Learning Objectives
Upon completion of this activity, participants should be better able to:
- Differentiate the clinical features and natural history of ulcerative colitis (UC) from those of other gastrointestinal disorders to facilitate early referral for endoscopic assessment
- Integrate updated practice guideline recommendations into effective strategies for controlling symptoms and inducing remission in patients with mild to moderate UC
- Formulate long-term management plans to maintain remission while minimizing treatment-related adverse effects
- Evaluate patients for UC treatment adherence at regular intervals to facilitate prompt correction of any issues contributing to nonadherence

Introduction
Ulcerative colitis (UC) is a chronic, immune-mediated disease characterized by inflammation of the large bowel. The inflammation typically begins in the rectum and extends in a symmetrical, circumferential pattern to regions of the large intestine. Epidemiologic studies suggest that the incidence and prevalence of UC is increasing worldwide. In North America, 780,000 individuals are affected, with 7000 to 46,000 new cases diagnosed each year. The symptoms of UC (ie, bloody diarrhea, rectal urgency, and tenesmus) may substantially impair patients’ quality of life. UC is associated with a more negative impact on patients’ lives than many other chronic diseases, including rheumatoid arthritis, asthma, and migraine headaches.

UC can be controlled—but not cured—with medical therapy. A 2-phase treatment approach is required: rapid, safe induction of clinical remission and long-term maintenance of remission. Treating inflammatory symptoms with appropriate medication may improve a patient’s quality of life and diminish both short- and long-term disease-related complications. Because the disease is chronic and progressive, lifelong medical therapy is usually required. Cancer surveillance is also a key component of care because of the
increased risk of colorectal cancer (CRC) associated with UC (see Recommendations for Colorectal Cancer Surveillance on page 6).\textsuperscript{1,5}

**Differentiating UC From Other Disorders**

Hallmark symptoms of UC include bloody diarrhea, often accompanied by rectal urgency and tenesmus.\textsuperscript{1} Because these symptoms often overlap with those of other inflammatory bowel diseases (IBDs), notably Crohn’s disease (CD) (Table 1)\textsuperscript{1,6-8} and other gastrointestinal (GI) disor-

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**Table 1. Differential Diagnosis of UC and CD\textsuperscript{1,6-8}**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Feature</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>Absent</td>
<td>Possible</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Varies</td>
<td>Common</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Very common</td>
<td>Fairly common</td>
</tr>
<tr>
<td>Fever</td>
<td>Occasional</td>
<td>Common</td>
</tr>
<tr>
<td>Growth failure in children/adolescents</td>
<td>Occasional</td>
<td>Common</td>
</tr>
<tr>
<td>Perianal disease</td>
<td>Absent</td>
<td>Fairly common</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>Very common</td>
<td>Fairly common</td>
</tr>
<tr>
<td>Signs of malnutrition</td>
<td>Fairly common</td>
<td>Common</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Fairly common</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Anatomic and Radiologic Features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site</td>
<td>Large intestine only</td>
<td>Any part of GI tract, from mouth to anus</td>
</tr>
<tr>
<td>Distribution</td>
<td>Contiguous mucosal inflammation</td>
<td>Noncontiguous, asymmetric, transmural inflammation; “skip” lesions typical</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Fine, superficial</td>
<td>Deep, with submucosal extension</td>
</tr>
<tr>
<td>Fissures</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>Fistulas and strictures</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Environmental Factor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Negative association</td>
<td>Exacerbates disease activity</td>
</tr>
</tbody>
</table>
ders such as collagenous colitis, infectious colitis, and irritable bowel syndrome (IBS) (Table 2), the diagnosis cannot be made solely on clinical symptoms. Endoscopy is required to confirm the histologic diagnosis, determine the extent of the disease, and assess severity. The initial assessment of a patient with suspected UC should include a thorough medical history to identify risk factors for UC and other possible causes of chronic diarrhea. For example, a history that includes recent use of antibiotics or a recent bowel infection might suggest pseudomembranous colitis or infectious colitis, respectively. However, infections can trigger IBD in some patients. Certain environmental factors may impact the risk of UC. Dietary factors (eg, a diet high in fat) are considered to be likely risk factors for the development of UC, but a consistent association has not been shown. Appendectomy for appendicitis reduces the risk of UC and is associated with a less severe clinical course.

Assessments of disease severity are based on both clinical and endoscopic findings, including rate of bowel movements and signs of systemic toxicity (Table 3). The severity of the disease and the extent of colonic involvement determine the treatment strategy. The focus of this review is the management of mild to moderate UC, which accounts for 50% of the UC patient population in any given year and which is characterized by ≤6 stools daily and no or minimal signs of systemic toxicity (ie, fever, tachycardia, and anemia).

### Inducing Remission

Aminosalicylates are the cornerstone of first-line therapy for inducing remission in patients with mild to moderate UC. The 5-aminosalicylic acid (5-ASA) agents—which include mesalamine and the azo-bonded prodrugs sulfasalazine, olsalazine, and balsalazide—are available in oral and topical formulations (Table 4). The selection should be matched to disease severity and loc-
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Aminosalicylates generally exert their therapeutic effects within 2 to 4 weeks.\(^1\) 5-ASA therapy alone induces remission in approximately one-third of patients with UC.\(^{17,18}\) A meta-analysis of 11 randomized controlled trials involving patients with mildly to moderately active UC (N = 2086) found remission was not achieved in 887 (60.3%) of 1470 patients randomized to treatment with 5-ASA compared with 494 (80.2%) of 616 patients given placebo; there was no statistically significant difference between the type of 5-ASA therapy used and efficacy at inducing remission.\(^\text{18}\)

The American College of Gastroenterology (ACG) guidelines for the management of UC recommend oral aminosalicylates, topical mesalamine, or topical corticosteroids (ie, foams, enemas, suppositories) as first-line therapy for inducing remission in mild to moderate distal UC.\(^1\) These recommendations are based on level A evidence (ie, consistent evidence from randomized controlled trials). Topical mesalamine is considered superior to topical corticosteroids or oral 5-ASAs. Combination therapy with oral and topical 5-ASAs is more effective than monotherapy with either treatment. In a double-blind comparison of oral mesalamine (2.4 g/d), mesalamine enema (4 g/d), and combination therapy with both agents, the combination achieved both an earlier response and greater improvement.\(^\text{19}\) Mesalamine suppositories or enemas may be effective for disease that is refractory to oral 5-ASAs or topical corticosteroids.\(^1\)

For patients with extensive mild to moderate UC, the ACG recommends oral sulfasalazine or another oral 5-ASA agent as first-line therapy for inducing remission (level A evidence). For disease refractory to combination oral and topical 5-ASA therapy or for rapid control of severe symptoms, the ACG recommends oral corticosteroids based on evidence from cohort studies or case-control studies (level B). For moderate disease refractory to oral corticosteroids, thiopurine therapy (azathioprine or 6-mercaptopurine) is recommended, but the ACG also notes that infliximab, a biologic agent, is effective in patients who have corticosteroid-refractory or corticosteroid-dependent disease despite thiopurine therapy or in those who are intolerant to corticosteroids or

### Table 3. Severity Classification of UC\(^1\)

<table>
<thead>
<tr>
<th>Severity</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>• &lt;4 stools daily with or without blood</td>
</tr>
<tr>
<td></td>
<td>• Absence of systemic signs of toxicity(^a)</td>
</tr>
<tr>
<td></td>
<td>• Normal ESR</td>
</tr>
<tr>
<td>Moderate</td>
<td>• &gt;4 stools daily</td>
</tr>
<tr>
<td></td>
<td>• Minimal signs of toxicity</td>
</tr>
<tr>
<td>Severe</td>
<td>• &gt;6 bloody stools daily</td>
</tr>
<tr>
<td></td>
<td>• Evidence of toxicity or elevated ESR(^b)</td>
</tr>
<tr>
<td>Fulminant</td>
<td>• &gt;10 stools daily</td>
</tr>
<tr>
<td></td>
<td>• Continuous bleeding</td>
</tr>
<tr>
<td></td>
<td>• Toxicity</td>
</tr>
<tr>
<td></td>
<td>• Abdominal tenderness and distension</td>
</tr>
<tr>
<td></td>
<td>• Blood transfusion requirement</td>
</tr>
<tr>
<td></td>
<td>• Colonic dilation on abdominal plain films</td>
</tr>
</tbody>
</table>

\(^a\)Signs of toxicity include fever, tachycardia, and anemia; \(^b\)Note: some patients with severe disease may not have elevated ESR.

ESR = erythrocyte sedimentation rate.

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1. Patients may find topical therapies impractical and uncomfortable. Common complaints include leakage and abdominal bloating, leading to poor treatment adherence.\(^\text{16}\)

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This recommendation was largely based on the results of the multicenter double-blind placebo-controlled Active Ulcerative Colitis Trials (ACT1 and ACT2), which involved patients with moderate to severe UC and either corticosteroid- or thiopurine-refractory disease (ACT1) or 5-ASA–refractory disease (ACT2). These trials showed that patients treated with infliximab were more likely to achieve clinical response and less likely to have mucosal

Table 4. 5-ASA Therapy Options for UC: Oral and Topical Agents

<table>
<thead>
<tr>
<th>Azo-bonded Prodrugs</th>
<th>Oral Agents</th>
<th>Site of Delivery</th>
<th>FDA-Approved Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sulfasalazine</td>
<td>Colon</td>
<td>Mild to moderate UC and as adjunctive therapy in severe UC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prolongation of remission period between acute UC attacks</td>
</tr>
<tr>
<td></td>
<td>Olsalazine</td>
<td>Colon</td>
<td>Maintenance of remission of UC in patients who are intoler-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ant of sulfasalazine</td>
</tr>
<tr>
<td></td>
<td>Balsalazide</td>
<td>Colon</td>
<td>Mildly to moderately active UC in patients aged ≥5 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mesalamine</th>
<th>Dosage Form</th>
<th>Site of Delivery</th>
<th>FDA-Approved Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Formulations</td>
<td>Delayed-release tablet (800 mg)</td>
<td>Distal ileum, colon</td>
<td>Moderately active UC</td>
</tr>
<tr>
<td></td>
<td>Delayed-release tablet (1.2 g)</td>
<td>Distal ileum, colon</td>
<td>Induction of remission in active, mild to moderate UC</td>
</tr>
<tr>
<td></td>
<td>Delayed-release capsule (400 mg)</td>
<td>Distal ileum, colon</td>
<td>Mildly to moderately active UC and maintenance of remission of UC</td>
</tr>
<tr>
<td></td>
<td>Extended-release capsule (250 mg; 500 mg)</td>
<td>Distal stomach, small intestine, colon</td>
<td>Mildly to moderately active UC and induction of remission of UC</td>
</tr>
<tr>
<td></td>
<td>Extended-release capsule (0.375 g)</td>
<td>Colon</td>
<td>Maintenance of remission of UC in adults</td>
</tr>
</tbody>
</table>

| Topical Formulations | Suppository (1000 mg) | Rectum | Active ulcerative proctitis                                  |
|                      | Liquid enema (4 g/60 mL) Kit (4 g) | Proximal sigmoid colon up to splenic flexure | Active mild to moderate distal UC, proctosigmoiditis, or proctitis |

FDA = Food and Drug Administration.
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Recommendations for Colorectal Cancer Surveillance
Patients with UC carry an increased risk for CRC due to chronic colonic inflammation. Extensive disease, young age at UC onset, severe bowel inflammation, history of pseudopolyps, family history of CRC, and primary sclerosing cholangitis (PSC) have been considered risk factors for the development of CRC.\(^1\)\(^3\)\(^9\)\(^-\)\(^4\)\(^2\)

However, more recent data from a chart review of a nationwide IBD cohort in the Netherlands (most of whom were male patients with UC) suggest that diagnosis of IBD at an older age is associated with early development of CRC (hazard ratio for age ≥10 years, 2.25; 95% CI, 1.92-2.63).\(^4\)\(^3\)

Early recommendations dated the initiation of CRC surveillance from the date of diagnosis of IBD, but it is now recognized that surveillance is better dated from onset of symptoms.\(^4\)\(^3\)\(^4\)\(^4\) In a recent study of an IBD cohort (primarily male patients with extensive UC), approximately 20% of all IBD-related CRCs occurred in the first decade after disease onset.\(^4\)\(^5\) Current recommendations from the American Gastroenterological Association advise beginning colonoscopy screening 8 years after disease onset\(^4\)\(^4\)\(^6\); the Crohn’s & Colitis Foundation of America Consensus Conference recommendations specify 8 to 10 years after symptom onset.\(^5\)

Repeated screenings are recommended every 1 to 2 years thereafter for most patients with UC; for patients with UC and coexisting PSC, screening should begin at PSC diagnosis and be continued annually.\(^5\)\(^4\)\(^4\)\(^6\)

However, despite the recommendation by the ACG, the Food and Drug Administration (FDA)-approved biologic agents for patients with UC (infliximab as well as adalimumab, golimumab, and vedolizumab) received approval only for use in patients with moderate to severe UC.

The 5-ASA agents are generally well tolerated. A recent meta-analysis found no statistically significant increase in the likelihood of experiencing adverse effects or in the frequency of adverse effects with 5-ASAs compared with placebo (Table 5).\(^1\)\(^8\) The one exception was a decreased risk of lower abdominal pain with 5-ASA therapy. Nephrotoxicity has been reported in patients treated with 5-ASAs, but evidence suggests it occurs rarely.\(^2\)\(^1\)

Although they are potent anti-inflammatory drugs, systemic corticosteroids are limited by their multiple adverse effects (eg, infections, glucose intolerance, osteoporosis, psychiatric disturbances, dependence); prolonged use (eg, >2-3 months) is not recommended.\(^2\)\(^2\) For mild to moderate UC, corticosteroids are generally reserved for disease that is refractory to 5-ASA therapy; however, these agents also may be used in the short term for managing disease flares.\(^1\)

An alternative to systemic corticosteroids is budesonide, an oral nonsystemic corticosteroid that undergoes nearly 90% first-pass hepatic metabolism and acts topically, with fewer adverse effects than systemic corticosteroids.\(^1\)\(^2\)\(^3\) The controlled ileal-release formulation delivers the drug to the distal ileum and proximal colon but not to the left colon; thus, its role in UC has been limited.\(^1\)\(^2\)\(^3\)\(^2\)\(^4\) The extended-release formulation utilizes a colonic release system that delivers the drug to the entire colon and was recently approved for inducing remission in mild to moderate UC.\(^2\)\(^3\)\(^2\)\(^5\)\(^2\)\(^7\) In October 2014, the FDA
approved a rectal foam formulation of budesonide for inducing remission in mild to moderate distal UC.\textsuperscript{28}

### Maintaining Remission

The choice of maintenance regimen is largely determined by the regimen used to induce remission. Patients who achieve clinical remission on aminosalicylate therapy can remain on it for maintenance. However, if a thiopurine or biologic agent was needed to achieve remission, that agent should be continued for maintenance.\textsuperscript{1} The 5-ASA agents are highly effective for maintaining remission in patients with mild to moderate UC. A meta-analysis of 11 randomized controlled trials found that the risk of relapse in patients with quiescent UC was significantly lower with 5-ASAs compared with placebo (relative risk, 0.65; 95% CI, 0.55-0.76).\textsuperscript{18}

As first-line agents for maintaining remission in mild to moderate UC, the ACG guidelines recommend mesalamine suppositories for patients with proctitis and mesalamine (enemas or oral), sulfasalazine, or balsalazide for those with distal colitis.\textsuperscript{1} As for induction, the ACG notes that combination treatment with oral and topical mesalamine is more effective for maintenance than monotherapy with either treatment. Second-line agents for maintenance recommended by the ACG include thiopurines and infliximab.\textsuperscript{1} However, other biologic agents that were FDA-approved after publication of the guidelines would be effective as well, although their indication is for moderate to severe disease.

For patients with extensive mild to moderate UC, the ACG recommends sulfasalazine, olsalazine, mesalamine, or balsalazide as first-line maintenance and thiopurine therapy when disease is corticosteroid-dependent or remission is unsustainable with 5-ASA therapy. Infliximab is considered effective in maintaining remission after use as an induction agent. Corticosteroids are not recommended for maintenance treatment due to adverse effects associated with long-term use.\textsuperscript{1}

<table>
<thead>
<tr>
<th>AE</th>
<th>No. of Trials</th>
<th>AE Rate in Patients Given 5-ASAs</th>
<th>AE Rate in Patients Given Placebo</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>7</td>
<td>46.2% (427/924)</td>
<td>43.4% (165/380)</td>
<td>1.02 (0.81-1.29)</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>7</td>
<td>3.8% (41/1070)</td>
<td>3.0% (14/462)</td>
<td>1.18 (0.63-2.18)</td>
</tr>
<tr>
<td>Headache</td>
<td>7</td>
<td>5.1% (54/1065)</td>
<td>6.3% (29/457)</td>
<td>0.82 (0.45-1.47)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6</td>
<td>1.9% (17/903)</td>
<td>4.7% (18/379)</td>
<td>0.44 (0.23-0.84)</td>
</tr>
<tr>
<td>Rash</td>
<td>4</td>
<td>2.4% (10/425)</td>
<td>2.3% (4/177)</td>
<td>1.02 (0.35-2.99)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>3.3% (19/577)</td>
<td>5.5% (13/235)</td>
<td>0.53 (0.23-1.24)</td>
</tr>
</tbody>
</table>

AE = adverse event; RR = relative risk.
Managing Disease Flares
Strategies for managing disease flares include increasing the mesalamine dosage from a maintenance level (2.4 g/d) to a therapeutic level (4.8 g/d or the equivalent), adding topical therapy to an oral regimen (for proctitis or left-sided disease), or using a short course (<2-3 months) of corticosteroids. Escalation of therapy (e.g., with an immunomodulator or biologic) may be appropriate for patients who experience frequent (>2-3 times per year) disease flares. In addition to an appropriate treatment regimen, stress management may be useful in maintaining remission. Patients should be educated about how stressful life events such as moving, changing employment, undergoing relationship problems, and taking exams may trigger flares.29 They also need to understand that frequent disease flares increase their risk of CRC.1,5

Evaluating Treatment Adherence
Treatment nonadherence is a major challenge for clinicians in managing UC. Overall rates of nonadherence range from 40% to 60%.30 As shown in one interview-based study of patients with UC, nonadherence rates can vary based on the treatment regimen: 42% (5-ASAs), 45% (topical corticosteroids), 40% (systemic corticosteroids), and 29% (immunosuppressants).31 Treatment nonadherence is associated with increased morbidity.32,33 Nonadherent patients in remission are more than 5 times as likely to experience a recurrence of symptoms than those who are adherent to medication.30 In a recent case-control study of disease flares, only nonadherence was significantly associated with an increased frequency of flares; other triggers such as stressful life events, nonsteroidal anti-inflammatory drug (NSAID) use, antibiotic use, recent infection, recent travel away from home, and cigarette smoking were not found to increase flare frequency.34 In addition, nonadherence in the UC patient population has been shown to reduce quality of life35 and increase the risk of CRC.33,36

The underlying reasons for treatment nonadherence are multifactorial and can include a poor clinician-patient relationship, need for prolonged treatment (even when disease is asymptomatic), complexity of the prescribed treatment regimen, medication side effects, cost, and patient misperceptions about UC or its treatment.31,36,37 Among patients with UC, risk factors for nonadherence include male gender, single marital status, left-sided disease (as opposed to pancolitis), and need for ≥4 concomitant medications.35 Symptom remission also may contribute to nonadherence, as patients may believe that they are well and therefore no longer need medication.35

Validated Tools to Foster Greater Adherence
Primary care clinicians can play a key role in encouraging treatment adherence (Table 6).36,38 The Modified Morisky Medication Scale (MMS) and the Medication Adherence Report Scale (MARS) are useful predictive tools that clinicians may use to identify patients who may be at
an increased risk for treatment nonadherence. The primary care setting is also the site at which interventions may be conducted to improve treatment adherence.

Patient education is a key component of disease management in patients with UC. Clinicians may overestimate patient comprehension of UC and its treatment; in one study of patients with UC, 62% reported that they felt ill-informed about their disease. Other strategies that may be employed to improve adherence include modifying the treatment regimen and encouraging patients to incorporate self-management techniques into their care. Patients should be directed to resources to help them participate in their care (see Resources for Patients With Ulcerative Colitis on page 8). Finally, establishing an effective patient-clinician dialogue in which patients play an active role in disease management and are kept informed about how their own behavior may affect long-term treatment outcomes is critical to improving adherence.

### Controlling Mild to Moderate UC: Clinical Pearls

- Always investigate complaints of bloody diarrhea and do not automatically attribute it just to hemorrhoids or IBS (which is not characterized by bloody diarrhea).
- Consult the ACG guidelines for current evidence-based recommendations for inducing and maintaining remission in UC.
- Limit the use of corticosteroids to induction of remission or short-term treatment of flares; to minimize their adverse effects, do not use these agents for long-term (ie, >2-3 months) management of UC.
- Monitor patients with UC frequently for treatment adherence—during well visits as well as during visits for acute care of non-IBD issues—and counsel them about the risks associated with nonadherence. When barriers to adherence are identified, offer patients solutions.
- Make sure patients with UC are undergoing CRC surveillance colonoscopies with biopsies at recommended intervals.
- Establish an effective patient-clinician dialogue in which patients play an active role in disease management and understand the effects of their behavior on long-term treatment outcomes.

### Table 6. Strategies to Improve UC Treatment Adherence

<table>
<thead>
<tr>
<th>Patient education</th>
<th>Clinician-patient communication</th>
<th>Treatment individualization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explain rationale for the use of medications</td>
<td>Maintain open communications</td>
<td>Adjust regimen to patient’s best time to take medications</td>
</tr>
<tr>
<td>Discuss chemoprotection for CRC</td>
<td>Provide ability to call about prescription concerns</td>
<td>Decrease pill burden whenever possible</td>
</tr>
<tr>
<td>Discuss adverse effects of medications and how to deal with them</td>
<td></td>
<td>Ensure new medication will not interact with current medications</td>
</tr>
<tr>
<td>Establish procedure for prescription refills</td>
<td></td>
<td>Schedule frequent office visits for maintaining adherence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use adherence aids: pill boxes, dosing reminder, refill reminder programs at pharmacies, mobile device apps</td>
</tr>
</tbody>
</table>
CASE 1: A 19-Year-Old Man With Rectal Bleeding

History and Presentation
Mark, a 19-year-old sophomore in college, presents to the Student Health Center reporting a change in bowel habits and persistent rectal bleeding. He says he has been working out in the gym more often than usual and attributes the rectal bleeding to hemorrhoids, which have bothered him since he was a weightlifter in high school. His previous bowel habits were 1 to 2 formed stools per day without urgency or discomfort. During the last 2 to 3 months, he has had 3 to 5 soft stools per day, occasionally with mucus and blood streaks, accompanied by urgency. He also reports lower left quadrant abdominal cramping pain that is relieved with a bowel movement. He is occasionally awakened during the night to have a bowel movement. He denies a history of GI infection, cigarette smoking, or frequent NSAID use and has no family history of IBD.

Initial Findings
- Vital signs: stable
- Abdomen: normal bowel sounds, no organomegaly; mild lower left quadrant tenderness but without palpable mass or fullness
- Perianal examination: no anal fissures, hemorrhoids, or tenderness; grossly blood-streaked stool detected on digital rectal examination
- Blood test results: comprehensive metabolic panel (CMP), within normal limits; white blood cell count (WBC), 11,100/µL; hemoglobin, 11.2 g/dL; hematocrit, 34%; mean corpuscular volume (MCV), 81 fl; platelet count, 425 × 10³/µL; C-reactive protein (CRP) level, 12.0 mg/L

Clinical Decision Point
What clues in Mark's history suggest that he should be referred for endoscopy?
A. Abdominal cramping relieved by defecation
B. Blood-streaked stools and nocturnal bowel movements
C. Hemorrhoids and increased physical activity
D. No recent GI infection or frequent NSAID use

Comment
Soft stools over a 3-month period and abdominal cramping relieved by defecation could indicate IBS. Recent GI infection and NSAID use are potential triggers of IBD, but their absence in Mark’s case does not rule out IBD. Hemorrhoids are not among the physical findings, and Mark’s increased physical activity would not account for his change in bowel habits. However, his history of blood-streaked stools, which were also present on the digital rectal examination, is a hallmark of IBD. Bloody stools always warrant investigation and should not be automati-
ally attributed to hemorrhoids or IBS. The other major clue to the presence of IBD in Mark’s history is his report of nocturnal bowel movements. The clinical suspicion of IBD should be high, and the absence of perianal disease on physical examination suggests UC rather than CD. 

Correct answer: B

**Diagnosis and Treatment Decision**

Mark was referred for endoscopy. The colonoscopy revealed left-sided continuous colitis from the anal verge to 50 cm, normal mucosa proximally, and a normal terminal ileum. Biopsies of the rectum and left colon showed acute and chronic inflammation and crypt abscesses consistent with UC. The diagnosis is left-sided UC.

Remission was induced with a mesalamine enema and oral mesalamine, 4.8 g/d in divided doses. After remission was achieved, topical mesalamine was discontinued and oral mesalamine was reduced to 2.4 g/d as maintenance therapy.

**CASE 2: A 32-Year-Old Woman With UC Flare**

**History and Presentation**

Deborah is a 32-year-old woman recently hospitalized for a UC flare who presents to her primary care clinician for a postdischarge follow-up, as she was unable to schedule an earlier appointment with her gastroenterologist. She was given the diagnosis of pancolitis 12 years ago, at age 20 years. During her hospitalization, she was treated with intravenous corticosteroids and was discharged last week on a corticosteroid taper and oral mesalamine, 1.2 g 4 times a day. She is currently having 2 to 3 soft stools per day with less urgency and no bleeding. She is a non-smoker and does not use NSAIDs. She has no family history of IBD.

The patient states that she did well for the first 10 years after her diagnosis, when her disease was maintained in remission with oral mesalamine only; however, during the last 2 years, she has had 4 to 5 flares per year requiring a course of corticosteroids. She travels frequently for work as a buyer for a national retail chain and is frustrated at the frequency of her flares.

On questioning, she admits that she frequently misses doses of her medication and sometimes forgets to take her medications with her on business trips. Instead, she will use loperamide as needed, with mild improvement. Despite her diagnosis more than 12 years ago, she has not had a surveillance colonoscopy.

**Initial Findings**

- Vital signs: stable
- Abdomen: normal bowel sounds; mild left upper quadrant and lower left quadrant tenderness but without palpable mass or fullness
Optimizing Control of Mild to Moderate Ulcerative Colitis

- Perianal examination: no anal fissures, skin tags, fistulae, or tenderness; nonbloody soft stool on digital rectal examination
- Blood test results: CMP, within normal limits; WBC, 13,2000/µL; hemoglobin, 10.4 g/dL; hematocrit, 31.2%; MCV, 78 fL; platelet count, 380 × 10³/µL; CRP level, 21 mg/L
- Computed tomographic scan of abdomen and pelvis (performed during hospitalization): inflammatory stranding of entire colon with mild thickening but no fluid collection; normal-appearing small bowel

**Clinical Decision Point**

*What is the most likely cause of Deborah's UC flares?*

A. CD misdiagnosed as UC  
B. Nonsmoking status  
C. Poor treatment adherence  
D. Treatment-refractory disease

**Comment**

The physical and radiographic findings are consistent with a diagnosis of UC. Although recent smoking cessation may trigger UC flares in some patients, Deborah has always been a non-smoker, and her disease had been maintained in remission until 2 years ago. Thus, it is unlikely that her smoking status influenced the onset of her disease flares. Deborah’s UC is responding to oral mesalamine as she tapers corticosteroid use, so treatment-refractory disease is probably not the cause of her flare. The most likely cause is her admitted poor adherence to her maintenance regimen. **Correct answer: C**

**Management Approach**

By not adhering to her maintenance regimen, Deborah is risking disease progression due to repeated flares as well as adverse effects, including osteoporosis, from her frequent corticosteroid use. She is also increasing her risk of CRC due to the chronic inflammation. She is counselled about the risks associated with treatment nonadherence and other possible triggers of disease flares. Just as important is offering her potential solutions, including mobile apps for dosing and prescription refill reminders and stress management techniques. A follow-up consultation with her gastroenterologist is recommended for consideration of advancing treatment to an immunomodulator or biologic and for scheduling a surveillance colonoscopy to screen for CRC.

References

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