

## REGULAR REVIEW

## Chronic inflammatory bowel disease

I W Booth

To be consigned to a life spent searching for the aetiology of inflammatory bowel disease remains as much a cause for supplication to St Jude as it ever did. Over the last decade new forms of inflammatory bowel disease have been described, the surgical management of ulcerative colitis has seen the impact of restorative proctocolectomy, and major changes have taken place in the medical management of Crohn's disease in childhood and adolescence. It is therefore appropriate to review some of these developments.

**Epidemiology**

The rapid increase in the incidence of Crohn's disease that took place in all age groups from the mid-1950s (0-2, increasing to 5-6 per 100 000 per year) may now have levelled off, although results in this respect are conflicting.<sup>1</sup> In contrast, the incidence of ulcerative colitis has remained virtually unchanged and still varies between five and 10 per 100 000 per year.

No single dietary factor has been unequivocally implicated in the pathogenesis of the classical forms of inflammatory bowel disease, but it is of interest that further evidence has appeared which suggests that lack of breast feeding, and episodes of diarrhoeal disease during infancy, predispose to the development of childhood Crohn's disease.<sup>2</sup>

**Crohn's disease**

## PRESENTATION AND DIAGNOSIS

*Anorexia nervosa*

The need to consider carefully the diagnosis of Crohn's disease in adolescents with apparent anorexia nervosa is well recognised, but mistaken diagnoses continue.<sup>3</sup> There are almost always sufficient symptoms, signs, or abnormal laboratory results to suggest underlying organic disease and the abnormal ideation relating to body image is absent.

*Panenteric disease*

Crohn's disease has long been recognised as affecting potentially the entire gut, but the frequency of proximal gastrointestinal involvement in childhood has been recognised only recently. Thirty per cent of affected children and adolescents in a large Canadian series,<sup>4</sup> and 42% in a French series,<sup>5</sup> had evidence of

Crohn's disease on upper gastrointestinal endoscopy.

Multiple aphthous ulcers in the oesophagus, gastric antral rigidity, granularity, linear ulceration and irregular thickening of the folds or cobblestoning in the duodenum were the commonest lesions. Upper gastrointestinal endoscopy may therefore be helpful in evaluating patients with suspected Crohn's disease in whom histological evidence is lacking and in patients with so called indeterminate colitis.

*Growth failure and sexual immaturity*

Up to a third of patients experience growth failure, usually with associated delayed skeletal maturation and sexual immaturity. The corresponding figure for ulcerative colitis is probably between 5 and 10%. The definition of growth failure varies, but must be a dynamic one, and a reduction in height centile of more than 0.3 SDs per year, a growth velocity of less than 5 cm per year, or a decrease in height velocity of at least 2 cm from the previous year during early to mid-puberty are all reasonable.<sup>6</sup> Bone age is usually at least two years behind chronological age.

A recent study from Scotland, where three quarters of children with inflammatory bowel disease were in the hands of physicians or surgeons, provides a strong argument for such patients being cared for by paediatric gastroenterologists.<sup>7</sup> In contrast to paediatricians, who invariably recorded height, physicians and surgeons rarely did so. Growth failure often went unrecognised and therefore untreated.

*Atypical Crohn's disease*

In addition to panenteric involvement, Crohn's disease may also involve structures remote from the gut. Recent reports of pulmonary and cutaneous granulomatous reactions in children with Crohn's disease emphasise the potentially multisystem nature of the disorder.<sup>8</sup>

Orofacial granulomatosis is a term used to describe the characteristic constellation of enlargement of the lips, diffuse facial swelling, gingival hyperplasia, oral ulceration, and buccal mucosal tags, which on biopsy are shown to contain non-caseating granulomata. It is becoming clear that up to a one third of such patients have evidence of more widespread involvement of the gastrointestinal tract,<sup>9</sup> and the term oral

University of  
Birmingham,  
Institute of Child Health,  
Francis Road,  
Birmingham B16 8ET

Correspondence to:  
Dr Booth.

Crohn's disease is therefore probably preferable.<sup>10</sup>

#### NUTRITIONAL TREATMENT

##### *Induction of remission*

An elemental, chemically defined diet, with exclusion of all other foods for six weeks is now recognised to be at least as effective as steroids in inducing remission of active disease.<sup>11</sup> Diet induced remission occurred in over 80% of a recent retrospective series, irrespective of the site of the disease, and remission was at least as long as when steroids were used (22% relapsed within six months, and 8–10% each subsequent year.<sup>12</sup> There is an additional benefit for children and adolescents in that linear growth six months after treatment with an elemental diet is substantially better than in those patients given steroids.<sup>13</sup>

The precise mechanism of the beneficial effect of elemental diets is uncertain, but the observation that successful induction occurs twice as commonly with an elemental, amino acid based feed (75%), as with a polymeric feed (36%), suggests that exclusion of intact protein from the gut is an important factor.<sup>14</sup>

##### *Reversal of growth failure*

Growth failure in Crohn's disease is sensitive to both enteral or parenteral nutrition, an outcome which is consistent with the notion that long standing undernutrition is important in the pathogenesis.<sup>15</sup> Overall, studies of nutritional repletion have shown that it is possible to convert a low initial height velocity of between 0.5–0.9 cm per six months to between 3.0–4.5 cm per six months after intervention.

Two recent publications are of interest, each of which has used nutritional supplementation to address the problem of growth failure in prepubertal patients. One used an intermittently administered elemental diet given by overnight nasogastric feeding for one month in four. This resulted in significant increases in growth velocities and reductions in both prednisolone intake and disease activity scores.<sup>16</sup> The second study used an overnight nasogastric supplement to increase energy intake in growth retarded adolescents by between 4.18 and 6.27 MJ (1000 and 1500 kcal) per day. The formula was non-elemental and, in contrast to the previous study, patients were encouraged to eat normally. In non-treated controls, height velocity remained unchanged, whereas in supplemented patients substantial improvements occurred in both height and weight during the year (6.98 cm and 11.75 kg respectively).<sup>17</sup>

Although there is convincing evidence to support energetic nutritional treatment in the management of growth failure, it is also important not to overlook the role of surgery. Two recent publications support early surgical intervention in adolescents with growth failure due to resectable disease. In addition to relieving symptoms, each study demonstrated an improvement in growth after surgery.<sup>18 19</sup> In one study nearly three quarters of operated patients had at least a doubling of preoperative growth velocity.<sup>19</sup>

#### Ulcerative colitis

##### EXTENSION OF PROCTOSIGMOIDITIS

Proctosigmoiditis is fairly common in children and adolescents, and data on the likelihood of progression to more extensive disease, with a poorer prognosis and a higher cancer risk, have recently been published.<sup>20</sup> In contrast to adults, in whom extension occurs in only 10%, proctosigmoiditis remained stable in only 42% of children. Extension into the descending colon occurred in 20%, into the transverse colon in 12%, and more proximally in the remaining 26%. Extension was unpredictable, but usually occurred within five years of onset.

##### COLONOSCOPY

Since early descriptions of colonoscopy in infancy and childhood it has become increasingly clear that this investigation is invaluable in the diagnosis and management of inflammatory disease of the colon.<sup>21</sup> The barium enema in this context is now virtually redundant. The procedure is safe and well tolerated, allows multiple mucosal biopsies to be taken, and often adds important information to the diagnosis. For example, over half the patients in a recent study who had endoscopically confirmed colitis had no radiological evidence of inflammatory disease, although only a single contrast barium examination had been used.<sup>22</sup>

##### DRUG TREATMENT

Sulphasalazine is valuable in the management of ulcerative colitis, particularly as a prophylactic. Side effects, which include reversible male infertility, are common, although probably less troublesome in children. Alternatives to sulphasalazine now exist, and most patients will tolerate mesalazine (delayed release 5-aminosalicylic acid) or olsalazine (altered carrier molecule of salicylate), both of which appear to be as effective as sulphasalazine.<sup>23</sup>

A number of case reports, including two children,<sup>24</sup> and the results of an uncontrolled trial,<sup>25</sup> have recently appeared which suggest that cyclosporin may be useful in patients with severe refractory ulcerative colitis. A controlled trial also suggests a beneficial effect in adults with active Crohn's disease.<sup>26</sup> At present, it is too early to define the precise role of cyclosporin in the management of inflammatory bowel disease, and the results of further trials are awaited, but preliminary results are certainly hopeful.

##### SURGERY

Although restorative proctocolectomy with an ileal reservoir has offered a highly attractive alternative to an ileostomy, the result is unsatisfactory in 5–10% of children and young adults because of excessive stool frequency and/or faecal incontinence.<sup>27</sup> Moreover, pouchitis, a chronic inflammatory disorder of the ileal reservoir producing painful diarrhoea, urgency, and systemic upset, occurs as a long term complication in up to 20% of patients. The long term risks of mucosal dysplasia and neoplasia are uncertain.<sup>28</sup>

### Newer forms of inflammatory bowel disease

#### ALLERGIC COLITIS

Food allergy is an important cause of colitis in the first few months of life.<sup>29</sup> It usually follows a benign course, and most foods are tolerated by 5 years of age.<sup>30</sup> It has been reported in preterm infants, in whom toxic dilatation of the colon can occur.<sup>31</sup> Interestingly, abnormalities after cows' milk challenge may be found in both the jejunum and the rectum of infants with cows' milk sensitive enteropathies.<sup>32</sup> In some infants the abnormality may be expressed only in the colon and not in the proximal small intestine.

Allergic colitis should be suspected in any infant, including a neonate in whom necrotising enterocolitis is an important differential diagnosis,<sup>33</sup> who presents with blood in the stool with or without diarrhoea. A family history of atopy, an eosinophilia, raised serum IgE concentration and positive radioallergosorbent tests are common, but the diagnosis rests upon prompt resolution of symptoms after antigen withdrawal. It is worth noting that the disorder has been described in exclusively breast fed infants.<sup>34</sup> Endoscopy is useful and permits mucosal biopsy. The specimen usually shows an acute and chronic inflammatory cell infiltrate of mainly plasma cells and eosinophils in the lamina propria. Cows' milk is nearly always the offending antigen, but intolerance to soya and beef have been described.

#### COLLAGENOUS AND MICROSCOPIC COLITIS

Patients have recently been described who present with severe diarrhoea, but without blood loss or tenesmus. The colon is macroscopically normal on endoscopy, but histological examination shows appreciable mucosal inflammatory change<sup>35</sup> sometimes with collagenous thickening of the basement membrane.<sup>36</sup> However the existence of collagenous colitis as a separate pathological entity remains somewhat controversial. Patients seem to respond to conventional medical treatment.

#### MISCELLANEOUS DISORDERS

New associations between colitis and systemic disorders have recently been reported in Behçet's syndrome<sup>37</sup> and hypereosinophilic syndrome.<sup>38</sup> Both children reported with Behçet's colitis required subtotal colectomy. The colitis in hypereosinophilic syndrome was steroid responsive.

- 1 Rose JDR, Roberts GM, Williams G, Mayberry JF, Rhodes J. Cardiff Crohn's disease jubilee: the incidence over 50 years. *Gut* 1988;29:346-51.
- 2 Koletzko S, Sherman P, Corey M, Griffiths A, Smith C. Role of infant feeding practices in development of Crohn's disease in childhood. *BMJ* 1989;298:1617-8.
- 3 Jenkins AP, Treasure J, Thompson RPH. Crohn's disease presenting as anorexia nervosa. *BMJ* 1988;296:699-700.
- 4 Lenaerts C, Roy CC, Vaillancourt M, Weber AM, Morin CL, Seidman E. High incidence of upper gastrointestinal tract involvement in children with Crohn disease. *Pediatrics* 1989;83:777-81.
- 5 Mashako MNL, Cezard JP, Navarro J, et al. Crohn's disease lesions in the upper gastrointestinal tract: correlation between clinical, radiological, endoscopic, and histological

- features in adolescents and children. *J Pediatr Gastroenterol Nutr* 1989;8:442-6.
- 6 Kleinman RE, Balistreri WF, Heyman MB, et al. Nutritional support for pediatric patients with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 1989;12:8-12.
  - 7 Barton JR, Ferguson A. Failure to record variables of growth and development in children with inflammatory bowel disease. *BMJ* 1989;298:865-6.
  - 8 Puntis JWL, Tarlow MJ, Raafat F, Booth IW. Crohn's disease of the lung. *Arch Dis Child* 1990;65:1270-1.
  - 9 Scully C, Cochran KM, Russell RL, et al. Crohn's disease of the mouth: an indicator of intestinal involvement. *Gut* 1982;23:198-201.
  - 10 Field EA, Tyldesley WR. Oral Crohn's disease revisited—1 10-year-review. *Br J Oral Maxillofac Surg* 1989;27:114-23.
  - 11 O'Morain C, Segal AW, Levi AJ. Elemental diet as primary treatment of acute Crohn's disease: a controlled trial. *BMJ* 1984;288:1859-62.
  - 12 Teahon K, Bjarnason I, Pearson M, Levi AJ. Ten years' experience with an elemental diet in the management of Crohn's disease. *Gut* 1990;31:1122-37.
  - 13 Sanderson IR, Udeen S, Davies PSW, Savage MO, Walker-Smith JA. Remission induced by an elemental diet in small bowel Crohn's disease. *Arch Dis Child* 1987;62:123-7.
  - 14 Gaffner MH, North G, Holdsworth CD. Controlled trial of polymeric versus elemental diet in treatment of active Crohn's disease. *Lancet* 1990;335:816-9.
  - 15 Kirschner BS. Nutritional consequences of inflammatory bowel disease on growth. *J Am Coll Nutr* 1988;7:301-8.
  - 16 Belli DC, Seidman E, Bouthillier L, et al. Chronic intermittent elemental diet improves growth failure in children with Crohn's disease. *Gastroenterology* 1988;94:603-10.
  - 17 Aiges H, Marcovitz J, Rosa J, Daum F. Home nocturnal supplemental naso-gastric feedings in growth retarded adolescents with Crohn's disease. *Gastroenterology* 1989;97:905-10.
  - 18 McLain BI, Davidson PN, Stokes KB, Beasley SW. Growth after growth resection for Crohn's disease. *Arch Dis Child* 1990;65:760-2.
  - 19 Davies G, Evans CM, Shand WS, Walker-Smith JA. Surgery for Crohn's disease in childhood: influence of sites of disease on operative procedure on outcome. *Br J Surg* 1990;77:891-4.
  - 20 Mir-Madjlessi DH, Michener WM, Farmer RG. Course and prognosis of idiopathic ulcerative proctosigmoiditis in young patients. *J Pediatr Gastroenterol Nutr* 1986;5:570-5.
  - 21 Williams CB, Laage NJ, Campbell CA, et al. Total colonoscopy in children. *Arch Dis Child* 1982;57:49-53.
  - 22 Holmquist L, Rudic N, Ahren C, Fallstrom SP. The diagnostic value of colonoscopy compared with rectosigmoidoscopy in children and adolescents with symptoms of chronic inflammatory bowel disease of the colon. *Scand J Gastroenterol* 1988;23:577-84.
  - 23 Robinson MG. New oral salicylates in the therapy of chronic idiopathic inflammatory bowel disease. In: Ginsberg AI, ed. *Gastroenterology Clinics of North America. Management of inflammatory bowel disease* 1989;18:43-50.
  - 24 Hyams JS, Treem WR. Cyclosporin treatment of fulminant colitis. *J Pediatr Gastroenterol Nutr* 1989;9:383-7.
  - 25 Lichtiger S, Present DH. Preliminary report: cyclosporin in treatment of severe active ulcerative colitis. *Lancet* 1990;336:16-9.
  - 26 Brynskov J, Freund L, Rasmussen SN, et al. A placebo-controlled, double-blind, randomized trial of cyclosporin therapy in active chronic Crohn's disease. *N Engl J Med* 1989;321:845-50.
  - 27 Stryker SJ, Telander RL, Perrault J. Anorectal evaluation after colectomy and endorectal ileoanal anastomosis in children and young adults. *J Pediatr Surg* 1985;20:656-60.
  - 28 Shepherd NA. The pelvic ileal reservoir: apocalypse later? *BMJ* 1990;301:886-7.
  - 29 Jenkins HR, Pincott JR, Soothill JF, Milla PJ, Harries JT. Food allergy: the major cause of infantile colitis. *Arch Dis Child* 1984;59:326-9.
  - 30 Hill SM, Milla PJ. Colitis caused by food allergy in infants. *Arch Dis Child* 1990;65:132-40.
  - 31 Harrison CJ, Puntis JWL, Durbin GM, Gornall P, Booth IW. Atypical allergic colitis in pre-term infants. *Acta Paediatr Scand* (in press).
  - 32 Inyngkaran N, Yadav M, Boey CG. Rectal mucosa in cows' milk allergy. *Arch Dis Child* 1989;64:1256-60.
  - 33 Dupont C, Badoual J, Le Luyer B, Le Bourgeois C, Barbet J-P, Voyer M. Rectosigmoidoscopic findings during isolated rectal bleeding in the neonate. *J Pediatr Gastroenterol Nutr* 1987;6:257-64.
  - 34 Perisic VN, Filipovic D, Kokai G. Allergic colitis with rectal bleeding in an exclusively breast-fed neonate. *Acta Paediatr Scand* 1988;77:163-4.
  - 35 Sanderson IR, Boyle S, Williams CB, Walker-Smith JA. Histological abnormalities in biopsies from macroscopically normal colonoscopies. *Arch Dis Child* 1986;61:274-7.
  - 36 Perisic VN, Kikai G. Diarrhoea caused by collagenous colitis. *Arch Dis Child* 1989;64:867-8.
  - 37 Chong SKF, Wright VM, Nishigame T, et al. Infantile colitis: a manifestation of intestinal Behçet's syndrome. *J Pediatr Gastroenterol Nutr* 1988;7:622-7.
  - 38 Falade AG, Darbyshire PJ, Raafat F, Booth IW. Hypereosinophilic syndrome in childhood presenting as inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* (in press).