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Cryptosporidial Infection Presenting as Relapse in Children With Inflammatory Bowel Disease

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Introduction: Cryptosporidiosis is an enteric parasitic infection that is associated with a self limiting illness in healthy patients. However, it can cause prolonged and severe life threatening complications especially in immunocompromised patients. The most common symptoms associated with Cryptosporidial infection include abdominal pain and diarrhea. In the absence of appropriate stool studies, Cryptosporidiosis in patients with inflammatory bowel disease (IBD) can be misdiagnosed as disease relapse and can lead to inappropriate therapy. Cryptosporidial infection has been well described among transplant recipients however; there is only a limited data available among children with IBD. Aim: The aim of this study is to describe the clinical characteristics and outcomes of Cryptosporidial infection among children with IBD. Methods: All the stool studies from children with a known diagnosis of IBD presenting with presumed relapse during the period 2004-2011 were reviewed after obtaining institutional review board approval. A positive Cryptosporidial infection is confirmation by identification of Cryptosporidial cysts on microscopic examination of stool sample. Results: Medical records of 170 patients treated for IBD were reviewed. Cryptosporidial infection was found in seven patients (four with Crohn's disease and three with ulcerative colitis) presenting with symptoms of disease relapse. Five patients were female and the median age was 13 years (range: 3-17). Four patients were on immunosuppressive medications (one on 6-mercaptopurine and three on infliximab) as their maintenance therapy and all required hospitalization due to worsening of symptoms. Inflammatory markers (CRP and ESR) were elevated in all but one patient. Three of the five patients treated with nitazoxanide had a shorter duration (mean = 6 days) of illness. All patients had complete resolution of symptoms with or without steroids by three weeks and no infection related complications were noted. No significant association between disease location and severity of infection was identified. However, all patients who required hospitalization were on immunosuppressive therapy. Conclusion: Cryptosporidiosis can cause significant illness and lead to increased need for hospitalization in patients receiving immunosuppressive therapy. It is important that all children presenting with IBD flare should have their stools examined for Cryptosporidium along with other pathogens. Nitazoxanide appears to be effective in addition to supportive therapy.

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Mucosal Healing With the Specific Carbohydrate Diet in Pediatric Crohn's Disease: Preliminary Results of a Prospective Pilot Study

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Due to both perceived and real risks of current medical therapies for Crohn's disease (CD), other safe and effective approaches, particularly those utilizing nutrition and enteral therapy, have been sought. The specific carbohydrate diet (SCD) has become one alternative for CD considered by parents and patients, yet no prospective pediatric trials which employ mucosal healing as an outcome exist. Methods: Pts with active CD (PCDAI $\geq$ 15) interested in the SCD as adjunctive therapy and able to swallow a video capsule (VC), were eligible for this study. Subjects underwent a patency capsule, and if passed intact, VC was administered. They were maintained on their prescribed medications and reviewed the SCD with a dietician who then monitored their intake. VC was then repeated at 12 weeks(wk). Demographic, dietary and clinical information were collected at both time points. VC at wks 0 and12 were evaluated by a reader blinded to patient results and timing. PCDAI, Harvey Bradshaw (HB) and Lewis score (LS) were calculated at study visits as well. Means for outcome variables are reported here because of the few pts enrolled as yet. Results: The SCD has been offered to 10 pts to date. Two declined because of the stringency of the SCD; 2 were unable to ingest the VC; with 6 enrolled. Four (2 M, 2 F; average age 13.5 y; disease duration 4.5 y) have completed the trial to date; 1 (20 yo F) ceased at 8 wk because of difficulty with the SCD. The 4 completers received an average of 72.4 % of their estimated caloric needs, respectively, prior to the SCD, and 82.6 % on the SCD. Weight, Hgb, WBC, ESR, and albumin were essentially unchanged. Mean HB decreased from 3 to 1 and PCDAI from 20 to 6.2. Small bowel (SB) ulcers seen on initial VC in 3 were not seen on the 12 wk VC, with LS decreasing in all pts. In1 pt not rigidly adherent to the SCD, the number of stenotic areas decreased and the LS declined, but additional aptha developed in a new location. Impressions: Mucosal and clinical improvement were seen in the first 4 patients completing this pilot study (with SB mucosal healing in 2). VC appears to offer an important means to monitor mucosal improvement even over a relatively short interval. Completion of this trial and additional studies are needed to understand the changes described here and the mechanisms contributing to this improvement.

4 CD Patients at 0 and 12 Weeks on SCD

				Week 0				Week 12			
Patient	Gender	Age	CD Duration (yrs)	Kcal	HB	PCDAI	LS	Kcal	HB	PCDAI	LS
1	M	13	1.3	1705	3	30	562	3000	0	5	0
2	M	10	8.0	1861	3	15	412	1971	1	5	112
3	F	15	4.2	1210	2	20	3710	1700	0	5	1350
4	F	16	4.6	1273	2	15	6228	1090	1	10	3720

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Nutritional Influences Upon CEACAM6 Expression by Intestinal Epithelial Cells

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Background and Aims: Exclusive enteral nutrition is established as an initial therapy to induce remission in active Crohn disease (CD), especially in children, but the mechanisms of action of this therapy are yet to be fully defined. The adhesion molecule CEACAM6 is upregulated in active CD, is implicated in the attachment of AEIC and has roles in innate immune defence. We hypothesised that nutritional stimuli as provided by enteral formula, modulate the activity and expression of CECAM6 by human intestinal epithelial cells. Methods: The human adenocarcinoma cell line Caco-2, is an established *In Vitro* model of epithelial cells and commonly used in studies of intestinal inflammation. This model was utilised to explore the effects of enteral formula (EF) upon CEACAM6. Caco-2 cells were treated with EF (Osmolite™, Abbott) or the proinflammatory cytokine, interferon-gamma as a positive control. The effect of EF on Caco-2 viability was assessed by Trypan blue exclusion assay. mRNA expression was defined by quantitative real-time polymerase chain reaction assay, while the expression of CEACAM6 protein within the cells was determined by dot blotting. In addition, the levels of secreted CEACAM6 protein were quantified by enzyme-linked immunosorbent assay. Results: Up to 30% v/v EF exposure for 24 hours had no effect on the viability of Caco-2 cells compared to unexposed controls ($p>0.05$). EF stimulation lead to a dose dependent increase (up to 48%) in the production of CEACAM6 protein after 24 hours, while 20% v/v EF significantly upregulated CEACAM6 mRNA expression 3-fold. Furthermore, PF doubled the shedding of CEACAM6 protein from the cells in the media. Conclusions: CEACAM6 expression is modulated by nutritional exposure, suggesting that innate defence activities may be mediated by PF in the setting of CD.

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Efficacy of Infliximab for Japanese Paediatric Crohn's Disease Patients

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Background: In recent years, the therapeutic application of the anti-tumour necrosis factor (TNF)-α antibody, infliximab (IFX) has expanded for both inducing and maintaining remission in young Crohn's disease (CD) patients. However, there are very few outcome reports from Japan in this clinical setting. With this in mind, we became interested to evaluate the clinical efficacy and safety of IFX in paediatric CD patients. Patients and Methods: In a single centre setting, we enrolled 15 paediatric CD patients, age 11-17yr, with mild to severe disease, CD activity index (CDAI) 256.3±88.7, and CD duration 4.1±2.5yr. All patients had received 5-aminosalicylic acid based medications, but none had received an immunomodulator (IM) like azathioprine or 6-mercaptopurine. The primary and secondary end points were weeks 10 and 52 following the first IFX infusion. Clinical response was defined as a decrease in CDAI by at least 70 points, while clinical remission was defined as CDAI <150. Further, loss of response was defined as the need for escalating IFX dose to maintain clinical remission. Results: At the primary end point, 12 of 15 patients (80%) responded, of these, 10 patients (66.7%) achieved clinical remission (Remission group). The age at CD diagnosis was younger in the non-remission group vs remission group, 15.2±1.5 vs 12.8±1.5 ($P<0.05$). At the secondary end point, 6 of 15 patients (40%) had maintained clinical remission (IFX effective group). Nine of 15 patients (60%) had lost response to IFX (IFX failure group). Patients' weight at first IFX infusion was smaller in the IFX failure group vs IFX effective group, 42.5±11.7 vs 53.4±7.2 ($P<0.05$). Additionally, the L2 type (disease location, colon) and high serum C-reactive protein (CRP) before the first IFX infusion were associated with IFX failure. Only one patient developed mild dyspnoea at the 15th IFX infusion. No other serious adverse event or opportunistic infection during our observation time. Discussion: The short-term response and remission rate in the present paediatric cohort are similar to the levels in the REACH study (1) and also the study in France (2), while the long-term outcome is less impressive. Likewise, IFX-failure rate was higher in our study as compared with the aforementioned studies. We believe that IFX mono-therapy (without IM) s one factor for weaker long-term efficacy in our cohort vs earlier studies. Accordingly, IFX therapy in paediatric CD patients may be influenced by concomitant IM, CD refractoriness, poor nutrition, and disease location. (1) Hyams J, et al. Gastroenterol. 2007., (2) Crombe V,et al. Inflamm Bowel Dis. 2011.

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Video Capsule Endoscopy Improves Clinical and Growth Outcomes in Pediatric IBD Patients

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Background: Video capsule endoscopy (VCE) can be an effective tool in the evaluation of Inflammatory Bowel Disease (IBD). In patients with known Crohn's disease (CD), VCE can help determine extent and severity of small bowel involvement and monitor for treatment response. VCE has also shown to be beneficial in unmasking small bowel CD in patients previously diagnosed with IBD unspecified (IBDU) or ulcerative colitis (UC). Aim: to identify the added value of VCE in pediatric patients diagnosed with or suspected to have IBD, by evaluating changes in treatment and clinical outcomes following VCE. Methods: A retrospective chart review was performed on confirmed IBD (N=66) and suspected IBD (N=17) patients who underwent VCE, at a tertiary care Pediatric IBD center between 2002 and 2011. Diagnostic classifications as well as treatments before and after VCE were analyzed. Clinical outcomes (Harvey Bradshaw Index (HBI) and laboratory parameters (ESR, CRP) including growth (z score) prior to VCE and 12 months after were also collected. Results: The mean age of the patients (N=83) was 12.5 +/- 2.9 yrs. The most common indication for VCE was patients with treated CD requiring further evaluation due to change in clinical status: decreased height velocity (43%) or worsening symptoms (17%). Other indications included patients with presumed UC or IBDU requiring additional small bowel examination to "rule out" CD (19%) and those with suspected IBD (20%). In those with IBD, 60% had a change in treatment following VCE. 85% underwent escalation in therapy: 56% added a biologic,