affected by severe (Intelligent Quotient $\leqslant$35) psychomotor retardation; and group C included 14 children without esophageal or bowel disorders, matched for age and sex. One 22-channel customized water-perfused silicone catheter was used. Pressure data were acquired and displayed using software especially designed for EHRM.
Results: In our study the most common esophageal motility abnormalities were failed esophageal peristalsis in group A and simultaneous esophageal activity with a low amplitude of the esophageal contractions in group B. No significant differences among the groups were observed for basal LES pressure, esophago-gastric junction relaxation and pressurization front velocity. Distal contractile integral (DCI) and DCI adjusted for esophageal length (DCIa) were significantly lower in group A and in group B compared to the control group ($p < 0.01$ for all comparisons).
Conclusion: This study confirms the applicability of EHRM both in NIC and in EA patients. In addition we showed that DCIa represents a valid parameter to measure the differences in the contractile activity of the distal esophagus in children with normal and abnormal motility.

PO63
NATURAL HISTORY OF CELIAC DISEASE IN A LARGE COHORT OF 419 PROSPECTIVELY ENROLLED TYPE ONE DIABETES CHILDREN: A SINGLE CENTRE EXPERIENCE

S. Castellaneta[1], E. Piccinno[2], E. Frezza[2], M. Oliva[3], C. Fontana[3], T. Capriari[3], F. Indrio[3], L. Cavallo[3], R. Francavilla[3]. *[1]Clinica Pediatrica, Ospedale San Paolo, Bari, Italy; [2]Endocrinologia Pediatrica, Giovanni XXIII, Bari, Italy; [3]Dipartimento Interdisciplinare di Medicina, Università di Bari, Italy*

Background and Aim: The aim of the present study is to describe the natural history of Celiac disease (CD) in a large cohort of diabetic children (T1DM) consecutively enrolled in a tertiary referral centre to: (a) establish the prevalence of CD; (b) investigate the prevalence and extent of spontaneous normalization of TTG antibody levels in a diabetic pediatric population.
Materials and Methods: All T1DM children referred from 2002 and 2011 were prospectively screened for CD. Demographic

and clinical data were recorded. All underwent the following serological determinations at the onset of T1DM and every 6–12 months: anti-TTG-IgA antibody, anti-endomisial antibody and total serum IgA; HLA class II antigens; haemoglobin A1c (HbA1c) concentration; nutritional parameters (cholesterol, triglycerides, iron, ferritin, haemoglobin). Celiac disease was diagnosed according to the ESPGHAN criteria. In order to compare the clinical and laboratory data of diabetic children with and without CD a group of children with T1DM without CD was frequency matched for sex, age (±1 year), and T1DM duration (±1 year). The data presented for the groups with serological/histological evidence of CD was that of the time of first appearance of CD serology (anti-TTGA and EmA).

Results: 419 children (F: 44%) were diagnosed in the study period. During follow-up, 58 children (13%) had a positive serological evidence of CD: 31 (56%) were symptomatic and diagnosed as CD and started a gluten free diet; 37 (46%) were asymptomatic and entered a follow-up while on a gluten containing diet with progressive decline/negativity of serological titres for CD. 15 children (26%) normalized CD serology and three became subsequently positive. Two children had a diagnosis of CD before that of T1DM. Overall, the prevalence of CD in T1DM is 7.8% (95%CI: 5.2–10.3) while the prevalence of positive CD autoimmunity is 14.3% (95%CI: 10.8–17.5); therefore children with T1DM have a 7 times higher risk of having CD as compared to healthy children (OR: 7.2; CI 95%: 4.4–11.8). Female gender is at higher risk for developing CD ($p < 0.03$) and children born by caesarean section developed biopsy proven CD at a younger age as compared to those who were born by vaginal delivery (3.7±3.2 vs. 7.1±3.5; $p < 0.01$). The age at first anti-TTGA positivity was significantly lower in children who had developed CD as compared to those who became negative (5.5±3.7 vs. 8.6±3.6; $p < 0.006$).

Conclusion: Our study in a large cohort of children with T1DM confirms that the prevalence of CD is significantly higher than expected in the general paediatric population and that the prevalence of positive CD autoimmunity doubles the prevalence of the disease. Females are at higher risk of developing CD and those born from caesarean section have a higher risk of CD diagnosis at younger age.

PO64

COMPARATIVE STUDY OF *HELICOBACTER PYLORI* ERADICATION RATES WITH 10-DAY QUADRUPLE "CONCOMITANT" THERAPY AND SEQUENTIAL THERAPY IN CHILDREN

C. Fontana[1], F. Indrio[1], L. Mastrototaro[1], S. Castellaneta[2], T. Capriari[1], L. Cavallo[1], R. Francavilla[1]. *[1]Dipartimento interdisciplinare di Medicina, Università di Bari, Italy; [2]Clinica Pediatrica, Ospedale San Paolo, Bari, Italy*

Background and Aim: The currently recommended first-line eradication treatment of *Helicobacter pylori* (HP) in children is usually successful in about 75%. Recently, a novel 10-day sequential treatment (omeprazole plus amoxicillin for 5 days, followed by omeprazole plus clarithromycin plus tinidazole for another 5 days) has achieved an eradication rate of 90% in children although it has been criticized for the difficult scheme and a simpler strategy has been proposed (concomitant: omeprazole plus amoxicillin plus clarithromycin plus tinidazole for 10 days) with high success rate in adults. The aim of the study was to assess the HP eradication rate of the concomitant compared to sequential treatment in children.

Materials and Methods: Eighty-five consecutive children with HP infection were randomized to receive either concomitant [n: 44; median age: 10.8 years (4.5–16 years)] or sequential therapy [n: 41; median age: 9.8 years (4.8–16 years)]. HP infection was based on 2 out of 3 positive tests results: ^{13}C-urea breath test, rapid urease test, and histology. Side effects and compliance were assessed during treatment. Eradication was assessed by ^{13}C-urea breath test 8 weeks after therapy. All children completed the Gastrointestinal Symptom Rating Scale (GSRS) at entry, during and after treatment.

Results: HP eradication was achieved in 40 children receiving sequential treatment (91%; 95% confidence interval: 87.1–98.5) and 35 children receiving concomitant treatment (85%; 95% confidence interval: 81.5–93.1) (P = NS). Compliance with therapy was good (>95%) in all. Overall, GSRS score were similar in both groups during and at the end of treatment (P = NS); however, children treated with concomitant treatment complained more often abdominal pain (18% vs. 42%; difference: –24%; $P < 0.03$). Concomitant treatment doubles the costs of antibiotic treatment as compared to sequential regimen.

Conclusion: Our study shows that concomitant is not superior to sequential treatment that provides the best eradication rates, optimal compliance with the lowest risk of antibiotic associated side effects and costs.

PO65

ROLE OF PARIS CLASSIFICATION AND OF THE PCDAI (PEDIATRIC CROHN'S DISEASE ACTIVITY INDEX) AT DIAGNOSIS AND FOR THE PROGNOSIS OF CHILDHOOD ONSET CROHN'S DISEASE

L. Garassino[2], M. Baldi[1], P.L. Calvo[1], M. Surace[1], D. Dell'Olio, C. Barbera[2]. *[1]Dipartimento Scienze Pediatriche Università OIRM Torino, Italy; [2]Università di Torino, Italy*

Specific objectives: Childhood onset Crohn's disease (CD) is a polymorphic entity with regard to predisposing factors, clinical presentation, course and response to treatment. The aim of this work was to analyze the diagnostic and predictive effectiveness of PCDAI in relation to the Paris classification (PC), the most recently introduced instrument for the evaluation of pediatric CD.

Materials and Methods: After the analysis of clinical data of 55 CD patients, referred to our service in the years 1991–2011, a database was created. Of each patient PCDAI was determined at onset and the disease phenotype described according to PC. The two parameters have been subsequently each other correlated.

Results: In our series the average PCDAI at diagnosis was 31.4 (range 7.5 to 50), regardless of age of the patients. Stratification of our patients according to PC some observations emerged: patients aged between 10 and 17 years have a more pronounced inflammatory situation, indicated by the alteration of the median values of ESR, albumin and haematocrit values and confirmed by significantly increased acute phase proteins. Stratifying patients according to the location of the lesions according to the PC, it was possible to note a prevalence of colic ones, while in patients with ileo-caecal localization a significantly higher age at diagnosis. The inflammatory situation, is more marked in colic locations, where they also had higher values of gamma-GT, as consistent with the known association between IBD and the localization of colonic autoimmune liver disease (sclerosing cholangitis). Dividing the patients for disease prevalent forms of behavior is not complicated. Considering the evolution of the MC one, two and five years after diagnosis, in one third of cases the disease activity may become extinct within the first year of therapy and the PCDAI is reduced in line with this trend. At one year follow up 73% of patients still have persistent symptoms and this condition is associated with younger age at diagnosis and less weight recovery. Even the classification of Paris captures this phenomenon, since a greater number of patients with persistent MC belongs to the group of age <10 years.

Conclusions: In conclusion we can argue that the properties of the PCDAI are sufficient to support its use in the clinical application and research, since they provide a uniform standard approach to the patient by different operators and by the same operator at different times. PCDAI and Classification of Paris were not directly related to each other but the same elements essential to the calculation of the PCDAI are distributed differently according to the classification of Paris. This proves therefore useful to integrate the PCDAI in the description of the disease in individual patients MC, as it allows to identify subpopulations with different phenotype.

PO66
PROBIOTIC SUPPLEMENTATION FOR PREVENTION OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN THE FIRST MONTH OF LIFE: AN ITALIAN MULTICENTRIC STUDY

F. Indrio[1], G. Riezzo[2], A. Di Mauro[1], E. Civardi[3], F. Garofoli[3], A.C. Intini[4], V. Vitacco[4], L. Corvaglia[5], E. Mariani[5], P. Guerrini[6], E. Ballardini[6], U. Corapi[7], M. Bisceglia[7], M. Cinguetti[8], A. Grezzani[8], G. Ricciardi[9], A. Loscalzo[9], A. del Vecchio[10], R. Francavilla[1]. *[1]Department of Pediatrics, University of Bari, Bari, Italy; [2]Lab of Experimental Pathophysiology, IRCCS, Castellana Grotte, Italy; [3]Neonatal Unit and Neonatal Intensive Care Unit, IRCCS, Policlinico San Matteo, Pavia, Italy; [4]Neonatal Unit and Neonatal Intensive Care Unit, Hospital SS. Annunziata, Taranto, Italy; [5]Neonatal Unit and Neonatal Intensive Care Unit, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [6]Neonatal Unit and Neonatal Intensive Care Unit, S. Anna Hospital, Ferrara, Italy; [7]Neonatal Intensive Care Unit, Crotone Hospital, Crotone, Italy; [8]Department of Pediatrics, Fracastoro Hospital, San Bonifacio (VR), Italy; [9]Department of Pediatrics, ICP, Sesto S. Giovanni Hospital, Sesto S. Giovanni (MI), Italy; [10]Neonatal Unit and Neonatal Intensive Care Unit, Di Venere Hospital, Bari, Italy*

Aims: Colic, regurgitation and constipation are common feeding problems in infants. The onset of these disturbances in the neonatal period not only required a over load work for pediatrician but also could act as an early traumatic experience that might influence the onset of gastrointestinal tract disturbances late in life. In animal models the role of microbiota has been demonstrated to be crucial for the adaptation to environmental stresses but is not been studied in infant. The aim of this prospective study was to evaluate the effects of probiotic supplementation in reducing the onset of these "minor" gastrointestinal disorders.
Methods: A double-blind placebo controlled multicentre study was performed among 8 Pediatric and Neonatology Centre over Italy. Both formula fed-infants and breast fed-infants a term were enrolled in the study at the 3rd day of life from October 2010 to December 2011. The infants were randomly assigned in a double-blind manner to receive either *L. reuteri* at dose of 1×10^8CFU a day (5 drops of an oil suspension) or placebo for 30 days. Parents were given a structured diary to record daily episodes of colic, regurgitation and number of stools.
Results: Demographic characteristic of the infants were similar. Of the 589 infants enrolled, 468 completed the study. The newborns receiving probiotics had a significant decrease in mean of minute of crying time per day (45.07 ± 12.34 vs 96.36 ± 34.67 $p<0.01$) and a larger number of stools per day compared to the placebo group (4.01 ± 1.1 days vs 2.8 ± 0.6 $p<0.01$). The number of regurgitation per day did not show any statistical significance between the two groups of infants at one month of follow up. No infant showed any adverse effect related to the trial.
Conclusions: These findings show that supplementation with *L. reuteri* DSM 17938 reduce the onset of colic and constipation in the first month of life. This could represent a new therapeutical strategy for preventing these potential harmful condition

PO67
PEDIATRIC SEDATION IN GASTROINTESTINAL ENDOSCOPY: OUR EXPERIENCE

R. Gallo[1], N. Dodaro[2], A. Paternostro[1]. *1. Department of Anesthesiology, Cosenza Hospital, Italy; 2. Department of Pediatrics and Pediatric Intensive Care, Cosenza Hospital, Italy*

Objective: The aim of the study was to assess the safest and most effective way to provide procedural sedation (PS) in children undergoing gastrointestinal endoscopy (GIE).
Methods: "Endoscopy" was combined with "conscious sedation". All pediatric patients (165) were included in this retrospective study (2008–2011):
Group A (16 patients 0–10 kg) midazolam 0.3–0.6 mg/kg was used;
Group B (54 patients 10–20 kg) midazolam 0.1–0.3 mg/kg and propofol 1 mg/kg was used;
Group C (95 patients >20 kg) midazolam 0.1 mg/kg and propofol 1–2 mg/kg was used.
In all three groups no atropine was used, moreover the drug dosage was adequately titrated by slow and repeated supplies in order to obtain the wanted sedation level.
Results: All three groups A, B, C showed high comfort level, endoscopist satisfaction, recovery time was significantly short, all of the three regimens were safe and effective.
Conclusions: Our data suggest that a synergic sedation, with Midazolam and Propofol in children over 10 kg or just Midazolam in children below 10 kg, in GIE was a suitable and safe sedation.

PO68
FOCAL NODULAR HYPERPLASIA OF THE LIVER IN CHILDREN SHOULD SUGGEST AN ENDOCRINE ILLNESS

A. Manna[1], M. Tufano[1], D. Liccardo[1], E. Mozzillo[1], A. Franzese[1], R. Iorio[1]. *[1]Department of Paediatrics, Federico II University, Naples, Italy*

Background: Focal nodular hyperplasia (FNH) is the second most common benign liver tumour after liver haemangiomas and it is most often found in females between the ages of 30 and 50 under oral contraceptives. In children, FNH represents 2% of the primary tumors of the liver.
Case Report: A 12-year-old girl with a previous ultrasonographic diagnosis of hepatic steatosis was admitted for evaluation of right abdominal pain. Physical examination showed obesity, hirsutism and acne in absence of clinical signs of liver disease. Menarche occurred at the age of 9 years and her cycles were irregular for oligomenorrhea and menorrhagia. She was not under treatment with oral contraceptives. Liver function tests were within the normal ranges. Abdominal ultrasonography showed a hypoechoic, $30\times24\times28$ mm, well-defined mass in V segment of the liver with a central scar. Abdominal contrast magnetic resonance and ultrasonography imaging confirmed the diagnosis of FNH. Alpha-fetoprotein, carcinoembryonic antigen, Ca-19–9 and Ca-125 were negative. A brain CT-scan and an electroencephalography did not show abnormal findings. Thyroid profile and sexual hormones were in the range of normality. Pelvic ultrasonography showed ovaries with sizes at the high range of normality in the absence of cysts. Due to an episode of hypoglycaemia (glucose: 45 mg/dl) which occurred two hours after dinner, she performed a metabolic screening

(negative) and evaluation of serum levels of GH (0.09 ng/ml, normal), insulin (37.8 μU/ml, high), and cortisol (47 ng/ml, low). Oral glucose tolerance test indicated a normal tolerance to glucose with hyperinsulinism. 17-OHP values after ACTH stimulation test suggested a status of carrier of heterozygous mutation of 21-hydroxylase deficiency (late onset form).

Conclusions: Although in the described patient a definite causal relationship between heterozygous carrier state for 21-hydroxylase deficiency (late onset form), hyperinsulinism and FNH was not clearly documented, our case report suggests that in children with diagnosis of FNH is desirable to investigate for an endocrine disorder. This recommendation is further supported not only by the well known association of FNH with long-term use of oral contraceptives, but also in some cases with diabetes mellitus.

PO69
SUCCESSFUL SHORT-TERM TREATMENT OF GIANT CELL HEPATITIS WITH AUTOIMMUNE HEMOLYTIC ANEMIA

S. Gatti[1], V. Romagnoli[1], C. Proietti Pannunzi[1], M. Grilli[1], V. Albano[1], G. Maggiore[2], C. Catassi[1]. *[1]Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy; [2]Department of Pediatrics, Università di Pisa, Pisa, Italy*

Background: Giant cell hepatitis (GCH) is a histological finding in infants with neonatal cholestasis that can be rarely seen after this period. Autoimmune hemolytic anemia (AIHA) is characterized by massive and acute red blood cell destruction due to antibody production, and favorably responds to corticosteroid therapy. The combination of GCH and AIHA is a rare distinct entity that carries poor response to immunosuppressive therapy and often progresses to fatal liver disease. The etiology of GCH-AIHA is unknown and no direct evidence exists for an autoimmune pathogenesis.

Case Presentation: A 10-month-old girl was referred to our department with severe anemia (hemoglobin 4.3 g/dL, mean blood cell volume 88 fL, reticulocytes 10.4%), jaundice (total bilirubin 4.2 mg/dL, conjugated bilirubin 3.63 mg/dL), hypertransaminasemia (ALT 2375 U/L, AST 2944 U/L) and liver enlargement. Laboratory investigations excluded all known causes of liver disease and showed positive Coomb's test result, so AIHA was diagnosed. A liver biopsy showed a mild inflammatory infiltrate in the lobules with activation of Kupffer cells and scattered foci of giant cell transformation with mild fibrosis, while liver stiffness measurement by FibroScan showed intense fibrosis (F4). Initial treatment consisted of erythrocytes transfusions and steroids administrations only (prednisone, 2 mg/kg orally per day). Due to lack of response, azathioprine 2 mg/kg was added to the steroid regimen. The AIHA improved, but the hepatitis was refractory to this conventional immunosuppressive regimen, so cyclosporine (5–8 mg/kg orally per day) was added with progressive and marked decrease of liver function tests. After 6 months of treatment she has mild hypertransaminasemia (AST: 64 U/l; ALT: 160 U/l, normal levels of bilirubin, albumin and PT) and liver stiffness re-evaluation showed mild hepatic fibrosis.

Conclusions: The association of AIHA with GCH is an uncommon condition that can be life threatening. Most patients initially respond to immunosuppressive agents, but the disease has shown a chronic and aggressive course. In this case the AIHA responded to steroid and immunosuppressive therapy, however liver disease required the addition of cyclosporine.

PO70
PRIMARY PROPHYLAXIS OF ESOPHAGEAL VARICES IN CHILDREN WITH PORTAL HYPERTENSION: PRELIMINARY DATA OF A RETROSPECTIVE ITALIAN MULTICENTER STUDY

F. Ferrari[1], S. Mallardo[1], S. Oliva[1], G. Di Nardo[1], P. Rossi[1], R. Iorio[2], S. Arrigo[3], P. Gandullia[3], A. Barabino[3], C. Romano[4], S. Cucchiara[1]. *[1]Pediatric Gastroenterology Endoscopy and Liver Unit, "Sapienza" University of Rome, Italy; [2]Department of Pediatrics, University of Naples "Federico II", Italy; [3]Gastroenterology and Endoscopy Unit, G. Gaslini Institute for Children, Genoa, Italy; [4]Pediatric Department, University of Messina, Italy*

Background: Portal hypertension (PH) can be caused by many diseases. Variceal hemorrhage can be the first symptom of PH. Management of PH differs among pediatricians, because there are few data about primary prophylaxis of children at risk of variceal hemorrhage.

Patients and Methods: This retrospective trial was conducted, actually, in two hospitals (Policlinico Umberto I of Rome and University of Naples Federico II). Consecutive patients (pts) with PH referred between 1996–2011 to any of the two hospitals were considered. A full clinical history, physical examination, electrocardiogram, laboratory tests and abdominal ultrasound scan with measure of spleen length were recorded. It was also recorded if pts received medical therapy with propranolol. Esophagogastroduodenoscopy (EGDS) was performed in all pts within one year from the diagnosis of PH under general anesthesia. The varices were graded based on the endoscopic criteria developed by the Japanese Research Society for Portal Hypertension. F2 (moderately enlarged, beady) and F3 (markedly enlarged, nodular, or tumor shaped) varices with red color signs (RCS) were prophylactically treated with endoscopic variceal ligation (EVL) or endoscopic variceal sclerotherapy (EVS) according to the skill of the endoscopic unit. After eradication, clinical and endoscopic control was performed at 3, 6 and 12 to monitor any complications and variceal recurrence.

Results: Data of 20 pts (8 males; median age 12 years, range 1–23) with PH and esophageal varices, detected on routine EGDS, were retrospectively analyzed. The causes of PH were: biliary atresia in 6 pts; portal cavernoma in 7; primary sclerosing cholangitis in 5; and the cause was unknown in 2 pts. In 17/20 children there was thrombocytopenia. All pts presented splenomegaly at ultrasound scan. Propanolol was admistered in 10 of the 20 pts. The dosage was variable according to patient. Among 20 pts with esophageal varices: 7 had F1 varices; 10 had F2 varices and 3 had F3 varices (6 had RCS). In 13/20 pts esophageal varices were prophylactically treated: in 6 pts EVL was performed and sessions of ligation were repeated every 4 weeks until the complete eradication; 4 pts underwent to EVS; only 3 pts required combined EVL and EVS procedures to achieve emergency hemostasis for active bleeding. Variceal eradication was achieved in 8 (61%) of the 13 pts treated: 5 of these (62%) underwent to EVL (mean of sessions 7.5); instead EIS was performed in 3 (37%) of 8 pts. In 4 pts having undergone EIS, there was a variceal recurrence. Median follow-up period was 38 months.

Conclusions: Our preliminary data show that children with PH, especially associated with splenomegaly and thrombocytopenia, should be screened for varices. Primary prophylaxis with EVL can be considered in pts with F2 and F3 varices with RCS. In our study, EVL is well tolerated with a low subsequent bleeding rate and no reports of major complications. Prospective multicenter trials are needed to identify children at high risk of variceal bleeding, to describe the

effect of propanol and its appropriate dosing and to define the best prophylactic endoscopic treatment.

PO71
A SYSTEMATIC REVIEW OF PEDIATRIC NAFLD THERAPY: YEAR 2012

I. De Micco[1], R. D'Aniello[2], M. Sangermano[2], C. Mandato[1], G. Paolella[2], S. Lenta[1], P. Vajro[2,3]. *[1]Department of Pediatrics, University of Naples "Federico II" and [2]Chair of Pediatrics, University of Salerno, [3]ELFID-European Laboratory for Food Induced Diseases, Naples, Italy*

Background: The epidemics of overweight and obesity in pediatric population has reached worldwide proportion over the last two decades. Nowadays Non Alcoholic Fatty Liver Disease (NAFLD) has become the most common cause of chronic liver disease also in children and adolescents. The disease includes a spectrum of clinical and histological conditions, ranging from simple steatosis, to nonalcoholic steatohepatitis, cirrhosis and liver failure. Early diagnosis and appropriate therapy is therefore essential to prevent its evolution. We conducted a systematic review to define most recent treatment options of pediatric NAFLD for the correction of etiopathogenetic mechanisms (e.g., insulin resistance, oxidative stress, intestinal microbiota).

Methods: Literature search was conducted using PubMed with the following keywords: NAFLD, NASH, fatty liver, treatment AND/OR therapy, weight loss, lifestyle intervention, antioxidant AND/OR vitamin E, metformin, thiazolidinediones, probiotics, ursodeoxycolic acid, omega-3-fatty acids AND/OR docosahexaenoic acid, incretin mimetics and dipeptidyl peptidase-4 (DPP-4) inhibitors AND/OR sitagliptin, pentoxifylline, farnesoid X receptor agonist, toll like receptors modifiers, statins and fibrates, angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers, bariatric surgery, adults, children, animal model.

Results: Our analysis showed that the cornerstones of NAFLD therapy are still lifestyle changes pointing toward weight loss, and physical activity. A gradual loss of weight is indeed associated in children to a rapid normalization of laboratory indices (Vajro 1994) with a significant improvement also in liver histology (Nobili 2008). Patients with poor compliance to diet and lifestyle changes have often resorted to antioxidants (e.g. vitamin E), oral insulin sensitizers (e.g. metformin) and cytoprotective (e.g. ursodeoxycholic acid) agents. Despite expectations for a large multicenter pediatric randomized, double-blind, placebo-controlled trial (TONIC), it showed that neither vitamin E nor metformin are clearly superior to placebo (Lavine 2011). New therapeutic approaches based on other pathogenetic mechanisms are still being evaluated both in children [e.g. probiotics and docosahexaenoic acid (Vajro 2011, Nobili 2011)] and/or in adults (surgery, pentoxifylline, and anti-TNFa) and/or in animal models [incretins and DPP-4 inhibitors, and Toll-Like Receptors modifiers (TLR2, TLR4 and TLR9)]. Agonists of the farnesoid X receptor (e.g. FXR agonist INT-747 NIDDK-sponsored NASH Clinical Research Network, and obeticholic acid) are now being tested also in humans.

Conclusion: Up to June 2012 there are still uncertainties about the most valid treatment options of pediatric NAFLD: Randomized Clinical Trials and/or case studies are few, often with methodological biases, and rarely documented by histological findings. Although a number of new drugs are under investigation, future efforts should focus also on the development of universal prevention strategies.

PO72
CHILDREN UNRESPONSIVE TO HEPATITIS B VIRUS VACCINATION NEED CELIAC DISEASE TESTING

G. Paolella[1], P. Pisano[2], I. De Micco[1], M. Sangermano[1], R. D'Aniello[1], V. Nobili[3], P. Vajro[1,2]. *[1]Chair of Pediatrics, Faculty of Medicine, University of Salerno, Salerno and European Laboratory of Food Induced Disease (ELFID), Naples, Italy; [2]S. Giovanni di Dio e Ruggi D'Aragona Hospital, Salerno, [3]Hepatometabolic Unit of the Bambino Gesù Pediatric Hospital, Rome, Italy*

Background and Aims: Hepatitis B surface antibody (HBsAb) response is associated with immunogenetic factors. Multiple candidate genes have been implicated, including human leukocyte antigen phenotype DQ2, strongly linked to Celiac Disease (CD). We aimed to verify how strong is the literature evidence of the association between these two conditions (HBV vaccine response and CD status). The need of adding individuals who are hypo-responder to HBV vaccination to the categories at increased CD risk recently proposed by the ESPGHAN as requiring specific CD antibodies testing (Husby et al., JPGN 2012) is discussed.

Materials and Methods: We have performed a systematic literature review of the articles reporting that, after HBV vaccination, naïve CD patients on a gluten-containing diet have low titers of HBsAb.

Results: We found 9 studies reporting low titers of hepatitis B surface antibodies, and percentages of protective (>10 U/L) values lower than in controls. HBsAb response after an i.m. or i.d. booster normalized following starting a proper gluten-free diet (GFD) (Table 1).

Table 1

1st author, year	HBV vaccine response in naïve CD patients	HBV vaccine response CD patients on GFD, after booster	HBV vaccine response in healthy age-matched controls
Park et al, 2007	12/26 (46.1%)	–	16/18 (88.9%)
Nemes, 2008	50/106 (50.9%)	36/37 (97.3%)	85/113 (75.2%)
Blasco, 2009	54% recently diagnosed 68.5% early diagnosis	86.1% recently diagnosed 89.5% early diagnosis	65.4%
Leonardi, 2009	30/60 (50.0%)	–	53/60 (88.3%)
Ertem, 2010	27/40 (67.5%)	96.4%	46/54 (85.2%)
Leonardi, 2010 (intradermic)	–	18/20 (90.0%)	-
Balamtekin, 2011 (2 different protocols)	50/64 (78.1%)	–	47/49 (95.9%)
Ertekin, 2011	32/52 (61.5%)	–	18/20 (90.0%)
Leonardi, 2011	31/66 (47.0%)	–	42/50 (84.0%)

Conclusions: The still worrying high prevalence of HBV infection both in some industrialized and in most developing countries requires pediatric gastroenterologists' alertness to the relevance of poor HBV vaccine response in CD patients. In fact, the latter could signal undiagnosed CD, requiring patient's investigation by specific antibody testing and/or duodenal biopsy, and possible correction by an appropriate booster program during a strict GFD. On the other hand, every new diagnosis of CD in a previously HBV-vaccinated individual should trigger the evaluation of HBsAb titers in order to take appropriate action in case of non-response, and to alert patients on their possible lack of full protection against HBV.

Our results suggest the need to add individuals who are hypo-responder to HBV vaccination to the list of categories at increased CD risk recently proposed by the ESPGHAN as requiring specific CD antibodies testing (Husby et al., JPGN 2012).

PO73
VIRAL HEPATITIS TREATMENT: WHAT ARE THE NEW WEAPONS?

C. Veropalumbo[1], S. Maddaluno[1], G. Paolella[2], I. De Micco[1], L. Ferrante[1], N. Di Cosmo[1], P. Vajro[2,3]. [1]*Department of Pediatrics, University of Naples "Federico II",* [2]*Chair of Pediatrics, University of Salerno,* [3]*ELFID – European Laboratory for Food Induced Diseases, Naples, Italy*

Objectives and Study: Standard therapy in pediatric chronic hepatitis (CH) B and C is currently still based on few drugs, most of them being burdened by side effects and/or unsatisfying serum conversion rates, and/or drug-resistance. Here we reviewed possible therapeutic options appearing on the horizon, already successfully adopted or presently tested in adult and/or children-adolescent preclinical trials.
Methods: Medline search from January 2009 to May 2012 on novel therapeutic options against CH B and C.
Results: *CH B*: Newer oral Nucleos(t)ide analogues are more advantageous than the standard of care (SOC) lamivudine because induce a much lesser drug-resistance. In USA Adefovir and Entecavir are used starting from age 12 and 16 years, respectively (Entecavir efficacy and safety is currently studied in a phase III trial involving children aged 2–17 years), whereas Telvibudine and Tenefovir may be offered only to adults. Also in this case however clinical trials at different ages (children aged 2–18, and 12–17 years respectively) are ongoing. In other countries these 4 drugs are all are off label in pediatrics.
"Therapeutic" vaccines [recombinant HBsAg and HBeAg, or HBV DNA pre S region (the latter tested also in pts aged >15 years)] aim to increase immunologic response in infected subjects. Hitherto, they have proven safe but effectiveness is still unconvincing.
CH C: At the present time the new adult SOC treatment includes PegIFN + Ribavirin + an oral NS3/4a protease inhibitor, such as telaprevir and boceprevir: both drugs in association with IFN and ribavirin are more effective than previous SOC therapy, which is still the current pediatric SOC. The group of new drugs acting on different phases of viral replication cycle presently studied in adults preclinical trials with promising results is now very large. It includes: HCV polymerase inhibitor viramidine with lesser hematological side effects than ribavirin, immunoglobulins against surface antigens aiming to avoid cellular entrance of HCV, HMG CoA reductase inhibitor, cyclophilin, lipoprotein, α-glucosidase inibithors, which aims to interfere with viral assembly, and Toll like receptors agonists (enhancing immune response against HCV) have also been tested.
AlbIFN [IFNα conjugated with albumin which confers longer IFN half life] in adults has shown to permit easier administration with similar effectiveness compared to IFN.
HCV vaccines [peptides or HCV genomic sequence] are tested both as preventing [surface recombinant peptides E2] and as therapeutic [alone or in combination with standard therapies] agents. Preliminary results in adults however are still inconclusive.
Conclusions: Different novel therapeutic strategies are currently tested in CH B and C, but most studies have so far prevalently involved only adult or adolescent population. The current promising results of several drugs, in near future will most probably shed light on their role, alone or in combination with present SOC, also in pediatric age.

PO74
BENEFICIAL EFFECT OF DIETARY SUPPLEMENTATION WITH GLUCOMANNAN IN CHILDREN WITH NAFLD: PRELIMINARY RESULTS

C. Della Corte[1], A. Alterio[1], B. Papadatou[1], M.R. Sartorelli[1], D. Comparcola[1], V. Nobili[1]. [1]*HepatoMetabolic Department, Bambino Gesù Children Hospital, Rome, Italy*

Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is becoming the most common pediatric liver diseases in industrialized countries. As in adults, children with NAFLD have several metabolic impairments (increased waist circumference, hypertension and insulin-resistance) that increase the risk of developing type 2 diabetes mellitus, metabolic syndrome and cardiovascular disease (CVD). The pathogenesis of NAFLD is generally considered the result of a series of liver injuries ("multi-hit" hypothesis). Insulin resistance and increased serum levels of free fatty acids are considered the main primary hits that lead to the excessive lipid accumulation in hepatocytes resulting in steatosis. Recently, it has been reported that a diet rich in high-viscosity fiber improves glycemic control and lipid profile, suggesting a therapeutic potential role in the treatment of NAFLD. Therefore, the aim of the present study was to evaluate the efficacy of a dietary fiber (glucomannan supply by Dicofarm©) in children with NAFLD.
Methods: Forty children with NAFLD (median age 10.8 yrs, 23 males) were enrolled. They were randomly assigned to take either glucomannan enriched biscuits (5 g/day) or placebo-biscuits (Reg Trial NCT01553500). Liver function tests, lipid profile, glycemic and insulinemic homeostasis were evaluated at baseline and after six months.
Results: Glucomannan treated group showed decreased values in low-density lipoprotein (LDL) vs. control group after 6 months of treatment ($p = 0.005$). Regarding liver function tests, although a trend toward decreased alanine-aminotransferase (ALT) level was observed in the treated group, the 95% confidence intervals were again too wide to judge on its clinical significance ($p = 0.126$).
Conclusions: The reduction in LDL (significantly different from the control group) observed in treated children suggested that glucomannan could potentially improve lipid profile in this population. Considering the association between lipid profile, fatty liver and metabolic syndrome in children, our results suggest that glucomannan may represent a rationale adjunct to diet therapy in the treatment of NAFLD.
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PO75
SUCCESSFUL LIVER TRANSPLANTATION IN TWO INFANTS WITH BILIARY ATRESIA AND COMPLEX SPLANCHNIC MALFORMATIONS

M. Gasparetto[1], E. Gringeri[2], M. Polacco[2], M. Cananzi[1], D. Neri[2], F. D'Amico[2], G. Zanus[2], U. Cillo[2], G. Guariso[1]. [1]*Department of Paediatrics, Unit of Gastroenterology, Digestive Endoscopy, Hepatology, and Care of the Child with Liver Transplantation University Hospital of Padova, Italy;* [2]*Department of Surgical Oncological and Gastroenterological Sciences, DiSCOG, Hepatobiliary and Liver Transplant Unit, University Hospital of Padova, Italy*

Background: Liver Transplantation in infants with biliary atresia (BA) associated with complex spanchnic malformations (i.e. splenic malformations in BASM Syndrome) is associated to a worse prognosis, especially due to vascular complications [1].

Specific aim: Within the last decade (2002–2012), 80 liver transplantations were performed on paediatric patients at our Centre; 25 of them were infants aging <1 year and/or weighting <10 kg. We report two paediatric cases affected by BA and splanchnic complex malformations who were successfully treated with liver transplantation.

Case reports: (1) An infant with BA, asplenia, intestinal malrotation and anomalous splanchnic vascularisation was surgically treated with Kasai portoenterostomy at 63 days of life. The outcome was inefficacious since the child presented impaired liver function, persistent jaundice, partially adequate nutritional status (body weight and middle brachial circumference <3rd percentile despite adequate caloric intake). An Angiographic CT detected patent superior and inferior mesenteric arteries (displaced on the right of the superior mesenteric vein and of the aorta respectively, in intestinal malrotation); thin portal vein (lumen 1.5 mm); absence of the middle hepatic vein; the inferior vena cava was interrupted at the level of its supra-renal infra-hepatic tract; the infra-renal tract of the inferior vena cava was connected to the Azygos vein. The child completed the first year vaccination schedule, before undergoing a left split liver transplantation at the age of 1.1 year. The post-operative Doppler study (day 2) evidenced patency and adequate fluxes at all vascular anastomoses. No major peri-operative complications have occurred. The liver function and hepatic tests are normal and the child is being fed regularly with normal formula, with an adequate growth. (2) An infant with Situs Viscerum Inversus (Left-sided liver, right-sided stomach, left-sided cecum, right-sided heart, interrupted inferior vena cava and Azygos continuation, pre-duodenal portal vein) was surgically treated with Kasai portoenterostomy at 55 days of life. The outcome was inefficacious and the child presented persistent cholestasis. An episode of cholangitis was associated with acute liver failure, so an urgent liver transplantation was required at the age of 6 months. Post-operative Doppler controls (day 2) were regular and no major complications have occurred.

Discussion: The presence of splanchnic malformations is no longer a contraindication to liver transplantation, even in infants weighing <10 kg, in Liver Transplantation Centres with an appropriate expertise. A careful attention to major complications has nevertheless to be considered, given the anatomical and surgical complexity of these children who basically have a worse prognosis.

Reference(s)

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PO76
HYDATID LIVER DISEASE: OUR 5-YEAR EXPERIENCE

L. Costa[1], A. Carabaich[1], S.F. Chiarenza[1]. [1]*Pediatric Surgery Department, S. Bortolo Hospital, Vicenza, Italy*

Echinococcus granulosus remains a clinical problem in sheep and subsistence farming communities. Human cystic echinococcosis caused by *E. granulosus* is the most common presentation and probably accounts for more than 95% of the estimated 2–3 million annual worldwide cases. The liver (70–80%) and lungs (15–25%) are the most frequent locations for echinococcal cysts. The diagnosis is made through the combined assessment of clinical, radiological, and laboratory findings.

Despite the fact that a number of scolecoidal agents have been developed against liver hydatid disease, the cornerstone of the definitive treatment remains surgery. Both the classic surgical techniques and the recently developed minimally invasive and laparoscopic methods target the eradication of the disease by simultaneously avoiding perioperative spillage and dissemination or recurrence of echinococcosis.

The most effective chemotherapeutic agents against the parasite are albendazole and mebendazole. Medical treatment alone is not an effective and durable treatment option. PAIR (puncture, aspiration, injection, reaspiration) is the newest minimally invasive technique with encouraging results, but it requires considerable expertise. Surgery remains the most accessible and widely practised method of treatment. The options are either radical (pericystectomy and hepatic resection) or conservative (deroofing and management of the residual cavity). Various scolicidal agents are used intraoperatively (Eusol, hypertonic saline and others). Complicated cysts (intrabiliary rupture and secondary infection) may require ERCP to obtain biliary clearance.

We report 4 cases of pediatric age. The age of patients was from 6 to 17 years. All had emigrated from sheep and farming communities in other countries (Morocco and Moldavia) as a child. They presented with abdominal fullness and nausea and were found to have 1 to 4 echinococcal cysts of the liver, in one or two lobes, range 15 to 30 cm. They were successfully treated with laparoscopic pericystectomy, deroofing and management of the residual cavity, because of a very favorable location. Lethal outcomes were not observed. In 2 cases long-term bile spillage from the cyst required conservative treatment with drainage, ERCP and biliary stent, removed after 2 or 4 months.

Conclusion: The treatment is mainly surgical, and, with appropriate diagnosis and treatment, prognosis is good. With advances and increasing experience in laparoscopic surgery, many more attempts have been made to offer the advantage of such a procedure to these patients. Laparoscopic surgery is used increasingly for hydatid disease.

PO77
ACUTE LIVER FAILURE IN CHILDREN AT A TRANSPLANTATION REFERRAL CENTRE: ETIOLOGY AND OUTCOME

A. Di Giorgio[1], M. Bravi[1], V. Casotti[1], A. Sonzogni[2], E. Bonanomi[3], M. Colledan[4], L. D'Antiga[1]. [1]*Paediatric Liver, GI and Transplantation,* [2]*Liver Pathology,* [3]*Paediatric Intensive Care,* [4]*General Surgery and Transplantation, Ospedali Riuniti Bergamo, Italy*

Background and Aim: Acute liver failure (ALF) in children is rare but may be fatal. Etiology is various but in a significant percentage of cases it remains unknown. Complications (encephalopathy and sepsis) can lead to both neurological sequelae and death. Survival of patients with ALF has been reported as lower than children with a different indication to LTX. In such a scenario the management of children with ALF is challenging. This study reports the experience of a single Transplantation Centre with the aim to assess etiology and outcome of children with ALF.

Methods: We retrospectively reviewed the notes of children referred to our Hospital between 1996–2011 because of ALF. ALF was defined, regardless of encephalopathy, by high transaminases and INR $\geqslant$2.0 due to impaired liver synthetic function, irrespective of underlying liver disease. We reviewed clinical and laboratory features of the eligible patients, the presence of encephalopathy, the need for LTX and the outcome.

Results: 48 patients were affected by ALF (M/F = 30/18); median age at presentation was 2.7 years (range 0.1–15.1). The etiology of ALF was autoimmune hepatitis in 10 pts (20.8%), acetaminophen overdose in 6 (12.5%), metabolic disease in 4 (8.3%), Wilson's disease in 3

(6.25%), mushroom poisoning in 2 (4.1%), neonatal hemochromatosis in 1 (2.0%), viral infection in 1 (2.0%) and indeterminate in 21 (43.7%). Thirty-nine pts (81.2%) developed jaundice and forty (83.3%) had hepatic encephalopathy (grade 2 = 8 pts; grade 3 = 8 pts; grade 4 = 24 pts). Median values for blood tests were: ALT 2010 U/L (range 90–18400), INR 3.8 (2.5–9.0), ammonia 156 μmol/l (41–368), bilirubin 17.6 mg/dl (0.6–50). After a median follow up time of 0.9 years (0.1–7.9), 23/48 pts (48%) had a good transplant-free survival, 25/48 pts (52%) underwent LTX. Two pts (4.1%) developed aplastic anemia (of whom one after LTX) and 1 (2%) neurological sequelae. Overall survival was of 91.7% (44/48). Four pts (8.3%) died (2 pts before and 2 after LTX). ALF was an indication for transplantation in 25 out of 501 pts (4.9%) who underwent LTX in our Centre.

Conclusion: Autoimmune hepatitis and acetaminophen overdose were the most common causes of ALF in our cohort of patients, but the etiology remained unknown for a significant percentage of cases. Encephalopathy was very common but we observed neurological sequelae only in one patient. LTX was required in over half of the patients. The overall outcome of children with ALF in our experience is good and not different from that of children with end-stage liver disease of other etiologies.

PO78
PRIMARY SCLEROSING CHOLANGITIS: A FAST ROAD TOWARD LIVER TRANSPLANTATION

C. Barbera[3], P.L. Calvo[1], M. Baldi[1], L. Garassino[3], A. Brunati[2], G. Carbonara[2], A. Cerrina[2], R. Romagnoli[2], M. Salizzoni[3].
[1]Gastroenterologia Dipartimento di Scienze Pediatriche e dell'Adolescenza, OIRM, Italy; [2]Centro trapianti di fegato "E.S. Curtoni" ASOU S. Giovanni Battista, Italy; [3]Università di Torino, Italy

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease of unknown etiology that is often associated with inflammatory bowel disease (IBD), predominantly ulcerative colitis (UC).

In the pediatric Service of Gastroenterology of Turin we diagnosed 11 IBD associated PSC.

There were 6 females and 5 males, mean age 9 yrs (range 2–14 yrs) at diagnosis.

PSC diagnosis was done by liver biopsy, ERCP (Endoscopic retrograde cholangiopancreatography) or CRMN (cholangio magnetic resonance) and colonoscopy. A mild form of UC was present in all children, but only in a minority of patients flares of disease occurred. Nevertheless in 6 of these boys a severe liver pain and recurrent cholangitis became the main medical problem, unresponsive to conventional medical treatment and only temporary responsive to stent application in the biliary tree by ERCP in 4 of them. Growth impairment was a coexisting complaint in a boy and in a girl. Both the two males were transplanted 14 yrs after PSC diagnosis; the 3 females after a shorter time of mean 11 years, and one girl even only after 2 yrs for severe liver failure. After OLT (Orthotopic Liver Transplant) a mild form of UC was observed in 2 (a boy and a girl), and a severe but transient UC recurrence after treatment for rejection in another girl followed by chronic aspecific diarrhea. None required proctocolectomy. One boy required re-olt one month after transplantation and has now developed another relapse, however he regained height and quality of life. Within a total of 2340 transplants performed in the Turin Liver Transplantation Unit in adult patients and a total of 109 in children patients PSC was the indication in 2.1% of adult pts and 7.8% in children.

Conclusions: Our data indicate that OLT is a succesful treatment for advanced liver disease due to IBD-PSC in children. Even if complicated it significantly ameliorates the quality of life of the patients.

PO79
PEDIATRIC MALNUTRION IN WESTERN COUNTRIES: TWO PECULIAR CASES

S. Gatti[1], V. Romagnoli[1], C. Proietti Pannunzi[1], M. Grilli[1], M. Rossi[1], C. Giorgetti[1], V. Albano[1], C. Catassi[1]. *[1]Department of Pediatrics, Università Politecnica delle Marche, Ancona, Italy*

Background: Failure to thrive associated with severe anemia can be a sign of nutritional vitamin deficiency. Hypocalcemia in infants can be related to vitamin D deficiency. Here we report two cases of severe nutritional vitamin deficiency in inadequately fed infants. The hazards of dietary "fads" in infancy and the importance of adequate nutritional follow up by health care professionals is emphasized.

Case presentation: Case 1: A 22-month-old girl was admitted to our department for failure to thrive and neurological delay. Physical examination revealed a pale, irritable and hypotonic infant; head circumference, length and weight were below the 3rd percentile. She was unable to walk and made no attempt to crawl or vocalize, she showed hyperreflexia and clonic movements of the hands, eyelids and mouth. Her mother followed a strict vegan diet. The infant was exclusively breast-fed when seen at the age of 22 months. Laboratory investigations showed haemoglobin of 9 g/dl, megaloblastic erytrocites and serum albumin of 3.4 g/l. Her B12 vitamin level was 0.01 ng/l (n.v. 0.25–1.10). Serum folate was 3.1 ng/ml (n.v. 1.5–13.5) and ferritin levels were low (6 ng/ml). Her mother's B12 vitamin level was 0.13 ng/ml. Vitamin D levels were low (21.3 ng/ml). B12 vitamin was given initially intramuscularly and then orally, together with iron and vitamin D supplements. Within 48 hours, the infant became more alert and active. Weaning with solid foods was started. Three months later, her development was appropriate for age. Her height, weight and head circumference were on the 25th percentiles. All blood parameters had returned to normal.

Case 2: A 4-month-old boy was admitted for multiple apneic episodes. Lenght, weight, head circumference and physical exam were normal. Laboratory exams showed hypocalcemia (Ca^{++} 3.2 mg/dl), low vitamin D levels (4.0 ng/ml), elevated PTH (477 pg/ml n.v. <65) and alkaline fosfatase (3345 U/l n.v. <1.100). In the previous three months this baby had been exclusively fed with yogurt. Oral supplement with vitamin D was started and milk-based formula was reintroduced. After few days calcium levels were within normal range and after one month vitamin D levels were normalized.

Discussion: In developed countries, vitamin deficiency is supposed to be rare in infants. However, in western countries, vegan diets (diets from which all animal protein has been excluded) have become increasingly popular and in most cases these diets are deficient in B12 vitamin leading to severe neurological symptoms combined with anemia. In the second case the vitamin D deficiency and the subsequent hypocalcemia are probably related to the low amount of vitamin D in the yogurt and to the low content of lactose (lactose enhances calcium absorption). In both cases inadequate diets were the origins of symptoms, favourably resolved with appropriate supplementations. An adequate nutritional evaluation by health care professional is strongly recommended in infants, particularly in those coming from families with restrictive eating habits.

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GASTROINTESTINAL AND HEPATIC DISORDERS IN CHRONIC GRANULOMATOUS DISEASE

I. Salfa[1], G. Angelino[1], N. Cantarutti[1], A. Claps[1], F. Rea[2], E. Romeo[2], P. De Angelis[2], F. Torroni[2], A. Finocchi[1]. *[1]Unit of Immunology and Infectious Disease, University-Hospital Pediatric Department, Bambino Gesù Children Hospital, IRCCS, Rome, Italy; [2]Unit of Digestive Endoscopy and Surgery, Department of Surgery and Transplant Center, Bambino Gesù Children Hospital, IRCCS, Rome, Italy*

Introduction: Chronic granulomatous disease (CGD) is a genetically heterogeneous primary immunodeficiency due to defective nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity. In addition to recurrent life-threatening infections, patients with CGD may also experience exuberant inflammatory responses characterized by tissue granuloma formation. Although pulmonary infections predominate in CGD, other sites are also commonly affected, such as skin, lymph nodes, gastrointestinal tract and liver. Symptomatic inflammatory bowel disease (IBD) affects up to 30% of patients and may be occasionally their presenting symptom; whereas hepatic abscesses occur in about the 30% of CGD patients and their management is often problematic because of their low responsiveness to antibiotic therapy, the frequent relapses after drainage and the need of surgical hepatic resection.

Objective: 15 patients with CGD were prospectively evaluated to assess the frequency, the clinical and the laboratory features of IBD and the hepatic manifestations.

Methods: We prospectively collected data regarding diagnosis of GI involvement and hepatic abscesses.

Results: Overall 60% of patients (9) experienced GI or liver manifestations. In 5 patients IBD-like disease occured whereas the other 3 patients presented liver abscesses; *Staphylococcus aureus* and *Aspergillus* sp. were isolated in three cases; one patient suffered from celiac disease. All patients received full standard prophylactic treatment comprising cotrimoxazole and itraconazole. In 3 patients symptoms started early in life leading to previously unknown diagnosis of CGD. In one patient remission of IBD was obtained after a combination of polymeric diet, mesalizine, steroids and azathioprine. In the other patients symptoms improved after treatment with mesalizine. Liver abscesses has been successfully treated with combined prolonged medical therapy and surgical drainage. In one patient remission was obtained after percutaneous transhepatic alcoholization.

Conclusions: IBD and hepatic disorders are a significant cause of morbidity in CGD patients. Early recognition of gastrointestinal involvement is critical to minimize morbidity and improve quality of life. Clinicians and pathologists need to be alerted that CGD is a differential diagnosis of IBD and liver abscesses especially, but not exclusively, when occuring early in life. Despite the immunocompromised state of patients, immunosuppressive treatment should be considered and it should not be withheld because of concern over risk of infection.

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