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Alimentary tract and pancreas

Long term prognosis of Crohn's disease with onset in childhood and adolescence

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SUMMARY The long term outcome has been determined in 67 children with Crohn's disease whose symptoms started at or before 16 years of age. The mean period of follow up was 15·0 years (range 1·5–47 years). The number of children diagnosed in each quinquennium has not increased. Nearly all patients had gastrointestinal symptoms at presentation, but in some cases these were only elicited on careful enquiry. Only four children presented with growth retardation alone. Twenty one per cent of the children had diffuse small bowel disease at onset or during the period of review and posed major problems in management with high morbidity and mortality. They were generally treated medically to suppress disease activity and surgical intervention was restricted to resection of local stricture formation. The outcome in distal ileal ± right colonic disease was similar to that in the adult. Patients with colonic disease (27% of total) were treated medically but 83% required surgical resection after a mean interval of only four years (range 0–9 years). Growth failure occurred in 21 children (height and weight less than 3rd centile) and 11 of these had a period of catch up growth; 10 after resection (ileal ± right colon resected, eight; colonic resection, two) and one after medical treatment. Ten have permanent growth and height retardation, of whom four had diffuse small bowel disease and three had early recurrence after surgical resection. Nine children have died during the period of review, of whom six had diffuse small bowel disease. Despite the high morbidity, 38 of the 58 survivors are now well with no evidence of recurrent disease. A further 14 are well, but with radiological evidence of residual (colon, three; diffuse small bowel, eight) or recurrent (three) disease. Only six have symptomatic disease at present.

Awareness of the problems of Crohn's disease in childhood has increased in recent years.[1–5] The insidious onset with growth arrest and, at times, minimal gastrointestinal symptoms; the relationship between malnutrition and growth failure;[6] the choice and timing of an operation;[7] the role of drugs;[8] and nutritional supplements;[9] have all deservedly received emphasis.

Faced with an individual child with Crohn's disease the clinician who tries to look beyond the immediate problems to the long term prognosis finds little guidance. Gryboski and Spiro[3] reviewed the course of 86 children for a mean period of six years, and emphasised the chronic morbidity of the disorder. Farmer and Michener[10] followed a very large series of 522 patients whose disease had been diagnosed before 21 years, for a mean period of 7·7 years and considered that only 17–27% (depending on the site of disease) had a 'good' quality of life.

At the General and Children's Hospitals, Birmingham, a large combined series of patients with Crohn's disease of childhood onset have been under long term review for up to 47 years (mean 16·5 years). This paper describes their history, management and present status.

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PATIENTS

The series comprised 67 children (37 boys, 30 girls) whose symptoms started at or before 16 years of age. They were referred either to the Gastroenterology Unit of the Children's Hospital or the General Hospital, Birmingham, between 1935 and 1980. The age at onset ranged between 3 and 16 years. The mean length of follow up since onset of symptoms was 16·5 years (range 1·5–47 years) and from diagnosis 15·0 years.

DISTRIBUTION OF DISEASE

The initial site of macroscopic disease in these children and for comparison that found in an unselected group of more than 400 patients referred to the Gastroenterology Unit at the General Hospital is summarised in Table 1. Nine children presented with diffuse small bowel disease, five other children who presented with focal disease in either the ileum or colon subsequently also developed diffuse small bowel disease, making 14 (21%) in all. There were no examples of ileal or colonic disease progressing to diffuse small bowel disease in the adult population.

DATE OF ONSET OF DIAGNOSIS

The date of onset and diagnosis is shown in Figure 1. There has been no marked change in the number of children presenting in each succeeding quinquennium despite evidence that the overall incidence of Crohn's disease is increasing.[11]

AGE AT ONSET OF DIAGNOSIS

The age at onset and diagnosis is shown in Figure 2. The mode for both onset and diagnosis was 16 years.

SYMPTOMS AT PRESENTATION

Nearly all the children (60 out of 67) presented with abdominal symptoms – diarrhoea, abdominal pain, or rectal bleeding either alone or in combination. Abdominal symptoms may be the only presenting feature but are commonly present in association with weight loss or growth retardation (n=19). In this series, presentation with weight loss or growth retardation alone was rare (n=4) (Table 2).

GENERAL PRINCIPLES OF MANAGEMENT

The approach to management was to identify the site and extent of macroscopic disease and to exclude or correct metabolic problems and nutritional deficiencies. Corticosteroid therapy had been used sparingly for symptomatic patients with

Table 1 *Initial site of macroscopic in childhood onset Crohn's disease compared with that observed in the adult population in the series from the General Hospital, Birmingham*

Macroscopic site of disease	*Childhood onset (n=67)*		*Adult onset (n=447)*	
	n	*%*	*n*	*%*
Diffuse small bowel	9	13	17	4
Distal ileum	25	37	207	46
Distal ileum±right colon	13	19	64	14
Colon alone	18	27	156	35
Other	2	3	3	1

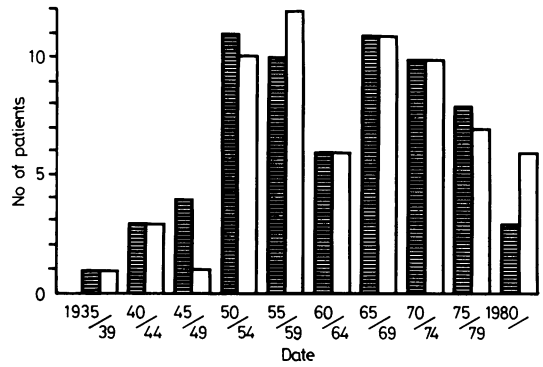


Fig. 1 *Date of onset of symptoms (■) and diagnosis (□) in childhood onset Crohn's disease (n=67).*

non-obstructive ileal disease, extensive Crohn's colitis, or diffuse small bowel disease. Surgical resection of small bowel disease was undertaken for complications (obstruction, abscess, or fistula formation). The principal surgical indication in extensive colonic Crohn's disease was chronic ill health. The rectum was preserved whenever possible.

Diseases at specific sites

DISTAL ILEUM ± RIGHT COLON (Table 3)

SYMPTOMS

This is the largest group and comprised 38 children

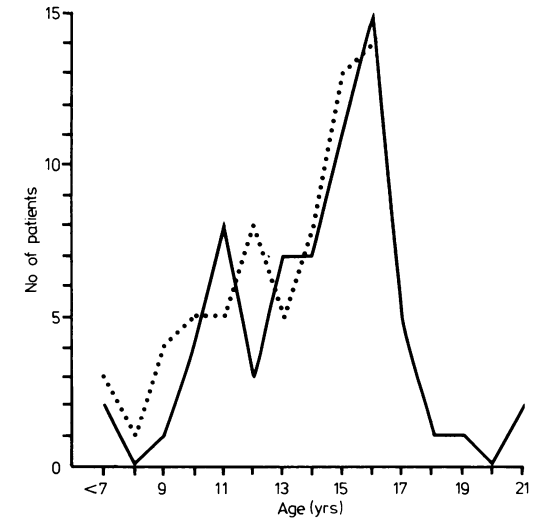


Fig. 2 *Age at onset of symptoms (·····) and diagnosis (——) in childhood onset Crohn's disease (n=67).*

Table 2 *Symptoms at presentation in childhood onset of Crohn's disease*

Abdominal symptoms (diarrhoea ± abdominal pain)		60
Abdominal symptoms alone	23	
With weight loss and/or growth retardation	19	
With weight loss and/or growth retardation and fever	2	
With anaemia	8	
With fever	3	
With anaemia and fever	5	
Weight loss and/or growth retardation alone		4
Anaemia only		2
Mouth ulcers		1
		67

(56%). They usually presented with intermittent obstructive symptoms often associated with general malaise and diarrhoea. They presented occasionally with an obvious mass in the right iliac fossa (n=4) or were found to have Crohn's disease unexpectedly at laparotomy where appendicitis had been suspected (n=4).

SURGICAL TREATMENT

All but two patients had been treated surgically at some time during the period of review. The mean interval between diagnosis of Crohn's disease and resection was 1·7 years. Nineteen of the children have subsequently undergone a second resection and nine a third resection. The cumulative reoperation rates after an initial resection for histologically proven recurrent disease are shown in Figure 3. The cumulative reoperation rates for distal ileal resection and right hemicolectomy after an initial resection in the whole series from the General Hospital, Birmingham, are included for comparison.

GROWTH RETARDATION

Reversal of growth retardation occurred in eight of 12 children in this group who had a resection of the distal ileum or right hemicolectomy before or during puberty. Of those who failed to grow one child had a resection in late puberty, two others subsequently developed diffuse small bowel disease, and one developed an early ileal recurrence.

MEDICAL TREATMENT

Corticosteroids were used in patients with persistent symptoms associated with mucosal inflammatory change without stricture formation. They were prescribed as part of the initial treatment of 10 patients, and for recurrent disease in six, and for an exacerbation in one.

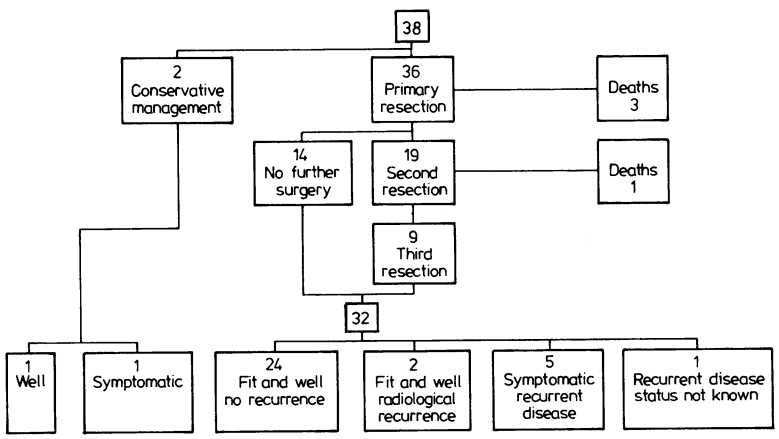
DEATHS

Two patients developed and subsequently died from diffuse small bowel disease (see below). The others died from perforated recurrent disease (one) and an unrelated viral pneumonia (one).

CURRENT STATUS

Of the 34 survivors, 26 are currently fit and well although two have radiological evidence of recurrence. Five have symptomatic recurrent disease. Two have been treated without surgical resection and one is well. The current status of one patient with recurrent disease is not known (Table 3).

Table 3 *Childhood onset Crohn's disease. Long term outcome of distal ileal ± right colon disease*



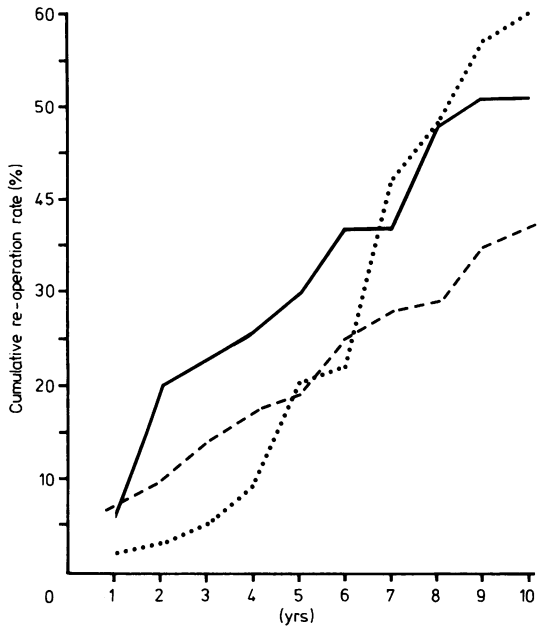


Fig. 3 *Cumulative reoperation rates after an initial resection of distal ileum ± right colon in childhood onset Crohn's disease (—). Results for whole series from General Hospital, Birmingham, after resection of distal ileum (----) or right hemicolectomy (·····) are included for comparison.*

COLONIC INVOLVEMENT (Table 4)

SYMPTOMS

Eighteen children (27%) presented with primary colonic involvement. All had diarrhoea and rectal bleeding either alone or in combination with weight loss and general malaise. When general malaise is the predominant feature the child may initially attract a functional label as happens in adults.[12] One of these children was said to have all the characteristics of a school phobia before her extensive Crohn's disease became more obviously manifest. Two girls were initially referred for psychiatric consultation because they were thought to be suffering from anorexia nervosa.

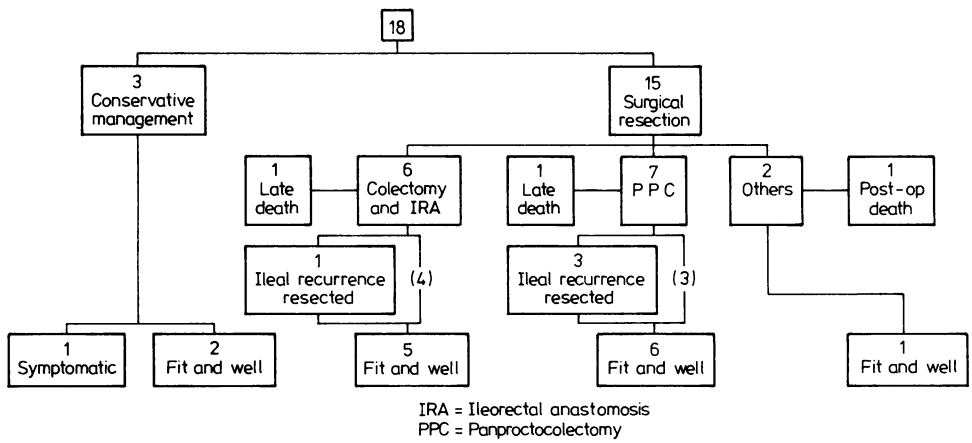
MANAGEMENT

The general management of these patients has been relief of symptoms, correction of metabolic problems and anaemia, with blood transfusions when necessary. Eleven children have received courses of prednisolone or ACTH for periods of more than six months.

SURGICAL TREATMENT

Because of persistent symptoms and general ill-health, often despite corticosteroid therapy, 15 of the 18 patients have undergone surgical resection during the period of review. The mean interval between diagnosis of Crohn's disease to the initial resection was only four years (range 0–9 years). The surgical treatment included colectomy and ileorectal, or ileosigmoid anastomosis (n=6), panproctocolectomy (n=7), local sigmoid resection (n=1), and emergency surgery for a colonic perforation (n=1).

Table 4 *Childhood onset Crohn's disease: long term outlook of colonic involvement*



(i) Growth failure
Only four of these patients who underwent resection before or around puberty had growth failure. Two have responded and one has been followed for less than 12 months. One child developed early ileal recurrence.

(ii) Colectomy and ileorectal anastomosis
The mean interval since resection among the six patients undergoing colectomy and ileorectal anastomosis was six years. One child developed recurrent disease and has been treated medically, the others have remained well, though one patient has since died from a carcinoma arising in the rectal stump.

(iii) Panproctocolectomy
Of the seven patients undergoing panproctocolectomy, four had a single stage procedure, and three a two stage procedure. During the long period of review since panproctocolectomy (mean 13·5 years) one patient developed diffuse small bowel disease and subsequently died from amyloidosis, but all the others are well.

(iv) Other
The patient undergoing emergency surgery for colonic perforation also had diffuse small bowel disease and died postoperatively.

CURRENT STATUS
Overall, of the 15 patients undergoing resection, 12 are alive and well, although four have had further resections for recurrent disease during the period of review. Of the three treated conservatively, two are well, while a third has received corticosteroid therapy, but none of these three are growth or height retarded.

DIFFUSE SMALL BOWEL DISEASE
MEDICAL MANAGEMENT
Nine children presented with diffuse small bowel disease. They posed major problems in management as they often had severe symptoms and major metabolic problems. All but two of these children have received prednisolone or ACTH for periods of more than six months.

SURGICAL TREATMENT
Surgery was restricted to resection of local stricture formation. Five children have undergone surgical resection (three multiple resections, two single resections for local stricture formation), and are now all well. Two have had prolonged periods of ill health of whom one has died. The other required prolonged treatment with corticosteroids in order to suppress disease activity. Two children ran a mild course for many years, one of which was complicated by fatal small bowel cancer.

FOCAL LESIONS PROGRESSING TO DIFFUSE DISEASE
Five further children developed diffuse small bowel disease during the period of review of whom four have since died. Two developed diffuse small bowel disease after ileal resection and eventually died from complications of corticosteroid therapy. One child with colonic involvement developed diffuse small bowel disease complicated by fatal amyloidosis. One patient undergoing emergency surgery for colonic perforation also had diffuse small bowel disease. A fifth presented with ileal disease progressed to diffuse small bowel disease and is currently well.

Other sites

One patient had a duodenal stricture treated surgically but also has residual colonic disease, is addicted to steroids, and is currently stunted but well. Another presented with oral and perianal Crohn's disease, developed a rectal stricture, was ultimately treated by panproctocolectomy, and is now well.

PERIANAL DISEASE
Perianal disease was an important feature in only four patients who all had extensive colonic disease. It did not affect the clinical management in any other patient.

GROWTH FAILURE
Growth failure, defined as height or weight below the third centile for age,[13] occurred in 21 (31%) of our children at some time during their illness. There was permanent retardation in 10 (15%) but the others (11) underwent catch up growth (at least to the 10th centile), eight after resection of the ileum with or without the right colon, two after colonic resection, and one patient with diffuse small bowel disease treated medically. Of the 10 patients with permanent retardation (of whom five have died), two were treated conservatively, four had local surgical resection of strictures in diffuse small bowel, one underwent resection during late puberty, and three patients failed to grow because of early recurrent disease after surgical intervention.

Current status

The outcome in the nine patients who died are summarised in Table 5. Fifty eight of the 67 children studied are still alive. Three are below the 3rd

Table 5 *Deaths*

Initial illness				*Subsequent course*					
								Age and date of death	
Sex	*Onset*	*Age (yrs)*	*Initial site of macroscopic disease*	*Surgical treatment*	*Date*	*Age (yrs)*	*Outcome and cause of death*	*Date*	*Age (yrs)*
M	1951	14	Ileum + right colon	Right hemicolectomy	1955	18	Recurrent disease 1964 Perforated colon 1965	1965	28
M	1951	9	Ileum + right colon	Right hemicolectomy	1954	11	Stunted – but remained well. Acute viral pneumonia	1982	31
M	1951	15	Colonic	Right hemicolectomy Ileo-rectal anastomosis	1954 1967	18 31	Cancer in retained rectum	1977	41
F	1954	10	Diffuse small bowel	Appendix Right hemicolectomy Ileal resection Fistula/bypass	1954 1963 1971 1973	10 19 27 29	Prolonged ill health. Gross weight loss. Died of postoperative sepsis	1974	36
M	1958	14	Diffuse small bowel	Laparotomy	1968	24	Anaplastic carcinoma of jejunum	1968	24
M	1958	9	Distal ileum Diffuse small bowel	Distal ileal resection	1961	12	Prolonged ill health Treated with ACTH	1971	27
M	1952	12	Distal ileum Diffuse small bowel	Ileal resection Resection of recurrence Resection of recurrence	1953 1962 1963	13 22 23	Pneumonia and ACTH induced hypertensive renal failure	1964	24
F	1951	15	Colon Diffuse small bowel	Laparotomy for perforated colon	1953	17	Postoperative death	1953	17
F	1947	3	Colon Diffuse small bowel	Panproctocolectomy	1963	19	Renal amyloidosis – renal transplant Died postoperatively	1975	28

centile for height, of whom one has recurrent episodes of weight loss, and one patient had permanent weight loss.

Thirty eight of the 58 survivors are fit and well with no evidence of recurrent disease. A further 14 patients are well but with radiological evidence of either residual colonic disease (three), diffuse small bowel disease (eight) or recurrent disease (three). Five have recurrent symptomatic disease (three with obstructive symptoms and small bowel recurrence, one with ileal recurrence and weight loss, one with residual colonic disease after ileal resection). One patient has residual symptomatic colonic disease which has been treated conservatively.

Discussion

Throughout the period of review patients have been subject to regular reappraisal, together with the identification and correction of metabolic problems.

DIAGNOSIS

While a diagnosis of inflammatory bowel disease must be considered in children presenting with growth retardation, we agree with Burbige and his colleagues[2] that most children have gastrointestinal symptoms at presentation. The diagnosis of Crohn's disease may sometimes be overlooked as the children often do not volunteer that they have gastrointestinal symptoms which are elicited only on careful enquiry. Abnormal laboratory indices (haemoglobin, serum albumin, and acute phase proteins) may suggest the correct diagnosis particularly in children with anorexia or apparently functional symptoms. At least one of these indices was abnormal at the time of presentation.

DISTAL ILEAL DISEASE ± RIGHT COLON INVOLVEMENT

The pattern of clinical presentation in distal ileal ± right colon disease was similar to that observed in adults.[3] Surgical resection was an effective option in those children with persistent symptoms and local complications. It resulted in rapid reversal of growth retardation in most children undergoing resection before late puberty.

Recurrent disease is commoner in children than in adults[7] but was usually confined to a short segment at or around the anastosis which was amenable to further resection if symptoms persisted.

COLONIC CROHN'S DISEASE

Colonic Crohn's disease has a higher morbidity than small intestinal disease.[10] Although the interval between diagnosis and resection was short, medical treatment played a useful contribution in delaying surgical resection for four to five years. The outcome after colectomy and ileorectal anastomosis or panproctocolectomy has been remarkably good, particularly considering the long period of follow up. Only one child has developed recurrent disease, though there have been two deaths (one from amyloidosis and one from cancer in the rectal stump).

DIFFUSE SMALL BOWEL DISEASE

More than 20% of the children developed diffuse small bowel disease, a figure similar to the incidence reported by Gryboski and Spiro[3] and much commoner than in adults.[14] Children with diffuse small bowel disease (either at presentation or developing during review) pose major problems in management and carry a high morbidity and mortality. Surgical intervention is limited to resection of local strictures to relieve obstructive symptoms which often develop during the course of follow up. Despite the problems determined and persistent management in this group was worthwhile as healing of diffuse small bowel disease may occur with time and residual stricture formation can be relieved by local resection. Permanent growth or height retardation was a common problem in this group and was only reversed by medical treatment in one child.

GROWTH FAILURE

Growth failure in children with Crohn's disease results from prolonged inadequate caloric intake and can be reversed by adequate nutritional support[6] either orally,[15] by continuous elemental enteral alimentation,[9] or after parenteral alimentation either in hospital[16] or at home.[17]

When resection of macroscopic disease permits oral nutritional restitution and adequate caloric and protein intake, growth and maturation are frequently re-established.[18] Homer and his colleagues[7] have emphasised that this expectation may not be achieved if surgery is undertaken in late puberty or if recurrent disease supervenes.

There were 21 (31%) children whose height, weight, or both were below the third centile at some time during their illness. Eleven of the 21 children showed catch up growth, all but one after surgery, and their height and weight have improved at least to the 10th centile. Of the seven patients whose height was below the third centile, five have improved to above the 90th centile. The most dramatic postoperative weight increases occurred in those with sudden preoperative weight loss.

Catch up growth occurred mostly in children after ileocolonic resection as persistent medical treatment was often attempted in extensive colitis to avoid

colectomy in childhood so that surgery was usually delayed until after puberty.

Of the 10 children permanently retarded, two with extensive disease have not grown despite medical treatment. There was no growth spurt after surgery in eight children because four had local resections of stricture in the presence of residual small bowel disease, three children failed to grow after ileal resection because they developed early recurrent disease and one had a resection in late puberty.

In this series presentation with growth failure alone was rare (6%). Almost invariably gastrointestinal symptoms could be elicited on careful enquiry.

LONG TERM PROGNOSIS AND CURRENT STATUS

The prognosis of childhood onset Crohn's disease has been considered by a number of workers.[3 7 10] The long period of review since onset of symptoms (mean 16·5 years) has enabled us to temper the pessimism commonly associated with a diagnosis of Crohn's disease in childhood. Although a disorder of high morbidity and excess mortality, the long term prognosis for most children is good. During the period of review nine patients have died. The causes of death are summarised in Table 4. Fifty two of the 58 survivors, however, are currently well although 14 have radiological evidence of residual or recurrent disease. Even in patients with diffuse small bowel disease persistent effort is worthwhile as the long term prognosis in some of these patients is good.

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