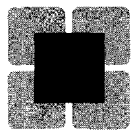

Management of inflammatory bowel disease: 30 years of observation

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■ Management of inflammatory bowel disease has become more precise and effective in the last 30 years, ensuring long, productive lives for most patients. Data such as family history, duration of disease, the onset of complications, and type of therapy are presented from 450 patients with inflammatory bowel disease treated during a 10-year period ending in 1984. The incidence of general complications over three decades is compared. Perianal disease and intestinal obstructions dominate complications of Crohn's disease. The most common nongastrointestinal complication for patients with either disease is monarticular large joint arthritis. Approximately 75% of patients with Crohn's disease will eventually undergo surgery. In the first decade of data collection, 50% of patients with ulcerative colitis had surgery; in the second decade, 26%; and in the third decade, 39%. The changing percentages correspond initially to advances in medical therapy and then to advances in surgical therapy.

□ INDEX TERM: INFLAMMATORY BOWEL DISEASE □ CLEVE CLIN J MED 1990; 57:685–691

THE CAUSES of ulcerative colitis and Crohn's disease in children and young people remain unknown, but the last 30 years have seen remarkable progress in therapy.[1] The medical approach has been refined, and the indications for surgical intervention have become more specific. Moreover, newer surgical procedures have eliminated the need for a permanent ileostomy in most young people. A combination of treatment alternatives can ensure long and productive lives for these patients.

The clinical features of Crohn's disease and ulcerative colitis with onset in childhood or adolescence and the long-term prognosis of these diseases have been described previously.[2–11] This paper adds to our earlier observations data from new cases seen from January 1, 1975, through December 31, 1984. Comparison of this group of patients with the previously reported 1955-through-1974 group gives us patient data for 30 years in some areas. The information gained by following our patients has allowed us to modify our treatment programs to provide better care for children and young people with these diseases.

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PATIENTS AND METHODS

Clinical, radiographic, and histologic data were collected on 858 patients with inflammatory bowel disease (IBD) seen at the Cleveland Clinic between January 1, 1955, and December 31, 1974. All patients were 20 years of age or younger at the time of diagnosis. The results of these studies have been reported.[4,6,7] An additional 450

TABLE 1
CHARACTERISTICS OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE, 1955 THROUGH 1984

	1955 through 1974		1975 through 1984	
	Ulcerative colitis	Crohn's disease	Ulcerative colitis	Crohn's disease
Patients	336	505	121	329
Sex				
Male	168 (50.6%)	289 (59%)	57 (47%)	184 (56%)
Female	166 (49.4%)	207 (41%)	64 (53%)	145 (44%)
10 years or younger at time of diagnosis	43 (12.8%)	28 (5.6%)	13 (10.7%)	10 (3.0%)
Years of follow-up	11.8	7.7	7.1	7.4
Died	18 (5.3%)	13 (2.8%)	3 (2.4%)	3 (0.9%)
Colonic cancer	9	0	1	2

TABLE 2
CHARACTERISTICS OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE, 1975 THROUGH 1984

	Ulcerative colitis		Crohn's disease	
	Nonoperated (61%)	Operated (39%)	Nonoperated (25%)	Operated (75%)
Average age at first visit (years)	14.3	15.4	15.3	17.0
Age at diagnosis (years)	14.3	15.2	15.4	17.2
Age at onset of symptoms (years)	12.9	13.1	14.6	14.8
Duration of symptoms to diagnosis (years)	16.5	24.7	9.8	29.9
Age at follow-up (years)	21.1	22.5	22.5	24.8
Length of follow-up (years)	6.9	7.3	7.1	7.5
Age at first surgery (years)	0	16.7	0	17.6

patients with IBD were seen between January 1, 1975, and December 31, 1984, and the resulting information has been added to the original data (*Table 1*).[4,6,7,10]

Patients were classified as having Crohn's disease or ulcerative colitis, according to established criteria.[2] All medical records were carefully reviewed, and follow-up studies were accomplished by the techniques previously described.[2–4,6] Whenever needed, trained interviewers contacted the patients by telephone to obtain information regarding complications, family history, and the clinical course of the diseases. Crohn's disease was diagnosed in an additional 329 patients and ulcerative colitis in 121 patients during this new 10-year period. The data from this new period are reported in this paper. (In each decade, information was not always available in all areas.)

RESULTS

Medical histories from the 121 patients with ulcerative colitis and the 329 patients with Crohn's disease were recorded as in the earlier study. The histories were tabulated according to whether or not the patients had had surgery. This offered the opportunity to assess the effect of surgery on the course, treatment, and complications of the disease.

Ulcerative colitis

Age and Sex. In this group, there were 57 males and 64 females—a ratio of 47% to 53% (*Table 1*). A positive family history of IBD was recorded in 21 of 116 (18%) of the ulcerative colitis patients. The mean ages of the patients at time of their first visit, diagnosis, onset of symptoms, follow-up, and first surgery are listed in *Table 2*. The duration of symptoms until diagnosis and the length of follow-up are also listed in this table. At the time of diagnosis, 3 patients were under 5 years of age, 13 were between 5 and 10 years of age, 40 were between 11 and 15 years of age, and 63 were between 16 and 21 years of age. At the time of diagnosis, 30% of the patients in the nonoperative group and 60% of the patients in the operative group had total involvement of the colon.

Complications. The intestinal complications in this group of patients are listed in *Table 3*. Vigorous bleeding was the most commonly observed complication. Extraintestinal complications are listed in *Table 4*. Arthritis was noted in 10 (8.3%) of patients. Erythema nodosum was the most common skin lesion. Other general complications are listed in *Table 5*.

Surgery. The indications for surgery were: chronic symptoms or symptoms intractable to medical therapy (25 patients); acute colitis intractable to medical therapy (8); excessive bleeding (3); toxic dilatation of the colon (3); and perforation of the colon (1).

Forty-seven (39%) of the patients underwent surgery, with 23 procedures performed at the Cleveland Clinic (*Table 6*). Surgery was elective in 76% of the patients, semi-elective in 20%, and imperative (emergency) in 4%. The death rate from ulcerative colitis for these patients was 0.83% (n=1). One other patient died of unrelated causes and another died of unknown causes.

One patient, at the time of surgery, was found to have a cancer of the cecum (Duke's classification of "D": moderately differentiated, with dysplasia). In 95% of the surgical specimens the entire colon was ulcerated. Postoperative complications included wound infections (2.3%) and pelvic abscesses (6.7%)

Follow-up. At the time of follow-up, 70% of the nonsurgical patients were asymptomatic, and an additional 20% described themselves as having a "few" symptoms (*Table 7*). Six patients were lost to follow-up. In the surgical group, 66% of the patients were asymptomatic and 27.7% reported "few" IBD symptoms. One patient was lost to follow-up. Among both treatment groups, 97% of the patients described their activity level as normal; 96% also described their work capability as normal.

TABLE 3
LOCAL COMPLICATIONS OF INFLAMMATORY BOWEL DISEASE, 1975 THROUGH 1984

	1975 through 1979		1980 through 1984	
	Ulcerative colitis (44 cases)	Crohn's disease (157 cases)	Ulcerative colitis (77 cases)	Crohn's disease (172 cases)
Bleeding	16 (36%)	61 (38.8%)	19 (24.6%)	25 (14.5%)
Perforation	1 (2.3%)	13 8.2%)	1 (1.3%)	11 (6.4%)
Abscess (internal)	4 (9.0%)	37 (23.5%)	2 (2.6%)	29 (16.8%)
Obstruction	7 (15.9%)	71 (45%)	9(11.6%)	55 (31.9%)
Fulminant colitis	6 (13.6%)	5 (3.2%)	5 (6.5%)	5 (2.9%)
Toxic dilatation	4 (9%)	7 (4.6%)	2 (2.6%)	7 (4.1%)
Perianal disease	6 (13.6%)	89 (57%)	12 (15.6%)	47 (27%)
Internal fistula	2 (4.5%)	49 (31%)	0	37 (21.5%)

TABLE 4
EXTRAINTESTINAL COMPLICATIONS IN INFLAMMATORY BOWEL DISEASE, 1955 THROUGH 1984

	1955 through 1974		1975 through 1984	
	Ulcerative colitis	Crohn's disease	Ulcerative colitis	Crohn's disease
Patients	333	505	121	329
Arthritis	24 (7.2%)	37 (7.5%)	10 (8.3%)	45 (13.6%)
Pyoderma erythema nodosum	17 (5.0%)	21 (3.8%)	6 (5.0%)	30 (9.0%)
Iritis	3 (0.9%)	1 (0.2%)	2 (1.6%)	10 (8.3%)
Liver disease	5 (1.5%)	3 (0.6%)	2 (2.5%)	2 (1.6%)
Urolithiasis	0	0	7 (5.8%)	21 (6.4%)
Cholelithiasis	0	0	3 (2.5%)	13 (4.0%)
Cancer	9 (2.7%)	0	1 (0.8%)	2 (1.6%)

Crohn's Disease

Age and sex. Of the 329 patients diagnosed as having Crohn's disease during this 10-year period, 184 were males and 145 were females (*Table 1*). In this group, 248 patients (75%) required surgery. A positive family history was recorded for 20% (64 of 320) of these patients. The death rate from Crohn's disease was 0.44% (n = 2); one death occurred postoperatively. Two more patients died of unrelated causes. At the time of diagnosis, no patients were under the age of 5 years, 9 patients were between 6 and 10 years of age, 78 were between 11 and 15 years of age, and 235 patients were between 16 and 21 years of age.

The age at time of first Cleveland Clinic visit, diagnosis, onset of symptoms, follow-up, and first surgery are listed in *Table 2*. The duration of symptoms until time of diagnosis is also listed. In the 238 patients for whom we had accurate information, the disease was thought to be in the small bowel in 118 (49.6%), localized in the large bowel in 39 patients (16.4%), and confined to the ileocolic area in 81 patients (34%).

Complications. Local bleeding, internal abscess, obstruction, perianal disease, and internal fistula were the most commonly observed complications (*Table 3*). The extraintestinal complications are listed in *Table 4*. Arthritis was the most common general complication; others included the eyes, joints, and skin lesions (*Table 5*). Approximately 10% of the patients were below the third percentile in height. Delayed puberty also occurred in some patients.

Surgery. The major indications for surgery among Crohn's disease patients were: intestinal obstruction (14 patients); mass with internal abscess (13); internal fistulas (9); severe perianal disease (33); and chronic symptoms intractable to medical therapy (20).

Surgery was performed at Cleveland Clinic in 44.8% of the cases (*Table 6*). Surgery was considered to be elective in 84% of the patients, semi-elective in 12%, and imperative (emergency) in 4%. Perianal lesions were present in 35% of the patients.

Follow-up. At the time of follow-up, 67% of the nonsurgical patients and 54% of the surgical patients considered themselves to be asymptomatic (*Table 7*). Twenty-six percent of the nonsurgical patients and 31% of the

TABLE 5
GENERAL COMPLICATIONS IN INFLAMMATORY BOWEL DISEASE, 1955 THROUGH 1984

	1955 through 1964		1965 through 1974		1975 through 1984	
	Ulcerative colitis	Crohn's disease	Ulcerative colitis	Crohn's disease	Ulcerative colitis	Crohn's disease
Patients	132	114	201	391	121	329
Perianal disease	1 (0.8%)	43 (37.7%)	5 (2.5%)	94 (24.0%)	18 (15.0%)	186 (53.5%)
Intestinal obstruction	7 (5.3%)	24 (21.1%)	4 (2.0%)	99 (25.3%)	16 (13.0%)	126 (38.0%)
Internal fistulas	2 (1.5%)	15 (13.2%)	1 (0.5%)	68 (17.4%)	2 (0.01%)	86 (26.0%)
Growth retardation	1 (0.8%)	3 (2.6%)	6 (3.0%)	37 (9.5%)	6 (0.05%)	31 (9.4%)
Megacolon	3 (2.3%)	8 (7.0%)	7 (3.5%)	24 (6.1%)	6 (0.05%)	14 (4.3%)
Chronicity	36 (27.3%)	19 (16.7%)	37 (18.3%)	56 (14.3%)	28 (23.0%)	113 (34.0%)
Surgery	65 (49.2%)	83 (74.1%)	53 (26.6%)	228 (59.5%)	47 (38.8%)	248 (75.4%)

TABLE 6
INDICATIONS FOR SURGERY AMONG PATIENTS, 1975 THROUGH 1984

	Ulcerative colitis	Crohn's disease
Bleeding	6.4%	8.0%
Medical failure or toxic colitis	26.1%	7.5%
Intractability or chronicity	69.5%	35.3%
Obstruction	0	13.4%
Mass abscess	0	11.7%
Internal fistula	0	7.9%
Perianal disease	0	23.3%
Operated at CCF	48.9%	44.8%
Condition at surgery (elective)	75.6%	83.6%

surgical patients reported a "few" symptoms. One patient died from complications of Crohn's disease, and two others died from other, unrelated causes. Twenty-three patients were lost to follow-up. At time of follow-up, 96% of the patients in the nonsurgical group considered themselves normal and capable of working full-time (*Table* 8). Ninety-two percent of the surgical patients considered themselves to be normal, and 90% indicated that they were able to work full-time.

DISCUSSION

Thirty years of observations on new patients seen at the Cleveland Clinic and then followed for extended periods has enhanced the care of children and young people with ulcerative colitis and Crohn's disease.

Diagnostic issues

In most patients, it is not difficult to confirm a diagnosis of ulcerative colitis or Crohn's disease.[12] Crohn's disease that involves only the colon may present with symptoms identical to those of ulcerative colitis. While it is rare that a diagnosis of Crohn's disease of the colon is subsequently changed to ulcerative colitis, occasionally, what is thought to be ulcerative colitis will eventually prove on biopsy to be Crohn's disease of the colon. Because therapy for the acute state of both diseases is almost identical, excessive testing and procedures to obtain biopsies are not justified initially when the patient is acutely ill. Usually, the diseases differentiate in time. The diagnosis in 75% of the patients with IBD is Crohn's disease.

Family history

The multiple occurrence of IBD in families is well documented.[1–3,13–16] Perhaps most important is that new cases in the immediate family be detected. Our unpublished data suggest that about 17% of patients with IBD have two or more immediate family members with IBD. In most cases, the disease will appear in another family member within 4 years of the first diagnosis. It is our impression that starting therapy when symptoms are minimal gives better long-term results.

Age distribution

The age distribution at the onset of disease is comparable for both conditions. Crohn's disease occurs most often in the mid teens and ulcerative colitis tends to occur in a slightly younger age group. It is striking to note that patients often have 1 year of symptoms before a diagnosis is established—an observation that should raise the index of suspicion for diagnosis in the immediate family.

Managing ulcerative colitis

The pattern of presenting symptoms (diarrhea with or without blood) and the treatment protocol is standard in ulcerative colitis.[12,13,17,18] Prednisone and sulfasalazine (Azulfidine) are used routinely.

The usual starting prednisone dosage is 1 mg/kg of

body weight per day, with a maximum dose of 40 mg/d. After 2 to 3 weeks, when the patient's symptoms are usually improving, the daily dosage can be reduced by 5 mg at weekly intervals until a dose of 20 mg/d is reached. Then the dosage should be reduced by 2.5 mg/d, again at weekly intervals. It is standard to try to discontinue prednisone therapy in children. If relapse occurs, the treatment protocol regimen is repeated. Then, if prednisone is necessary for maintenance, we convert the dosage schedule over 4 to 6 weeks to an every-other-day regimen. Symptoms are usually controlled by 20 to 30 mg orally every other day.

TABLE 7
STATUS AT TIME OF FOLLOW-UP, 1975 THROUGH 1984

	Crohn's disease		Ulcerative colitis	
	Nonoperated(%)	Operated(%)	Nonoperated(%)	Operated(%)
Alive and asymptomatic	66.7	54.4	70.3	66.0
Alive with few symptoms	25.9	31.0	20.3	27.7
Alive with severe symptoms	2.5	5.2	0.0	0.0
Alive and unknown	0	0.4	0.0	0.0
Dead from IBD	0	0.4	0.0	2.1
Other causes	0	0.8	1.4	2.1
Lost to follow-up	4.9	7.7	8.1	2.1

TABLE 8
ACTIVITY LEVEL AT TIME OF FOLLOW-UP, 1975 THROUGH 1984

	Crohn's disease		Ulcerative colitis	
	Nonoperated(%)	Operated(%)	Nonoperated(%)	Operated(%)
Normal for age	97.3	97.8	96.3	91.8
Limited by IBD	95.9	95.7	96.3	90.3
Inactive because of IBD	1.4	2.2	0	0
Work full-time	95.9	95.7	96.3	90.3

Managing Crohn's disease

Treatment for Crohn's disease is less standardized.[17,19] The determining factor is the location of the disease—perianal, colonic, ileocolonic, or small bowel. Patients with perianal disease seldom need systemic steroids, but respond to local therapy. Colonic disease is perhaps the most difficult to treat, has the most severe symptoms, and almost always needs steroid therapy.

Ileocecal disease is the most common. Usually steroids are used initially, but there are often internal complications such as abscess, fistula, or a permanent mass. Other complications are usually already present by the time a mass has formed in the right lower quadrant. In most cases, removing the mass and creating an ileocolonic anastomosis results in dramatic improvement.[6]

Morbidity and discomfort are significant when the disease involves multiple segments of the small bowel. Usually these patients have pain or cramps, anorexia, poor oral intake, and diarrhea, with consequences that include poor nutrition and growth retardation. Surgery is not often indicated. Occasionally, the initial treatment involves parenteral nutrition, both in the hospital and at home, and low-dose prednisone therapy.[20–26] Azathioprine and 6-mercaptopurine have also been helpful.

General complications

The general complications of IBD are compared over three decades in *Table 5*. Perianal disease is a significant problem in Crohn's disease, with an incidence of 53.5% during the last 10-year period. The incidence of intestinal obstruction increased over the 30-year period, particularly among patients with Crohn's disease. Perhaps prolonged medical therapy and healing accompanied by scar formation accounts for the increase. The incidence of internal fistulas is also increasing, but the incidence is lower than that for intestinal obstruction.

Growth retardation, defined as measurements below the third percentile, is a well-recognized complication, particularly of Crohn's disease.[11,13,21,23] Anorexia, coupled with the typical nutritional intake of teenagers, contributes to retarded growth.

Extraintestinal complications

The most common extraintestinal complication for patients with inflammatory bowel disease is monarticular large-joint arthritis.[11,12,17,19] The most common skin lesion is erythema nodosum, which accounts for nearly 90% of all of the skin lesions seen in IBD. Liver disease (pericholangitis) is rare. Urolithiasis and cholelithiasis complications are not unusual. The occurrence of only one colon cancer among patients with ulcerative colitis during our 30-year review should reassure those with concerns about an association between the two diseases.[7,27,28]

Early recognition of relapse

Children and adolescents need to be followed carefully and regularly once the acute attack of IBD has been terminated. Detecting relapses and complications is extremely important. Because some teenagers are reluctant to communicate clearly, "detective work" may be needed to adequately assess the child's health. Careful height and weight measurements should be taken and plotted. Growth velocity, which is perhaps the most sensitive indicator we have of the presence of disease, must be assessed every 6 months.[23] An unsatisfactory growth velocity (less than 4 cm/yr) indicates that disease, poor nutrition, or an excessive steroid effect is impairing growth. More accurate determinations of the patient's status can be made with growth curves that include expectations for growth during puberty, and with bone-age radiographs.

Vague abdominal pains, anorexia, irritability, decrease or change in appetite, amenorrhea, and continued delay in the onset of puberty often indicate the presence of subclinical disease. Gastrointestinal "flu-like" illnesses also can trigger relapses.

Surgery

Surgical intervention is necessary when internal abscess, excessive rectal bleeding, toxic megacolon, or partial or complete intestinal obstruction occur. Often, though, the failure of a medical regimen to return the patient to good health and to ensure good quality of life is sufficient indication for surgery.

Approximately 75% of the patients with Crohn's disease will eventually undergo surgery. The number of patients who undergo surgery is similar from one institution to another.[11,17,19] In the first decade of our observations, 50% of our patients with ulcerative colitis had surgery; in the second decade, 26%; and in the third decade, 39%. These changing percentages accurately reflect the quality of medical therapy compared to surgical options in the second decade and, in the third decade, the development of outstanding surgical operations (ileo-anal-rectal anastomoses and small bowel stricturoplasty) for both inflammatory bowel diseases.

Status at follow-up

Between 55% and 70% of the patients seen in the third decade with ulcerative colitis or Crohn's disease were asymptomatic. Another 25% had only a few symptoms. Fewer than 5% had severe symptoms. Only rarely does a patient die from IBD—a point that must be emphasized to the patient and the family.

At follow-up, 90% to 97% of the patients considered their activity normal for their age (*Table* 8). Only a few, particularly those with Crohn's disease, indicated that their illness limited their activities. Ninety-five percent of all the patients were able to work full-time.

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