Paediatrics Nutrition

A paediatric gastrostomy audit – does gastrostomy placement with concurrent fundoplication increase the risk of gastrostomy related complications?

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**Aims** To compare the incidence of gastrostomy complications with a primary gastrostomy versus gastrostomy with concurrent fundoplication and neurologically impaired versus neurologically normal children. Additionally two low profile devices (LPD) one with balloon retention the other with silicone bolster retention were compared for their longevity.

**Methods** Ninety eight patients (58 males, mean age 4.66 years) with 107 gastrostomies inserted between April 2004 and May 2008 were included in this retrospective, single institution audit. Follow up data was obtained up June 2009, enabling a minimum follow up period of one year. The specific complications reviewed were tube related (malinsertion and malposition post LPD placement), site related (wound infection/breakdown confirmed with swab, hypergranulation requiring treatment and skin excoriation requiring dressings). Logistic regression analysis was used with a statistical significance defined as p value < 0.05.

**Results** There were 63 primary gastrostomies and 44 with concurrent fundoplication, 71 children were neurologically impaired and 36 were neurologically normal. The mean follow up time was 35.6 ± 1.41 months. There were 4 malinsertions and 5 malpositions post low profile device insertion with no association between primary gastrostomy and concurrent fundoplication or neurological status. While hypergranulation was a problem with 71–91% in all groups there was no statistical significance between the groups. The odds of an infection with gastrostomy plus concurrent fundoplication were 2.38 times greater than for gastrostomy alone (95% CI, 1.02, 5.56; p = 0.02). The odds of excoriation are 2.50 times greater in patients receiving gastrostomy plus concurrent fundoplication than for gastrostomy alone (95% CI 1.09–5.71; p = 0.015). There was no statistical association with neurological impaired or neurological normal children. Low profile device replacement rates were significantly higher for those with balloon retention (1.77 per year) compared with silicone bolster retention (0.56 per year).

**Conclusion** There was a higher incidence of site infection and skin excoriation for gastrostomy placement with concurrent fundoplication. There was no significant difference between neurologically impaired compared with neurologically normal children. Low profile balloon devices were changed three times more often than those with silicone bolster retention.

Defective bile acid transport and synthesis in a piglet model of short bowel syndrome associated-liver disease

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SBS-ALD occurs in ~65% of infants following small bowel resection (SBR) however the cause remains unknown. We have recently described a piglet model which mimics many of the features of SBS-ALD including hepatic fat droplet and bile acid accumulation. The aim of the current study was to characterise changes in enterohepatic bile acid synthesis and transport in our piglet model of SBS-ALD.

**Methods** 4-week old piglets underwent a 75% small bowel resection (SBR) or sham operation and were studied at 0, 2, and 6 weeks post-operation. Stool and serum was taken weekly for LFTs and total bile acid determination (TBA). At sacrifice ileum and liver was removed for histological analysis, RT-PCR determination of target genes and bile acid tissue levels.

**Results** In the liver there was no change in NTCP, BSEP, CYP7A1 or FXR mRNA. Significant changes are tabled below.

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<tr>
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<th>Week 0</th>
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<tr>
<td>Ileum</td>
<td>21.7 ± 11.7</td>
<td>23.6 ± 9.8</td>
<td>26.5 ± 8.6</td>
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<td>Liver</td>
<td>52.5 ± 7.5</td>
<td>36.3 ± 14.8</td>
<td>42.6 ± 5.4</td>
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<td>Stool</td>
<td>39.9 ± 9.4</td>
<td>41.8 ± 6.1</td>
<td>71.4 ± 8.7*</td>
<td>53.3 ± 9.3</td>
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<tr>
<td>Serum</td>
<td>3.9 ± 1.0</td>
<td>9.5 ± 0.7</td>
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<td>9.4 ± 2.8</td>
<td>18.6 ± 3.5*</td>
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<td>ASBT</td>
<td>12.0 ± 3.2</td>
<td>19.3 ± 4.5</td>
<td>53 ± 6***</td>
<td>15.3 ± 2.8</td>
<td>31.5 ± 6.4</td>
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<td>IL-BP</td>
<td>15.6 ± 4.5</td>
<td>36.0 ± 10.2</td>
<td>62.4 ± 8.4*</td>
<td>23.9 ± 5.1</td>
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<td>OSTA</td>
<td>15.0 ± 5.2</td>
<td>13.5 ± 5.2</td>
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<td>16.0 ± 4.5</td>
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<tr>
<td>OSTB</td>
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<td>FXR</td>
<td>1.5 ± 0.3</td>
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<td>1.5 ± 0.4</td>
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**Conclusion** We have performed the first concurrent study of intestine and liver using a model of SBS-associated liver disease. We have observed dysregulation of key molecules involved in bile acid synthesis and transport, including the nuclear receptor FXR.

BMI and gastroesophageal reflux disease in children, is there an association?

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**Introduction** Obesity is an epidemic in both adults and children with approximately 18% of Australian Children aged 2–18 yrs being overweight and a further 7% being obese. In adults, a positive association between weight and gastroesophageal reflux has long been established however this association currently remains unclear in children. The aim of this study was to correlate Body Mass Index (BMI) with the occurrence of gastroesophageal reflux (GOR) in children.

**Methods** A retrospective analysis of 24 h pH studies completed at the Women’s & Children’s Hospital between 2006 and 2010 was performed. Patient body weight and height were recorded and BMI was calculated. Patients were divided into four BMI categories (underweight, normal weight, overweight and obese according to the WHO guidelines). GOR episodes and total acid exposure was recorded using a pH probe which remained in place for 24 h.

**Results** 316 children (mean age 9.46 ± 4.5, 53% male) were included. When compared to normal weight children, overweight children had significantly higher acid exposure and a greater frequency of acid reflux (p = 0.004 and p < 0.001 respectively). Furthermore overweight children...
were more likely to have a reflux index of more than 5% indicating a positive GOR diagnosis, compared to normal weight children (p < 0.001). Male gender was an independent risk factor for a higher acid exposure (p = 0.019).

**Conclusion** Obesity increases oesophageal acid exposure and the risk of GOR in children. The identification of this risk factor may indicate weight reduction as a potential therapy for GOR in overweight children.

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**Grape seed extract: a potential adjunct to chemotherapy?**

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**Introduction** Mucositis is a serious disorder of the gastrointestinal tract that results from cancer chemotherapy. Previously, we have demonstrated that grape seed extract (GSE) partially reduced indicators of intestinal damage in a rat model of intestinal mucositis (Cheah et al. 2010); however, its impact on the effectiveness of chemotherapy against cancer cells is currently unknown. We investigated the combined effects of GSE and chemotherapy on colorectal cancer cells.

**Methods** Caco-2 cells (5000 cells/well) were cultured in a 96-well tissue culture plates in DMEM media with 10% FCS for 48 hrs. Culture medium was replaced with serum free medium containing GSE (10, 25, 50, or 100 μg/mL) and 5-FU (5 Fluorouracil, 100 μM). The proliferative activity of cells was determined by MTT (3,4,5-Dimethylthiazol-2,5-diphenyltetrazolium bromide) assay at 24 and 48 hrs. Significance was assumed at p < 0.05 using one-way ANOVA.

**Results** GSE treatments significantly (p < 0.05) reduced the proliferative activity of Caco-2 cells compared to control value in a time- and dose-dependent manner (IC50 = 50.2 μg/mL, 24 hrs; IC50 = 37.8 μg/mL, 48 hrs). At 24 hrs, 5-FU significantly reduced cell viability to 86% (p < 0.05) of control value. The combination of 5-FU and GSE significantly (p < 0.05), and dose-responsively, decreased the proliferative activity of Caco-2 cells (GSE 25 = 35%; GSE 50 = 67% and GSE 100 = 71%) compared to 5-FU control. At 48 hrs, 5-FU reduced Caco-2 cell viability to 71% (p < 0.05) of control value. 5-FU and GSE in combination significantly (p < 0.05), and dose–responsively, decreased the proliferative activity (p < 0.05) of Caco-2 cells (GSE 25 = 23%; GSE 50 = 72%; GSE 100 = 73%) compared to 5-FU control.

**Conclusions** We conclude that GSE not only reduced the proliferative activity of Caco-2 cells but also enhanced the capacity for 5-FU to reduce the proliferative activity of Caco-2 cells. Further studies are warranted to determine GSE effects on tumour growth in vivo. Our data provides the first evidence of GSE enhancing the impact of chemotherapy on cancer cells. Dietary GSE could be a promising adjunctive approach to combat intestinal mucositis.

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**Duodenal bulb biopsy in paediatric coeliac disease: experience from Perth, WA**

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**Background** Coeliac disease (CD) is a gluten sensitive enteropathy characterized by small intestinal intraepithelial lymphocytosis and villous atrophy. Duodenal involvement in CD is frequently patchy and at times difficult to interpret histologically. The distal duodenum is routinely biopsied as part of the diagnostic evaluation but not the duodenal bulb. However, recently there have been few reports of CD changes limited to duodenal bulb only.

**Aim** To assess the usefulness of a duodenal bulb biopsy in the diagnosis of celiac disease in a paediatric population.

**Methods** Since Feb 2009, in our institution we have routinely included duodenal bulb biopsy in addition to distal duodenal biopsies in children suspected of having CD. All children diagnosed with CD between Feb. 2009 and May 2011 were identified and those children who had biopsy finding consistent with CD limited to the duodenal bulb were reviewed with regards to clinical, serological (anti tissue transglutaminase antibodies) and histopathological parameters.

**Results** A total of 101 children were diagnosed with CD during study period. The mean age was 8.21 years (±3.63), 33 males and 68 females. Eight of 101 (7.92 %) had histological changes consistent with CD limited to the duodenal bulb (Marsh III) with normal histology in the distal duodenum.

**Conclusions** This study demonstrates the importance of the duodenal bulb biopsy in children suspected of having CD. We therefore recommend that duodenal bulb biopsies be included routinely in children undergoing endoscopic biopsies for the diagnosis of CD.

**Key Words:** Coeliac disease, duodenal bulb.

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**Magnetic resonance evaluation of small bowel in paediatric Crohn’s disease – a single centre experience**

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**Objectives** Small bowel imaging is recommended in all children suspected or diagnosed to have Crohn’s disease (CD) at diagnosis. Traditionally this was done by barium meal follow through. In recent years, experience has accumulated with the use of MRI to evaluate small bowel in CD. In this study, we aim to describe our experience with this modality of imaging. We attempted to correlate the Paediatric Crohn’s Disease Activity Index (PCDAI) with the MRI features of small bowel children with Crohn’s disease at diagnosis.

**Methods** Princess Margaret Hospital is the only tertiary paediatric service in the state of Western Australia. Our centre has been using MRI imaging of small bowel in children with CD since 2004. Hospital records of all children with CD diagnosed since 2004 were reviewed for demographic details, PCDAI and MRI findings. MR enterography is performed at 1.5 T field strength with oral (Polyethylene glycol) and intravenous (Gadolinium) contrast and images were assessed by an experienced radiologist who was blinded to the PCDAI. Various MR imaging characteristics and overall MRI impression were reviewed for association with PCDAI using statistical software.

**Results** A total of 57 children were diagnosed with Crohn’s disease since 2004, of whom 43 had MRI evaluation of their small bowel, the majority with in 2 months of diagnosis. There were 25 males and 18 females. Median age at diagnosis was 12 years. The association between MRI diagnosis of small bowel involvement and PCDAI was statistically significant (p value 0.01) Certain features of MRI were found to correlate strongly with PCDAI.

**Conclusion** MR enterography correlates well with the disease activity of Paediatric Crohn’s disease. It has the advantage over barium of having no radiation exposure. MRI should be considered as the choice of imaging in paediatric Crohn’s disease, when available.
Long-term effects of transabdominal electrical stimulation on paediatric slow-transit constipation

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Transabdominal electrical stimulation (TES) was used to treat children with treatment-resistant slow-transit constipation (STC) for 1–2 months as part of a randomised control trial. In the short term (2 months after stimulation) TES produced improved colonic transit and quality of life. Aim: To determine long-term outcomes for STC children treated by TES.

Methods In 2006–9, 42 STC children started a trial using TES. Defecation was managed by timed-sits on the toilet after meals, laxative use or enema and antegrade continence enemas (8 patients). Patients were randomised into 2 groups receiving: (A) 1 month sham and 1 month stimulation or (B) 2 months of stimulation administered by physiotherapists (20-minutes, 3/wk) with 8 weeks between stimulation months in Group B. Thirty-nine completed the trial and in the 2 years following the trial, 19 patients also self-administered TES daily for 30 minutes for >2 months. Long-term follow-up of 30/39 patients was conducted by phone interviews and questionnaires 1–4 years (mean: 3.5 years) after the trial ended. Effects of TES on STC symptoms were evaluated (using confidence intervals, Chi-squared tests or paired t-test). Ethics approval HREC30116A.

Results All patients had at least one month of stimulation performed by physiotherapists and then 1/2 had home stimulation. There was no improvement in 1/3 of patients. Two thirds perceived they had improved with improvement lasting >6 months in 25–33% and >2 years in 33%. Compared to pre-stimulation, defecation frequency improved in 30% overall. Defecation frequency did not improve after 1 month but improved in 90% of patients after 2 months of stimulation. Soiling became wetter in 62% and then drier again. Soiling improved in 78% and abdominal pain in 59%. The Holschneider continence score improved in 81%. Laxative use stopped in 52% while 43% with stomas stopped antegrade continence enemas (washouts). Timed-sits switched to urge-initiated defecations in 12/21 patients. Eighty percent of relapsed patients elected to have home stimulation. Symptoms improved in 60% of home stimulation patients.

Conclusion TES is a promising treatment for STC children. Stimulation for 2 months was more effective than 1 month. Improvement occurred in 2/3 of children, lasting >2 years in 1/3 while symptoms recurred after 6 months in 1/3 of children. Children developed sensory input in the rectum and were able to feel the need to defecate suggesting the treatment activated sensory nerves in the intestine or spinal cord.

Radionuclear gastrointestinal transit studies at the Royal Children’s Hospital, Melbourne

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Chronic constipation is a common problem in childhood. Gastrointestinal transit (GIT) studies can be performed using plastic markers and x-ray images (Sitz marker studies) or a radioactive meal and gamma camera images (nuclear transit study, NTS). There is increasing worldwide interest in a shift to Nuclear Medicine techniques (Southwell 2009 Pediatr Surg Int 25: 559, Sutcliffe et al 2010 Semin Pediatr Surg 9: 81). The Royal Childrens Hospital (RCH) has used the NTS since 1998 and developed considerable experience.

Aim To review the NTS technique at RCH to identify methods for widespread implementation.

Methods Patients stop taking laxatives for 5 days, fast the night before and take a radioactive milk drink containing technetium or gallium. Gamma camera images are taken at 0, 2, 4, 24, 30 and 48 hours. Radioactivity is quantified in stomach, small bowel, ascending colon, transverse colon, descending colon, recto-sigmoid colon and evacuated activity and plotted in 3D plots. The median point (Geometric Centre, GC) of radioactivity is calculated for each time point and plotted in 2D graphs. The radiation dose relative to body mass is calculated.

Results Since 1998, >800 studies have been performed on 680 patients. Gastric emptying, small bowel transit and colonic transit have been characterised, and a reporting method developed to provide referring clinicians with results in an easily understood format. Subgroups of patients with rapid transit, slow transit through the whole intestine, slow transit in the proximal colon, anorectal retention and normal colonic transit have been identified. Multiple studies from one patient are plotted on the same graph to compare results to previous studies and normal values.

Conclusion Attention to patient preparation, positioning, camera acquisition settings and raw/processed data presentation make it possible to achieve accurate and reproducible results. A simple report method has been developed that is easily interpreted by clinicians and provides valuable information on transit through stomach, small bowel and large bowel for diagnosis and monitoring a patient’s response to treatments.

Accuracy of coeliac serology as a marker of duodenal mucosal recovery in children with coeliac disease on a gluten-free diet

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Background The diagnosis of Coeliac Disease (CD) is based on demonstration of characteristic small intestinal villous damage supported by positive serological tests. Follow-up in children on a strict gluten-free diet (GFD) is generally based on resolution of clinical features and normalisation of the serological markers as per the revised ESPGHAN criteria. Recent adult studies have shown that serologic markers do not necessarily correlate with dietary compliance or mucosal recovery. In view of these we have changed our practice to now routinely re-biopsy all children with CD who have complied with a GFD for at least 12 months.

Aim To determine whether IgA anti-tissue transglutaminase (tTG) and IgG anti-deamidatedgliadin peptide (DGP) antibodies are sensitive and specific markers of mucosal recovery in children with CD on a GFD.

Methods All children with known CD (on the basis of Marsh type 3 changes) who have been re-evaluated with duodenal biopsies paired with repeat tTG and DGP serology were audited over a 24-month period. Mucosal recovery was defined as a return to Marsh type 0 (blinded assessment by a single paediatric histopathologist). In addition, a standardised questionnaire of dietary compliance was administered with parents.

Results The interim results of the ongoing audit are presented. To date103 children have been re-evaluated. Of these children, 17 (17%) had positive serology, and 86 (83%) had negative serology (normal or equivocal as defined by laboratory cut-off values). Of the 86 children with negative serology, 2 (2%) had Marsh type 3 endenteropy. Of the 17 patients...
with positive serology, 3 had Marsh type 3 changes. Eight patients had mucosal abnormalities graded as Marsh type 1 and 2, 1 associated with positive serology and 7 associated with negative serology. The sensitivity and specificity of serology as a marker of mucosal healing was 60% and 86% respectively. 78 (76%) questionnaires were completed, with 92% reporting good or excellent compliance with a GFD including 62% of those with abnormal biopsies.

**Conclusions** The preliminary findings of this audit suggest that serology may not be an optimum tool to detect mucosal healing in a child with CD on a GFD. Parent-reported dietary compliance determined by a validated questionnaire also did not correlate with mucosal findings. Ongoing recruitment in this study is awaited to confirm these findings, and determine the ideal monitoring strategy for long-term follow-up of children with CD.