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The State of the Art in the Management of Inflammatory Bowel Disease



A CASE STUDIES NEWSLETTER SERIES

The fifth in a series of educational newsletters based in part on the proceedings of a roundtable.



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THE STATE OF THE ART IN THE MANAGEMENT OF INFLAMMATORY BOWEL DISEASE: A CASE STUDIES NEWSLETTER SERIES

INTRODUCTION

The complexity and lifelong course of ulcerative colitis (UC) and Crohn's disease (CD) require that gastroenterologists recognize, treat, and manage a range of clinical challenges. This newsletter explores several of these using a case study approach. In the first case study, diagnosis is the central issue. In a second case, the issue centers on treatment in a difficult scenario in which the patient has 2 perianal fistulae. The third case provides an opportunity to explore risk factors for relapse in inflammatory bowel disease (IBD) and the challenges of nonadherence to medical therapy in UC. The final case addresses the important issue of colorectal cancer (CRC) and means of monitoring and managing dysplasia and CRC.

Case 1

A 74-year-old woman presents to your clinic with continuing complaints of weight loss, fever, abdominal pain, and diarrhea. A former dancer now suffering from osteoarthritis, she has taken NSAIDs daily (ibuprofen 1200 mg/d) for the past 18 months. You are the third gastroenterologist she has consulted within a year — she has had previous diagnoses of infectious colitis and medication (NSAID)-induced colitis. At colonoscopy, you find diverticula, erythema, and ulceration in the left colon. The terminal ileum and the remainder of the colon are normal. What is the diagnosis?

LEARNING OBJECTIVES

By the end of the program, participants will be able to discuss and summarize

- The differential diagnosis of inflammatory bowel disease in elderly patients with late-onset disease
- Approaches to diagnosis and management of perianal fistula in Crohn's disease
- Risk factors for relapse in ulcerative colitis
- Factors in nonadherence and strategies for maximizing medication adherence
- Recommended approaches for dysplasia-surveillance colonoscopy in patients with ulcerative colitis

There is a bimodal distribution in the pattern of IBD onset, with a first peak occurring in the third decade of life and a second, smaller peak occurring between ages 50 and 60.² Epidemiologic studies indicate that approximately 12% of UC patients and 16% of CD patients experience disease onset after age 60.³ Even though later-onset IBD is not uncommon, many older patients present with atypical symptoms that may be confused with other bowel disorders, including ischemic colitis, infectious colitis, and diverticulitis. Our current case is further complicated by the fact that this patient takes NSAIDs regularly. NSAIDs themselves can cause damage in both the small and large intestine and are associated with relapse in patients with IBD.^{4,5} In some gastroenterology centers, as many as 20% to 50% of patients newly diagnosed with IBD may be taking NSAIDs.⁶ The diagnosis of IBD in elderly patients therefore can be difficult, or it may be missed altogether, thus delaying therapy. Indeed, in CD, the interval between onset of symptoms and diagnosis is 4 years longer in the elderly than in younger populations.⁷

The evaluation of patients is the same irrespective of age and includes clinical, laboratory, endoscopic, histologic, and radiographic assessment. The differential diagnosis of colitis in elderly patients is presented in Table 1, page 2. Table 2, page 4 provides features of UC, CD, infectious colitis, ischemic colitis, and diverticulitis that can assist in the differential diagnosis. Infectious colitis is common and should be the initial consideration in the differential diagnosis. Multiple stool and blood cultures and repeated fecal examinations should be performed to identify pathogens. Infectious colitis typically lasts no longer than 4 weeks.⁸

Although she had received a previous diagnosis of infectious colitis, this patient's intestinal symptoms had continued unabated, and the results of stool and blood cultures and fecal examinations have failed to identify bacterial, parasitic, or viral causes of her colitis.

Ischemic colitis also is frequent in the elderly. Epidemiologic studies suggest that it affects men and women equally and occurs most commonly after the seventh decade of life.⁹ Often there is no clear cause for an ischemic episode, although it is assumed that many are associated with small-vessel disease.⁹ Symptoms include sudden onset of mild, crampy left-lower-quadrant pain followed by bloody diarrhea. These symptoms may be accompanied by nausea, vomiting,

State of the Art in the Management of Inflammatory Bowel Disease: A Case Studies Newsletter is the fifth in a series of newsletters based, in part, on the proceedings of a roundtable that was held in Washington, DC. Although discussions at the roundtable covered the spectrum of management issues in inflammatory bowel disease, each newsletter expands on topics of particular importance or explores treatment issues using a case-presentation approach. Learning objectives of that roundtable were as follows:

By the end of the program, participants were able to discuss what is known about sex differences and to summarize current findings and identify knowledge gaps as they apply to the:

- Epidemiology and proposed etiologies of ulcerative colitis and Crohn's disease
- Clinical and diagnostic findings in adults and children with inflammatory bowel disease (IBD)
- Clinical utility of traditional and evolving therapies in the everyday management of ulcerative colitis and Crohn's disease
- Psychosocial challenges IBD patients face
- Relationship between adherence and disease relapse to optimize adherence in clinical practice

STATEMENT OF NEED: Strategies for the management of inflammatory bowel disease (IBD) are continuing to evolve as the result of research advances, growing clinical experience, and an expanding therapeutic armamentarium. However, IBD afflicts approximately 1 million Americans at various points in the life cycle, and the management of its complications remains a challenge for physicians treating the disease. These complications have serious implications for the long-term welfare of patients with IBD and can even be elicited by the very medications used to treat the conditions. The clinical approach must be customized to the needs of the patient and must take many factors into consideration. As many as 25% of all patients with IBD will experience extraintestinal manifestations of their disease at some point, not including such insidious morbidities as osteoporosis and colorectal cancer.¹ An appreciation of these clinical challenges of IBD is critical to developing appropriate therapeutic regimens that can positively impact the spectrum of disease presentation and its systemic effects on the patient. Awareness of these issues will help physicians become better equipped to meet the challenges of IBD in daily clinical practice and will support the practice of evidence-based medicine.

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and tenesmus.⁸ Colonoscopy or a barium enema performed within 48 hours of symptom onset usually can confirm the diagnosis. Colonoscopy reveals hemorrhagic nodules that represent bleeding into the submucosa. These correspond to "thumbprints" found on barium studies. Bluish-black mucosal nodules may signify gangrene.⁹ In most cases, signs and symptoms of ischemic colitis resolve within 24 to 48 hours, recovery usually is complete, and recurrences are rare.⁹ Management consists of supportive care and fluid replacement.⁸

For the patient in our case, colonoscopy did not reveal typical features of ischemic colitis, and the chronic nature of her symptoms indicates that an ischemic cause of colitis is unlikely.

Long-term NSAID use by this patient complicates the diagnosis. NSAIDs can cause a range of gastrointestinal adverse events, including gastric and duodenal ulceration, small-bowel inflammation, and the catastrophic consequences of bleeding and perforation. They rarely cause colitis but may increase the risk of appendicitis in elderly patients, cause diverticular complications such as fistulae or abscesses, or play a role in relapse in IBD patients.⁶ Analgesia is an important aspect of treatment for patients with osteoarthritis; however, if NSAID use is causing undesirable gastrointestinal symptoms, NSAIDs should be withdrawn, and a non-NSAID analgesic should be prescribed. If this patient has IBD, withdrawal of NSAIDs may or may not reduce symptoms.⁶

This patient's history indicates that previous NSAID withdrawal (for 2 months) had little or no effect on symptoms.

Colonoscopy did reveal diverticula in the left colon, raising the possibility that this patient's symptoms are due to diverticulitis, or inflammation of diverticula. Diverticula are common in the elderly,

TABLE 1

DIFFERENTIAL DIAGNOSIS OF COLITIS IN THE ELDERLY

Infection	
• <i>Clostridium difficile</i>	• <i>Escherichia coli</i> O157:H7
• Salmonella	• Entamoeba histolytica
Ischemia	
Inflammatory bowel disease	
Diverticulitis	
Neoplasia	
Medication	
• NSAIDs	• Allopurinol
• Estrogen	• Gold
• Antibiotics	• Laxatives
Microscopic colitis	
• Collagenous type	• Lymphocytic type
Systemic disease	
• Vasculitis	• Amyloid
Diversion colitis	
Autoimmune deficiency syndrome	

Adapted from Tokayer AZ. Ideopathic inflammatory bowel diseases in the elderly. In: Kirsner JB, ed. *Inflammatory Bowel Disease*. 5th ed. Philadelphia, Pa: WB Saunders Company; 2000:335-341, with permission from Elsevier Science.

being found in 35% to 60% of people older than 60 and in more than 50% of elderly patients with newly diagnosed IBD.⁸ It is difficult to distinguish between diverticulitis and IBD on clinical grounds, because the clinical manifestations are similar.³ CD and diverticulitis are especially

difficult to differentiate, and a diagnosis of CD may not be apparent until after an unsuccessful operation for diverticulitis.⁸ Features favoring a diagnosis of CD are insidious onset, previous colonic resections for presumed diverticulitis, extraintestinal manifestations, fistulae in atypical locations, and endoscopy demonstrating mucosal inflammation with friability, granularity, and ulceration. Diverticulitis is characterized by acute onset of symptoms and endoscopically normal mucosa. Bleeding is rare, but when it occurs it is brisk and self-limited.^{3,8}

The patient in our case has had an insidious disease onset and superficial ulceration and inflammation in the left colon, suggesting that her condition is due to IBD. Serologic testing for perinuclear antineutrophil cytoplasmic antibody (pANCA) and anti-Saccharomyces cerevisiae antibody (ASCA) revealed a positive titer for ASCA and no pANCA. What is the diagnosis?

Numerous epidemiologic reports have shown that elderly patients with CD are predominantly female and that left-sided colonic involvement is particularly prevalent.³ Though this patient's clinical features are nonspecific, superficial ulceration and erythema found in colonoscopy fit the profile of CD. Results of serologic testing also point to a diagnosis of CD. ASCA expression occurs in 61% of CD patients and 12% of those with UC, and pANCA is detected in 66% of UC patients and 15% of those with CD.¹⁰

Your diagnosis is mild to moderate CD involving the rectosigmoid area. What is your approach to treating this patient?

As with much late-onset CD, you find that this patient's disease is more distal and is confined to the colon.¹¹ The medical and surgical treatment of patients with CD is the same irrespective of age. The treatment goals are to induce and then maintain remission. Therapeutic options include 5-aminosalicylates (5-ASAs), corticosteroids, azathioprine/6-mercaptopurine (AZA/6-MP), metronidazole, cyclosporine, and infliximab.¹²⁻¹⁴ The overall response to medical treatment in both young and elderly populations appears to be similar, with a success rate for elderly patients of approximately 80%.⁷

The sequence of inductive treatment for patients with mild to moderate disease begins with the 5-ASAs. For patients whose treatment has been delayed because of a missed diagnosis and who consequently have more severe disease, it may be necessary to initiate therapy with more aggressive treatment. In such a case, the sequence may be initiated with corticosteroids and then progress to AZA/6-MP, metronidazole, cyclosporine, or infliximab, depending on therapeutic response.¹²⁻¹⁴ As is the case with medical management, the indications for and choice of surgery are the same regardless of age. Studies have suggested that the need for surgical intervention in CD is smaller for late-onset disease, although when it is required, surgery is performed earlier in the disease course.⁷

Special considerations for elderly patients

The treatment of late-onset IBD is often complicated by the presence of comorbid medical conditions, necessitating careful consideration in the selection of therapy. In this regard, corticosteroid use, with its potential for dependence, loss of bone mineral density, and increased osteoporosis risk, is of particular concern.¹⁵ Glucocorticoid therapy

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Generic Name	Trade Name	Approved Use (if any)	Unapproved/ Investigational Use
Alendronate	Fosamax®	Treatment and prevention of osteoporosis in postmenopausal women, treatment of glucocorticoid-induced osteoporosis in women and men, treatment of Paget's disease	N/A
Azathioprine (derivative of 6-mercaptopurine)	Imuran®	Rheumatoid arthritis, renal transplantation	Crohn's disease, ulcerative colitis
Calcitonin	Miacalcin®	Paget's disease, postmenopausal osteoporosis	N/A
Ciprofloxacin	Cipro®	Various aerobic bacterial infections	Crohn's disease
Cyclosporine	Sandimmune®, Neoral®	Allogeneic transplantation, rheumatoid arthritis, psoriasis	Crohn's disease, ulcerative colitis
5-Aminosalicylate mesalamine	Asacol®, Pentasa®, Rowasa®, Canasa®	Ulcerative colitis	Crohn's disease
olsalazine sodium balsalazide disodium	Dipentum® Colazal™		
Estrogen	Various	Symptoms associated with menopause, vulvar/vaginal atrophy, prevention of osteoporosis	N/A
Infliximab (anti-tumor necrosis factor- α monoclonal antibody)	Remicade®	Moderately to severely active Crohn's disease refractory to conventional treatments, fistulizing Crohn's disease, rheumatoid arthritis	Ulcerative colitis, other inflammatory disorders
Methotrexate	Various	Neoplastic disease, psoriasis, rheumatoid arthritis	Crohn's disease, ankylosing spondylitis, primary sclerosing cholangitis
6-Mercaptopurine	Purinethol®	Chemotherapy, leukemia, transplantation	Crohn's disease, ulcerative colitis
Metronidazole	Flagyl®	Trichomoniasis (Trichomonas vaginalis), amebiasis, anaerobic bacterial infections	Crohn's disease
Raloxifene	Evista®	Treatment and prevention of osteoporosis in postmenopausal women	N/A
Risedronate	Actonel®	Treatment and prevention of osteoporosis in postmenopausal women, treatment and prevention of glucocorticoid-induced osteoporosis in women and men, treatment of Paget's disease	N/A
Sulfasalazine	Azulfidine®	Ulcerative colitis	Crohn's disease
Tacrolimus (FK506)	Prograf®	Allogeneic transplantation	Primary sclerosing cholangitis, Crohn's disease, ulcerative colitis
	Protopic®	Atopic dermatitis	

N/A=not available

also can exacerbate concomitant conditions such as diabetes, hypertension, and congestive heart failure.³ With our patient, a postmenopausal woman already at risk for osteoporosis, dual-energy x-ray absorptiometry scanning should be performed to assess bone mineral density status and therapy prescribed to prevent or treat osteoporosis. Agents that have been approved by the Food and Drug Administration for the prevention and/or treatment of osteoporosis include estrogens, raloxifene, calcitonin, parathyroid hormone, and 2 bisphosphonates, alendronate and risedronate.¹⁶ Alendronate and risedronate are both effective in the treatment of glucocorticoid-induced osteoporosis in patients with IBD, and risedronate also has been demonstrated to prevent glucocorticoid-induced bone loss.¹⁷⁻²⁰

The patient in this case requires analgesia to control pain from osteoarthritis, a common condition in elderly patients. Because NSAIDs may exacerbate IBD symptoms and/or be a factor in relapse, they should be avoided if possible. Non-NSAID medications should be considered, including a simple analgesic such as acetaminophen or, if pain is not well controlled, an opioid/acetaminophen combination.²¹

Adherence by elderly patients is another special concern. Care must be taken to ensure that explicit directions are given and understood by the patient and that the patient is capable of administering her medication. Verbal communications and counseling should be supported with written information. The purpose of the medication or intervention must be made clear to the patient, as must the need to adhere to therapy. Important advice should be repeated and should be consistent to minimize confusion.²² A simplified regimen and techniques to help patients remember to take medications may be particularly helpful for elderly patients. Pharmacoeconomics and other issues related to ability to procure medication should be addressed. Finally, efforts should be made to assess and involve the patient's support system — a family member or friend can be enlisted to help ensure adherence.²²

Case 2

A 32-year-old man with a 3-year history of colonic CD controlled with mesalamine now presents with fever, diarrhea, abdominal tenderness, perianal pain, and persistent discharge. Physical examination reveals 2 fistulae, but the patient is too uncomfortable for digital examination. What is your approach to evaluating this patient?

Perianal complications in CD include edematous skin tags, cyanotic discoloration, fissures or anal ulceration, abscesses, fistulae, and anorectal strictures.²³ Depending on the classification scheme used, they are reported to occur in 20% to 80% of patients at some point in the course of disease.²⁴ Perianal fistulae occur with a frequency ranging from 17% to 43% and are most common in CD involving the colon and/or rectum.²⁵ They can cause substantial morbidity and disability, including scarring, continual seepage, and fecal incontinence.

Examination under anesthesia (EUA) involving digital rectal examination and probe insertion to determine the fistula tracts is standard practice for evaluating perianal fistulae.²⁵ Other nonsurgical methods of evaluation include endoscopic ultrasound (EUS), magnetic resonance imaging (MRI), fistulography, and computed tomography. A recent study of the accuracy of EUA, EUS, or MRI in determining fistula anatomy found that EUS and EUA were accurate in 91% of cases and MRI was accurate in 87%. When any 2 tests were combined, the accuracy was 100%,

	UC	CD	Infectious colitis	Ischemic colitis	Diverticulitis
Rectal involvement	+	±	±	—	—
Submucosal hemorrhage	—	—	±	+	—
Segmental disease	—	+	+	+	±
Rapid resolution	—	—	+	+	±
Histology	Nonspecific	Granuloma in 30% - 50%	Nonspecific	Infarct	Nonspecific

Adapted from Grimm IS, Friedman LS. *Gastroenterol Clin North Am.* 1990;19:361-389, with permission from Elsevier Science.

leading the authors to suggest that an optimal approach would use any 2 of the 3 methods.²⁶

The diagnostic evaluation revealed 2 high-transsphincteric fistula tracts, which pass from the intersphincteric plane through the external sphincter and into the ischioanal fossa. What is the optimal approach for patient care?

The optimal approach combines medical and surgical treatments, which, in turn, depend on the location and type of fistula and overall disease activity. There are various classification schemes for describing perianal fistulae, one of which is shown in Figure 1. If there is no proctocolitis, most simple low-transsphincteric, intersphincteric, and superficial fistulae can be treated with fistulotomy.²⁵ In the case of active rectal inflammation, however, fistulotomy is contraindicated because of poor wound healing, and placement of noncutting setons plus medical therapy is the better treatment option.²⁵ Complex and high fistulae (high-transsphincteric, suprasphincteric, or extrasphincteric fistulae) also require noncutting setons. Setons maintain drainage while medical therapy is initiated and reduce the risk of perianal abscess.²⁵ Our patient has 2 high-transsphincteric fistulae tracking from the intersphincteric space through the external anal sphincter. Two setons were threaded into the cutaneous orifice of the fistulae, through the fistula tract, and into the rectum and anal canal.

Medical management

Medical treatments for perianal fistula include the antibiotics metronidazole and ciprofloxacin, AZA/6-MP, cyclosporine, infliximab, and tacrolimus. Although randomized, controlled data from trials specifically designed to evaluate the efficacy of various treatments on fistula healing are limited, several positive reports on infliximab and tacrolimus were published recently.²⁷⁻²⁹ The data are reviewed below. It should be noted that although neither 5-ASAs nor corticosteroids play a major role in fistula management in the setting of active mucosal disease,²⁴ treatment should be directed at controlling the luminal disease as well as the fistula.

Antibiotics. Metronidazole and ciprofloxacin have been evaluated in several small, uncontrolled studies. Bernstein and colleagues studied the effects of metronidazole 10 mg/kg/day in 21 consecutive patients with chronic unremitting perianal disease.³⁰ All patients experienced dramatic clinical improvement, and 15 of 18 patients experienced complete or almost complete healing.³⁰ In a second study, metronidazole was evaluated in 8 consecutive patients with CD and perianal fistulae, all of whom responded to therapy. The number of draining fistulae was reduced 20-fold, and significant reduction of symptoms was experienced by all of the patients.³¹

Although it appears to be effective in fistulizing disease, metronidazole use is hampered by side effects. The most common are nausea, headache, anorexia, vomiting, diarrhea, epigastric distress, and abdominal cramping. Use is also accompanied by an unpleasant, metallic taste, and there are potential serious adverse events including peripheral neuropathy and convulsive seizures.³²

In part because of the side effects of metronidazole, clinicians have begun to use ciprofloxacin. As in the case of metronidazole, efficacy data supporting the use of ciprofloxacin for fistulous disease are from

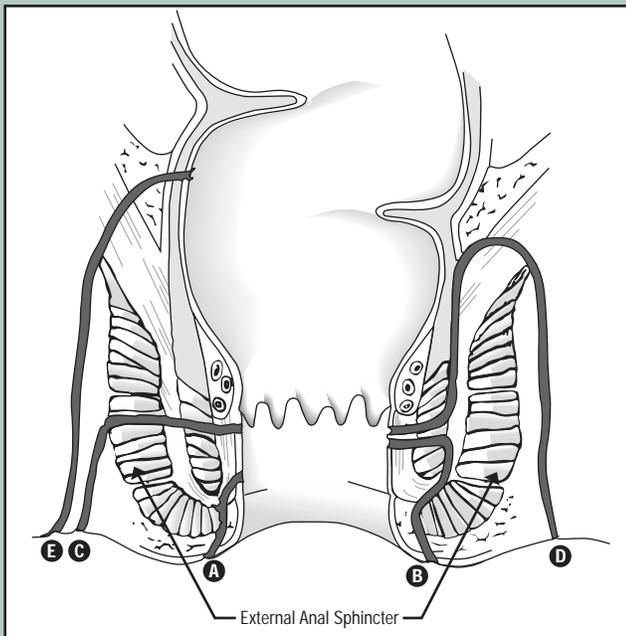
small, uncontrolled trials. Turunen and coworkers described long-term outcomes following ciprofloxacin treatment in 10 patients with severe perianal or fistulous CD.³³ Patients received 1.0 to 1.5 g/day of ciprofloxacin for a minimum of 3 months and were followed for 4 years. Two patients experienced healing of perianal lesions for more than 2 years and five patients experienced recurrences that were treated successfully following subsequent courses of ciprofloxacin. Solomon et al retrospectively analyzed the combination of ciprofloxacin and metronidazole in 14 patients with severe perianal CD. Patients received ciprofloxacin 1.0 to 1.5 g/day plus metronidazole 500 to 1500 mg/day. At assessment, which was performed between 4 and 20 weeks, 85% of patients had improved, including 3 who had healed completely.³⁴

AZA/6-MP. Present was the first to report randomized, controlled data on the effects of 6-MP on fistula healing. Of the 29 patients with fistula in the study who received 6-MP, 9 (31%) had closing of fistula compared with 1 of 17 (6%) placebo-treated patients.²⁴ A further report on 27 patients in the original study and an additional 7 patients with fistulizing CD found that 13 (39%) had complete fistula closure, and 9 (26%) experienced obvious improvement with a minimum of 6 months of 6-MP therapy. For the patients with healing or improvement, the mean time to response was 3.1 months.³⁵ Pearson and colleagues conducted a meta-analysis of 9 randomized, placebo-controlled trials evaluating the efficacy of AZA/6-MP in CD. Of these, 5 studies reported fistula responses. Of the 41 patients receiving therapy, 22 (54%) responded (95% confidence interval [CI], 37% to 69%) compared with 6 of 29 placebo-treated patients (21%; 95% CI, 8% to 40%), giving a pooled odds ratio of 4.44 (95% CI, 1.50 to 13.20) favoring fistula healing.³⁶

Cyclosporine. A number of small, open-label trials have reported the efficacy of cyclosporine in fistula healing. Hanauer and Smith reported outcomes of 5 CD patients with 12 chronic draining fistulae unresponsive to surgery, steroids, antibiotics, total parenteral nutrition, or AZA/6-MP. Patients received intravenous (IV) cyclosporine at 4 mg/kg/day for 6 to 10 days, followed by oral dosing initiated at 8 mg/kg/day that was adjusted to maintain a trough level of 100 to 200 ng/mL. All fistulae responded to treatment, with decreased drainage, improvement in inflammation and patient comfort, and complete resolution of drainage in 10 of 12 fistulae. Although 5 fistulae recurred once patients were on oral treatment, IV cyclosporine was useful for initial management of refractory fistulae.³⁷ Present and Lichtiger evaluated cyclosporine in 16 CD patients with active fistulae refractory to standard medical therapy (antibiotics, steroids, 5-ASA, or AZA/6-MP). Patients were treated with IV cyclosporine 4 mg/kg/day followed by oral dosing at 6 to 8 mg/kg/day. Fourteen (88%) of the patients responded to IV cyclosporine, with 7 experiencing complete fistula closure, and 7 demonstrating moderate improvement. Once on oral therapy, 5 patients (36%) relapsed, and 9 (64%) maintained improvement.³⁸ In a retrospective chart study, Egan and colleagues evaluated the response to IV cyclosporine 4 mg/kg/day of 9 patients with complex fistulizing CD. Seven patients experienced partial response; this was maintained or improved in 4 patients during subsequent oral cyclosporine therapy and in 1 patient who was initially unresponsive. Relapse occurred in 5 patients, however, once oral cyclosporine was discontinued, despite concomitant AZA/6-MP treatment.³⁹

Infliximab. Present and colleagues established the efficacy of infliximab for the treatment of fistula in a randomized, placebo-controlled trial involving 94 adult patients, of whom 85 (90%) had perianal fistulae.²⁷

FIGURE 1
PERIANAL CLASSIFICATION SYSTEM
OF PARKS AND COLLEAGUES



- A. A superficial fistula tracks below both the internal anal sphincter and external anal sphincter complexes.
- B. An intersphincteric fistula tracks between the internal anal sphincter and the external anal sphincter in the intersphincteric space.
- C. A transsphincteric fistula tracks from the intersphincteric space through the external anal sphincter.
- D. A suprasphincteric fistula leaves the intersphincteric space over the top of the puborectalis and penetrates the levator muscle before tracking down to the skin.
- E. An extrasphincteric fistula tracts outside of the external anal sphincter and penetrates the levator muscle into the rectum.

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Patients were randomly assigned to receive infliximab 5 mg/kg or 10 mg/kg or placebo by IV infusion at weeks 0, 2, and 6. The primary endpoint of the study was a reduction of at least 50% in the number of draining fistulae at 2 or more consecutive evaluations. Closure of all fistulae was a secondary endpoint.²⁷ Significantly more patients receiving either dose of infliximab achieved the primary endpoint in comparison with placebo-treated patients (68% percent of patients receiving infliximab 5 mg/kg [$P=.002$], 56% receiving infliximab 10 mg/kg [$P=.02$], and 26% receiving placebo). Furthermore, 55% of patients who received infliximab 5 mg/kg and 38% who received infliximab 10 mg/kg experienced complete closure of all fistulae, in comparison with 13% of placebo-treated patients ($P=.001$ and $P=.04$, respectively). Median duration of fistula closure was 3 months.²⁷

Tacrolimus. Several small case series have reported positive results with oral tacrolimus in the healing of treatment-refractory perianal fistulae,⁴⁰⁻⁴² and a 10-week, randomized, double-blind, placebo-controlled study of tacrolimus in 48 patients with perianal or enterocutaneous fistulae recently was reported in preliminary form. In this study, patients received oral tacrolimus 0.2 mg/kg/day or placebo. Dosages of other medications (5-ASAs, antibiotics, prednisone, and AZA/6-MP) were held constant. The primary outcome measure was more than a 50% reduction from the number of baseline fistulae for at least 4 weeks; a secondary outcome was closure of all fistulae for at least 4 weeks. Nine of 21 patients (43%) who received tacrolimus achieved the primary endpoint, in comparison with 8% (2/25) of placebo-treated patients ($P=.004$). Ten percent of tacrolimus-treated patients and 8% of placebo-treated patients experienced closure of all fistulae. Adverse events occurred in 95% of tacrolimus-treated patients and in 76% of patients receiving placebo. Treatment-related adverse events included paresthesias, insomnia, tremor, and headache, and 38% of tacrolimus-treated patients (vs no placebo-treated patients) met the definition of nephrotoxicity. Adverse events were managed with dose reductions; the efficacy of lower doses remains to be determined.²⁸

Following seton placement and institution of medical treatment with infliximab, this patient has responded with complete fistula closure. How would you maintain remission?

There are few good data regarding maintenance treatment for patients with fistulizing CD. The best efficacy evidence to date is from the ACCENT II trial, which has been reported in preliminary form.²⁹ This trial evaluated infliximab in both inductive and maintenance treatment for 306 patients with draining fistulae. In the inductive phase, patients received 5 mg/kg infliximab at weeks 0, 2, and 6. Patients who responded to treatment with more than a 50% reduction in number of draining fistulae at weeks 10 and 14 were subsequently randomized to a maintenance phase consisting of placebo or infliximab 5 mg/kg every 8 weeks through week 46. One hundred ninety-five patients achieved fistula response at 14 weeks and were randomized to the maintenance phase of the study. Maintenance infliximab therapy was more effective than was placebo. Patients receiving maintenance infliximab had a significantly longer time to loss of response, higher rates of fistula closure, greater duration of fistula closure, and greater improvement in the Crohn's Disease Activity Index and Inflammatory Bowel Disease Questionnaire than did placebo-treated patients. Serious infections occurred in 5% of patients, and 30% of patients experienced infections necessitating treatment. Four percent of patients had infusion reactions.

It is clear that strategies for the treatment of patients with fistulizing CD are still evolving, and there are many unanswered questions regarding this most challenging aspect of CD. The long-term safety and efficacy of newly available agents are still to be established. Furthermore, optimal treatment sequences for induction and maintenance must be determined. The introduction of new agents provides an opportunity to test these agents in combination with older therapies to identify approaches for optimal efficacy, safety, and improved quality of life.

Case 3

Your 21-year-old female patient with distal UC continues to experience flares. You suspect that she is not adhering to her prescribed regimen of a once-nightly rectal suspension enema. How does nonadherence impact disease course in UC?

The course of IBD is typified by periods of quiescence interrupted by relapse. One theory regarding the remitting and relapsing nature of the disease holds that as long as exacerbating and protective factors are held in check with maintenance treatment, remission will continue. However, when the balance is tipped toward exacerbating elements, either by external or internal causes, the result is relapse.⁴³ Researchers have sought to uncover the factors that contribute to relapse to optimize patient management and ensure that remission is maintained. Although data from retrospective and prospective studies sometimes have been contradictory regarding certain contributors, there is general agreement that nonadherence to medication, inadequate doses of maintenance therapy, adverse reactions to therapy, emotional stress, NSAID use, seasonal factors (perhaps seasonal eosinophil activation), oral contraceptive use, or change in smoking status can all play roles in relapse.^{5,43-47} The relative significance of these factors remains to be established, although inadequate maintenance therapy (due either to nonadherence or to inadequate prescribed doses) may be among the most common reasons patients relapse.⁴³

Though relapse due to nonadherence is a particular focus of this case presentation, the impact of IBD on issues specific to women, such as changes in disease status that may occur over the menstrual cycle, birth control, and general sexual health, also deserve attention. The relationship between IBD activity and the menstrual cycle has been studied by Kane and colleagues. Women with UC (N=49) and CD (N=49) were more likely than healthy women (N=90) to experience menstrual and premenstrual bowel-habit changes with concomitant disease symptom exacerbation. Further, women with IBD were more likely to report a cyclical pattern to their bowel habits, with diarrhea being the most frequent symptom.⁴⁸ Therefore, with a woman who reports symptom exacerbation, it may be worthwhile to determine how exacerbation relates to her menstrual cycle before making major changes to her therapy⁴⁸; conservative treatment such as antispasmodics or herbal preparations to alleviate temporarily occurring symptoms may be a more appropriate approach.⁴⁹

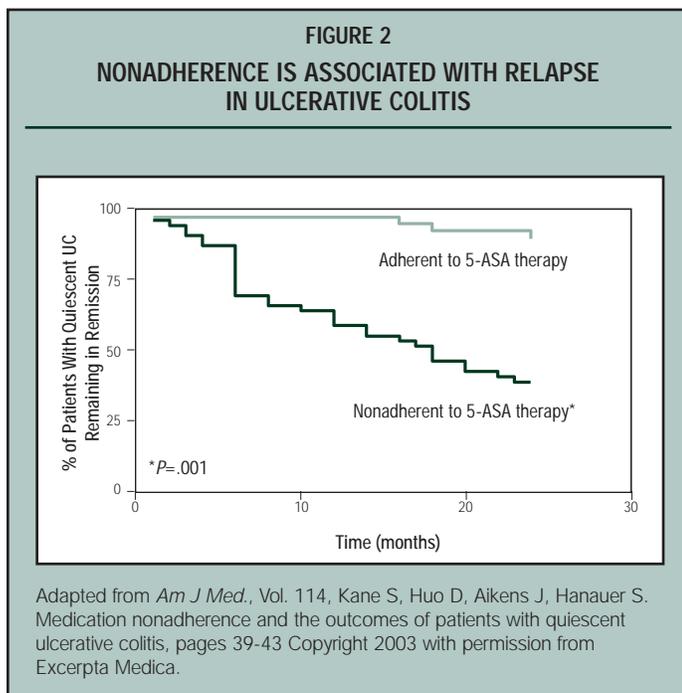
Counseling women on the choice of birth control requires additional considerations. Intrauterine devices usually are not recommended, because complaints of abdominal pain could be related to either pelvic inflammatory disease or IBD — distinguishing between these may delay diagnosis and treatment of active IBD. Regarding oral contraceptives, some studies have suggested that their use may increase the

incidence of IBD, could exacerbate symptoms, and, as noted above, is associated with an increased risk of relapse.^{45,49} Although data have been conflicting, if the woman in this case takes birth control pills, they may be contributing to IBD symptom exacerbation, and another method of birth control should be suggested.

New attention is being paid to the potential impact of IBD on overall sexual health. The gynecologic histories of women with IBD tend to include numerous conditions, including menstrual abnormalities, vaginal discharge, and infertility.⁵⁰ It is important that clinicians be aware not just of the medical aspects but of how IBD and accompanying gynecologic problems may raise women's concerns regarding sexual functioning and partner relationships.⁵¹

Factors impacting adherence

Nonadherence is a particularly difficult issue in IBD. The chronic course of IBD typically requires continued medical treatment across the lifespan, but adherence in such circumstances often is problematic. In one study, the overall adherence rate of patients taking maintenance therapy for UC was only 40%.⁵² The impact of nonadherence on relapse is clear. Recent evidence suggests that medication adherence is associated with improved outcomes in IBD. Conversely, nonadherence is an important contributor to relapse. Nonadherence was evaluated prospectively by Kane et al in a cohort of 99 patients taking a maintenance regimen of mesalamine for quiescent UC. Nonadherence was defined as refilling less than 80% of the prescribed supply of medication. Patients were evaluated at 6, 12, and 24 months from inclusion. At 24 months, 82% of the 39 patients experiencing clinical recurrence were nonadherent, while 34% of the 59 patients who remained in remission were nonadherent ($P=0.01$). Overall, adherent patients had an 89% chance of maintaining remission compared with 39% in those who were nonadherent ($P=.001$) (Figure 2).⁵³ The many factors that affect adherence fall into 3 general categories: illness related, treatment related, and patient related.



Illness-related factors. Illness-related factors affect the patient's perception that therapy is needed. They include the severity, extent, and duration of disease; frequency, duration, or intensity of flare-ups; and type and severity of complications. There is an inverse relationship between the overall impact of disease and the likelihood that a patient will be adherent: the greater the overall impact of disease, the higher the likelihood that patients will take medication. Conversely, it is more difficult to get patients with well-controlled disease and few flare-ups to continue maintenance therapy, because the need for continued treatment is less clear.⁵²

Treatment-related factors. Two treatment factors of paramount importance to adherence are efficacy and safety. It is important to balance an agent's ability to control symptoms and maintain remission with its side-effect profile. Although all 5-ASA compounds are equally effective for maintaining remission in mild to moderate UC, for example, mesalamine doses can be increased without a concomitant increase in the side-effect rate. In contrast, sulfasalazine is associated with dose-related side effects because of the toxicity of the sulfapyridine moiety. Fortunately, almost all sulfasalazine-intolerant patients will tolerate other 5-ASAs well.⁵⁴ Furthermore, though the efficacy of steroids, immunomodulators, and biologic therapies in IBD is undisputed, these agents are associated with a range of short- and long-term side effects that must be considered carefully before therapy is initiated.

Convenience of the treatment is also an important factor. Less frequent dosing or a smaller number of pills can be more convenient for patients and may promote better adherence to therapy, as Kane and Magnanti demonstrated in a recent pilot study with 11 patients on a qd regimen.⁵⁵ The formulation, which includes pill size and mode of delivery, plays a role. Patients may find it easier to swallow smaller and/or fewer pills, for example, or may express a preference for oral or topical treatment. Finally, treatment costs and reimbursement issues may impact the patient's ability to procure treatment. These issues have become more significant with the advent of more expensive biologic therapies.

Patient-related factors. There are a range of patient-related factors in adherence, including the type of disease (UC or CD) and concomitant medical conditions. The failure of patients to discuss major concerns with their physicians is an important, but sometimes overlooked, factor. Bell and colleagues identified characteristics of patients who did not voice their concerns. These patients were more likely to be younger, less educated, unmarried, less trusting of their physicians, and less satisfied with their overall care.⁵⁶ Patients with this profile may benefit when their physicians promote openness about their perceived needs.

Inadequate education has a negative impact. Based on responses to a questionnaire that explored the adequacy of patient knowledge, only 30% of patients with IBD believe they have adequate knowledge of their own disease.⁵⁷ Other patient-related factors are lack of skills or knowledge necessary to follow the treatment regimen, refusal to believe that treatment will help or that benefits will outweigh side effects, or circumstances (financial need, child care problems, transportation difficulties, or employment issues) that interfere with treatment.⁵⁸ Finally, patient characteristics are also important. For example, for men, gender has been identified as a chief characteristic in nonadherence, particularly for men who are young and unmarried.⁵²

What are the keys to improving adherence by patients with IBD? What are the available options?

The primary element in improving adherence is individualization. Therapy should be based on the patient's disease and therapeutic history, response to previous medications, "track record" of taking therapies as prescribed and attending scheduled visits, and cost considerations. Patients must be educated regarding the disease, accompanying lifestyle changes, the need for continued treatment, and the role that nonadherence plays in relapse, including the potential for serious relapse and disease progression.

For the patient in this case, there are a number of treatment options flexible enough to "work around" impediments to adherence that may be related to her regimen of a nightly mesalamine enema. The need for nightly topical treatment often becomes a quality of life issue for patients. If this is so, oral therapy should be considered.⁵⁹ Patients can be maintained successfully on oral 5-ASAs provided the dose is high enough. Oral 5-ASAs are added, up to 4.8 g/d of mesalamine,¹³ as topical therapy gradually is tapered.

Physicians should address any potential inconveniences related to dosing regimens for patients on oral mesalamine therapy, as this may contribute to nonadherence. Kane and Magnanti examined this issue by assessing the effect of a once-daily dosing regimen on adherence in patients taking mesalamine for maintenance in quiescent UC. Twenty consecutive patients were randomized to receive mesalamine either once daily or with usual dosing, which was either bid or tid. At 3 months, no patients in either group had experienced relapse. All of the patients in the qd group versus 78% of patients in the usual-dosing group were adherent to their prescribed medication. At 6 months, 1 patient in each group had experienced a relapse. In the qd group, 90% of patients were adherent compared with 75% in the usual-dosing group. More patients in the qd group expressed satisfaction with treatment.⁵⁵ In this small pilot study, adherence and satisfaction were improved, and short-term clinical outcomes appeared to be similar. These promising results warrant further investigation of qd dosing in larger trials.

One also can consider a combined oral/topical approach that decreases the enema frequency to twice per week. d'Albasio and coworkers found that combined treatment (oral 5-ASA 1.6 g/day and 5-ASA enemas twice weekly) was more effective than oral therapy alone in preventing relapse.⁶⁰ In this study, intermittent enema therapy was well accepted, and it may be a particularly good approach for patients with a high risk of relapse.⁶⁰

This patient has announced her plans to transfer to an out-of-state college. How would you monitor her treatment and help ensure adherence? Is there a role for self-monitoring of drug therapy in UC?

The potential for nonadherence could be increased if your patient plans to go away to college. For example, if a decision is made to continue topical treatment and she plans to live in a dormitory, she may not have the privacy needed to self-administer enemas. In this case, you might ask the college housing authority to assign a single room for her based on medical need. Furthermore, the necessity for treatment monitoring continues despite the fact that this patient will be away. Visits can be scheduled far in advance, or the patient can be monitored by telephone as well as in the office.

A recent study reported the success of an alternate approach to traditional patient care: guided self-management. Robinson and colleagues randomly assigned 203 patients with UC to traditional treatment and follow-up or patient-centered self-management training and follow-up on request.⁶¹ Patient-centered management involved a personalized, guided regimen consisting of a single 15- to 30-minute session during which patients were trained to recognize signs of relapse and were provided with agreed-on treatment regimens. Copies of the treatment protocol were given to each patient's primary care physician.⁶¹

In the self-guided group, the time to treatment of relapse was significantly shorter (14.8 hours, $P=.0001$ vs 49.6 hours), the number of outpatient visits smaller (0.9 vs 2.9, $P<.0001$), and time spent visiting a doctor shorter (1 hour vs 6.2 hours; $P<.0001$). Further, although they did not reach statistical significance, there were several positive trends for the self-guided group: There were fewer relapses and a shorter duration of relapse when treatment was initiated within 24 hours.⁶¹ An overwhelming proportion of patients (82%) preferred the self-management technique, and, even more importantly, 95% of patients in the control group elected to adopt a self-management approach when the trial was concluded.⁶¹

There are many options for increasing adherence. They depend, overall, on a good patient-physician partnership that fosters open communication. A productive partnership enables the physician to provide emotional and psychological support. Directly addressing concerns or impediments specific to the patient, and a flexible approach that bears the individual needs of the patient in mind, will do much to help ensure good adherence. Only if the patient understands the need for continued therapy and commits to the therapeutic objectives will it be possible to realize the benefits of treatment. You can direct your patients to the Crohn's & Colitis Foundation of America (CCFA; www.cffa.org), an organization committed to educating and supporting patients affected by these diseases.

Case 4

A 55-year-old patient with pancolitis of 11 years' duration (in remission for 7 years), a family history of CRC, and no prior findings of dysplasia has transferred to your care. He has not had a routine colonoscopy for the past 3 years. Has he been managed adequately? What is your approach for assessing dysplasia or cancer in this patient?

Epidemiology and risk factors of CRC

Addressing the increased CRC rate associated with IBD is an important priority in patient care. Since the first reports of CRC in patients with IBD, population-based studies have confirmed the increased incidence of cancer initially reported.⁶²⁻⁶⁶ The most recent study demonstrated an increased incidence rate ratio of colon cancer for both CD and UC patients (CD: 2.64; 95% CI, 1.69 to 4.12; UC: 2.75; 95% CI, 1.91 to 3.97). Patients with UC (but not CD) had an increased incidence rate ratio of rectal cancer (1.90; 95% CI, 1.05 to 3.43). Conversely, patients with CD (but not UC) had an increased risk for small-intestine cancer (17.4; 95% CI, 4.16 to 72.9).⁶⁷

The overall risk of CRC for patients with UC is influenced by a number of factors. Risk increases with increasing disease duration. A meta-analysis

by Eaden et al found that the cumulative probabilities of CRC were 2% by 10 years, 8.5% by 20 years, and 18% by 30 years.⁶⁸ Extent of disease also contributes to risk, with the risk highest for patients with more extensive disease.⁶² Early age of onset also appears to be an important factor, although data are conflicting regarding the increased risk to patients who have early-childhood onset of UC.^{62,69}

Several studies have established that a family history of CRC increases the risk. In a case-control study of 102 patients with UC and CRC, a family history of sporadic CRC in any relative increased the risk 5-fold.⁷⁰ A second, population-based cohort study found that familial CRC increased the risk of CRC more than 2-fold for patients with IBD.⁷¹ A concomitant diagnosis of primary sclerosing cholangitis (PSC) also increases CRC risk. Kornfeld and colleagues demonstrated a cumulative CRC risk of 25% after 10 years for patients with UC and concurrent PSC.⁷² It is interesting to note that disease activity does not appear to affect CRC risk. Because of this, CRC tends to manifest in patients with quiescent disease who have been able to retain their colons over the long term.⁶⁹

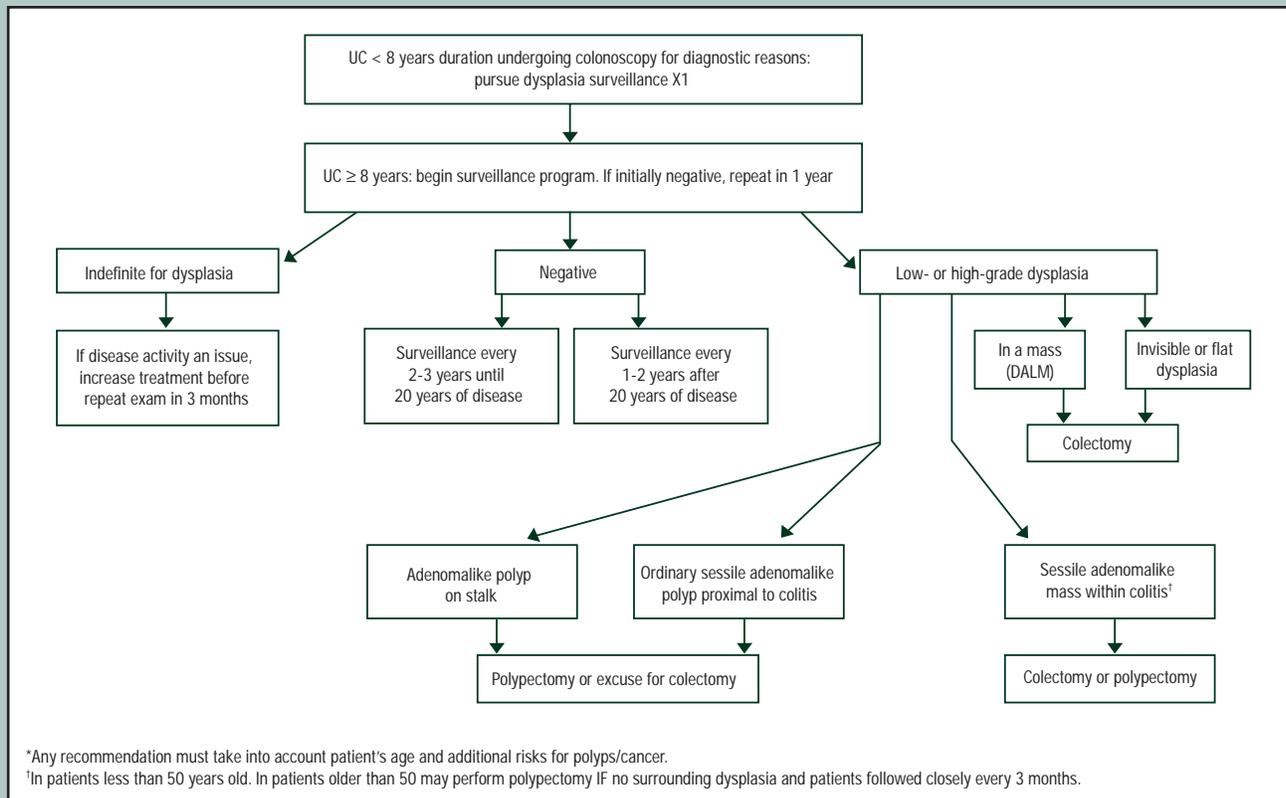
The patient in this case has pancolitis, which places him at a higher risk of CRC than patients with less extensive disease. He has a family history of sporadic CRC, which also increases his risk. In his favor, he does not have PSC or evidence of dysplasia on his previous colonoscopy. His disease duration is 11 years, so his risk of CRC is

still relatively low. His last colonoscopy was 3 years ago, and, because this patient's UC is well controlled, it is likely that he will retain his colon and thus require continued periodic monitoring.

Mitigating the risk of CRC

Two studies have shown that 5-ASAs are chemopreventive of CRC. In a retrospective case study of 175 patients with UC, Moody et al found that 3% of patients on long-term sulfasalazine treatment developed CRC, in comparison with 31% who had had their treatment stopped or were not adherent to therapy. The difference was highly significant ($P < .001$).⁷³ The second retrospective study also demonstrated that the risk of CRC can be substantially reduced if patients are adherent to regular 5-ASA therapy. One hundred two UC patients with a diagnosis of CRC were matched with UC patients without CRC (controls).⁷⁰ Variables such as age at diagnosis of UC, pharmacotherapy, average frequency of contacts with physicians, number of barium enemas and colonoscopies, activity of UC, smoking history, presence of PSC, and positive family history of UC were assessed. The most significant finding was the strong protective effect of regular 5-ASA therapy. Both sulfasalazine and mesalamine conferred protection, although the protective effect of sulfasalazine was less pronounced and seen only at dosages of at least 2 g/day. Mesalamine reduced the CRC risk by 81%. Though protection was independent of dose, it was significant at

FIGURE 3
RECOMMENDED APPROACH TO DYSPLASIA-SURVEILLANCE COLONOSCOPY*



Adapted with permission from Bernstein CN. Cancer prevention strategies in inflammatory bowel disease. In: Bayless TM, Hanauer SB, eds. *Advanced Therapy of Inflammatory Bowel Disease*. Hamilton, Ontario: BC Decker; 2001:257-261.

mesalamine doses of at least 1.2 g/day. Of note, the protective effects were independent of disease activity.⁷⁰

Dysplasia and cancer surveillance

The increased risk of CRC for patients with IBD has led physicians to use endoscopic surveillance as a potential means of identifying dysplasia or cancer at an early, curable stage. The patient in this case has not had a routine colonoscopy for 3 years, and most experts would agree that he is due for another dysplasia-surveillance colonoscopy. Whether he should have undergone cancer surveillance at more frequent intervals remains a matter of debate, with controversy arising from several areas. First, no randomized controlled clinical study has ever been performed to prove the benefit of dysplasia-surveillance colonoscopy.⁷⁴ Further, there is no standard approach to the number of biopsies or sites of biopsy. Finally, surveys have found that physicians may not fully understand the implications of low- or high-grade dysplasia if it is found.^{75,76} Despite the shortcomings, endoscopic dysplasia surveillance is the best currently available tool.

A recommended approach to screening is provided in Figure 3, page 9. Any approach must take into account the patient's age and additional risks for polyps or cancer. Dysplasia surveillance should be initiated at 8 years of disease, and as many biopsies as possible should be obtained. At least 4 large-cup biopsies should be taken from each of at least 8 sites. An even higher number should be obtained from the sigmoid colon and rectum, because these sites have a higher incidence of CRC in patients with UC.⁷⁷ Future monitoring is based on initial results.

- If the initial endoscopy findings are negative, surveillance should be performed every 2 to 3 years after 8 years of disease until disease duration reaches 20 years. After 20 years, the frequency of surveillance should be increased to once every year.⁷⁷
- A second pathologist's opinion should be sought if the findings are indefinite, low-grade, or high-grade dysplasia.
- If the results are indefinite, a repeat endoscopy should be performed within 3 to 6 months, and an increased number of biopsies should be obtained.^{74,77}
- A finding of definite dysplasia, regardless of grade (high grade or low grade), or a dysplasia-associated lesion or mass (DALM) indicates a likelihood of cancer and is an indication for colectomy.⁷⁷
- An adenomalike polyp on a stalk or an ordinary sessile adenomalike polyp proximal to colitis requires polypectomy or consideration of colectomy⁷⁶ if the patient is symptomatic, has disease that is refractory to treatment, or is unwilling to undergo more intense surveillance.

Because the risk for CRC increases exponentially with duration of UC, the patient may be presented with the option of prophylactic colectomy once disease duration reaches 20 years⁷⁷ if the patient is unwilling to comply with surveillance guidelines. Indeed, patient education is an important aspect of any surveillance program. Patients should be counseled on the need for surveillance and on any implications of their particular risk profiles. This approach enables patients to address

changes in their usual patterns of disease in a timely fashion and to participate in decisions regarding surveillance; it may even be adopted by physicians for their patients with chronic, extensive Crohn's colitis.

A sessile, <2-cm, smooth, regular adenomalike mass within the colitis zone was removed. No dysplasia surrounded the mass. What is your approach now?

The distinction between a DALM and an incidental adenoma is important for patients with UC, because DALMs are an indication for colectomy. On the other hand, adenomas in noncolitic mucosa, although by definition dysplastic, can usually be removed definitively via colonoscopy.⁷⁸ In addition, small polypoid adenomas or small sessile adenomas (<1.5 cm), without evidence of surrounding dysplasia, can be removed via polypectomy if the patient is willing to adhere to heightened surveillance (eg, repeat surveillance colonoscopy within 3 to 6 months).^{78,79}

What about the patient in our case, who was found to have an adenomalike mass within the colitis zone, with no dysplasia surrounding the mass? The previous standard for such situations has been to consider the mass a DALM and proceed with colectomy. A recent study, however, suggests that a more conservative approach may be possible — provided there is no demonstrable coexistent dysplasia in flat colonic mucosa. Rubin and colleagues performed colonoscopic polypectomy in 48 patients, in whom 70 polyps were resected (60 in colitic mucosa and 10 in noncolitic mucosa). Low-grade dysplasia was found in 57 polyps, 2 patients demonstrated high-grade dysplasia, and 1 patient was found to have carcinoma. All patients received follow-up colonoscopies with a mean follow-up of 4.1 years. Although subsequent colonoscopies revealed additional polyps in 48% of patients, no carcinomas were found.⁷⁸ Surgical resection was recommended for 6 patients who had recurrent polyps in the same vicinity. Postsurgical pathology was consistent with the preoperative diagnosis, with no addition of higher-grade dysplasia.⁷⁸

The authors recommended that patients with UC found to have discrete dysplastic polyps within the colitis zone undergo colonoscopic polypectomy. Biopsy specimens should be taken both adjacent to the polypectomy site and throughout the colon to ensure that the polypectomy is complete and to seek other areas of dysplasia. Patients should be followed up with surveillance colonoscopy at yearly intervals. If the polyp recurs after several polypectomies or if dysplasia is found in flat mucosa, colectomy is recommended.⁷⁸

Overall results of surveillance programs

In a review of 15 studies of dysplasia surveillance involving 2030 patients, 21% were found to have neoplasia (dysplasia or cancer) during surveillance. Cancer was found in 1% of patients, with 71% identified at an early stage. These results indicate that dysplasia-surveillance colonoscopy can detect cancer earlier than it is typically found in unscreened populations and also enables prevention of CRC via colectomy when dysplasia is detected.⁶⁹ Therefore, although it is an imperfect tool, dysplasia-surveillance colonoscopy provides the best approach to preventing CRC or managing it when it is in an early, more curable stage.

CONCLUSION

The treatment of patients with IBD brings a spectrum of challenges to the gastroenterologist. As illustrated by these case studies, they may include how to determine a correct diagnosis in a difficult case in which symptoms overlap between IBD and other common bowel disorders, how to address difficult-to-treat complications such as perianal fistula in CD, how to enhance medication adherence, and when and how to monitor periodically for dysplasia and CRC. These

cases reflect some of the many dimensions of this lifelong illness and highlight the need for ongoing integration of newly available information. Fortunately, the past several years have seen many advances in basic scientific understanding, addition of diagnostic tools, a growing number of therapeutic options, and a new awareness of quality of life issues. These advances, as well as those on the horizon, will enable physicians to continue to improve the health and well-being of all patients with IBD.

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THE STATE OF THE ART IN THE MANAGEMENT OF INFLAMMATORY BOWEL DISEASE:

A CASE STUDIES NEWSLETTER 5th in a Series

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- Which of the following statements is true regarding IBD in the elderly?
 - Approximately 26% of CD patients and 22% of UC patients have disease onset after age 60
 - There is a bimodal distribution in onset of IBD, with a major peak before age 20 and a second, smaller peak between the ages of 50 and 80
 - Elderly patients with IBD have symptoms that overlap with other bowel disorders. However, serologic testing to determine ASCA and pANCA levels have not proven useful in reaching a diagnosis
 - All of the above
 - None of the above
- Which of the following is suggestive of a diagnosis of ischemic colitis?
 - Endoscopic findings that include aphthous, irregularly shaped, or linear ulcers and a cobblestone appearance
 - Acute onset of gastrointestinal symptoms with endoscopically normal mucosa
 - A colonoscopy that reveals hemorrhagic nodules that may be bluish-black in appearance
 - Diverticula
- How does medical and surgical treatment of elderly CD patients differ from that in younger populations?
 - The medical and surgical management of patients with CD is the same irrespective of age
 - Because surgery for elderly patients is complicated by increased morbidity and mortality due to an overall poorer health status, surgery is rarely performed
 - Corticosteroid treatment, because of its potential negative impact on coexisting medical conditions, is contraindicated for elderly patients
 - The overall response of medical treatment of elderly patients is similar to that of younger populations, with a success rate of about 65%
 - All of the above
- Which of the following is true regarding perianal complications in CD?
 - Perianal fistula occur in between 17% and 43% of CD patients at some point in the course of disease
 - A recent study has shown that combining any 2 of these 3 diagnostic procedures—EUA, fistulography, or EUS—will determine fistula anatomy accurately in virtually every case
 - Low transsphincteric fistulae can be treated with fistulotomy or seton placement, depending on patient preference
 - Daily oral mesalamine is effective inductive therapy for patients with fistulizing CD
 - All of the above
- Although few randomized, double-blind studies specifically have investigated the efficacy of therapeutic agents in the treatment of perianal fistula, available evidence suggests that
 - Corticosteroids do not play a major role in the management of fistula healing
 - Periodic infliximab infusion following infliximab-induced remission is effective for long-term maintenance of fistula healing
 - Tacrolimus may be more effective than placebo in reducing fistula number
 - AZA/6-MP, cyclosporine, and the antibiotics metronidazole and ciprofloxacin may have a role in treatment of fistulizing CD
 - All of the above
- Which of the following has NOT been shown to be a factor in relapse in IBD?
 - Pregnancy
 - Change in smoking status
 - Emotional stress
 - Inconvenient treatment regimens
 - None of the above is a factor in relapse
- Which of the following was found by Robinson and colleagues to significantly favor self-guided treatment in UC?
 - The self-guided group had fewer relapses
 - Patients in the self-guided group spent less time visiting doctor
 - Time to treat relapse was significantly shorter in the self-guided group
 - The self-guided group had fewer outpatient visits.
 - All of the above
- Which of the following factors does NOT influence CRC risk in patients with IBD?
 - Duration and extent of disease
 - A family history of sporadic CRC
 - Presence of PSC
 - Disease activity
 - All of the above influence CRC risk
- Which of the following is true regarding the role of 5-ASAs in the prevention of CRC?
 - 5-ASAs appear to reduce the risk of CRC, provided patients are adherent to therapy
 - Sulfasalazine protects against CRC, but only at dosages of at least 2 g/day
 - The protective effects of mesalamine appear to be independent of dose as well as of disease activity
 - In a study by Eaden and coworkers, mesalamine reduced CRC risk by approximately 80%
 - All of the above
- Under what circumstance is colectomy NOT mandated based on results of dysplasia-surveillance endoscopy?
 - Small adenomas with no surrounding dysplasia
 - Definite low-grade dysplasia
 - Definite high-grade dysplasia
 - DALM
 - All of the above necessitate colectomy

Evaluation

Please record your posttest answers: 1. ___ 2. ___ 3. ___ 4. ___ 5. ___ 6. ___ 7. ___ 8. ___ 9. ___ 10. ___

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