Gastroenterology, hepatology, and nutrition

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 pHmetry 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 intragastrically underwent 12 hours 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 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-acidic and therefore are missed using standard pHmetry. 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.

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


Introduction: We have evaluated in vivo release and fate of enteric-coated microspheres, to examine why therapy fails to correct malabsorption 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 enteric coated microspheres, to examine why therapy fails to correct maldigestion /malabsorption.

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 1.25 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 malabsorption seen in CF patients.

MATERNAL FISH OIL SUPPLEMENTATION AND VISUAL DEVELOPMENT IN TERM INFANTS: A POSITIVE ASSOCIATION BETWEEN DOCOSAHEXAENIC 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-conceptional age (PCA).

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

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

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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 (Kendall’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


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-colic: n=27 and colonic: n=15) defined by barium follow through and macroscopic appearance at ileo-colicoscopy. 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 (♂:♀=p=0.5) and pubertal status (♂:♀=p=0.2). Children with ileo-colic disease had a higher PCDAI (Kruskal Wallis, p=0.03) and CRP (Kruskal 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. 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 after 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 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% CI: 0.1–6.3, 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 improvements in biochemical markers of nutritional status including haemoglobin, IGF-I, thyroxin, and folate.

Conclusions: 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 neurodevelopmental 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, ‘left-ergy’ with left colonic activity, ‘abdominal pain’ with oral, transverse colonic and peri-anal activity, ‘diarrhoea’ with jejunal 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 95%CI –1.06, p=0.02) 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 symptoms 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


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
MATERIONAL 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 of lambs with characteristic phenotypes.

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 (6.5 MJ/day). A1-A5, 21-25, 34-38, and 1-45, respectively. All animals consumed 6.8–7.5 MJ/day, sufficient to 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 significantly higher in NR than control groups (p<0.001). 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.

Conclusions: 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 increased pressor response to catecholamines.

LONG TERM OUTCOME OF ELEMENTAL DIET AS PRIMARY THERAPY FOR CROHN’S DISEASE


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 6.0–15.8) 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 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 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.

UNITED KINGDOM EXPERIENCE WITH INFlixIMAB IN CHILDHOOD CROHN’S DISEASE


Background: Infliximab is a chimeric monoclonal antibody to tumour necrosis factor. It has been shown to be beneficial in adults with severe unresponsive 8/ 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 in children, 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.
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 infiximab, 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), liver & lupus like reaction (1), candidal endophthalmitis (1).

Conclusion: The UK experience suggests that infiximab 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 (Group1). 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 I patients seen with IF from 1989-1998, compared with 52 Group 2 patients seen 1998–2001.

**Results:**

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<th>Control</th>
<th>CF + Enzyme</th>
<th>CF + Placebo</th>
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<tr>
<td>Peak (%/h)</td>
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<td>Cum(%)</td>
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<td>3±0.5</td>
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<td>v Placebo vs Enzyme, Ω CF vs Control, p&lt;0.05</td>
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**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 CO2 BREATH TESTS OF LABELED LIPID SUBSTRATES WITH DIFFERING CHAIN LENGTH**


Introduction: Stable isotope breath tests of lipid substrates have been used to evaluate digestive events in patients with CF. Mixed triglyceride, a 1,3-diesteryl, 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 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 13CO2 enrichment by isotope ratio mass spectrometry. VCO2 production, measured by indirect calorimetry, was used to calculate appearance of label (V13CO2= VCO2x enrichment).

**Results:** Cumulative V13CO2 (Cum %) and peak V13CO2 (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 V13CO2 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 postlipolysis 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.

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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 6%, p<0.03). A significant 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 6%, p<0.03). 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 ≥ 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 Wi/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=0.53) 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

<table>
<thead>
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<th>Changes</th>
<th>‘100% Group’</th>
<th>‘50% Group’</th>
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<td>p=ns</td>
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<td>+ 0.53 (p&lt;0.001)</td>
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<td>Haemoglobin</td>
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<td>p&lt;0.001</td>
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<td>Platelets</td>
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