

## Gastroenterology, hepatology, and nutrition

### G43 ACID AND NON-ACID GASTRO-OESOPHAGEAL REFLUX IN NEUROLOGICALLY IMPAIRED CHILDREN

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**Aim:** In addition to acid gastro-oesophageal reflux (GOR), non-acid GOR (pH > 4) may be clinically relevant in neurologically impaired children. However, standard pH metry can only detect the former. The aim of this study was to quantify acid and non-acid reflux in a group of these patients using a new catheter-related technique.

**Methods:** Ten children (9 cerebral palsy, 1 Trisomy 21) fed intra-gastrically underwent 12 hour studies of intra-oesophageal 6 channel impedance and dual channel pH monitoring. All patients were off medication influencing gastric pH. Recordings were analyzed for the frequency of acid and non-acid GOR and the height reached by the refluxate.

**Results:** Three hundred and sixty nine reflux events were detected with the combined technique. One hundred and ninety one (51.8%) were non-acid events (mean pH 5.6) and of these 138 (72.2%) reached the uppermost (1) impedance channel. Of the 178 acid reflux events (mean pH 3.1), 81.5% reached the uppermost channel.

**Conclusions:** Over half of reflux events in neurologically impaired children are non-acid and therefore are missed using standard pH metry. Most of these refluxes reached the upper oesophagus. Simultaneous intraoesophageal impedance and pH measurements proves to add valuable information that may improve therapeutic management in this patient group.

### G44 IN-VITRO FATE OF EXOGENOUS ENZYMES IN PATIENTS WITH CYSTIC FIBROSIS (CF): LONG-TUBE LUMINAL STUDIES

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**Introduction:** We have evaluated in vivo release and fate of enteric-coated microspheres, to examine why therapy fails to correct maldigestion in most CF patients with pancreatic insufficiency (PI).

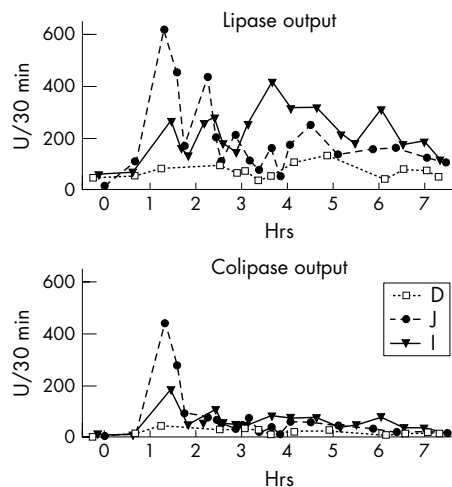
**Methods:** Postprandial events were studied in the duodenum, jejunum and ileum of 3 CF subjects by a validated multi-lumen intestinal tube and marker perfusion technique. After the tube was inserted, marker equilibrated baseline samples were obtained from each intestinal site. Subjects ingested a standard solid meal, fixed dose of enzyme and a gastric marker. Serial intestinal samples aspirated over 7.5 h were evaluated for pH, markers, enzyme activities and bile acids.

**Results:** Duodenal delivery of the gastric marker and endogenous bile acids peaked within 3 h. Duodenal pH showed considerable inter-individual variation (range- 4.5-7.75); mean jejunal (6.69) and ileal (6.97) pH were more alkaline and stable. Sequential activities for each enzyme were similar to that shown for total lipase and colipase (Figure). Postprandial enzyme activities showed: (a) a small rise from baseline in the duodenum throughout the 7.5 h period; (b) a large rise in jejunal activity, peaking at 1-2.5 h; (c) a sustained increase in activity in the ileum after 1.5 h for total lipase but not colipase. After 3 h, the colipase to lipase ratio was markedly reduced in the jejunum and ileum, suggesting impaired colipase survival.

**Conclusions:** Unlike normal digestion, very little exogenous enzyme is released proximally. Consequently, there is a mismatch of enzyme release with peak duodenal nutrient and bile acid delivery. This may in part explain the persistent maldigestion /malabsorption seen in CF patients.

### G45 LONG TERM CALCINEURIN INHIBITOR THERAPY IS NOT ASSOCIATED WITH DETERIORATING RENAL FUNCTION IN CHILDREN AFTER LIVER TRANSPLANTATION

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Abstract G44 Figure

**Introduction:** Calcineurin inhibitor drugs (CNI), Cyclosporin (CyA) and Tacrolimus (Tac) are potent immunosuppressants which have improved survival after liver transplantation (LTx) at the expense of nephrotoxicity.

**Aim:** To evaluate the long-term renal function in children who underwent LTx from 1989-99.

**Subjects and Methods:** Retrospective analysis of children who underwent LTx from 1989-99 and survived at least one year. CNI doses were reduced at 3m followed by monotherapy after 1 yr. Glomerular filtration rate (GFR ml/min/1.73m<sup>2</sup>) was calculated from the Schwartz formula<sup>1</sup> pre-LTx, 3,6,12 m post LTx and then annually.

**Results:** 116 patients (67M:49F) were included in the analysis. Median age at LTx was 2.2 yrs (0.2-1.8). 28% of the children were less than 1yr of age. Median (range) cGFR was 124 mls/min/1.73m<sup>2</sup> (99-236) pre LTx and it fell to 74 at 3m (64%; p=0.001). It increased to 87 (80% of pre LTx value) by 60 m. Children less than one year of age had better recovery of renal function (89% of pre-LTx). There was no correlation of the cGFR with the primary liver disease.

**Summary:** There was a temporary reduction in renal function post LTx which improved following reduction of CNI drugs at 3m.

**Conclusion:** Effective immunosuppression is possible without nephrotoxicity

1. Schwartz GJ, Haycock GB, Edelmann CM, et al. A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. *Paediatrics* 1976;**58**:259-63.

### G46 MATERNAL FISH OIL SUPPLEMENTATION AND VISUAL DEVELOPMENT IN TERM INFANTS: A POSITIVE ASSOCIATION BETWEEN DOCOSAHEXAENOIC ACID (DHA) STATUS AND RETINAL MATURATION

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**Aims:** The long-chain polyunsaturated fatty acid, DHA, is an essential structural component of cell membranes, present in high proportions in the brain and retina. Recent studies have demonstrated that a dietary supply of DHA is of functional importance to the visual development of preterm and term infants. We investigated whether the supplementation of pregnant women with fish oil affects the visual development of term infants.

**Methods:** In a double blind prospective study, 100 women were randomly assigned to receive dietary supplementation with either a fish oil rich in DHA (n=50) or a placebo (n=50) from 15 weeks gestation until delivery. Total fatty acids (%TFA and concentration) in red blood cells (RBC) and plasma were analysed at 15, 28 and 40 weeks gestation and at delivery in umbilical cord blood. The visual evoked potential (VEP) and electroretinogram (ERG) were used to measure visual development. Full-field ERGs, including dark-adapted intensity-response functions, were recorded shortly after birth. VEPs were recorded to flash stimuli after birth and to both flash and pattern stimuli at 50 and 66 weeks post-conceptual age (PCA).

**Results:** Maternal supplementation did not significantly alter the level of DHA in cord blood. Moreover, there were no differences in

measures of visual maturation based on supplementation. However, maturity of the retina at birth was associated with the DHA status of the infants. Specifically, retinal sensitivity measured from the intensity-response function of the ERG, was correlated with DHA %TFA in cord blood (Kendal's Tau,  $p < 0.01$ ). Maturation of the visual pathways, as measured by VEPs, was not associated with maternal or infant DHA status.

**Conclusions:** Retinal sensitivity is mediated by the rod photoreceptors that accumulate DHA during their rapid growth in the perinatal period. We have demonstrated that retinal sensitivity is associated with the DHA status of the infant. However, the retina and visual pathways mature adequately over a wide range of maternal DHA status so that no direct benefit of supplementation was demonstrated.

#### G47 ENTERAL NUTRITION TREATS CHILDREN WITH CHRONIC CROHN'S DISEASE MORE EFFECTIVELY IF THE ILEUM IS ALSO INVOLVED

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**Introduction:** Crohn's disease has several different phenotypes and the response of disease at different sites to different therapies has been poorly documented.

**Aim:** To examine clinical and biochemical response to enteral nutritional therapy of Crohn's disease at differing intestinal sites.

**Methods:** We enrolled 62 consecutive children (age: 8–17 years) with acute intestinal Crohn's disease (PCDAI > 20). Patients were treated with Polymeric diet (8 weeks). Patients were grouped according to disease site (ileal: n=20, ileo-colonic: n=27 and colonic: n=15) defined by barium follow through and macroscopic appearance at ileo-colonoscopy. Children treated with immunosuppressants/steroids in the past 4 months were excluded from the study.

**Results:** Before treatment there was no significant difference between the three groups with respect to: age (Median = 13.6 yrs, ANOVA,  $p=0.8$ ), sex ( $+2$ ,  $p=0.5$ ) and pubertal status ( $+2$ ,  $p=0.2$ ). Children with ileo-colonic disease had a higher PCDAI (Kruskall Wallis,  $p=0.03$ ) and CRP (Kruskall Wallis,  $p=0.012$ ). After 8 weeks of treatment, all groups had an overall increase in weight (median = 2.46 kg, t test,  $p < 0.05$ ) and fall in PCDAI, ESR and CRP (Wilcoxon Rank  $p < 0.05$ ). However, the remission rate (PCDAI < 20) varied between groups being lower for the isolated colonic group.

#### Abstract G47

| Remission | ILEAL    | ILEO-COLONIC | COLONIC   |                       |
|-----------|----------|--------------|-----------|-----------------------|
| YES       | 18 (90%) | 23 (85.2%)   | 7 (46.7%) | $\chi^2$ , $p = 0.04$ |
| NO        | 2        | 4            | 8         |                       |

**Conclusions:** The nature differences in remission rates for disease at different sites highlights the need for detailed pre-treatment assessment of cases in order to achieve individualised tailoring of treatment. The observation that children with disease in the colon respond better to enteral nutrition if the ileum is also involved may point to different underlying inflammatory mechanisms for these different Crohn's phenotypes.

#### G48 A 12-MONTH PROSPECTIVE STUDY OF GASTROSTOMY FEEDING IN DISABLED CHILDREN

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Gastrostomy-tube (G-tube) feeding is used for disabled children but there have been few prospective studies to evaluate this intervention. This study aimed to investigate the effect of G-tube feeding on growth and nutritional status of disabled children. 55 children with cerebral palsy (CP) (mean age 5.67 yrs) were studied before and 6 & 12 months after G-tube insertion. Anthropometry, dietetic evaluation, and a range of biochemical indices were undertaken at each visit.

**Growth:** There was a statistically significant improvement in weight gain with mean weight increase over 12 months of 33% (range: 6.5% to 80%). The first six months showed the greatest weight gain (20% of initial body weight). This was in accordance with the parent's perceptions of growth in their children. Before intervention 75% (n=48) of parents said their child had grown in the last six months but at 6 and 12 months afterwards, this had risen to 95% (n=38) and 100% (n=29) respectively.

**Body Composition:** Body fat % was calculated from anthropometry (Brook, 1971) and the average increase in the first six months post G-tube insertion was 4% (95% c.i. = 1.4–6.5,  $p=0.004$ ).

**Nutritional Status:** At 6 & 12 months after G-tube placement mean intake of energy ( $p=0.05$ ) and protein ( $p=0.05$ ) had significantly increased. Twelve months of G-tube feeding was associated with increases in biochemical markers of nutritional status including haemoglobin, IGF-BP, thyroxin, and folate.

**General Health:** Before G-tube placement 46% (n=52) of children had no serious chest infections within the preceding six months and 69% had no hospital admissions (due to chest infections). In the six months post intervention 58% (n=38) were free of chest infections and 84% reported no hospital admissions. At twelve months 63% (n=30) reported no recent infections and 100% no admissions.

**Conclusion:** This study has demonstrated the positive effect of G-tube feeding on body composition and nutritional status and parent's perceptions of general health, in children with neurological impairment.

#### G49 RELATIONSHIP BETWEEN PRESENTING SYMPTOMS, SITE OF DISEASE ACTIVITY, AND HEIGHT AND WEIGHT Z SCORE AT DIAGNOSIS OF CROHN'S DISEASE

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**Aim:** To determine the relationship between presenting symptoms, site of disease activity and height/weight Z scores at the time of diagnosis of Crohn's Disease (CD).

**Methods:** Data collected prospectively from the 1998/9 BPSU survey (*Lancet* 2001; **357**: 1093–4) from 364 CD cases aged < 16 years were analysed.

**Results:** The following correlations between symptoms and site of disease were found: 'weight loss' with jejunal and ileal activity, 'lethargy' with left colonic activity, 'abdominal pain' with oral, transverse colonic and peri-anal activity, 'diarrhoea' with colonic and rectal activity, 'bleeding' with jejunal, ileal, and colonic (but not rectal) activity (all  $p < 0.05$ ). Anorexia was not associated with any specific site activity. Mean height and weight Z scores were reduced at diagnosis (-0.54, 95%CI -0.67 to -0.41, and -1.06, 95%CI -1.21 to -0.92 respectively), with a correlation between these variables of  $r = 0.72$  (all  $p < 0.0001$ ). There was a negative correlation between the time from recall of onset of symptoms to diagnosis (ie 'delay') and height ( $r = -0.22$ ,  $p < 0.001$ ), but no such relationship with weight. The symptom of 'weight loss' was associated with reduced weight (mean Z -1.3 versus -0.7,  $p < 0.001$ ), as was 'anorexia' (mean Z 1.9 versus -1.0,  $p = 0.01$ ), but there were no correlations with height. The symptom of 'abdominal pain' was associated with reduced Z score for height (mean -0.76 versus -0.45,  $p = 0.03$ ), but not for weight. Jejunal activity was associated both with a lower Z score for weight and height (mean Z -1.6 versus -1.1,  $p = 0.017$  and mean Z -0.9 versus -0.5,  $p = 0.041$ , respectively). Ileal activity was associated with a lower Z score for weight (mean Z -1.2 versus -0.8,  $p = 0.02$ ) but there was no relationship with height. Fascinatingly there was a relationship between oesophageal disease activity and height (mean Z -0.6 versus -0.2,  $p = 0.045$ ), but not for weight.

**Conclusions:** Prolonged symptoms are associated with decreased height at diagnosis, suggesting that earlier recognition of CD may be important. Jejunal and to a lesser degree ileal disease are associated with impaired height and weight Z scores at diagnosis. Symptoms give some indication of sites affected.

#### G50 THE OUTCOME OF THE OLDER INFANT (100 DAYS +) WITH BILIARY ATRESIA

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**Introduction:** There is a detrimental effect of increasing age on the results of the Kasai portoenterostomy for biliary atresia and some centres routinely advocate primary liver transplantation for the older

infant, irrespective of other criteria. This perception that such infants are indeed irretrievable was tested by single centre retrospective analysis.

**Methods:** All infants who had undergone surgery for biliary atresia during the period 1980–2000 and who were aged 100 days or greater were reviewed. Actuarial survival was calculated using two end-points (death / transplantation). A retrospective review of their ultrasonography (n = 12) and pre-operative liver histology (n = 22) was also undertaken to ascertain possible predictive criteria. Non-parametric statistical tests were used throughout. p=0.05 was regarded as significant.

**Results:** 422 infants had BA during this period of which 32 (7.6%) were 100+ days at surgery [median 133 (108 - 180) days]. Surgery included portoenterostomy (n = 23) and hepaticojejunostomy (n = 9). Overall 5 and 10 year actuarial survival with native liver was 41% and 36%. Currently 11 (34%) are alive with their native liver (9 are anicteric), 9 (28%) have undergone transplantation and 12 have died. While there were survival advantages for Type 1 or 2 BA and absence of macroscopic cirrhosis at surgery (p>0.05). No individual histological feature (including degree of fibrosis, giant cell transformation, bile duct destruction etc.) in the retrospective review of available material was discriminatory at all. The finding of a "heterogeneous" parenchyma on ultrasonography was predictive of poor outcome but lacked sensitivity.

**Conclusions:** The potential for reasonable medium-term survival is present in about one-third of infants (100 days +) coming to primary hepatobiliary surgery. In the absence of accurate discrimination, we continue to favour this option rather than subject all to transplant simply on the basis of age.

#### G51 MATERNAL NUTRITIONAL PROGRAMMING OF BLOOD PRESSURE RESPONSES AND KIDNEY DEVELOPMENT DURING JUVENILE LIFE

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**Aims:** A reduction in maternal nutrition resulting in compromised placental and/or fetal growth is one factor contributing to adult cardiovascular disease. This effect may be mediated in part by abnormal mitochondrial function in the kidney whose growth we have shown to be compromised by nutrient restriction. The present study aimed to determine the consequences of maternal undernutrition on mitochondrial activity in the kidney and vasopressor responsiveness during juvenile life.

**Methods:** Twelve Welsh Mountain ewes were individually housed from 28 days gestation. Six were fed a nutrient restricted (NR) diet (3.5 MJ/day) until 80 days gestation and the remainder a control (C) diet (6.8–7.5 MJ/day). After 80 days gestation, until term (147 days), all animals consumed 6.8–7.5 MJ/day, sufficient to fully meet their energy requirements. Blood pressure was measured from chronically indwelling catheters at six months of age during continuous infusion of noradrenaline with dose increases (0.5–32ng/kg/min) at 10-minute intervals. Lambs were then euthanased for kidney sampling and mitochondrial analysis. Results are presented as means with their standard errors.

**Results:** Although body and kidney weights were similar between groups, the abundance of cytochrome c was raised in mitochondria of kidneys from lambs born to NR ewes (NR 119±17; C 87±10 % ref (p<0.05)). Basal plasma cortisol was similar between groups but lambs born to NR ewes exhibited an increased blood pressure response to noradrenaline infusion (NR 45.3 ± 4.8; C 32.0 ± 2.0 mmHg (p=0.07)).

**Conclusion:** Maternal nutrient restriction over the period of rapid placental growth, followed by adequate feeding up to term, results in enhanced mitochondrial cytochrome c in the kidney during juvenile life. Although basal blood pressure was similar, these offspring showed an increase pressor response to catecholamines.

#### G52 QUALITY OF LIFE IN CHILDREN ON HOME PARENTERAL NUTRITION AND FOLLOWING INTESTINAL TRANSPLANTATION

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Intestinal transplantation offers an alternative to long term parenteral nutrition (P.N.) in selected individuals. As survival increases, it is essential to examine the quality of life (Q.O.L) and the impact of transplantation on the child and family.

**Methods:** Parental reports (Child Health Questionnaire CHQ-PF50, Achenbach Child Behaviour Checklist, General health Questionnaire GHQ-28) and developmental measures (Bayley scales of Infant development II or Weschler Intelligence scale for children) were used. Prospective assessments were carried out pre-, 6, 12, 24, and 36 months post transplant, (I.T group, n=12, median age 21 months, range 8 months–10.1 years). Questionnaires were also completed once by parents whose children were stable on home P.N. (P.N. group, n=9, median age 45 months, range 11 months–15.3 years).

**Results:** P.N. and I.T (pre-transplant) patients had Q.O.L scores below the norm. I.T recipients scored worse for physical functioning (p=0.05), discomfort (p<0.05) and mental health (p=0.05). Parents of both groups were greatly impacted by their child's health and behaviour as measured by anxiety, depression, and impact on personal time. Family functioning was suboptimal with increased tension, social dysfunction and limitations in family activities. By 6 months' post I.T, there was an improvement in most domains so that general health and social functioning was better than the P.N. group. In contrast, there was deterioration in mental health, behaviour (attention and thoughts problems) and intellectual and motor development in infants for 24 months post I.T.

**Conclusion:** Intestinal failure, I.T and home P.N. compromise children's development and Q.O.L and their care has a significant impact on the family. Long-term rehabilitation is achievable after I.T and survivors can achieve a better Q.O.L than those who remain on P.N.

#### G53 LONG TERM OUTCOME OF ELEMENTAL DIET AS PRIMARY THERAPY FOR CROHN'S DISEASE

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In children with Crohn's disease (CD), clinical trials have demonstrated that polymeric or elemental diet therapy (EDT) is as effective as steroids in inducing remission, whilst avoiding steroid side effects. However, long-term outcome of EDT in managing paediatric CD is poorly documented and uncertain. Preliminary data from one study suggested that steroid use is only delayed by a median of 18.9 weeks.

**Aim:** To examine the impact of EDT on the long-term clinical course of CD, particularly in relation to clinical and biochemical remission, time to first and subsequent relapses, and first steroid usage.

**Material and methods:** 44 children (Median age at diagnosis 12.8 years, range 6.6–15.8) who had received EDT as their initial therapy were studied. Their clinical course and subsequent management were analysed. The time from diagnosis to analysis was 1 to 7 years (median 3.0 years)

**Results:** Initial EDT induced clinical remission in 40/44 cases (90 %). Median time to remission was 6 weeks (range 2–12 weeks). Median duration of first remission was 54 weeks (range 4–312 weeks). 17 (38%) have not relapsed. The remaining 27 suffered a total of 52 relapses; 16 (30%) were treated with EDT and in 12 (75%), remission was induced. Overall, 21 patients (47%) avoided steroids completely, and, in the remainder, the use of steroids was delayed by a median period of 68 weeks (range of 6–190 weeks).

**Conclusion:** These data suggest that there are significant long-term benefits to using EDT as first-line therapy for CD. Steroids may be avoided in nearly half the cases, or their use postponed by 68 weeks.

#### G54 UNITED KINGDOM EXPERIENCE WITH INFLIXIMAB IN CHILDHOOD CROHN'S DISEASE

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**Background:** Infliximab is a chimeric monoclonal antibody to tumour necrosis factor. It has been shown to be beneficial in adults with severe unresponsive &/or fistulising Crohn's disease but there are limited data in children.

**Aims & Methods:** In order to determine UK experience with infliximab in childhood Crohn's disease members of the British Society of Paediatric Gastroenterology Hepatology and Nutrition were asked to provide details of their experience. Data recorded included age of patients, reason for using infliximab, dosage, number of doses & outcome including side effects.

## Abstract G56

|     | Control    |          | CF + Enzyme |          | CF + Placebo |           |
|-----|------------|----------|-------------|----------|--------------|-----------|
|     | Peak (%/h) | Cum(%)   | Peak (%/h)  | Cum(%)   | Peak (%/h)   | Cum(%)    |
| MTG | 7.9±0.1    | 41.7±3.5 | 7.8±0.5     | 34.3±2.5 | 2.7±0.9ψΩ    | 9.3±3.4ψΩ |
| LTG | 4.9±0.4    | 24.6±1.7 | 3.3±0.5 Ω   | 20.6±1.8 | 0.6±0.2ψΩ    | 2.9±1.0ψΩ |

ψ Placebo vs Enzyme, Ω CF vs Control, p<0.05

**Results:** Nineteen children with Crohn's disease have been reported. The median age was 12 (range 5–17) years. Indications for treatment included: severe disease unresponsive to conventional therapy (including steroids, azathioprine & surgery) 12, perianal fistulae 11, other fistulae 5, steroid dependence 1. Most children received dosages of 5 (range 3–10) mg/kg. The median number of doses received was 3 (range 1–6). In 2 children there was no reported improvement after infliximab, improvement of fistulae was reported in 12, improvement in perianal disease in 11, avoidance of surgery in 5, reduced need for other drugs in 8 and improvement in symptoms/quality of life in 15. The median duration of response was 6 months (range 10 days - >9 months). Reported side effects included: hepatitis (1), fever & lupus like reaction (1), candidal endophthalmitis (1).

**Conclusion:** The UK experience suggests that infliximab may be beneficial in children with severe unresponsive &/or fistulising Crohn's disease as has been reported in adults. The limited duration of benefit suggests that repeated doses will be needed in most cases. More data are required about potential side effects.

### G55 IMPACT OF NEW STRATEGIES IN MANAGING INTESTINAL FAILURE (IF)

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Intestinal failure (IF) can be managed by parenteral nutrition (PN) with a high degree of success. However some patients develop complications (lack of venous access, cholestasis) stimulating the evaluation of new treatments.

**Aim:** To review children with IF from 1989–2001 in order to evaluate the effect of new strategies on outcome.

**Methods:** Between 1989 and 1998 combined size matched liver-bowel and isolated small bowel transplants were offered to patients with complications secondary to PN (Group 1). From 1998 reduced size combined liver bowel grafts, isolated liver transplant, non transplant surgery (bowel lengthening &/or bowel resection) and interventional radiology for venous thrombosis were included as management options (Group 2). Differences in outcome were evaluated by retrospective review of case notes of all 48 Group 1 patients seen with IF from 1989–1998, compared with 52 Group 2 patients seen 1998–2001.

### Abstract G55

|                                      | 1989–1998        | 1998–2001       |
|--------------------------------------|------------------|-----------------|
| Mean bilirubin at time of assessment | 253 µmol/l       | 200 µmol/l      |
| Listed for intestinal transplant     | 18               | 19              |
| Number of intestinal transplant      | 6                | 15              |
| Number of isolated liver transplant  | 0                | 4               |
| Number of non-transplant surgery     | 1                | 6               |
| <b>Total number of survivors</b>     | <b>15 (31 %)</b> | <b>35 (67%)</b> |

12 children died on the waiting list for transplantation in Group 1; only 2 children died in Group 2, indicating that the availability of other treatments in addition to intestinal transplantation (ie reduced size grafts, isolated bowel transplants and utilisation of interventional radiology to access inaccessible veins), is important in reducing mortality. In addition, eight children in Group 2 compared with 1 child in Group 1 have benefited from non-transplant treatment and are currently independent of PN.

**Conclusion:** A multi-disciplinary approach with access to innovative surgery and radiology tailored to individual needs has led to improved survival in managing children with IF.

### G56 EVALUATION OF THE RESPONSE TO ENZYME THERAPY IN CYSTIC FIBROSIS (CF) USING 13 CO<sub>2</sub> BREATH TESTS OF LABELED LIPID SUBSTRATES WITH DIFFERING CHAIN LENGTH

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**Introduction:** Stable isotope breath tests of lipid substrates have been used to evaluate digestive events in patients with CF. Mixed Triglyceride, a 1,3-distearyl, 2-octanoyl glycerol, with 13C label on the medium chain moiety (MTG), may be more useful for assessing intraluminal lipolysis. In contrast, the Long Chain Triglyceride mixture, Hiolein (LTG), which resembles dietary fat, should be capable of assessing all phases of lipid assimilation (lipolysis, absorption and metabolism).

**Methods:** We assessed lipid assimilation in 8 controls and 10 CF subjects with pancreatic insufficiency (PI) by comparing the metabolic fate of MTG and LTG. Each substrate was ingested on separate occasions with an isotopically neutral meal. CF subjects received each substrate with enzyme and placebo. Breath samples obtained serially over 12 h were analyzed for 13CO<sub>2</sub> enrichment by isotope ratio mass spectrometry. VCO<sub>2</sub> production, measured by indirect calorimetry, was used to calculate appearance of label (V13CO<sub>2</sub>= VCO<sub>2</sub>x enrichment).

**Results:** Cumulative V13CO<sub>2</sub> (Cum %) and peak V13CO<sub>2</sub> (Peak %/h) were expressed as a percentage of administered label (Table). In controls, cumulative recovery of label with MTG exceeded that for LTG (p=0.01). In CF subjects without enzymes, recovery of each substrate was markedly reduced. Peak recovery of label with MTG and LTG occurred at the same time (8.5–9.5 h) in controls and CF patients receiving enzymes. In CF, enzyme therapy normalized label recovery with MTG, but LTG peak V13CO<sub>2</sub> was reduced in comparison with controls (p<0.05)

**Conclusions:** In CF, enzyme therapy normalized assimilation of MTG but LTG remained impaired. These results provide indirect evidence that enzyme therapy corrects intraluminal lipolysis whereas postlipolytic assimilation of lipids (absorption or metabolism) is impaired.

### G57 FLOW CYTOMETRIC CHARACTERISATION OF INTESTINAL LYMPHOCYTE POPULATIONS IN CHILDREN WITH REGRESSIVE AUTISM

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**Background:** Enterocolitis has been reported in a group of children with a history of developmental regression into autism. The mucosal pathology is suggestive of an autoimmune lesion, but links with cognitive function remain unclear. We have presented immunohistochemical evidence of excess small and large intestinal lymphocyte infiltration and now characterise this infiltrate using flow cytometric analysis.

**Methods:** Duodenal (D4), ileal and colonic biopsies were obtained from 50 affected children (mean age 6.8, range 2–16, 33M), 26 histologically and developmentally normal controls (6.8y, 1–17, 15M) and 44 histologically inflamed controls (10.8y, 1–19, 29M). Prior to analysis, the epithelial compartment was isolated using EDTA and the lamina propria by collagenase digestion. Lymphocyte populations were visualised using fluorochrome-conjugated monoclonal antibodies and multi-colour flow cytometry, with gating performed using forward and side-scatter. Isotype controls were used throughout.

**Results:** Within the duodenal epithelial compartment, CD3 cells were significantly elevated in affected children above histologically normal controls (25 v 12%,  $p<0.01$ ) and reached levels similar to those for inflammatory conditions. In the affected children significant expansion of both IEL T cell sub-populations (CD8 and the usually minority population CD4) were observed. Within the duodenal lamina propria, CD3 cells were also increased above controls in affected children (36 v 16%,  $p<0.02$ ). This increase was seen for both CD4 (19 v 6%,  $p<0.03$ ) and CD8 cells (14 v 6%,  $p<0.03$ ). In addition, a significant increase was seen in CD19 B cells in the affected children (20 v 5%,  $p<0.01$ ). Similar findings were seen in both terminal ileal and colonic biopsies, where both T and B cell populations were more abundant in affected children compared with histologically normal controls, reaching levels similar to those seen in disease controls with well-recognised inflammatory conditions.

**Conclusions:** The data provide further evidence, using a separate technique, of excess infiltration of both T cells and B cells within the intestine of children with regressive autism. Whether this mucosal pathology relates directly to the developmental abnormality remains uncertain.

### G58 CAN INTENSIVE NUTRITIONAL SUPPLEMENTATION WITH AN ELEMENTAL DIET INDUCE A TRUE DISEASE REMISSION IN CROHN'S DISEASE? A RANDOMISED CONTROLLED TRIAL

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**Background:** A course of liquid enteral feeding can induce a remission in Crohn's disease. This may be due to a beneficial effect from the liquid feed or to discontinuation of normal foods. It has been suggested that liquid supplements improve long-term disease control. However, it is essential to distinguish nutritional benefits from anti-inflammatory actions. Our aim was to compare outcome using elemental diet therapy with and without normal foods.

**Methods:** 52 children with active disease (PCDAI  $\geq 25$ ) were randomised to receive either 100% or 50% of their requirements as EO28 for 5-7 weeks (n=26 per group). The '50% group' were encouraged to eat normally.

**Results:** Prior to entry the groups were comparable for disease severity. Dietetic monitoring confirmed that both groups received comparable overall amounts of nutrition. Treatment was discontinued before 5 weeks in 8/26 in the '100% group', and 6/26 in the '50% group'. At 6 weeks 61% of the '100% group' and 46% of the '50% group' were in remission ( $p=ns$ ). **Changes '100% Group' '50% Group' 100% v 50%** PCDAI -26 ( $p<0.001$ ) -13 ( $p<0.001$ )  $p=ns$  Wt/Ht SDS +0.69 ( $p<0.001$ ) + 0.53 ( $p<0.001$ )  $p=0.003$  Haemoglobin +0.7 ( $p=0.011$ ) -0.3 ( $p=0.056$ )  $p<0.001$  Platelets -151 ( $p<0.001$ ) -26 ( $p=0.39$ )  $p=0.006$  ESR -26 ( $p=0.004$ ) -4 ( $p=0.46$ )  $p<0.003$  CRP -15 ( $p=0.03$ ) -3 ( $p=0.55$ )  $p=ns$  After 6 weeks, relapse rates in the '100%' and '50%' groups were 44% v 58%.

**Conclusion:** The blood indices all improved significantly in the '100% group'. No such improvement was seen in the '50% group' indicating that inflammation was not suppressed. The complete absence of improvement suggests that this was not due to an elemental diet 'dose effect', but to continuation of normal foods. Weight gain may largely explain the fall in PCDAI in the '50% group', and the apparently similar remission rates in the two groups. The treatment received by the '50% group' may not have induced a true remission, and this is perhaps reflected in their tendency to earlier relapse.

#### Abstract G58

| Changes     | '100% Group'        | '50% Group'          | 100% v 50% |
|-------------|---------------------|----------------------|------------|
| PCDAI       | -26 ( $p<0.001$ )   | -13 ( $p<0.001$ )    | $p=ns$     |
| Wt/Ht SDS   | +0.69 ( $p<0.001$ ) | + 0.53 ( $p<0.001$ ) | $p=0.003$  |
| Haemoglobin | +0.7 ( $p=0.011$ )  | -0.3 ( $p=0.056$ )   | $p<0.001$  |
| Platelets   | -151 ( $p<0.001$ )  | -26 ( $p=0.39$ )     | $p=0.006$  |
| ESR         | -26 ( $p=0.004$ )   | -4 ( $p=0.46$ )      | $p<0.003$  |
| CRP         | -15 ( $p=0.03$ )    | -3 ( $p=0.55$ )      | $p=ns$     |