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### Neuro-Immune Interactions At Different Intestinal Sites of Pediatric Irritable Bowel Syndrome (IBS) and Their Correlation With Symptoms

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Introduction: neuro-immune interactions have previously been proposed as factors involved in sensory-motor dysfunction and symptom generation in adult IBS patients. No such studies have been performed in pediatric IBS. Thus, we investigated mast cell infiltration and mast cell-nerve interactions in the ileo-colonic mucosa of children with IBS, as well as the relationships between these parameters and symptoms; we also measured fecal calprotectin. Methods: IBS patients were diagnosed according to Rome III criteria and abdominal pain quantified with a validated questionnaire. Ileo-colonic mucosal mast cells and mast cell-nerve interactions were identified immunohistochemically and quantified with a computer-assisted method. Fecal calprotectin concentration was quantified by ELISA. Correlations between symptoms and biological parameters were carried out using Spearman's rho. Results: 21 IBS patients and 10 controls were enrolled. The number of mast cells in close vicinity of nerve fibers (MC-NF) was significantly higher in the ileum ( $P=0.01$ ), right colon ( $P=0.04$ ), and left colon ( $P<0.001$ ) of IBS patients as compared to controls. A significant correlation was found between mast cell count in the ileum and abdominal pain intensity score ( $rs=0.474$ ,  $P=0.030$ ). Similarly, a significant correlation was found between MC-NF count in the right colon and abdominal pain intensity score ( $rs=0.523$ ,  $P=0.015$ ). In addition, the pain frequency score was significantly correlated with mast cell count both in the ileum ( $rs=0.667$ ,  $P=0.001$ ) and right colon ( $rs=0.567$ ,  $P=0.007$ ) and with MC-NF count both in the ileum ( $rs=0.434$ ,  $P=0.049$ ) and right colon ( $rs=0.534$ ,  $P=0.013$ ). Discussion: in children with IBS mast cell-nerve interactions are increased in ileo-colonic mucosa: this interaction is strongly correlated with frequency and intensity of abdominal pain.

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### Gastrointestinal Manifestations of Ehler-Danlos Syndrome Type III (Hypermobility Type) : A Paediatric Cohort

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Background: Ehlers Danlos Syndrome (EDS) is a group of inherited connective tissue disorders caused by a defect in the synthesis of collagen. Ehlers Danlos Type III characteristically has associated gastrointestinal disorders. The clinical phenotype of EDS type III is well recognised in adults but there is very little data in children. Aim : To describe the clinical presentation of gastrointestinal symptoms associated with EDS type III in a paediatric cohort of patients. Methods: Retrospective review of notes and electronic patient record of all children with a diagnosis of EDS type III referred to the paediatric neurogastro clinic. Results: A total of 56 children were recruited with a median age of 13yrs (range 2yrs-18yrs). Gender distribution: female  $n=37(66\%)$ , male  $n=19(34\%)$ . Ethnic origin: White British  $n=42$ , MWC  $n=4$ , Asian  $n=3$ , AsianBritish  $n=1$ , Other  $n=6$ . 89% presented with symptoms of abdominal pain associated with either GOR( $n=27$ ), bloatedness( $n=35$ ) or constipation ( $n=46$ ). 33 patients had nausea and 23 patients had associated vomiting. 6 children complained of dysphagia and 2 children had oesophageal spasm. 11 patients had IBS type symptoms. 82% had constipation. 4 patients had faecal incontinence and soiling, 2 patients had painful rectal spasms suggestive of rectal evacuatory disorder. All patients had hypermobility and 52% has persistent chronic joint pain. 14 children had balance problems and this along with joint pain led to 9 patients using wheelchair for mobility. 15 children reported recurrent joint dislocation and 6 had fractures. 20 children reported chronic fatigue. Weight loss was noted in 18 children. 28 patients had autonomic dysfunction, 17 had postural orthostatic tachycardia syndrome and 20 had orthostatic hypotension. 8/20n who had impedance study showed pathological reflux while 5/ 15 children showed reflux on barium study. 13/16 children had delayed gastric emptying. High resolution oesophageal manometry showed dysmotility (hypertensive peristalsis) in 6/11, small bowel manometry abnormal in 3/5 and anorectal manometry abnormal in 2/3, delayed colonic transit with megarectum noted in 7/15 children. Medical management required for GI symptoms, orthostatic hypotension and joint pains. Nutritional management with exclusion diet and FODMAP were used in 6 children with some effect. 15 children received enteral feeds and 5 children parenteral nutrition. Surgical treatment was required in 6 patients. All of them required multidisciplinary input. Conclusion: Children with a diagnosis of EDS type 3 present with a wide spectrum of foregut, midgut and hindgut motility disorders. Associated autonomic dysfunction and hypermobility with lax joints can be quite debilitating. A holistic approach to management through the multidisciplinary team is required.

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### Gastric Electrical Stimulation for Teenage Children With Chronic Unexplained Nausea and Vomiting (CUNV)

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Introduction: Gastric electrical stimulation has been shown in clinical trials in adults to be safe and effective in drug refractory nausea and vomiting, with long term studies showing statistically significant improvement in gastroparesis symptoms. Objective: We performed a pilot study in 5 teenagers who had been referred after unsuccessful drug treatment. To assess the utility of gastric electrical stimulation (GES) in reducing the symptoms of chronic nausea and vomiting. Methods: Patients: Their median age was 15.5 (range 14-18 years). All were female. Two had presented with cyclic vomiting syndrome unresponsive to medication, one of which had three funduplications for GORD with no improvement. One on TPN with severe erosive oesophagitis and had numerous admissions, and one on long term enteral n/j feeds. They all had gastric emptying studies which showed delayed gastric emptying. None were diabetics. Electrogastrography showed gastric dysrhythmias in all five, with increased episodes of tachygastria in 3 and mixed dysrhythmias in 2. The surgical approach was via laparotomy in two patients; while the other three had laparoscopic surgery (two

had robotic assisted laparoscopic surgery). There were no complications following surgery. Main Outcome Measurements: All patients were evaluated at baseline for the primary outcome parameters associated with GI symptoms, gastric physiology and electrophysiology, and hospital admissions and patient diaries and compared to evaluate the long-term effect of GES. Patients were evaluated at baseline and at follow-up visits (3, 6 and 12 months and thereafter twice yearly in 4 patients). Results: Results- The median follow up time was 9.5 months (range 4 - 50 ). There was a significant reduction of nausea and vomiting in three patients in 6 months, marginal improvement in one and none so far in the patient with the shortest time to follow up of 4 months. Two patients who had assisted feeding (1 TPN, 1 NJ feeding) are now able to eat normally. Conclusion: GES has been shown effective in adults but has been done infrequently in children. This study and one other recent abstract presented at DDW last year (1), show that GES can be effectively applied to the pediatric population. GES is an effective and safe treatment in children with intractable nausea and vomiting. However, these results are limited by the small number of the patients and relatively short follow up period. Nevertheless, their clinical improvement in symptoms warrant further study of this new modality of treatment in children. Reference: 1. Lu P et al. Improvement of Quality of Life and Symptoms After Gastric Electrical Stimulation in Children with Gastroparesis and Functional Dyspepsia. DDW Abst;Gastroenterol May 2012. Disclosure of Interest: None Declared

Mo1224

### Combination PEG+E and Sodium Picosulphate Is Effective for Bowel Disimpaction in Pediatric Patients Presenting to a Surgical Clinic

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Background: Polyethylene glycol (PEG 3345 + electrolytes) and sodium picosulphate (SPS) are well-established treatments for constipation. PEG alone can produce disimpaction in 92 % of children (1) while SPS produced treatment response in 83% of adults with chronic constipation (2). This study investigated the effect of combined PEG/SPS to achieve bowel disimpaction in treatment-resistant pediatric patients presenting to a surgeon in a tertiary children's hospital. Method: Retrospective audit of 44 consecutive clinic records was conducted over 4 month period. All 44 patients previously had poor response to medical treatment by many clinicians including General Practitioners, pediatricians and gastroenterologists before referral to the surgeon. Patients had nuclear colonic transit studies. Dosage was 6-10 sachets PEG+E and 15-20 drops SPS on day 1, 6-8 sachets PEG+E/20 drops SPS on day 2 and 4-6 sachets PEG+E/10 drops SPS on day 3. Patients were provided instructions to administer the regimen at home over 3 days. PEG+E was dissolved in 125 ml water/sachet and mixed with an equal volume of juice, then drunk at 80 ml/30 min. RESULTS: By nuclear transit study, 27 patients had slow transit constipation (STC), 14 had anorectal retention (AR) & STC, and 3 AR. Autism Spectrum Disorder was diagnosed in 16/44. All 44 were dis-impacted. Mean ( $\pm$ SE) stool output per week shifted from  $0.88(\pm 0.213)$  to  $6.57(\pm 0.303)$  defecation/s/week. ( $t(43)=-8.349$ ,  $p=0.000$ ). Average stool output was 6-7 cups over the 3-day period. Stool consistency shifted from Bristol Stool Scale 2 to 4. Mean soiling incidents/week decreased from  $4.54(\pm 0.446)$ /week to  $1.05(\pm 0.274)$ /week. ( $t(39)=15.293$ ,  $p=0.000$ ) Conclusion: continued high-dose PEG+E/SP was effective in dis-impaction for treatment-resistant children with chronic constipation presenting to a tertiary referral surgical clinic. The combination of PEG+E and SPS produced dis-impaction in all patients without complication. This method could be useful for all patients with chronic constipation. 1. Candy DC, et al. J.Pediatric Gastroenterol. Nutr. 2006 Jul;43(1):65-70. 2. Wulkow R, et al. Int J Clin Pract. 2007 Jun;61(6):944-50.

Mo1225

### Is There an Association Between Esophageal Reflux and Pathologic Apneas in Infants? A Systematic Review

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Introduction: In infants, gastro-esophageal reflux (GER) is universally present and apneas are commonly encountered. Apneas can be centrally mediated, obstructive or both and have been proposed to be GER induced. It has also been suggested that apneas cause GER. Finally, both GER and apneas could be temporally related when both share a common etiological factor. Evidence for any of these relations has never been systematically reviewed. Objectives: To perform a systematic review to determine whether there is an association between GER and apnea in infants (<12 months). Methods: PubMed, EMBASE and Cochrane databases were searched for prospective studies investigating an association between GER and apnea in infants. Studies with  $n\geq 10$  infants per arm (aged <12 months) were included. GER had to be studied by pH-metry or pH-impedance (pHMII) and GER episodes were defined pH <4 for  $\geq 5s$  and/or a drop of >50% of baseline in impedance signal in the distal 2 channels. An apneic event was defined based on international criteria to be a cessation of breathing for >20s, or  $\geq 10s$  with hypoxemia or bradycardia. An epoch of  $\leq 2min$  was used to define a temporal relation between GER and apnea or vice versa. Quality was assessed using the Newcastle Ottawa Scale (NOS) for systematic reviews of cohort/case studies. Results: Of 1634 abstracts found, 6 met our inclusion criteria. Main reasons for exclusion were 1) definition of apnea did not meet inclusion criteria 2) duration of epochs was unclear or >2min and 3)  $n<10$  patients. All studies were prospective, observational patient series from tertiary centers. All had poor methodological quality according to NOS. Due to heterogeneity in design, outcome measures and analysis, pooling of results was impossible. A total of 289 infants (5 studies reported gestational age: range 24-43 weeks, 1 reported postnatal age: range 1-34 weeks) were evaluated for GER and apneas. All used respiration rate and heart rate to evaluate apneas, all but 2 included oxygen saturation measurement as well. Four studies used distal esophageal pH-metry to detect GER, 1 used pharyngeal pH-metry and 1 esophageal pHMII. The association of apnea induced by GER was assessed in all studies, epochs varied from 10s-2min. Recording time varied from 70min-21hrs. One study found an increase of apneic events after GER, 5 studies found no association. Only 1 study also assessed the association of GER induced by apnea. This was the case in 9% of GER events. No studies specifically looked for a common etiology. Conclusion: This systematic review showed no evidence for an association between GER and apneas in infants. The quality of included studies was low. Therefore, there is a need for high quality studies using uniform