Interest in inflammatory bowel disease (IBD) has been increasing for the past 20 years, and the clinical features have been well defined. The importance of determining the long-term prognosis has been emphasized as a result of the increasing incidence of IBD, particularly Crohn's disease, and the significant percentage of adolescent patients. Because of the nature of IBD and the relatively low mortality, a large number of patients have had the disease for more than ten years.

Although the increasing number of patients seen and the increasing number of children and adolescents among them are significant, a major factor of concern over the long-term prognosis of IBD is the relatively poor response to medication given for longer than two years. In addition, patients are often clustered in the same family, so that a positive family history for similar illness is relatively frequent. Further, patients with ulcerative colitis are at risk of developing carcinoma of the colon if the colitis is present for a long period, and patients with Crohn's disease are at risk of requiring an operation which may be followed by a recurrence. The most important factor in assessing the long-term prognosis of IBD is the effect on the patient of chronic illness characterized by diarrhea, rectal bleeding, abdominal pain, malnutrition and various extraintestinal manifestations and other complications. Several recent studies have emphasized that these patients feel their quality of life is suboptimal. In fact, the so-called psychologic features of IBD may predominate, leading to significant problems with interpersonal relationship and feelings of rejection.

Diagnosis of IBD

Accurate diagnosis is important for patients with IBD. The importance of differential diagnosis of Crohn's disease from ulcerative colitis was first recognized by Lockhart-Mummery and Morson two decades ago, and distinctive clinical features which can differentiate the two diseases in the vast majority of cases have been identified.

For virtually all patients with ulcerative colitis, whether localized or involving the total colon, the primary symptom is rectal bleeding. In addition, diarrhea and weight loss of 20% or more may be present. Abdominal pain is not usually a clinical feature, and perianal disease and internal fistula formation are not characteristic findings.

The most important diagnostic procedure in ulcerative colitis is proctosigmoidoscopy, which typically shows fine mucosal granularity, erythema, loss of mucosal vascular pattern, friability with bleeding, edema, and ulceration in inflamed mucosa. The findings begin at the dentate line and proceed proximally in a continuous fashion, and virtually all patients with ulcerative colitis have rectal involvement. Approximately 10% of patients have various extraintestinal manifestations. "Skip areas" (normal areas of bowel between involved segments) are not a feature of ulcerative colitis.

Crohn's disease has more protean manifestations. Studies by our group at the Cleveland Clinic and the National Cooperative Crohn's Disease Study have shown that the vast majority of patients have a triad of symptoms: diarrhea, abdominal pain, and weight loss. We have
emphasized the concept of a clinical pattern as being important in determining prognosis as well as defined indications for surgery for Crohn's disease. The initial location of disease plays a significant role in the long-term prognosis and the complications which occur. Approximately 40% of our patients — both adults and children — have ileocolic involvement. Another 25% to 30% have pure small-intestine involvement, and approximately 25% have pure colonic disease. In a small percentage of patients the initial manifestations of Crohn's disease are perianal, which is in sharp distinction with ulcerative colitis.

Development of an activity index for Crohn's disease has been a problem for many years. Although it has been shown that the primary symptoms of Crohn's disease are abdominal pain, diarrhea, and weight loss, these symptoms are somewhat variable and are not entirely accurate in the assessment of disease activity. Not only is the assessment of disease activity important in the day-to-day management of patients with Crohn's disease, it is also significant in clinical trials. Thus, the National Cooperative Crohn's Disease Study (NCCDS) developed a quantifiable disease index. However, this disease index did not provide all of the necessary solutions to this problem and has been reevaluated. It must be emphasized that the NCCDS Crohn's Disease Activity Index (CDAI) (Table 1) was developed primarily for evaluation of a randomized prospective clinical trial, and not for day-to-day clinical usage. Nevertheless, one might surmise that these two goals are not mutually exclusive of each other and there have been attempts to put the CDAI to clinical usage. Two problems have arisen: first, CDAI is a mixture of subjective and "objective" data and the weighing of the various factors makes considerable difference in the quantification of it; second, it is reasonably cumbersome and requires a fair amount of time to complete the required forms.

Partly because of these two factors and partly because of the stimulus provided by the CDAI, others have attempted to develop activity indices for patients with Crohn's disease. The Dutch group have developed an activity index with 18 variables based on the evaluation of data from 63 patients. However, this activity index has not been widely accepted, again because of its cumbersome and multi-variable nature.

Perhaps the most widely used of the newer activity indices is that developed by Harvey and Bradshaw called "A Simple Index of Crohn's Disease Activity" (Table 2). This has the advantage of being strictly clinical and of enabling the clinician to modify the variable factors on each evaluation of the patient. However, this index may be too "simple" in view of the complexity of Crohn's disease itself.

Our work in the assessment of patients with Crohn's disease has indicated the significance of the “clinical pattern" in which the anatomic location of disease plays an important role in the clinical course, prognosis, complications and indication for surgery for patients with Crohn's disease. In addition, symptoms from Crohn's disease may not be due to disease activity as such, but may be due to fibrosis, stenosis, and

### TABLE I

**Crohn's Disease Activity Index (CDAI; NCCDS)**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Liquid or very soft stools—number in one week: none, 1-4, 5-9, 10-19, 20-49, and 50-98</td>
</tr>
<tr>
<td>2.</td>
<td>Abdominal pain—sum of seven daily ratings: 0 = none, 1 = mild, 2 = moderate, and 3 = severe</td>
</tr>
<tr>
<td>3.</td>
<td>General well-being—sum of seven daily ratings: 0 = generally well, 1 = slightly below par, 2 = poor, 3 = very poor, and 4 = terrible</td>
</tr>
<tr>
<td>4.</td>
<td>Symptoms or findings presumed related to Crohn's disease: a) arthritis or arthralgia, b) skin or mouth lesions, pyoderma gangrenosum or erythema nodosum, c) iritis or uveitis, d) anal fissure, fistula, or perirectal abscess, e) febrile episode exceeding 100°F during past week</td>
</tr>
<tr>
<td>5.</td>
<td>Taking lomotil or opiates for diarrhea: 0 = no, 1 = yes</td>
</tr>
<tr>
<td>6.</td>
<td>Abdominal mass: 0 = absent, 1 = dubious, 2 = definite, and 3 = definite and tender</td>
</tr>
<tr>
<td>7.</td>
<td>Hematocrit (47 minus hematocrit), males; (42 minus hematocrit), females</td>
</tr>
<tr>
<td>8.</td>
<td>Body weight — 100 X (1 minus [body weight/standard weight])</td>
</tr>
</tbody>
</table>

### TABLE II

**The Simple Index of Crohn's Disease Activity**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>General well-being: 0 = very well, 1 = slightly below par, 2 = poor, 3 = very poor, 4 = terrible</td>
</tr>
<tr>
<td>2.</td>
<td>Abdominal pain: 0 = none, 1 = mild, 2 = moderate, 3 = severe</td>
</tr>
<tr>
<td>3.</td>
<td>Number of liquid stools per day</td>
</tr>
<tr>
<td>4.</td>
<td>Abdominal mass: 0 = none, 1 = dubious, 2 = definite, and 3 = definite and tender</td>
</tr>
<tr>
<td>5.</td>
<td>Complications: arthralgia, uveitis, erythema nodosum, apthous ulcers, pyoderma gangrenosum, anal fissure, new fistula, abscess (score one per item)</td>
</tr>
</tbody>
</table>
partial intestinal obstruction. Thus, at the time of operation and resection of the stenotic segment, there may be little or no actual inflammation, and the pathologist may find marked fibrosis and stenosis, but without significant evidence for inflammatory change or granulomas. This creates yet another problem in the assessment of the “disease activity” for patients with Crohn’s disease.

In light of all of these observations, an international study group has been formed to develop a new disease activity index for patients with Crohn’s disease. Those involved with the development of the previous indices are active in the current study group, and computer modeling and testing of the variables is currently underway. Whether or not this disease activity index (Table 3) will be modified by subsequent computer generated data remains to be seen. Nevertheless, the attempt to quantify the disease activity of Crohn’s disease is worthwhile, and is an ongoing project. However, the quantifiability of such an index, its clinical usefulness and reproducibility, and its widespread acceptance by both clinicians and clinical investigators remains to be seen.

Crohn’s disease: Prognosis

The most important factors in the long-term prognosis for patients with Crohn’s disease include: (1) accurate diagnosis and definition of clinical pattern, (2) complications, particularly those that necessitate surgery, (3) operation and postoperative problems, (4) recurrent disease following surgery, (5) chronicity of illness, which can encompass a great variety of aspects, (6) development of renal calculi, and (7) extra-intestinal manifestations, especially growth retardation in young patients.

As noted previously, our studies have indicated the value of definition of clinical pattern in determination of prognosis, particularly the need for operation. Patients with an ileocolic pattern of Crohn’s disease who require surgery typically do so because of development of intestinal obstruction, perianal fistulas, or internal fistula with abscess. Patients with small-intestine Crohn’s disease who require surgery characteristically do so because of development of intestinal obstruction or internal fistula with abscess. Those with colonic Crohn’s disease have a greater variety of complications, including poor response to medical therapy, perianal disease, intestinal fistulas, and toxic megacolon as the major indications for surgery.
Because of the nature of Crohn's disease, with transmural extension and often widespread intestinal involvement, chronicity of illness and malnutrition may be serious problems. Further, patients with Crohn's disease may have had one or two operations and may have recurrences necessitating further medical or surgical therapy. Additionally, response to and side effects of medical therapy may be more of a problem than in ulcerative colitis. Social and economic, as well as psychologic, factors may be of considerable clinical importance in long-term Crohn's disease. "Sick role" behavior and suboptimal quality of life may become dominant factors for the patient who has had Crohn's disease for many years.

Ulcerative colitis: Prognosis

Ulcerative colitis can be categorized as distal disease, total-colon disease, or an overlap of those two usually referred to as left-sided colitis. Our experience with distal disease over the past 20 years has indicated a good prognosis for 90% of patients. Approximately 75% of these have completed resolution of symptoms, approximately 15% continue to have periodic recurrences of rectal bleeding but no other significant symptoms, and approximately 10% have extension of disease to the entire colon. In most of this last group, extension occurs within four years after diagnosis.

Recently, we have attempted to assess the prognosis of patients with left-sided colitis by means of colonoscopy. Although initial studies have shown that the mucosal inflammatory changes often extend slightly higher than can be immediately recognized by proctosigmoidoscopy, the overall long-term prognosis remains similar to that of patients with distal-colon ulcerative colitis. The physician should emphasize the relatively benign prognosis to patients, particularly those with recurrences of rectal bleeding. Use of topical steroids, particularly hydrocortisone enemas, has been beneficial. However, reassurance by the physician can also play an important role in management.

Factors in the long-term prognosis for patients with ulcerative colitis involving the entire colon (ulcerative pancolitis) include: (1) age at onset and duration of disease, (2) severity of the clinical course and chronicity of illness, (3) response to and side effects of therapy, (4) extraintestinal manifestations, (5) need for operation, and (6) long-term surveillance for the development of dysplasia or colonic cancer.

Patients with ulcerative colitis, particularly those with onset at a young age, may have an initial acute episode followed by complete resolution of symptoms. The long-term prognosis, however, relates to the general pattern of disease: (1) severe onset with an inexorable downhill course requiring operation, usually within a short time following diagnosis, or (2) an intermittent or chronic continuous clinical course. With the latter pattern, patients often have recurrent rectal bleeding, diarrhea, weight loss of 20% or more, anemia, hypoalbuminemia, and extraintestinal manifestations (in about 10% of cases). Although these patients may be maintained on sulfasalazine and steroids for a long time, the response is often unsatisfactory. This pattern constitutes the most common single indication for surgery in our experience in patients with ulcerative colitis.

Some of the more interesting manifestations of ulcerative colitis are those involving the hepatobiliary system, particularly sclerosing cholangitis. With the increased use of endoscopic retrograde cholangiopancreatography, sclerosing cholangitis is being recognized more often. This manifestation characteristically occurs in patients with long-standing, often relatively quiescent, ulcerative colitis and is initially suggested by an abnormal serum alkaline phosphatase value. Our experience with sclerosing cholangitis has shown that secondary biliary cirrhosis is unusual, and the presence of sclerosing cholangitis itself is not considered a surgical indication. Other hepatobiliary complications that can occur include pericholangitis, chronic active hepatitis, and rarely, carcinoma of the bile duct system.

Colonic carcinoma has been known to be a complication much more frequently associated with ulcerative colitis than with Crohn's disease, and has been found to be associated with a long duration of illness as well as total colon disease. However, the exact incidence and the factors that predispose to development of colonic carcinoma remain somewhat uncertain.

Two important advances in the understanding of cancer development in ulcerative colitis has been the evolution of the concept of dysplasia and the development of the technique of fiberoptic colonoscopy to carry out a surveillance program. Dysplasia has been known to occur in ulcerative colitis for many years but there has been confusion regarding the morphology, terminology and significance of the dysplastic lesion. Nevertheless, these lesions have been regarded as premalignant and have included epithelial atypia, villous change and reduced epithelial mucous content. Recent work has expanded the concept of dysplasia as a premalignant lesion which does not arise from normal mucosa somewhat analogous to the polyp-cancer sequence. It has also been recognized that dysplasia is a patchy lesion so that a single rectal biopsy may not detect it, nor does a
negative rectal biopsy preclude the presence of an invasive carcinoma in the more proximal colon. Several recent studies have looked at grading of dysplasia and its clinical significance as well as the presence of a mass lesion. Our recent study emphasized the significance of atrophic and non-inflamed mucosa and the following six characteristics of epithelial dysplasia: atrophic mucosa, goblet cell depletion, pseudo-stratification of nuclei, enlargement of nuclei, increased mitotic activity and minimal inflammation. These concepts have led to prospective studies as well as having been summarized succinctly recently. 

With the development of fiberoptic endoscopy and the ability to apply these techniques on the prospective basis to patients with ulcerative colitis, it is now possible to obtain data on a retrospective, continuing and prospective basis to evaluate the chance of risk. It is now generally accepted that total colon colonoscopy should be carried out at an appropriate (although not entirely defined) interval for patients determined to be at high risk for development of colonic carcinoma. Multiple sequential biopsies are taken for histologic presence and grading of dysplasia. Thus, it is now possible to follow patients with ulcerative colitis both on the basis of duration of disease as well as its extent.

Our previous experience emphasized the importance of risk factors to be (1) duration of ulcerative colitis, generally thought to be approximately ten years after onset or greater; (2) total colon disease rather than limited disease; (3) ulcerative colitis rather than Crohn's disease. Our studies did not indicate a higher risk based on a younger age of onset, other than for the long duration of disease. Subsequently, our studies have indicated the significance of inactive disease (usually associated with mucosal atrophy) as important in the development of colonic carcinoma. Further, a subset of patients having undergone ileorectal anastomosis has also been identified who must be followed because of danger of development of carcinoma in the rectal stump.

We have advanced the concept of surveillance colonoscopy versus "diagnostic" colonoscopy, the former being performed for presence of disease over a long period of time without other indication, and the latter being performed to investigate a clinical or radiographic abnormality. Although our study showed dysplasia and cancer in both categories, the association was understandably higher among those patients with a more "specific" reason for colonoscopy. Therefore, attention has been placed recently on the so-called surveillance group of patients with ulcerative colitis. Thus, our recent experience can be summarized as follows: colonic carcinoma in ulcerative colitis is rare before duration of ten years of disease. The colitis involves the entire colon in most cases. The colitis is inactive at the time of the diagnosis of carcinoma in most cases. The presence of cancer correlates well with the finding of severe dysplasia, usually in the vicinity of the lesion. Dysplasia may be consistently identified by multiple observers. Colonoscopy should be carried out every one to two years; if mild dysplasia is found, continued surveillance is indicated; if severe dysplasia is found, the examination should be repeated in approximately three months; if dysplasia is found a second time, then operation should be performed. The two areas in which there is incomplete agreement are the frequency of colonoscopy (and here other factors are considered such as cost effectiveness and use of double contrast barium enema) and whether or not the finding of severe dysplasia in an atrophic or otherwise uninfamed mucosa is an indication for colectomy immediately or whether it should be repeated. Because of the rarity of colonic carcinoma in Crohn's disease, as well as the rarity of mucosal dysplasia in Crohn's disease, surveillance programs are not recommended for patients with colonic Crohn's disease at the present time. Carcinomas in Crohn's disease have typically been found in bypassed loops of the small intestine but do not occur with numerical frequency to warrant a surveillance program at the present time.

For any surveillance program in ulcerative colitis to be successful, there must be adequate patient compliance, understanding, and follow-up. Therefore, explanation of the problem to the patient is important so that an appropriate perspective is kept by the patient and his family. It also should be emphasized that carcinoma in ulcerative colitis is a numerically uncommon lesion despite the statistical frequency when compared to the general population or the significance for the patient with long-standing total ulcerative colitis. Therefore the approach to the problem by the physician must be as scientific as possible and the approach to the patient must be as sensitive as possible given the set of circumstances involved.

Because of the mobility of the population, the relatively young age of the patients, and the often relatively quiescent nature of the disease, a system of surveillance is extremely important for patients with long-standing ulcerative colitis involving the entire colon. While we emphasize this to patients, we have not recommended prophylactic proctocolectomy because of the relatively small number of patients in whom colonic carcinoma actually develops. Nevertheless, concern over the potential development of cancer often is a dominant factor in the patient's own assessment of his or her quality of life. A study
at Mount Sinai Hospital in New York has shown that 11.2% of patients admitted with ulcerative colitis between 1960 and 1976 also had carcinoma of the colon. This and other studies have emphasized the importance of long-term surveillance and have attempted to define criteria for accomplishing it.

Comparison between Crohn's Disease and ulcerative colitis

The extraintestinal manifestations of Crohn's disease are similar in type and frequency to those of ulcerative colitis. Hepatobiliary manifestations are more common in ulcerative colitis. A study by our group has indicated that the frequency of growth retardation (defined as height or weight less than the third percentile for age) is significantly greater statistically in patients with childhood onset of Crohn's disease than in patients with ulcerative colitis. Because of concern about malnutrition, need for extensive intestinal resection, recurrence with further need for surgery, and the young age of the patient, the physician is often reluctant to recommend surgery for a patient who has not yet undergone sexual maturation. Evaluation of bone growth, comparison of development with that of other members of the patient's family, and evaluation of general nutritional status are all important in assessment of the severity of growth retardation. However, when less than the third percentile is achieved in growth, resection of the disease segment of the intestine may be necessary to improve the patient's nutritional status. Growth or lack thereof can be an important factor in the patient's assessment of quality of life.

Our recent study of family history of IBD has shown that over one third of patients with childhood onset Crohn's disease have a positive family history for a similar illness, usually the same disease. Of 552 patients with Crohn's disease, 35% had a positive family history; 336 patients with ulcerative colitis were also studied, and 29% of them had a positive family history, for an overall incidence of approximately one third. Although no pattern was predominant and no evidence of a specific genetic pattern of inheritance was found, sibling-sibling association was most commonly encountered. Fifteen percent of patients in each group had a positive family history of a similar (usually the same) disease in the immediate family.

While the family history has no specific prognostic implications, the presence of the same or similar disease among multiple family members can certainly affect the family socially, psychologically and economically. We are continuing this study with evaluation of kindred and assessment of factors which may be implicated in the increased incidence of IBD among family members of those afflicted.

Summary and Conclusions

Because of an increasing number of patients with IBD observed over the past 20 years, it is now possible to assess factors in the long-term prognosis which are considerably more reliable than those previously noted. Both our experience at the Cleveland Clinic and that of others over this period have emphasized the validity of the following conclusions:

1. A system for long-term follow up is essential.
2. Diagnostic and therapeutic measures must be cost effective as well as medically effective.
3. Social and psychologic factors play an important role in prognosis and must be considered in long-term management.
4. In Crohn's disease, the major problem is the need for operation in over two-thirds of cases and for reoperation in about half of these.
5. In ulcerative colitis, surveillance for cancer of the colon is the most significant aspect of long-term follow up.

The physician who is involved in the long-term management of patients with IBD must take an active role in establishing a system for follow up and surveillance which recognizes the problems peculiar to these diseases and to the patients affected by them.

REFERENCES


---

**Calendar of Events**

**October 31 - November 2, 1983**
The ninety-second (92nd) Annual Meeting of ALIMDA will be held at the Hyatt Regency in San Antonio, Texas from October 31, 1983 through November 2, 1983. Gerzy Gajewski and his hard working committee have arranged a varied and exciting program. Formal participation at an organizational level has been obtained from The University of Texas Health Science Center, The Southwest Foundation for Research and Education, The U.S. Army Institute of Surgical Research, The U.S. Air Force School of Aerospace Medicine, and the Hyperbaric Medicine facilities. On-site presentations and demonstrations have been scheduled, as well as lectures and panels to take place at the hotel.

For information, contact: Dr. Frank Mansure  
P. O. Box 7378, Philadelphia, PA 19101  
Phone: (215) 472-5000

**November 2-3, 1983**
The eleventh Mortality & Methodology Seminar will be held immediately after the ALIMDA meeting.

Place: Hyatt Regency Hotel, San Antonio, Texas  
Fee: $100 per participant

For more information, contact: Dr. Robert G. Wood,  
P. O. Box 2465, Houston, Texas 77001.  
Phone: (713) 871-4958

**May 13-16, 1984**
The Thirty-Ninth Annual Meeting of the Canadian Life Insurance Medical Officers Association.

Place: Valhalla Inn  
Kitchener, Ontario, Canada

For information contact: Dr. R.D. Atkinson,  
Mutual Life Insurance Company of Canada,  
Waterloo, Ontario N2J 4C5  
Canada  
Phone: (519) 888-2249

---

**Please Note**

If anyone is interested in back issues of the *Journal of Insurance Medicine*, please write to Dr. Frank Mansure, Secretary of ALIMDA, P.O. Box 7378, Philadelphia, PA 19101.