Colonoscopy has assumed a pivotal role in the diagnosis and management of patients with inflammatory bowel disease (IBD). Visual inspection of the colon and in certain cases, the terminal ileum, is a crucial component of the workup of a patient with suspected IBD. The colonoscopic exam with accompanying biopsy specimens can often establish the diagnosis, determine the extent and severity of IBD, and establish the presence of dysplasia during surveillance to reduce the risk of colorectal cancer. New techniques such as chromoendoscopy have already enhanced our ability to detect dysplasia; other improvements in standard colonoscopy are in development.

INTRODUCTION

Ulcerative colitis and Crohn’s disease mimic other inflammatory conditions that affect the colon such as diverticulitis, infectious colitis, and ischemia. Colonoscopy, in combination with clinical history, physical examination, radiographic findings, and laboratory values, often helps to provide an answer to the question of “Is this chronic idiopathic IBD or acute self-limited colitis?” Current indications for colonoscopy in inflammatory bowel disease include the following:

INDICATIONS

A. Differential diagnosis  
B. Determination of disease extent  
C. Determination of disease activity  
D. Assessment of efficacy of medical therapy  
E. Screening/surveillance for dysplasia and cancer

Colonoscopy is frequently used when therapeutic decisions are needed, but does not by itself determine the need for surgery. This is true for every patient that faces the possibility for surgery, whether it be to prevent colon rupture from toxic dilation, severe hemorrhage, a spontaneous perforation or failure to thrive. There is no specific colonoscopic finding that mandates surgery.
When colonoscopy is indicated, complete inspection of the colon is the goal, except with severe inflammation where partial examination may provide the necessary information with a low risk of perforation. Total colonoscopy is essential when the goal is surveillance for dysplasia or cancer. Poor bowel preparation is a common reason for incomplete colonoscopy in inflammatory bowel disease. The decision to terminate the exam before complete inspection of the colon may be prudent in the presence of severe inflammation with large, deep ulcerations which carry an increased risk of perforation.

About 10% of all cases of IBD may not meet any criteria for a definitive diagnosis and fall into the category of indeterminate colitis. The features that are most helpful in endoscopically differentiating ulcerative colitis from Crohn’s disease are shown in Tables 1 and 2.

**EARLY LESIONS OF INFLAMMATORY BOWEL DISEASE**

The earliest lesions in Crohn’s disease consist of tiny punched-out ulcers in otherwise normal appearing mucosa. The pathogenesis of these diminutive ulcers involves a precursor lesion in colonic submucosal lymphoid nodules, which antedate visible aphthoid ulcers. Using chromoendoscopy and a magnifying colonoscope, findings on endoscopy have been correlated with electron microscopy and immunohistochemistry. On scanning electron microscopy, surface erosions on the order of one to two hundred microns in size can be observed in lymphoid nodules surrounded by a halo in areas which appear normal endoscopically (1). Biopsies of the smallest early visible lesions of Crohn’s disease will give the highest yield of granulomas, as enlarging ulcerations tend to obliterate the tiny granulomas. Although pathognomonic of Crohn’s disease, granulomas are not commonly seen on biopsy material with prevalence ranging from 5%–36% of cases (2).

The earliest tissue response in ulcerative colitis (3) is an increase in surface blood flow which produces an endoscopic picture of diffuse erythema and vascular congestion. The mucosal vascular architecture becomes dulled and obscured as a result of the associated edema. Endoscopically, edema is manifest by a fine granular appearance due to multiple highlights from individual mounds of edema interspersed with

**Table 1**

**Endoscopic Features of Ulcerative Colitis**

- Rectum involved
- Diffuse erythema replaces usual vascular pattern
- Mucosal granularity (Figure 1)
- Mucosal friability
- Ulcerations always in areas of mucosal inflammation (Figure 2)

**Figure 1.** Granular mucosa in ulcerative colitis.

**Figure 2.** Ulceration and erythema in ulcerative colitis.
Colonoscopy in IBD

INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #25

Table 2
Endoscopic Features of Crohn’s Colitis

- Rectum often normal
- Asymmetric and discontinuous disease common (Figure 3)
- Discrete ulcers may occur in normal mucosa (Figure 4)
- Linear ulcers common
- Mucosal friability unusual
- “Cobblestoning” often occurs in severe cases

colonic crypts. This endoscopic pattern has been described as “wet sandpaper.” In ulcerative colitis, the engorged mucosa bleeds readily when touched with the endoscope or a cotton swab, and this friability or contact bleeding is a typical early feature. As the inflammation progresses, minute surface ulcerations develop in the inflamed mucosa resulting in spontaneous bleeding. Multiple linear ulcers several centimeters in length (“bear-claw” ulcers) represent the coalescence of smaller surface erosions and are seen within a background of diffuse colonic inflammation.

Large ulcers are much more commonly seen in Crohn’s disease and represent the aggregation and enlargement of the initial small aphthous inflammatory erosions. In contrast to ulcerative colitis, ulcers in Crohn’s disease are usually surrounded by normal mucosa until late stages of the disease.

EXTENT OF DISEASE

Defining disease extent in inflammatory bowel disease is important in determining cancer risk, surgical decision-making, choosing appropriate medical therapy (suppositories versus enema therapy, for example), and assessing whether the disease has advanced proximally. Colonoscopy with multiple proximal biopsies remains the gold standard for defining extent of disease, as well as assessing activity and ruling out other forms of inflammation (eg. infectious or collagenous colitis). When assessment is being made for disease extent, biopsies should always be taken. This increases the diagnostic yield considerably over endoscopy alone or double-contrast barium enema, which tends to underestimate disease extent. In one older study (4), pancolitis was diagnosed in twice as many patients with endoscopy compared to double-contrast barium studies, and in three times as many patients using histology. Aphthoid erosions and fine granularity are usually easily identifiable with double-contrast barium enema, whereas inflammatory lesions without accompanying mucosal distortion and superficial erosions and ulcers that are few in number are not always detected (5). As many as 50% of patients with resistant proctitis and a normal appearing X-ray will manifest inflammation proximally when biopsied.

(continued on page 19)
Chromoendoscopy, spraying dye on the mucosal surface of the colon, has been reported to increase the ability to determine the extent of colitic involvement to levels similar to those found on histologic examination of biopsy specimens (6).

Mary and Modigliani in the GETAID group (7) found poor correlation in Crohn’s disease between clinical activity of colitis and the endoscopic findings, and clinical response was associated with endoscopic improvement in only 29% of patients. Clinical remission induced by corticosteroids or other modalities may not be accompanied by endoscopic remission. Landi, et al from France, in a prospective randomized trial of endoscopic monitoring for Crohn’s disease in patients who had achieved a clinical remission on high dose steroid therapy, found no value in repeated colonoscopy during the subsequent tapering of steroids (8) and there was no clear correlation between endoscopic determination of colonic or ileal inflammation and overall disease activity. In contrast, clinical improvement after infliximab therapy in Crohn’s disease is accompanied by significant endoscopic healing and resolution of the mucosal inflammatory infiltrate (9).

Although endoscopy with biopsy is still the best method to evaluate disease extent and activity, correlation between these findings and clinical severity remains poor. Modigliani (7) concluded “the clinical severity of an attack of Crohn’s disease is not dependent on the nature, extent or severity of the endoscopic lesion” and clinical judgement is paramount in any therapeutic decision in Crohn’s disease patients.

In contrast to the lack of correlation between disease symptoms and endoscopic severity in Crohn’s disease, the endoscopic response is much closer to the clinical symptomatology in ulcerative colitis.

**ACTIVITY OF COLITIS**

Although it is difficult to quantitate the degree of colitic activity, several “activity scores” have been generated. These are mainly of interest in clinical studies, and most clinicians successfully grade the severity of involvement as “none, mild, moderate, or severe” with experience as the only guide to this stratification.

Contrary to prior opinion, colonoscopy can probably be performed safely in the acutely ill patient and may add useful information in the decision for surgery (10). Most recent studies report no additional morbidity or mortality from colonoscopy in the acute setting.

Several reports from Europe have correlated ulcer depth on colonoscopy in acute colitis with the need for surgery (10–12) and with an aggressive course. The complication rate from performing colonoscopies in these patients is surprisingly low. In Carbonnel’s series of 85 consecutive colonoscopies in patients with acute disease extending to at least the descending colon, the only procedure-related complication was colonic dilation in one patient. Nonetheless, the decision for surgical intervention is still largely based on clinical evaluation of the patient’s status.

Although the use of I.V. cyclosporine or anti-TNF agents may alter colectomy rates in the future, colonoscopy may have a role in identifying patients who are at risk for losing their colons, namely, those in whom deep coalescent ulcerations can be identified. Moderate mucosal disease, instead of severe penetrating disease, may identify a subset of patients who despite initial resistance to medical therapy may be able to avoid colectomy.

There have been several recent reports of superinfection with CMV in severe colitis—in both steroid treated and steroid naïve patients. Colonoscopy with biopsy may be crucial in identifying these patients and instituting appropriate anti-viral therapy (13–15).
Inflammatory polyps (Figure 5), an indicator of previous severe colitis with sparing of mucosal islands, may be present in both ulcerative colitis and Crohn’s disease and have no malignant potential.

**DIFFERENTIAL DIAGNOSIS**

Acute onset of diarrhea in most patients is a self-limited illness and responds to symptomatic therapy. Although diarrhea is the hallmark of infectious colitis, mild to modest rectal bleeding is also relatively common. The endoscopic appearance of the mucosa and the histologic changes in infectious and inflammatory colitis may be virtually indistinguishable. It has been noted that about one-third of patients who present with mucoid bloody diarrhea and suspected inflammatory bowel disease actually have an infectious etiology. In addition, it is not uncommon for patients with inflammatory bowel disease to also be superinfected with an infectious agent (16). The correct differential diagnosis relies on the experience of the endoscopist, interaction between the endoscopist and pathologist who examines the biopsy specimen, and on the subsequent course of the disease as noted on follow-up of the patient. Colonoscopy in the differential diagnosis of acute, severe hemorrhagic colitis was evaluated by Mantzaris, et al (17), who found endoscopic findings to be similar in infectious colitis and ulcerative colitis groups. However, occasional rectal sparing and a patchy and uneven distribution of lesions in the more proximal colon were seen more often in infectious colitis.

As illustrated in the aforementioned study, colonoscopy has a definite role in the differential diagnosis of acute, severe, bloody diarrhea. In the patient with unexplained chronic non-bloody diarrhea in whom diagnostic evaluation, including history, stool cultures, and sigmoidoscopy are normal, colonoscopy with biopsy can also be an important diagnostic resource. In addition to visualizing surface lesions too mild to be visible by radiographic imaging, histologic examination of tissue biopsies may demonstrate more unusual forms of colitis, such as collagenous and microscopic (lymphocytic) colitis (18,19) or acute self-limited colitis (20). Histologic criteria can distinguish IBD from acute self limited colitis. Endoscopic findings are non-specific such as patchy erythema with and without ulcerations of varying size and depth.

Because of the limited capacity of the bowel to respond to various injuries, the endoscopist must always consider different diagnostic options, even when “typical” evidence of idiopathic inflammatory bowel disease is encountered. If the diarrheal syndrome advances to the subacute stage (longer than 4 weeks), the differential diagnosis remains difficult, since some infectious agents, including Campylobacter, tuberculosis, schistosomiasis, and amebiasis, may all cause prolonged diarrheal illness (21).

**COMPLICATIONS OF COLONOSCOPY**

Colonoscopy-related complications in the stable patient with inflammatory bowel disease are similar to those seen in the general population, where bleeding and perforation are the two most common serious complications. In their series of 151 colonoscopies and 70 polypectomies in patients with chronic ulcerative colitis and Crohn’s colitis, Rubin, et al reported no bleeding, perforation, post-polypectomy fever, or mortality occurring as a result of the procedure (22).

There are specific subgroups of patients with IBD in whom colonoscopy is more challenging and associated with a higher complication rate. These include the acutely ill patient with severe, fulminant colitis, and the patient with stricture formation in whom dilation or navigation of the stricture is performed. Colonoscopy is avoided in the patient with a megacolon, except in rare circumstances where endoscopic decompression is needed.

Many strictures can be successfully negotiated with the standard colonoscope, since gentle air insufflation may help to distend the narrowed lumen. However, the endoscopist must be prepared to terminate the examination when a stricture resists attempts at intubation. Endoscopic balloon dilation of strictures of Crohn’s disease has been described as “a safe alternative to surgery in selected patients (23).” In Crohn’s disease, single, short, fibrotic strictures, which frequently occur at the site of previous surgical resection, are the most suitable for transcolonic dilation. The use of fluoroscopy and a narrow caliber instrument (pediatric colonoscope) may add to the safety of this procedure. Strictures in ulcerative colitis must be considered cancer until proven to be benign.

(continued on page 23)
SURVEILLANCE COLONOSCOPY FOR DYSPLASIA/COLORECTAL CANCER

The risk of colorectal cancer in IBD can be correlated with both the extent and duration of the disease. In ulcerative colitis, the risk begins at 8 years of total colitic involvement. In Crohn’s colitis of the same duration of illness, the risk of colorectal cancer is similar if over one-third of the colon is involved, and it is prudent to enroll patients into surveillance programs. The general consensus is to obtain 4 quadrant biopsies in 8 or 9 stations throughout the colon every year. It has been estimated (24) that this number of biopsies will find 90% of dysplastic areas if they are present, and doubling the number of biopsies will provide a 95% probability of finding dysplasia if it is present.

Dysplasia is a neoplastic condition. High-grade dysplasia is ominous and requires surgery. Chromoendoscopy, using dyes sprayed on the surface of the mucosa to enhance the ability to visualize neoplastic lesions, may become the new standard for surveillance colonoscopy (Figures 6–8). Several authors note the increased yield of dysplasia after dye spraying, compared to the relatively low yield of standard 4 quadrant surveillance non-targeted biopsies (25–27). The standard for surveillance colonoscopy in chronic ulcerative colitis and chronic Crohn’s colitis may be to dye spray the mucosa and only biopsy or remove the abnormal areas.

Discrete polypoid dysplastic lesions in colitis can be totally removed colonoscopically and treated as sporadic adenomas, even if HGD is present (22,28). A high percentage of dysplastic lesions that cannot be removed colonoscopically are found to contain cancer. These lesions are often referred to as DALMs, or “Dysplasia Associated Lesions or Masses” and require surgical removal.

A report of the results of a 30 year surveillance program for 600 patients with extensive ulcerative colitis showed that 12.3% developed neoplasia including 30 colorectal cancers (29). Forty-six patients had low-grade dysplasia and 20% of these who had immediate surgery (continued on page 26)
were found to have colorectal cancer. It was reported that overall, 39% of patients with low-grade dysplasia developed HGD or colorectal cancer. Nineteen patients had HGD, and 7 (37%) developed colorectal cancer. Another report (30) noted that LGD has a high rate (50%) of neoplastic progression to HGD or colorectal cancer within 5 years. When to intervene with surgery for those patients in whom LGD is confirmed and discovered in a surveillance program remains controversial. The significance of LGD on a biopsy becomes less clear since interobserver agreement between pathologists reviewing the same slides is uniformly poor (31).

There have been two reports that show a lower incidence of colorectal cancer in IBD than was previously believed. In the St. Mark’s ulcerative colitis surveillance program (29), the cumulative index of cancer by disease duration was 0% at ten years, 2.5% at twenty years, 7.6% at thirty years, 10.8% at forty years, and 13.5% at 45 years. It has been suggested that the lower incidence of colorectal cancer in this study may be due to the possible protective effect of mesalamine. In spite of the superb surveillance program at St. Mark’s Hospital, 13 patients developed colorectal cancer. Clearly, surveillance is not 100% effective.

A report from the Mayo Clinic (34) on the risk of colorectal cancer in IBD patients who live in Olmsted County, Minnesota detailed the follow-up of 692 persons. Six cancers were found in 378 UC patients, and 5.4 were expected from an age-matched cohort as reported in the SEER data registry (a standardized registry of white persons in Iowa). In 315 Crohn’s disease patients, 6 cancers were observed, and these were not significantly different from the SEER data (Table 3).

In this Mayo Clinic study (32), the colorectal cancer risk was similar to that expected in the general population and the possible protective effect of maintenance therapy with mesalamine was also mentioned. These two studies were good news for doctors and their patients that regular surveillance colonoscopy and disease controlling therapies are worthwhile (33). On the other hand, a Cochrane Review (34) concluded with the statement that “there is no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive colitis, but there is evidence that patients in a surveillance program tend to have colorectal cancer detected at an earlier state than those who are not under surveillance.”

**THE FUTURE OF COLONOSCOPY IN IBD**

Colonoscopy can diagnose and determine the extent and severity of IBD along with clinical parameters. Colonoscopy with biopsy is the standard means of detecting dysplasia and thereby reducing the cancer risk in IBD. Chromoendoscopy has been shown to be of considerable benefit in the identification of dysplasia, and may become the standard technique for surveillance colonoscopy. Optical coherence tomography (OCT) detects the reflection of light from the surface of the colon in essentially an optical version of ultrasonography. It allows for a cross sectional image of the colonic wall with details below the mucosal layer. Preliminary evidence suggests that OCT may be useful in distinguishing Crohn’s disease from ulcerative colitis by detecting a disrupted layered structure indicative of transmural inflammation (35). Narrow band imaging (NBI) uses special filters to narrow the red, green, and blue wavelengths of light to produce a modification of a standard endoscopic image (36). This can highlight abnormal blood vessels that are suggestive of dysplasia. NBI is easily incorporated into standard colonoscopies and is now commercially available. NBI may be able to provide the benefit of dye spray (chromoendoscopy) in detection of dysplasia without requiring the application of dye. Other techniques in development that may improve dysplasia detection include fluorescence imaging (37), in which either a sensitizing agent or autofluorescence is used to detect subtle changes in mucosa, and confocal laser endoscopy which combines colonoscopy and microscopy (38). Confocal endoscopy allows the colonoscopist to observe details on a cellular level that were previously seen only by the pathologist.
The application of these new technologies may permit more accurate diagnosis and allow for the endoscopic removal of dysplastic lesions in IBD that were formerly thought to require surgery. However, with the most sophisticated tools, the colonoscopist needs clinical data to guide endoscopic management. In this respect, more data is needed on the prognosis of low-grade dysplasia in IBD, which will help determine which of the new endoscopic techniques will be appropriate tools.

References