

# Clinical presentation and course of Crohn's disease in southeastern Ontario

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**ABSTRACT:** Clinical records of 222 patients with proven Crohn's disease identified at Queen's University Medical School in Kingston, Ontario from 1966 to 1984 were reviewed. Four clinical patterns were identified. Ileocolic disease (44%) was most frequent. Small intestinal involvement alone occurred in 30% while colonic involvement alone was documented in 18%. Gastroduodenal Crohn's disease was diagnosed in 8.5% but in all such patients there was involvement of additional small or large bowel. Females (57%) out-numbered males (43%) with a female to male ratio of 1.3. The age range at diagnosis was seven to 73 years and 177 patients (80%) were diagnosed between the ages of 11 and 40 years. Patients with colonic disease only tended to be older and had fewer obstructive episodes, fewer surgical resections and more gross rectal bleeding. Patients with gastroduodenal disease were more often male, usually had additional small bowel involvement, experienced more local complications and required more surgical intervention than the other patterns. Only one patient was identified with disease restricted to the anorectum. Patients in this series were followed from two months to 24 years. The mean duration of follow-up was 4.9 years. The frequency of complications and the necessity for surgery were similar to other reported series. None of the patients had either large or small bowel cancer during the follow-up period and there were no deaths related directly to Crohn's disease, its complications or related surgery. *Can J Gastroenterol* 1988; 2(3):107-116.

**Key Words:** *Clinical course, Crohn's, Ontario*

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THE CLINICAL PRESENTATION AND course of Crohn's disease has been described in a number of reports from centres in the United States (1,2), the United Kingdom (3,4) and Scandinavia (5,6). In North America, most of the information reported is derived from patient populations evaluated in large urban teaching centres, thereby providing a description of Crohn's disease which tends to accentuate the more severe forms and complications. Apart from a description of 25 cases from Sherbrooke in 1972 (7) and a review of 98 cases with small bowel disease from Alberta in 1964 (8), the clinical aspects of Crohn's disease in Canada have not been extensively detailed.

To determine the clinical behaviour of Crohn's disease in a representative Canadian population the Divisions of Gastroenterology at Queen's University Medical School undertook a retrospective review of all patients diagnosed with

Crohn's disease since 1966. This report summarizes some important features which characterize the clinical spectrum of Crohn's disease in this predominantly English speaking, Caucasian patient population.

### PATIENTS AND METHODS

Queen's University Medical School is the only tertiary referral medical centre in southeastern Ontario and it is presently serving a population of approximately 670,000 (unpublished data) with both urban and rural areas represented.

Since 1966 it has been the custom of most community family physicians in the catchment area to refer all cases of suspected inflammatory bowel disease to the two affiliated teaching hospitals in Kingston for evaluation and assistance. These referral practices are well established and are independent of the severity of the inflammatory bowel disease in question. Furthermore, it is customary for consultant general surgeons at the medical school to involve members of the Divisions of Gastroenterology in the care of patients with inflammatory bowel disease admitted initially to surgical services. Consequently this centre evaluates and manages, both medically and surgically, most patients suffering from inflammatory bowel disease in the region. Patients are followed regularly in specialized hospital based ambulatory clinics and are identified in both hospital and divisional records.

The Crohn's disease population which forms the basis of this report was selected by a review of all divisional and hospital records. The review extends from 1966 to 1984 and includes all patients in whom a specific diagnosis of Crohn's disease, regional ileitis or granulomatous colitis was made. To ensure that cases of inflammatory bowel disease, managed primarily or exclusively by the Divisions of General Surgery at the two hospitals, were not excluded, the clinical records of the individual surgeons involved in intestinal surgery were also reviewed. Only four additional patients with Crohn's disease were discovered.

A simultaneous review for cases of ulcerative colitis, the clinical details of which form the subject of another report, permitted the correct identification of

cases of Crohn's disease initially misdiagnosed as ulcerative colitis in seven instances.

The hospital and divisional records of all identified patients were reviewed in detail. Relevant clinical information was extracted from the original records and transposed into specialized recording charts to facilitate data analysis.

During the review of the clinical information contained in the records, attention was directed specifically to the confirmation of the diagnosis of Crohn's disease according to accepted clinical, endoscopic, radiologic, histologic and surgical criteria. Patients with well documented, chronic inflammatory colitis which could not be classified as either Crohn's or ulcerative colitis were designated 'indeterminate'. Five patients with inflammatory colitis were excluded because there was inadequate data to permit a diagnosis. Patients with a single, self-limited episode of terminal ileitis were also excluded since it is probable that many were secondary to infections such as *Yersinia* and *Campylobacter*.

The patient data were arranged in four clinical patterns. These patterns were selected according to the anatomic distribution of disease and in consideration of previous reports (1,9). In each case the pattern was determined at the most recent follow-up by the maximum extent of disease using all available endoscopic, radiologic and surgical information. In all cases the investigation of extent included a barium meal with a small bowel follow through accompanied by a barium enema and sigmoidoscopy. In most, colonoscopy was also employed in staging, but upper endoscopy was only performed for specific indications (ie, symptoms, radiographic abnormalities). Consequently, clinically silent, microscopic involvement was not considered in the determination of anatomic distribution. Patients in the gastroduodenal group had gastric and/or pyloroduodenal involvement in addition to other intestinal sites.

Familial occurrence of Crohn's disease was determined prospectively by direct interview of 91 unselected patients in this series who were seen for evaluation or review over one year.

The significance of differences among

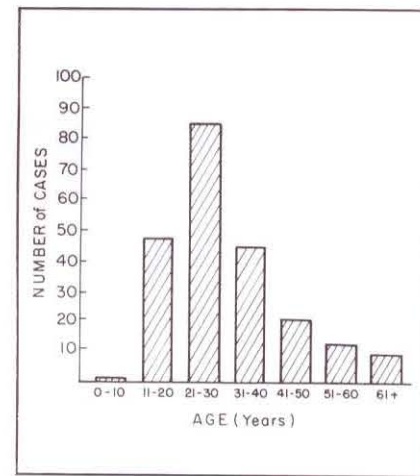


Figure 1) Age distribution at diagnosis

the four patterns was established using the  $\chi^2$  test.

### RESULTS

**Patient population:** The review identified 254 patients with proven or suspected Crohn's disease. The records in 12 cases were incomplete, making a specific diagnosis impossible and these cases were excluded. In 20 patients with colonic disease the clinical details did not permit satisfactory differentiation from ulcerative colitis. These patients were classed as 'indeterminate' and were also excluded, leaving a study population of 222 patients.

**Prevalence of disease:** For several reasons a precise determination of disease incidence and prevalence is not possible. For example, it is known that some cases of Crohn's disease in this region are diagnosed and managed elsewhere. In addition, some patients have been lost to follow-up.

Based on estimates of the maximum size of the catchment area provided by the Queen's University Department of Epidemiology (unpublished data), the minimum prevalence of Crohn's disease in southeastern Ontario is approximately 33 cases per 100,000 population.

**Age and sex distribution:** The study population included 126 females (57%) and 96 males (43%). The female to male ratio was 1.3. The age at diagnosis varied from seven years to 73 years. Figure 1 shows that the bulk of the patients (90%) presented between ages 11 and 40 with peak incidence in the third decade.

TABLE 1

## Clinical pattern of disease — Case distribution

Clinical pattern	Number	Total	Female/Male	Subgroup	Number	Subgroup
Ileocolic	98	44%	1.6	Ileum		
				Right colon only	20	21%
				Total colon	21	21%
				Segmental colon	57	58%
				Distal ileum		
Small bowel	66	30%	1.1	Nil else	43	65%
				Perianal	22	33%
				Other small bowel	1	2%
Colonic	39	18%	1.8	Total colon	17	44%
				Segmental colon	21	54%
				Anorectum	1	2%
Gastroduodenal	19	8%	0.6	Small bowel	18	95%
				Total colon	1	5%

## CLINICAL PATTERNS

**Patient distribution:** Four clinical patterns were identified (Table 1): ileocolic disease, identified in 98 patients (44%), was most common; 66 patients (30%) suffered from small intestinal involvement alone; 39 patients (18%) had disease restricted to the colon; and gastroduodenal Crohn's disease was identified in 19 patients (8%), but in each of the latter cases there was additional involvement of either the small bowel or the colon.

In those with ileocolic disease, colonic involvement was primarily segmental (58%). Contiguous right colonic disease or total colon involvement were equally represented (20 and 21%, respectively). The majority (65%) with small bowel disease had isolated distal ileal involvement. Distal ileitis associated with prominent perianal disease was documented in a third of this group while ileitis and jejunitis occurred in only one patient. Isolated colonic involvement was almost equally distributed between segmental (54%) and total (46%) colitis. The single patient with anorectal disease was arbitrarily assigned to this group. Gastroduodenal Crohn's was most frequently associated with variably severe small bowel disease (95%). In one case, gastroduodenal involvement was associated with both small bowel and colonic disease.

Females outnumbered males in all groups except the gastroduodenal group where the female to male ratio was 0.6. The female predominance was most

marked in the ileocolic and colonic patterns.

Figure 2 shows the age distribution at the time of diagnosis for the four clinical groups. The pattern for each is similar to that described for the entire patient population. The apparent lack of presentation of gastroduodenal Crohn's after age 40 and the suggested biphasic nature of the distribution in Crohn's colitis with a second peak in the sixth decade should be noted.

**Follow-up:** Of the patients in this particular study 98% have been followed by the Divisions of Gastroenterology at Queen's University Medical School. The follow-up intervals range from two months to 24 years with a mean of 4.9

years. Table 2 indicates that at least one-third of the patients in each clinical group have been followed for five years or longer. Less than 20% have been followed for less than one year. As discussed, the follow-up of these patients is extensive. Because of the special interest in inflammatory bowel disease, clinic records contained complete documentation of the course of the disease, the development of complications and the frequency of surgical intervention.

**Symptoms and signs:** The symptoms and signs of Crohn's disease have been well described (5,6). For the purpose of this retrospective study, a number of practical definitions were adopted. Diarrhea was considered present if the stool frequency was increased more than normal for the patient and if the consistency of the stool was more fluid than normal and the changes could not be explained by any other process. Abdominal pain was considered to be related to inflammatory bowel disease after exclusion of pain from other gastrointestinal and hepatobiliary conditions. Weight loss was identified when a reduction in weight (greater than 5%) occurred in the absence of some other obvious explanation. Rectal bleeding was recorded when there was visible blood in the stools. Such bleeding appeared in the form of bright red streaks of blood or was more substantial but infrequent tissue staining and occult bleeding were excluded.

Since symptoms commonly predated the diagnosis (Table 3), the earliest

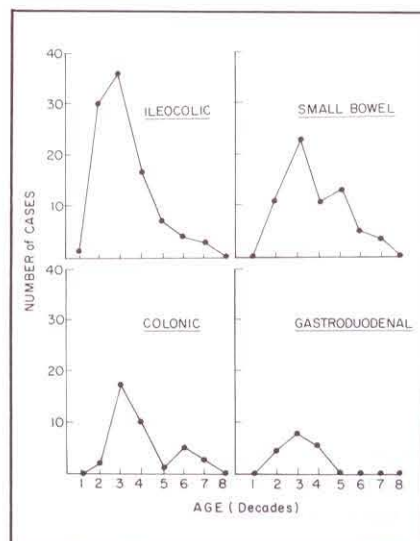


Figure 2) Age distribution at diagnosis according to clinical pattern

**TABLE 2**  
Duration of follow-up according to clinical pattern

Years of follow-up	Clinical pattern (number of patients/% of clinical pattern)				Total
	Ileocolic	Small intestine	Colon	Gastroduodenal	
0-1	16 (16%)	14 (21%)	7 (18%)	3 (15%)	40 (18%)
1-2	19 (19%)	10 (15%)	6 (15%)	1 (5%)	36 (16%)
2-5	26 (26%)	18 (28%)	14 (25%)	2 (11%)	60 (27%)
5-10	21 (21%)	16 (24%)	5 (14%)	7 (38%)	49 (21%)
>10	16 (16%)	8 (12%)	7 (18%)	6 (31%)	37 (17%)

**TABLE 3**  
Duration of symptoms prior to diagnosis according to clinical pattern

Duration	Clinical pattern				Total n = 218
	Ileocolic n = 96*	Small bowel n = 65*	Colonic n = 38*	Gastroduodenal n = 19	
< 6 months	44 (47%)	15 (23%)	8 (21%)	4 (21%)	71 (33%)
6 - 12 months	12 (12%)	18 (27%)	11 (29%)	5 (26%)	46 (21%)
1 - 2 years	24 (25%)	13 (20%)	6 (16%)	7 (37%)	50 (23%)
3 - 4 years	8 (8%)	3 (5%)	5 (13%)	1 (5%)	17 (8%)
5 - 10 years	6 (6%)	9 (14%)	5 (13%)	1 (5%)	21 (9%)
> 10 years	2 (2%)	7 (11%)	3 (8%)	1 (5%)	13 (6%)

\* In some cases (two, one, and one, respectively) the clinical record was inadequate to establish duration interval

**TABLE 4**  
Initial clinical features

	Clinical pattern				Total n = 218
	Ileocolic n = 96*	Small bowel n = 66	Colonic n = 38*	Gastroduodenal n = 18*	
Diarrhea	68 (71%)	44 (68%)	31 (79%)	12 (67%)	155 (71%)
Abdominal pain	69 (72%)	43 (66%)	26 (67%)	7 (39%)	145 (67%)
Weight loss	36 (38%)	12 (18%)	12 (31%)	7 (39%)	67 (31%)
Rectal bleeding	16 (17%)	12 (18%)	19 (49%)†	2 (11%)	49 (22%)
Pyrexia	15 (16%)	3 (2%)	5 (13%)	3 (17%)	27 (12%)
Perianal abscess	3 (3%)	5 (8%)	2 (5%)	0	10 (5%)
Perianal fistula	4 (4%)	3 (2%)	1 (3%)	1 (6%)	8 (4%)
Anal fissures	3 (3%)	2 (3%)	2 (5%)	0	7 (3%)

\* In some cases (two, one, and one, respectively) the clinical record did not allow accurate determination of the initial presenting features. † Significant difference  $P < 0.05$

clinical features of active Crohn's disease were sought. As depicted in Table 4, diarrhea was a prominent early feature and was one of the initial symptoms in more than two-thirds of cases. The occurrence of abdominal pain paralleled diarrhea, except in the gastroduodenal group where it was significantly less conspicuous. Weight loss was identified in about one-third of each group. As expected, rectal bleeding was significantly more common in colonic Crohn's.

The mean duration of clinically apparent symptoms until diagnosis was 3.6 years. Patients with ileocolic disease were more frequently identified within the

first six months following the onset while patients with small intestinal disease, colonic disease alone and gastroduodenal Crohn's tended to be diagnosed later. In 75% of the entire group the diagnosis was made within two years of the onset of symptoms but 15% suffered from chronic diarrhea, abdominal pain or fatigue accompanied by variable weight loss for more than five years before the diagnosis was established.

At the time of diagnosis, the pattern of symptoms was similar but the frequencies of each were increased (Table 5). Diarrhea was present in almost 90% of the patients. Abdominal pain was

evident in 80% of the patients except in the gastroduodenal group in which it was much less common (17%). Rectal bleeding in colonic Crohn's at the time of diagnosis was even more striking than at onset.

Pyrexia was not a common major finding at onset but it emerged as a predominant feature in 21% at diagnosis. Perianal disease (abscess, fistula) and anal fissures were relatively uncommon, both at onset (12%) and at diagnosis (11%).

In view of the recurrent and progressive nature of Crohn's disease, the accrual of clinical features over the total duration of disease was analyzed (Table 6). Diarrhea and abdominal pain occurred in 90 to 100% in all groups. Rectal bleeding remained significantly more common in Crohn's colitis but was well represented in the other patterns. Pyrexia, associated with disease activity, was seen eventually in almost half of the patients with both colonic and gastroduodenal Crohn's and in one-third of the patients with ileocolitis. Only 18% with small bowel disease alone suffered significant bouts of fever.

Although perianal disease was uncommon at both onset and diagnosis, at least one-quarter of the patients in each group developed some evidence of perianal involvement while under observation. There was no apparent difference in the frequency of perianal disease among the four clinical patterns. Despite the presence of colitis, some degree of constipation was reported at some point in nearly 20% with colonic and 10% with ileocolic disease. Although nausea and vomiting were common in gastroduodenal Crohn's, these symptoms did not specifically distinguish this group.

**Family history:** Familial clustering of Crohn's disease was determined in detail by direct interview in 91 unselected patients in this series. In 19 (21%) there was a clear history of familial inflammatory bowel disease. Of the 24 affected relatives so identified, five (21%) had ulcerative colitis rather than Crohn's disease. There were nine first degree, 12 second degree and three third degree relatives in this group. In four of the 19 patients, affected relatives were found in two degrees.

TABLE 5  
Clinical features at diagnosis

Feature	Clinical pattern				Total n = 220
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 38*	Gastroduodenal n = 18*	
Diarrhea	83 (85%)	58 (89%)	34 (89%)	16 (89%)	191 (87%)
Abdominal pain	78 (80%)	54 (83%)	31 (79%)	3 (17%)†	166 (75%)
Weight loss	52 (53%)	23 (35%)	22 (56%)	12 (67%)	109 (50%)
Rectal bleeding	16 (16%)	13 (20%)	24 (62%)†	3 (17%)	56 (25%)
Pyrexia	22 (23%)	7 (11%)	10 (26%)	7 (39%)	46 (21%)
Perianal abscess	3 (3%)	5 (8%)	2 (5%)	0	10 (5%)
Perianal fistula	4 (4%)	2 (3%)	1 (3%)	1 (6%)	8 (4%)
Anal fissures	2 (2%)	2 (3%)	1 (3%)	0	5 (2%)

\* In one case the clinical record was inadequate to specify the clinical features at diagnosis. † Significant difference  $P < 0.05$

**Complications:** Complications related to Crohn's disease were classified as local or systemic. Local complications included those related directly to intestinal inflammation.

Table 7 lists the major local complications encountered. Internal fistulae were common in each group. Intra-abdominal and pelvic abscesses occurred significantly more often with gastroduodenal involvement (37%) compared to all other groups (less than 10%).

As expected, bowel obstruction was uncommon in Crohn's colitis. In contrast, almost one-half with gastroduodenal involvement and one-third with either ileocolitis or small intestinal involvement alone experienced an obstruction at some stage.

Obstructive uropathy, limited to cases with ileal involvement, was rare (five cases). Similarly, massive hemorrhage (two cases) and toxic megacolon (two cases) occurred only in those with ileocolitis.

Free perforation developed in 8% with ileocolitis, 6% with small intestinal disease alone and 26% with gastroduodenal involvement. No patient with disease restricted to the colon alone experienced a free perforation.

Table 8 lists the systemic complications and closely related diseases by clinical pattern. Anemias of chronic disease and of iron deficiency occurred in almost one-third of each patient group. Folate and vitamin B12 deficiencies were much less common.

Iritis and uveitis, seen in all patterns, occurred in only 5% in total. Pyoderma gangrenosum (2%) and erythema nodosum (5%) were restricted to patients with

at least some involvement of the colon. Arthritis, characterized by joint pain and swelling with variable tenderness and limitation of motion, was diagnosed in 10%. The arthritis which involved large joints predominantly was asymmetric, pauci-articular, rheumatoid factor negative and acetylsalicylic acid (or steroid) responsive. It was more common with colonic involvement but it also occurred in patients with small intestinal disease

alone. Patients with arthralgia only were not included in this classification.

The numbers of patients with proven pericholangitis (two cases) and sclerosing cholangitis (two cases) were small. Since several patients with mildly abnormal liver tests but without signs of cholestatic liver disease were not investigated further, it is probable that these conditions are under-represented. Because of its persistent and progressive nature, it is less likely that sclerosing cholangitis was underdiagnosed, but in view of the failure to pursue mild liver test abnormalities with cholangiography or biopsy, patients with sclerosing cholangitis may have been missed. No cases of chronic active liver disease, cirrhosis or bile duct cancer were encountered.

**Surgery:** Table 9 depicts the surgical experience of the patient group by clinical pattern. One-hundred and twenty-five patients (56%) underwent a surgical procedure during the period of observation. In 90 patients there was surgical resection of involved bowel, while in 69

TABLE 6  
Cumulative clinical features

Feature	Clinical pattern				Total n = 222
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 39	Gastroduodenal n = 19	
Diarrhea	90 (92%)	60 (91%)	39 (100%)	17 (89%)	206 (93%)
Abdominal pain	84 (86%)	63 (95%)	35 (90%)	18 (95%)	200 (90%)
Weight loss	66 (67%)	36 (55%)	22 (56%)	15 (79%)	139 (63%)
Rectal bleeding	51 (52%)	20 (30%)*	28 (72%)*	8 (42%)	107 (48%)
Pyrexia	31 (32%)	12 (18%)	16 (41%)	9 (47%)	68 (31%)
Perianal abscess	14 (14%)	9 (14%)	9 (23%)	5 (26%)	37 (17%)
Perianal fistula	15 (15%)	9 (14%)	8 (21%)	5 (26%)	37 (17%)
Anal fissures	18 (18%)	20 (30%)	10 (26%)	5 (26%)	53 (24%)

\* Significant difference  $P < 0.05$

TABLE 7  
Local complications

Feature	Clinical pattern				Total n = 222
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 39	Gastroduodenal n = 19	
Internal fistula	16 (16%)	7 (11%)	6 (15%)	4 (21%)	33 (15%)
Abdominal/pelvic abscess	7 (7%)	5 (8%)	3 (8%)	6 (32%)*	21 (9%)
Obstruction	31 (32%)	24 (36%)	2 (5%)*	9 (47%)	66 (30%)
Free perforation	8 (8%)	4 (6%)	0	5 (26%)*	18 (8%)
Massive hemorrhage	2 (2%)	0	0	0	2 (1%)
Megacolon	2 (2%)	0	0	0	2 (1%)
Obstructive uropathy	2 (2%)	2 (3%)	0	1 (5%)	5 (2%)

\* Significant difference  $P < 0.05$

**TABLE 8**  
Systemic complications and related conditions

	Clinical pattern				Total n = 222
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 39	Gastroduodenal n = 19	
Anemia					
Chronic disease	31 (32%)	13 (20%)	13 (33%)	4 (21%)	61 (27%)
Iron deficiency	38 (39%)	13 (20%)	13 (33%)	5 (26%)	69 (31%)
Folate deficiency	15 (15%)	7 (11%)	3 (8%)	3 (16%)	28 (13%)
Vitamin B12 deficiency	5 (5%)	3 (5%)	0	1 (5%)	9 (4%)
Iritis/uveitis	7 (7%)	1 (2%)	1 (3%)	1 (3%)	10 (5%)
Arthritis	9 (9%)	8 (12%)	8 (21%)	0	25 (11%)
Renal calculus	5 (5%)	3 (5%)	2 (5%)	2 (11%)	12 (5%)
Pyoderma					
gangrenosum	3 (3%)	0	2 (5%)	0	5 (2%)
Erythema nodosum	6 (6%)	0	4 (10%)	1 (5%)	11 (5%)
Oral aphthous ulcers	10 (10%)	4 (6%)	6 (8%)	0	20 (9%)

**TABLE 9**  
Surgical intervention according to clinical pattern

	Clinical pattern				Total n = 222
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 39	Gastroduodenal n = 19	
Patients with surgery	59 (60%)	38 (58%)	14 (36%)	14 (74%)	125 (56%)
Total procedures	138	61	36	52	287
Patients with resection	50 (51%)	24 (36%)	5 (13%)*	11 (58%)	90 (41%)
Total resections	76	29	6	26	37
Mean resection frequency in resected cases	1.52	1.21	1.20	2.36*	1.52
Patients with non-resective procedures	27 (28%)	20 (30%)	12 (31%)	10 (53%)	69 (31%)
Total nonresective procedures	62	32	30	26	150
Patients with:					
Abscess drainage	12 (12%)	9 (14%)	8 (20%)	8 (42%)*	37 (17%)
Bypass	3 (3%)	0	0	2 (11%)	5 (2%)
Miscellaneous	23 (24%)	15 (23%)	9 (23%)	7 (37%)	54 (24%)

\* Significant difference  $P < 0.05$

patients, nonresective surgery was undertaken.

A total of 137 resections were performed in 90 patients. Resections were most frequent in the ileocolic (51%) and gastroduodenal (58%) groups. In contrast, only 13% of the colonic group required a resection (Table 10).

One hundred and fifty nonresective procedures were performed in 69 patients. Nonresective surgery was required in about one-half of the gastroduodenal group but in only about 30% of the other three patterns. The major nonresective procedure, drainage of an abscess, was performed in almost one-half of those with gastroduodenal involvement but in less than 20% of the other patterns.

Intestinal bypass was rarely used. A number of minor nonresective proce-

dures was frequent in all groups. These included fistulectomy, anal dilatation, rectal stricture dilatation, ileostomy stricture dilatation and revision and diagnostic laparotomy. In a few patients with severe perianal disease a proximal diverting colostomy was used.

Table 11 lists the indications for surgery. Perianal disease constituted the most common indication in all patterns and necessitated surgery of some form in 82 patients (37%). Obstruction was the indication in 53 patients (24%) while internal fistulae and abscesses, and intractable disease activity were each indications in about 15% of patients. Perforation (8%) and megacolon (1%) were considerably less frequent.

None of the patients operated on for Crohn's disease died during or following

surgery. Complications incurred as a direct result of surgery are not listed but were frequent. Fortunately, all operative complications resolved successfully without mortality.

**Medical treatment:** Patients in this study population were treated in the usual way. Sulfasalazine (Salazopyrin) was prescribed for almost 90% of the patients and there were no significant differences in the use of sulfasalazine among the four major groups. Systemic corticosteroids, either alone or in combination with sulfasalazine were prescribed for 59%. A larger percentage of patients in the gastroduodenal class were treated with systemic steroids (84%) compared to the colonic Crohn's group (54%), the ileocolic group (63%) and the small intestinal pattern (48%). Rectal steroids were administered primarily in the colon pattern. Immunosuppressives (Azathioprine) were employed in only 6% of the patients. Recently, metronidazole has been used irregularly, primarily for the treatment of perianal disease and on occasion for severely active disease unresponsive to sulfasalazine and corticosteroids.

Individualized nutritional therapy was delivered in a number of instances. Chemically defined diets and parenteral nutrition were given as treatment for severe exacerbations of disease or in preparation for a surgical procedure. Nutritional therapy has not been employed routinely as primary treatment for inflammatory bowel disease at this centre.

**Prognosis:** Although morbidity was as prominent in these patients as that recorded in other series, there has not yet been recorded any mortality related directly to the primary disease process or to the major associated complications. There have been four deaths during the entire follow-up. One patient died from a carcinoma of the lung, one from mid-brain hemorrhage and one from a subarachnoid hemorrhage secondary to a Berry aneurysm. One patient with colonic Crohn's died following a small bowel infarction believed secondary to a volvulus related to post surgical adhesions. Neither small bowel nor colon cancer has been found in any case in this series.

TABLE 10  
Resection frequency according to clinical pattern

Resections per patient	Clinical pattern				Total n = 222
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 39	Gastroduodenal n = 19	
1	36 (37%)	20 (30%)	4 (10%)	5 (26%)	65 (29%)
2	9 (9%)	3 (5%)	1 (3%)	2 (11%)	15 (7%)
3	2 (2%)	1 (2%)	0	1 (5%)	4 (2%)
4	1 (1%)	0	0	1 (5%)	2 (1%)
5	0	0	0	2 (11%)	2 (1%)
6	2 (2%)	0	0	0	2 (1%)

## DISCUSSION

Although it has been assumed that Crohn's disease in Canada is representative of the experience in other countries, only two earlier reports from Canada offer any clinical data. Nootens and Devroede (7) described 25 cases from Sherbrooke, Quebec. Most were female and most had colonic involvement. The clinical description was very general, providing only a simple overview of this group. In a similar report, Gilbert and Sartor (8) reported 98 cases from Edmonton. No attempt was made in either study to define the clinical course of disease or to examine its relationship to clinical patterns.

This review of 222 patients with Crohn's disease has many features in common with other surveys from the United States (1,2), the United Kingdom (3,4) and Scandinavia (5,6,10,11). In the present series, as in others, the disease afflicted primarily the young with the majority of cases (59%) occurring in the second and third decades. The number of children in this particular series was quite small. This reflects the uncommon occurrence of Crohn's disease in children under 10 years of age and the lack, until 1979, of local expertise in pediatric gastroenterology.

Although it is impossible to make a precise calculation of the incidence and prevalence of Crohn's disease in the area studied, it is reasonable to conclude that the minimum prevalence is approximately 33 cases per 100,000 population. This prevalence rate is higher than those found in the United Kingdom and the United States but it is significantly less than the prevalence rates recorded in Sweden and Wales (Table 12). Analysis of Table 2 shows that 62% of the patient population have been followed for less

than five years. The data suggest that the annual incidence of Crohn's disease has recently increased in the geographic area. Unfortunately, other factors, including both an increased total population and an increased geographic referral base obfuscate an accurate interpretation of this observation. It is important to consider, however, that claims of a recent

increase in the incidence of Crohn's disease (12,13) may account for these findings.

As suggested by Farmer (1) classification in one of four clinical patterns permitted recognition of particular trends in the clinical presentation and course of Crohn's disease. The distribution of cases among the four major clinical patterns was generally similar to other reports (1,3). However, in the present patients, the gastroduodenal pattern (8%) was distinctly more common than some reports indicate (1-6). It is interesting that the frequency of duodenal disease in the regional Copenhagen study (10) was also 8%. In contrast to the present series, almost two-thirds with duodenal disease in the Copenhagen series showed no other detectable involvement.

TABLE 11  
Indications for surgery

	Clinical pattern				Total n = 222
	Ileocolic n = 98	Small bowel n = 66	Colonic n = 39	Gastroduodenal n = 19	
Perianal disease (fissures, fistula, abscess, stricture)	37 (38%)	17 (26%)	15 (38%)	13 (68%)	82 (37%)
Perforation	8 (8%)	4 (6%)	0	5 (26%)*	17 (8%)
Internal abscess or fistula	8 (8%)	6 (9%)	5 (13%)	9 (47%)*	28 (13%)
Intractable disease (failure of medical treatment)	20 (20%)	3 (5%)	4 (10%)	6 (31%)*	33 (15%)
Bowel obstruction	24 (24%)	17 (26%)	4 (10%)	8 (42%)	53 (24%)
Toxic megacolon	2 (2%)	0	0	0	2 (1%)

\* Significant difference  $P < 0.05$

TABLE 12  
Crohn's disease prevalence

Centre	Series	Reference	Years	Prevalence (cases/100,000)
United Kingdom				
Oxford	Evans and Acheson	(14)	1951-1960	9
London	Wright	(21)	1970	13
Scotland	Kyle	(22)	1962-1968	32.5
Cardiff	Mayberry et al	(23)	1977	56
United States				
Stanford	Gelpi	(24)		13
Mayo Clinic	Sedlack et al	(25)		106
Scandinavia				
Stockholm	Hellers	(5)	1974	54.2
Malmö	Brahme et al	(12)	1965	20.9
Malmö	Brahme et al	(12)	1973	75.2
Canada				
Sherbrooke	Nootens and Devroede	(7)	1972	6.3
Kingston	Present series		1984	33.1

The reasons for prominent gastroduodenal involvement are not immediately clear. The diagnosis of gastroduodenal involvement was made using standard techniques when there were appropriate clinical or radiographic clues. In some patients, the diagnosis was suspected on clinical grounds when nausea and vomiting were unusually prominent or when there were acid/peptic complaints in the history. Some cases were discovered by chance when a barium meal, performed as part of a small bowel assessment, demonstrated changes typical of Crohn's disease (for example, mucosal fold thickening, aphthous ulceration, luminal narrowing) involving the gastric antrum, pylorus or duodenum. Whether this represents a trend for gastroduodenal involvement in this particular geographic area or is simply a manifestation of the relatively small numbers of patients studied remains to be determined.

While the age distributions in both the ileocolic and small bowel groups match the overall distribution, the colonic and gastroduodenal groups show some interesting variations (Figure 2). Gastroduodenal disease was not found after the fourth decade. The distribution curve for the colonic pattern shows a primary peak coincident with the other patterns but there is a secondary peak occurring in the sixth decade. It has been suggested that ischemic colitis may be misdiagnosed as Crohn's in older patients. In the present study, ischemia was excluded by strict adherence to the diagnostic criteria. Confusion with ulcerative colitis was avoided by excluding all 'indeterminate' forms. Alternatively, the second peak may indicate some age related environmental or vulnerability influence in etiopathogenesis. A similar unexplained biphasic distribution has been recognized in ulcerative colitis (14). Since the biphasic distribution in this series is entirely related to a paucity of cases diagnosed in the fifth decade and the total number of cases of colonic Crohn's is relatively small this second peak could also be spurious.

The delay in diagnosis has been well described (1,3). In the regional review from Denmark, Both *et al* (10) recorded a mean delay of 3.2 years which is similar

to the delay of 3.6 years in the present study. This delay probably represents a minimum, as this interval was established only after symptoms easily related to inflammatory bowel disease were unequivocally present.

Tables 4, 5 and 6 illustrate the progression of the major clinical features of Crohn's disease. The occurrence of the major clinical manifestations clearly increased in time in all groups. The relatively infrequent occurrence of abdominal pain early in the course in the gastroduodenal group should be noted. Important rectal bleeding was most commonly associated with colonic involvement as expected, but 30% of the small bowel group suffered this symptom as well.

In this retrospective study, as in others, the determination of the frequencies of certain clinical symptoms and signs at different stages of illness may underestimate the true frequencies because of the failure to specifically record relevant negatives. For major clinical findings this is not an important issue but for potentially less obvious features (such as perianal disease and fissures, pyrexia, aphthous stomatitis, joint involvement and skin lesions) such deficiencies may compromise these estimates, particularly early in the course prior to diagnosis.

However, in this series, it seems unlikely that underestimation, on the basis of a negative ascertainment bias, significantly distorts these determinations. For example, it is apparent from Tables 4 and 5 that the frequencies of perianal disease and fissures were similarly low both at onset and at diagnosis. Since the diagnoses were established and confirmed in almost all instances by the attending staff of the academic Divisions of Gastroenterology, who have a particular interest in inflammatory bowel disease, few if any cases with fissures and perianal suppuration would have been missed. Thus, the relatively low incidence of these conditions accurately reflects the true incidence in this patient population at these defined stages.

In the case of systemic complications and related conditions, the frequencies (Table 8) represent the cumulative experience of the patient groups up to the most recent patient contact. For each

complication or condition the results closely parallel the experiences of other groups making a negative ascertainment bias less likely.

Although the severity and clinical impact of the various disease manifestations were not specifically measured in this study, Table 6 suggests that patients with the gastroduodenal pattern are more likely to suffer the major disease manifestations during the course than any of the other three groups. As a result, this group appears to suffer a higher average disease related morbidity than the others. The occurrence of extraintestinal complications was also similar to that reported in other series (10,15).

Notwithstanding the evidence supporting an increased incidence of gastrointestinal cancer in Crohn's disease (16,17), no patient was identified with either large or small bowel cancer in the present series. Because the rate of surgical resection in this population is not substantially different from the rates of surgery in other series (1,3,11,18) and the approach to medical treatment is similar, it seems quite unlikely that resection of bowel at risk or the administration of particular drug treatments explain this observation.

Conceivably, selection bias could produce artificially high rates of intestinal cancer in series reporting an increased risk. In the regional review in Copenhagen (11) intestinal malignancy was similarly uncommon with only one cancer detected in the ileum in the study population of 185 cases followed for a mean of 5.5 years (range one to 18 years). In most reports the majority of cancers were detected only after observation periods longer than 10 years (17-19). In this series, only 37 cases have been followed for this length of time and exclusion of a Crohn's cancer association is impossible.

It is well known that the frequency of surgery is high in patients with Crohn's disease and that the cumulative risk of surgery rises with disease duration (1,3, 18). In the present series, 125 patients (56%) were operated on a total of 287 times. At least one resection was required in 41%, while 31% required some non-resective procedure such as abscess drainage. About one-half of the total operative



procedures were done for resection of diseased bowel. In the regional Copenhagen study of a patient group similar to the present series (11), the cumulative resection frequency after 10 years was slightly higher at 55%. These cumulative resection frequencies are substantially lower than those reported in some studies. This may reflect both shorter follow-up times and the inclusion of milder disease. Additional observation will be necessary to differentiate between these possibilities.

The indications for surgery were usually specific. Perianal disease was the most common indication for surgery in all groups. This was followed by intestinal obstruction and internal abscesses and fistulas. In each of these, gastroduodenal disease presented the highest risks for operative intervention. Only 26% of the patients were operated on for 'intractable disease'. In many such instances repeated bouts of subacute intestinal obstruction, individually manageable by conservative means, culminated in resection or bypass as definitive treatment. In some of these 'intractable' cases, however, the indication was progressive general debility, refractory to all forms of medical management.

Although it has been suggested that patients with ileocolic disease fare worse, in general, than other clinical groups, the present series suggests that clinically apparent gastroduodenal involvement predicts more frequent local complications and more frequent surgical intervention. In these cases, it was most often the associated small bowel disease which produced the complications and requirements for surgery but in this series gastroduodenal involvement identified a subgroup which experienced more frequent difficulties during disease progression. It is likely that more extensive and severe disease are the important factors contributing to this observation.

Few patients in this study population have died, and no deaths were related directly to Crohn's disease. This observation may be related to several factors. Since this study population includes patients who have never been admitted to hospital there is a smaller proportion of severely ill patients represented. This contrasts with other series reporting

## Tableau clinique et évolution de la maladie de Crohn dans le sud-est de l'Ontario

**RESUME:** Les dossiers cliniques de 222 patients souffrant de maladie de Crohn confirmée à la Queen's University Medical School de Kingston, Ontario, de 1966 à 1984, ont été étudiés. Quatre patterns cliniques ont été reconnus. L'iléo-colique était l'affection la plus fréquente (44%). Le petit intestin seulement était atteint dans 30% des cas tandis que la localisation au niveau du côlon seulement était évidente dans 18% des cas. La maladie gastroduodénale de Crohn a été diagnostiquée chez 8.5% des patients mais chez ceux-ci, le petit ou le gros intestin était également atteint. Les femmes (57%) dépassaient les hommes (43%) en nombre avec un rapport homme/femme de 1 à 3. L'âge des patients au moment du diagnostic se situait de sept à 73 ans. Cent soixante-dix-sept patients (80%) ont été diagnostiqués entre les âges de 11 et 40 ans. Les malades atteints d'affections du côlon seulement tendaient à être plus âgés et souffraient d'un nombre moindre de crises deus aux obstructions; ils subissaient moins de résections chirurgicales et plus de saignements rectaux massifs. Les hommes semblaient, plus souvent que les femmes, atteints de maladies gastroduodénales; le petit intestin était plus souvent touché, ils souffraient d'un plus grand nombre de complications locales et requéraient le plus grand nombre d'interventions chirurgicales. La maladie était limitée à l'ano-rectum chez un seul patient. Les patients de cette série ont été suivis durant une période allant de deux mois à 24 ans. La durée moyenne de la surveillance était de 4.9 années. La fréquence des complications et la nécessité d'interventions chirurgicales est similaire aux autres séries rapportées. Aucun des patients n'a été atteint d'un cancer du gros ou du petit intestin durant la période en question et aucun décès ne semble attribuable directement à la maladie de Crohn, à ses complications ou aux interventions chirurgicales qui lui sont reliées.

excess mortality in which referral and case identification biases favour the inclusion of more severe and complicated cases (9,19). A similar low mortality, not differing from the expected mortality, was reported from the Copenhagen regional review by Binder et al (11). These findings indicate that life expectancy in Crohn's disease is probably not altered substantially, a point of considerable importance when discussing prognosis with patients and relatives. Mayberry et al (20) found significant mortality in the first two to three years following diagnosis as well as after more prolonged observation (more than 13 years). The mean duration of observation in the present series was 4.9 years with 146 of 222 (66%) followed for longer than two years and it seems unlikely that an 'early' effect on mortality was missed. Earlier diagnosis of less severe disease (lead time bias) could account for the present observation but Mayberry et al (20) concluded that this was not a factor in their series. More prolonged observation may eventually expose an increased Crohn's related mortality documented by others.

### CONCLUSIONS

Patients with Crohn's disease were as-

signed to one of four clinical disease patterns. This allowed the identification of patient subgroups at particular risk for a variety of clinical manifestations. Both local and systemic complications were frequent and morbidity was a major problem, but mortality related directly to Crohn's disease was not encountered. Surgical treatment was necessary in more than 50% of patients but this requirement will undoubtedly rise as the follow-up period is extended. No cancers of the biliary tree, small intestine or colon have yet been discovered.

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