

Food allergy: the major cause of infantile colitis

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SUMMARY Forty six children presented with colitis between 1977 and 1981, and all 8 of those below the age of 2 years had food allergic colitis which resolved completely after exclusion of certain foods. In most of the 8 the onset was soon after starting foods other than breast milk. The most common offending food was cows' milk protein, but soya (3 cases) and beef (1 case) were also implicated. A history of allergy in the child or family was common as were blood eosinophilia, high concentrations of serum IgE, and positive IgE antibodies. Colonoscopic appearances were distinctive and biopsies showed a noticeable increase in eosinophils and IgE-containing cells in the lamina propria. We suggest that food allergy is the major cause of colitis in infancy and that an exclusion diet is the treatment of choice.

There are two peaks of age incidence in inflammatory bowel disease and the first peak, which occurs in infancy,^{1,2} may represent a different disease process from that occurring in older children. Food allergy has been implicated in the aetiology of colitis and rectal bleeding,³⁻⁶ and we have therefore studied the effect of dietary treatment in colitis in children who presented below the age of 2 years.

Patients and methods

The age distribution of 46 children with colitis seen between 1977 and 1981 showed two peaks—at less than 2 years and between 6 and 13 years (Fig. 1). All children over the age of 6 years suffered from typical ulcerative colitis (n = 15) or Crohn's disease (n = 23). We report on the 8 patients under the age of 2 years and compare them with 8 matched patients from the older age group (four with ulcerative colitis; four with Crohn's disease) whom we have called 'selected controls'. The 6 patients who presented under 4 months of age were taking cows' milk protein only; they were transferred to a soya milk diet (Cow & Gate 'S' formula) and the two older children, who were already receiving a mixed diet, were given a cows' milk and egg free diet.

The following features were studied: dietary history, the incidence of allergy in the patients and first degree relatives, full blood count, serum immunoglobulins, IgE and IgE antibodies to whole cows' milk, β -lactoglobulin, and ovalbumin. Faecal culture for bacteria and viruses were negative. The whole colon was visualised at colonoscopy in 7 of the

8 patients with food allergic colitis and in all the selected controls by an experienced endoscopist (PJM) using an Olympus PCF colonoscope. Multiple biopsies of the colon, taken before and after treatment with an exclusion diet, were examined by light microscopy; eosinophils were counted on haematoxylin and eosin stained sections and IgE-containing cells by an indirect biotin-avidin immunoperoxidase technique.⁷

Results

All 8 patients presented with bloody diarrhoea, often with mucus. In all 6 who presented before the

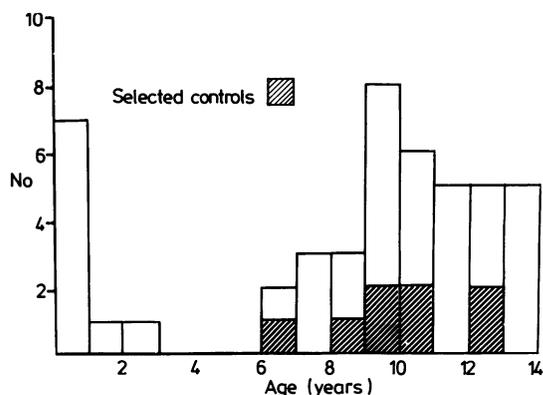


Fig. 1 Age of patients with colitis presenting between 1977 and 1981 (n = 46).

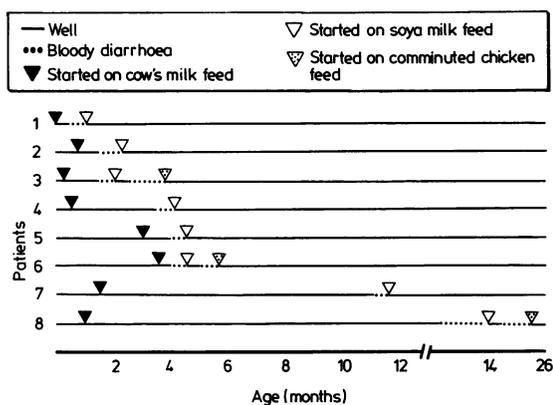


Fig. 2 Infant feeding and onset of symptoms in 8 patients with food allergic colitis. All were breast fed initially except patient 1.

age of 4 months, symptoms followed shortly after the first feed containing cows' milk (Fig. 2). Substitution of cows' milk for a soya protein based feed (Cow & Gate 'S' formula) resulted in the prompt resolution of their symptoms. In three of the 8 patients, however, symptoms recurred between two and 6 weeks after starting the soya milk but resolved when a chicken based feed (Cow & Gate, Chix) was substituted. Two patients were again given cows' milk (5 ml whole cows' milk) between 9 and 12 months after diagnosis but bloody diarrhoea returned within 24 hours. One patient was given beef (1 tin beef broth) for the first time at age 1 year and this precipitated bloody diarrhoea. On return to their exclusion diets, the patient's symptoms resolved and they have since remained well on the diet.

Allergic symptoms were more common in patients with food allergic colitis than in selected

Table 1 Features of atopy in 8 patients with food allergy colitis, 8 selected controls and their first degree relatives

	First degree relatives of:			
	Patients	Controls	Patients	Controls
Eczema	6	2	7	2
Angioedema	2	0	2	0
Asthma	1	0	3	0
Hay fever	0	0	3	1
Rhinitis	1	0	1	1
Eosinophilia	5	1	—	—
Raised IgE	4(5)	0(2)	—	—
Positive radio-allergosorbent test	2(3)	0(1)	—	—
Positive skin prick test	3(6)	—	—	—

Italicised number in parenthesis is number tested when less than 8.

Table 2 Distribution of colonic disease in patients and controls

Distribution	Patients (n = 7)	Controls (n = 8)
Pan-colon	3	7
Left colon	3	1
Transverse colon	0	0
Right colon	1	0

controls, as was a positive family history of atopy related disease ($P < 0.006$, Fisher's exact test) (Table 1). None of the patients was anaemic on presentation, but blood eosinophilia (greater than $350 \times 10^6/l$), high serum IgE concentrations,⁸ and IgE antibodies (greater than $2 \times$ cord blood binding⁹) were more common in the food allergic colitis group. Serum IgG, IgM, and IgA were normal in all patients. Skin prick testing for cows' milk and a number of other food and inhalant antigens was positive in half of the food allergic colitis patients tested (Table 1).

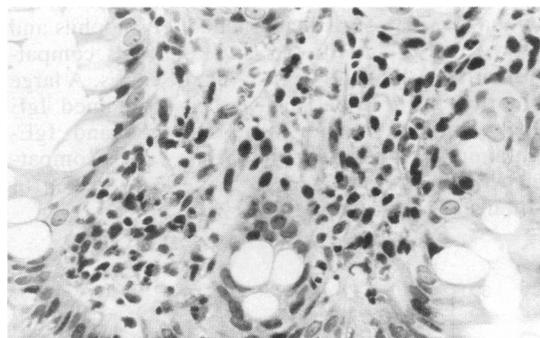


Fig. 3 The large intestinal mucosa of a patient with food allergic colitis (haematoxylin and eosin stain, photographed in green light containing large number of eosinophils ($\times 450$).

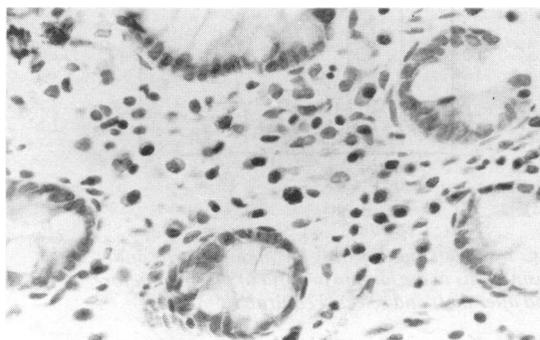


Fig. 4 Increased numbers of IgE-containing cells in the large intestinal mucosa of a patient with food allergic colitis, shown by immunoperoxidase ($\times 450$).

The endoscopic appearances before treatment in the 7 patients with food allergic colitis consisted of patchy erythema with loss of visible vascularity and very occasional mild superficial ulceration. These lesions were interspersed with apparently normal mucosa. In contrast, endoscopic appearances of the control group were typical of either ulcerative colitis or Crohn's disease. Most of the control patients had a pan-colitis, whereas in the patients with food allergic colitis the distribution was more regional (Table 2).

Biopsy specimens were taken from several sites in the inflamed colon. In contrast to the control group who had typical histological features of ulcerative colitis or Crohn's disease, biopsy specimens from the 7 food allergic colitis patients before diet showed preservation of crypt architecture with no evidence of branching of the crypts, no crypt abscess formation, and no depletion of goblet cell mucus. The lamina propria lacked the noticeable vascularity of active chronic ulcerative colitis and the granulomata often seen in Crohn's disease. In all there was an acute and chronic inflammatory cell infiltrate in the lamina propria consisting largely of eosinophils and plasma cells (Fig. 3); this appearance is compatible with the designation eosinophilic colitis. A large minority of the mononuclear cells contained IgE (Fig. 4). The number of eosinophils and IgE-containing cells fell after the diet to values compatible with biopsy specimens from the selected control patients (Fig. 5).

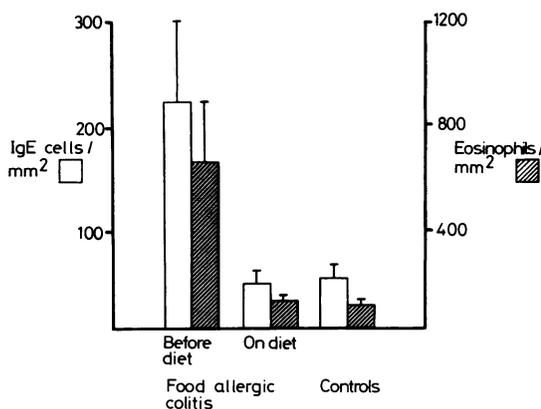


Fig. 5 Mean number of IgE containing cells and eosinophils in the lamina propria of patients (before and after diet) and selected controls.

Significance of Student's *t* test comparison: $P < 0.02$ for mean eosinophils in food allergic colitis group before diet and after diet and for food allergic colitis group before diet and controls; $P < 0.05$ for IgE cells in food allergic group before diet and after diet and for food allergic colitis group before diet and controls.

Discussion

We have shown that food allergic colitis, previously recognised in sporadic cases,³⁻⁵ accounts for most, if not all, children who present in the first year of life suffering from colitis. Previous studies of diet treatment in colitis patients presenting later suggests that their response to diet is, at best, slower and less consistent.¹⁰ We did not treat our older patients with diet.

All our patients presented with bloody, often severe diarrhoea, usually shortly after the introduction of cows' milk feeds. Resolution of symptoms on an appropriate exclusion diet is the only definitive criterion for diagnosis, preferably with appropriate subsequent challenge. Other features suggesting the diagnosis of food allergic colitis in infants with bloody diarrhoea are a history of other allergic diseases in the child or the family, blood eosinophilia, raised IgE concentrations and IgE antibodies, and positive skin prick tests. Though our series of 8 patients below the age of 2 years all had the same disease, there are other causes which require appropriate investigation including stool culture and microscopy and blood coagulation studies. Colonoscopy effectively excludes rare local causes such as angiodysplasia, but it also detects colitis, distinguishing, both microscopically and macroscopically, the food allergic form from others. The specific macroscopic and histological features of chronic ulcerative colitis are lacking in food allergic colitis and the inflammation is represented microscopically by a heavy eosinophilic infiltrate without excessive vascularity and an abundance of IgE-containing mononuclear cells. The appearances of bacterial or viral infection are quite distinct. The mucosal changes are usually not detected by a barium enema, and since they are often patchy, may be missed by sigmoidoscopy alone.

An excess of mucosal eosinophils has been reported in food allergic colitis¹¹ and we report in addition an excess of IgE-containing cells; these findings are compatible with an IgE mediated process. Several foods (cows' milk, soya, and beef) have been implicated in colitis in our patients and the symptoms have usually started soon after the ingestion of the particular food.

It has been suggested that colitis caused by food allergy is a transient phenomenon.^{3,6} Three of our patients who were challenged up to 9 months after diagnosis relapsed so severely that challenge of the other patients was felt to be unjustifiable. Further study is needed to determine their long term prognosis. Though it has been shown that milk allergy may cause anaemia through chronic gastrointestinal bleeding,⁶ none of our patients was

anaemic; presumably their severe symptoms led to diagnosis before this showed.

Ulcerative colitis is associated with a history of 'artificial' infant feeding^{12 13} but there are several other possible hypotheses for this association in addition to food (cows' milk) allergy. By contrast, Crohn's disease is not associated with a history of artificial infant feeding,¹³ but benefit has been reported after an oligoantigenic diet.¹⁴

Our data support the view that there is an identifiable minority of patients with colitis who respond quickly and completely to diet; we show that they constitute at least most of the first peak of the age distribution curve, but it is likely that some will present later. Whether this group is responsible for all the reports of the benefit of diet in ulcerative colitis and Crohn's disease, or whether some or all of these other patients would benefit too, will require further studies. The characteristics we outline of this responsive group will help in designing such studies.

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Sadly, Professor Harries died on 27 April 1983.

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