Factors Associated With Poor Outcomes in Adults With Newly Diagnosed Ulcerative Colitis

Walter Reinisch,* Andrew R. Reinink,‡ and Peter D. R. Higgins‡

*Department of Medicine, McMaster University, Hamilton, Ontario, Canada; and ‡Department of Medicine, Division of Gastroenterology, University of Michigan, Ann Arbor, Michigan

It is a challenge to accurately identify patients with early stage ulcerative colitis (UC) who are at highest risk for a poor outcome and therefore might require salvage therapy. Several epidemiologic and clinical studies have analyzed factors associated with poor prognosis and increased risk for colectomy. We review prognostic factors for adults with newly diagnosed UC and discuss which patients might benefit from rapid and progressive therapy. Patients with poor prognoses tend to be young nonsmokers with high levels of inflammatory biomarkers, low levels of hemoglobin, and extensive disease, based on colonoscopy. We examine these risk factors in 2 hypothetical patients who have been newly diagnosed with UC.

Keywords: IBD; Treatment; Prognosis; TNF Inhibitor; Tumor Necrosis Factor.

Ulcerative colitis (UC) is a chronic inflammatory disorder of the colon that varies in course, ranging from quiescent to chronic refractory disease. The main complications of UC are fulminant colitis, leading to emergency colectomy, and chronic smoldering inflammation, which contributes to the development of colorectal cancer and/or elective colectomy.1,2 Recent population-based cohort studies reported that approximately 10% of patients with UC require colectomy, and a significant number of colectomies occur during a patient’s first hospitalization for UC.1,3–5 Although rates of elective colectomy are decreasing with more progressive management strategies, which include immunosuppressants and anti-tumor necrosis factor agents, rates of emergency colectomy remain stable. Patients who receive emergency colectomies tend to require them soon after diagnosis with UC and to have short durations of disease flare, indicating their rapid progression to severe UC.6 Long-term studies have estimated that the colectomy rate among patients who have been hospitalized previously for disease flare is as high as 70% within 5 years of initial hospitalization.3–9 The risk of colectomy within 90 days of diagnosis is particularly high for patients diagnosed during hospitalization.5

Therefore, it is an important but difficult task to identify, at first presentation, patients who are likely to have a rapid and severe course of disease and who require more aggressive treatment to prevent colectomy. Epidemiologic and clinical studies have analyzed a large number of factors associated with a future need for colectomy in patients with UC.10–13 We review this literature in order to help clinicians better assess adult patients who are at risk for poor outcomes and who are most likely to benefit from early, progressive therapy. Many of these prognostic factors are useful not only at initial diagnosis, but also during subsequent flares and hospitalizations. We have applied these findings to 2 hypothetical patients who present with similar symptoms but have different prognoses when their risk factors are considered. Throughout this review, the evidence level for each risk factor has been graded based on the 2011 Oxford Centre for Evidence-based Medicine Levels of Evidence Grading System for Prognosis (Oxford grade [OG]),14 using the highest grade of evidence among the reports cited for each risk factor.

Factors Associated With Poor Outcomes

Patient Characteristics

In the hypothetical cases shown in Figure 1, patient A and patient B differ in 2 important characteristics associated with outcome: age and smoking status. Younger age at diagnosis is associated with a shorter time to clinical relapse, greater number of relapses, increased risk of colectomy, poorer response to treatment, greater disease severity, and a greater extent of progression of distal UC (OG2).4,13,15–18 (Table 1)14,5,14,15,17–27 In a 10-year, population-based cohort study of 519 patients with UC (the Inflammatory Bowel South-Eastern Norway [IBSEN] study), patients age 50 and older at diagnosis had a 72% lower risk for colectomy than patients younger than age 30 (OG2).1 The association between more severe disease and younger age is supported by the

Abbreviations used in this paper: ACT, Active Ulcerative Colitis Trial; CDI, Clostridium difficile infection; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FCP, fecal calprotectin; IBD, inflammatory bowel disease; IBSEN, Inflammatory Bowel South-Eastern Norway; OG, Oxford grade; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.
high rate of colectomy (20% within 5 years of diagnosis) reported from a pediatric cohort in France, which was twice the rate of adult patients (OG2).1,28

Among older adults, there are conflicting data on the association between age at diagnosis and outcome. Another population-based study performed in France concluded that the rate of surgery was 8% within 10 years of diagnosis for patients who developed UC after age 60 (OG3).29 However, a Canadian study reported that patients diagnosed with UC when they were age 65 and older had an increased risk for early colectomy, compared with patients diagnosed when they were younger than age 65 (OG3).5 Although these findings seem incompatible, they can be reconciled. Patients diagnosed at older ages might have a milder course of UC, but those who present with severe UC might be less likely to receive immunosuppressive rescue therapy because of concerns of an increased risk of infectious complications. The potentially more restricted use of rescue therapy could increase the chances of disease progression to colectomy. Results from several retrospective cohort studies indicated that patients who were nonsmokers or ex-smokers had more relapses, greater frequencies of hospitalization and colectomy, and a lower likelihood of disease regression than current smokers (Table 1) (OG2).4,20,21,23 There is conflicting evidence about the association between sex and outcome in patients with UC (OG2).4,24 In a European population-based cohort, rates of relapse were higher in women than in men, whereas men were found to be at increased risk for colectomy in a similarly designed study performed in Canada (OG3).5

**Clinical Signs and Symptoms**

In several studies, the severity of UC at diagnosis was associated with subsequent relapse and colectomy. For example, in 296 patients with UC managed at a single center over 10 years, moderate and severe disease at diagnosis increased the risk of relapse approximately 2-fold, and later colectomy more than 3-fold (OG3).20

---

**Table 1**

<table>
<thead>
<tr>
<th>Patient A</th>
<th>Patient B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brief history and initial symptoms:</strong></td>
<td><strong>Brief history and initial symptoms:</strong></td>
</tr>
<tr>
<td>A previously healthy 21-year-old female ex-smoker presents to her physician with a 2-day history of urgent bowel movements with traces of blood. On day 2, she had 5 urgent bowel movements with blood and some mucus.</td>
<td>A 45-year-old male smoker (1 pack/day x 20 years) presents with a 2-day history of urgent bowel movements; the bowel movements initially had mucus, but they turned bloody by evening of day 1 and increased in number to 5 urgent bloody stools on day 2.</td>
</tr>
<tr>
<td><strong>Initial laboratory results:</strong></td>
<td><strong>Initial laboratory results:</strong></td>
</tr>
<tr>
<td>• Hgb 9.1 g/dL</td>
<td>• Hgb 13.1 g/dL</td>
</tr>
<tr>
<td>• ESR 73 mm/h</td>
<td>• ESR 25 mm/h</td>
</tr>
<tr>
<td>• CRP 2.5 mg/dL</td>
<td>• CRP 0.5 mg/dL</td>
</tr>
<tr>
<td>• FCP 820 μg/g</td>
<td>• FCP 210 μg/g</td>
</tr>
<tr>
<td>• Serum albumin 28 g/L</td>
<td>• Other labs within normal limits</td>
</tr>
<tr>
<td><strong>Colonoscopy results:</strong></td>
<td><strong>Colonoscopy results:</strong></td>
</tr>
<tr>
<td>Endoscopic evidence of UC; pancolitis with ulcerations on left side.</td>
<td>Endoscopic evidence of UC; diffuse erythematous inflammation up to the splenic flexure.</td>
</tr>
<tr>
<td><strong>Initial treatment course:</strong></td>
<td><strong>Initial treatment course:</strong></td>
</tr>
<tr>
<td>Outpatient treatment with mesalamine oral (2.4 g qd) and suppository (1 g PR noon &amp; hs).</td>
<td>Outpatient treatment with mesalamine oral (2.4 g qd) and suppository (1 g PR noon &amp; hs).</td>
</tr>
</tbody>
</table>

---

**Figure 1**. Patients A and B presented with very similar symptoms. Initial laboratory results and colonoscopy indicated a worse prognosis for patient A. Initial treatment should be similar in the 2 patients, but patient A is more likely to need aggressive therapy as a next step. Hgb, hemoglobin; hs, at bedtime; PR, per rectum; qd, every day.
Among patient features, increased body temperature and pulse at time of hospital admission were associated with a higher risk of colectomy (OG2). These factors have been incorporated into scoring systems to determine risk for short-term colectomy (OG3). Stool frequency and blood in stool also have been incorporated into several predictive indices. 

**Biologic Markers**

Among several biomarkers that have shown prognostic value for patients with UC, level of C-reactive protein (CRP) is among the most studied and most evidence-based (Table 2). Levels of CRP increase by 500- to 1000-fold within 48 hours during inflammation and decrease with a half-life of 19 hours once the acute-phase response subsides (OG5). In the IBSEN study, levels of CRP greater than 23 mg/L at diagnosis of extensive colitis increased the risk of surgery nearly 5-fold within the next 5 years (OG2). In an analysis of the Active Ulcerative Colitis Trials (ACT-1 and ACT-2; N = 728) in patients with moderate to severely active UC, baseline levels of CRP of 20 mg/L or greater were associated significantly with the risk of colectomy during 54 weeks of follow-up evaluation (OG3). Increased CRP level also was an important predictor of outcomes of hospitalized patients with severe transmural UC (OG2). In 51 consecutive episodes of severe colitis at a single center, 85% of those with either CRP levels greater than 45 mg/L and 3 to 8 stools or with more than 8 stools on day 3 required colectomy during the same admission (OG2). Similarly, in a retrospective analysis of 97 acute attacks of UC requiring inpatient treatment, levels of CRP of 25 mg/L or higher and more than 4 stools on day 3 were associated independently with colectomy within 30 days (OG3).

Fecal calprotectin (FCP), a neutrophil protein, is an extensively studied marker of intestinal inflammation (OG5). A recent extensive review of how the level of FCP can be used to manage patients with inflammatory bowel diseases (IBDs) found a high correlation (range, 0.48–0.87) between FCP levels and endoscopic activity in patients with UC (OG5). In a study of 39 patients with UC, levels of FCP greater than 250 mcg/g identified those with active mucosal disease with 71% sensitivity and 100% specificity (OG4). In a prospective study of 90 patients with acute severe UC who were hospitalized for treatment, levels of FCP were significantly higher among patients requiring colectomy (a cut-off level of 1922.5 mcg/g yielded a positive likelihood ratio of 9.23 for colectomy, with 97.4 specificity and 24.0% sensitivity) (OG2).

Several studies have suggested that an increased erythrocyte sedimentation rate (ESR) is associated with the need for colectomy. An ESR of greater than 75 mm/h at admission increased the risk of colectomy 4.6-fold in a prospective study of 67 patients with severe colitis (OG2). In a population-based cohort of 519 patients with UC (the IBSEN cohort), an ESR of 30 mm/h or

### Table 1. Characteristics of Patients With UC That Are Associated With Poor Outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>Younger age at diagnosis has been associated with more severe disease, shorter time to relapse, and higher risk for colectomy (OG2)</td>
</tr>
<tr>
<td></td>
<td>Age of 65 years or older at diagnosis was associated independently with increased risk for early colectomy (OG3)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Nonsmokers and ex-smokers tend to have more extensive disease and a lower chance of disease regression; current smokers tend to have lower rates of relapse and fewer hospitalizations (OG1)</td>
</tr>
<tr>
<td>Sex</td>
<td>There is conflicting evidence for the association between sex and outcome (OG2)</td>
</tr>
<tr>
<td>Genetic factors</td>
<td>None of the genetic variants associated with specific outcomes can identify patients with sufficient levels of sensitivity or specificity. Specific haplotypes of CLEC7A have been associated with UC that is refractory to medical treatment and shorter time to colectomy (OG2)</td>
</tr>
</tbody>
</table>

NOTE. For each set of references, the evidence level was graded by the Oxford 2011 Levels of Evidence grading system for prognosis, using the highest grade among the articles cited. Lower numbers indicate better evidence.

### Table 2. Biologic Markers Associated With Poor Outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>Increased CRP level at time of diagnosis or during follow-up evaluation is associated with a higher risk of colectomy (OG2)</td>
</tr>
<tr>
<td>FCP</td>
<td>Increased level of FCP is associated with an increased risk of relapse and of colectomy (OG2)</td>
</tr>
<tr>
<td>ESR</td>
<td>A higher ESR is associated with an increased risk of colectomy (OG2)</td>
</tr>
<tr>
<td>Hematologic markers</td>
<td>Low levels of hemoglobin or fibrinogen and extended prothrombin time are associated independently with treatment failure (surgery, death, or discharge in a moribund state) in patients with severe or fulminant UC (OG2)</td>
</tr>
<tr>
<td>Body temperature and pulse</td>
<td>Increased body temperature and pulse in patients with severe colitis is associated with a higher risk of colectomy (OG2)</td>
</tr>
</tbody>
</table>

NOTE. For each set of references, the evidence level was graded by the Oxford 2011 Levels of Evidence grading system for prognosis, using the highest grade among the articles cited. Lower numbers indicate better evidence.
higher at the time of diagnosis increased the risk of colectomy 3-fold.\textsuperscript{1,13} CRP and ESR each were associated with negative outcomes, and with each other (OG4).\textsuperscript{13} However, because CRP levels increase and decrease more rapidly than ESR levels during acute UC, CRP is more useful in assessing risk and identifying a response to therapy, as illustrated in the University of Michigan severe ulcerative colitis protocol (OG5).\textsuperscript{50}

Hematologic markers of poor prognosis include low levels of hemoglobin (\(<9\ g/dL\) or fibrinogen (\(<220\ mg/dL\)), and extended prothrombin time (>14 s; average control time, 12 s). Each of these markers was associated independently with a lack of response to intravenous corticosteroids in multivariate analyses of a prospective study of 50 consecutive patients hospitalized for UC (OG2).\textsuperscript{38} For children newly diagnosed with UC, a scoring system based on hemocrutit and white blood cell counts had a high negative predictive value for colectomy at 1 and 3 years, although the positive predictive value for colectomy was low (OG4).\textsuperscript{51}

Initial laboratory results for patient A and patient B indicated a worse prognosis for patient A than patient B (Figure 1). Patient A’s increased level of CRP and ESR, high level of FCP, and low level of hemoglobin all predicted a more aggressive disease course than that of patient B, who had normal levels of CRP and hemoglobin and only a slight increase in FCP level.

**Serologic and Genetic Markers**

Perinuclear antineutrophil cytoplasmic antibodies and antibodies against *Saccharomyces cerevisiae* might be surrogate markers of an aberrant immune response in patients with IBD. Several studies have shown higher rates of relapse and lower rates of remission among patients with perinuclear antineutrophil cytoplasmic antibodies (OG4).\textsuperscript{15,52,53}

Genetic markers of disease course have been identified but are not yet used in clinical practice (OG2).\textsuperscript{16,54} Iliev et al\textsuperscript{27} found that a haplotype of the gene that encodes dectin1 (*CLEC7A*) was associated more strongly with UC that is refractive to medical treatment than UC that responds to treatment, and was associated with a shorter time to colectomy among 806 patients (OG3).\textsuperscript{27}

**Endoscopic and Histopathologic Factors**

Endoscopic measures of disease extent and activity also can predict outcomes of patients with UC (Table 3).\textsuperscript{17,18,19,30,35,36,55,68} The endoscopic findings for patient A and patient B (Figure 1), further suggest that patient A’s outcome is likely to be worse than patient B’s outcome because patient A has more extensive disease and more severe mucosal lesions. The severity of mucosal lesions directly reflects inflammatory activity and might be used to identify more aggressive disease, which carries a worse prognosis (OG5).\textsuperscript{59} In the ACT 1 and ACT 2 studies, the proportion of infliximab-treated patients with UC who were in clinical remission at week 30 was 4-fold greater among patients with mucosal healing (endoscopy subscore, 0 or 1) at week 8 (34%–46%) than among patients with endoscopy scores of 2 or 3 at week 8 (6.5%–11%) (OG3).\textsuperscript{56,59} Patients with lower Mayo endoscopy subscores were also less likely to progress to colectomy through week 54 of follow-up evaluation (OG3).\textsuperscript{59} Among 513 UC patients in the IBSEN study, mucosal healing after 1 year of treatment was associated with an almost 5-fold lower risk of colectomy (OG2).\textsuperscript{57}

In patients with quiescent UC, even when routine colonoscopies showed a normal appearance of the mucosa, indicating remission, histologic evidence of mild or moderate inflammation can persist and is associated with eventual relapse (OG3).\textsuperscript{66,70} Findings from magnifying

### Table 3. Disease and Treatment Factors Associated With Poor Outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal appearance and Mayo endoscopy subscore\textsuperscript{1,56–59}</td>
<td>Absence of mucosal healing and/or deep extensive colonic ulcerations are associated with an increased risk of colectomy (OG3)</td>
</tr>
<tr>
<td>Epithelial defects by magnifying chromoscopy\textsuperscript{50–62}</td>
<td>Associated with an increased risk of relapse (OG2)</td>
</tr>
<tr>
<td>Histopathologic parameters\textsuperscript{53–66}</td>
<td>Inflammation, deep ulceration, mononuclear cell infiltration, low numbers of eosinophils, wide extent of disease, frequent crypt abscesses and severe cryptitis (in patients &gt;38 y), and presence of lymphoid follicles (in patients ≤38 y) are associated with an increased risk of colectomy (OG3)</td>
</tr>
<tr>
<td>Disease severity\textsuperscript{10,12,30,38,67}</td>
<td>Moderate or severe disease at diagnosis is associated with a higher risk of relapse and colectomy (OG2)</td>
</tr>
<tr>
<td>Disease extent\textsuperscript{1,13}</td>
<td>Extensive colitis or pancolitis at diagnosis is associated with a higher risk of colectomy (OG2)</td>
</tr>
<tr>
<td>Disease duration\textsuperscript{10}</td>
<td>Shorter disease duration (&lt;3 y) is associated with a higher risk of colectomy (OG3)</td>
</tr>
<tr>
<td>Hospitalization\textsuperscript{7}</td>
<td>Associated with an increased risk of colectomy (OG4)</td>
</tr>
<tr>
<td>Treatment failure with azathioprine, corticosteroids, cyclosporine, and/or infliximab\textsuperscript{7,8,11,12,35,68}</td>
<td>Associated with an increased risk of colectomy (OG2)</td>
</tr>
</tbody>
</table>

NOTE. For each set of references, the evidence level is graded by the Oxford 2011 Levels of Evidence grading system for prognosis,\textsuperscript{14} using the highest grade among the articles cited. Lower numbers indicate better evidence.
colonoscopy with chromoendoscopy correlate better with histopathologic findings than do conventional colonoscopy findings in patients with UC (OG2).60,70 In studies examining the predictive value of this procedure, the presence of irregular crypt openings and/or an irregular fine architectural network and/or minute defects of epithelium were associated with higher relapse rates (OG2).60–62 However, it is not clear whether these findings predict the eventual need for colectomy. Several conventional histopathologic parameters have been found to predict the need for colectomy (Table 3) (OG3).63–66 In a retrospective study of 75 patients with endoscopically inactive disease, histologic examination showed basal plasmacytosis in 21% of patients, which increased the risk for clinical relapse by more than 5-fold at 1 year (OG3).66

The extent and duration of UC also can predict the need for colectomy. In a 5-year follow-up analysis of participants in the IBSEN study, levels of CRP increased with extent of disease, and extensive colitis was associated with an increased risk for surgery (OG2).39 At 10 years, the cumulative rate of colectomy was 19% in patients with extensive colitis at diagnosis, compared with 8% in patients with left-sided colitis and 5% in patients with proctitis (OG2).1 In a review of several epidemiologic studies, the 5-year rate of colectomy was 30% to 45% among patients with pancolitis at the time of diagnosis vs 2% to 14% among those initially diagnosed with proctitis or left-sided disease (OG5).71 For pediatric patients, a delay in diagnosis of more than 6 months was a risk factor for colectomy (OG3).28

**Treatment Factors and Comorbidities**

Patients who require early hospitalization for the management of UC are a subset with severe disease who could be more likely to require colectomy (OG4).7 In a retrospective case-control study of 246 patients with UC, at least 1 hospitalization and previous treatment with infliximab each were associated with the eventual need for colectomy (OG4).7

Another disease-related factor to consider during assessment is the possible coexistence of primary sclerosing cholangitis (PSC)—an extra-intestinal manifestation that develops in approximately 2% to 7.5% of patients with UC (OG2).72,73 Increased levels of alkaline phosphatase, often associated with increased activity of transaminases, is a marker of PSC in patients with UC, and indicates that the patient should be examined by magnetic resonance cholangiopancreatography (OG2).73–76 Some data indicate that the course of UC is less severe in patients with PSC, suggesting that PSC-associated UC could be a distinct phenotype of IBD, however, further studies are needed (OG4).72,77,78 In a regression analysis of data collected prospectively from 420 patients, the presence of PSC was 1 of only 2 independent predictors of UC disease progression (OG3).18 In a cohort of 113 pediatric patients with UC, the presence of extraintestinal manifestations at diagnosis was associated with a 3.5-fold increase in risk of colectomy (OG3).28

Several studies have reported that *Clostridium difficile* infection (CDI) increases the risk for poor outcomes in patients with UC (OG1).79,80 Because not all patients with IBD and CDI have typical risk factors for CDI (antibiotic therapy, hospitalization, pseudomembranes), their presence should not be required for CDI testing (OG3). Similarity, patients with UC are at increased risk for colonic reactivation of cytomegalovirus infection, which subsequently is associated with an increased risk for colectomy and mortality (OG5).81 However, there are few data on the prevalence of CDI and colonic cytomegalovirus infection at diagnosis of UC.

Cvancarova et al73 (OG4) used data from the IBSEN trial to develop a model to predict the need for colectomy within 10 years after a diagnosis of UC. They determined that the highest risk for colectomy within 10 years of diagnosis was associated with age younger than 40 years, use of corticosteroids, extensive colitis, and ESR of 30 or greater. The model accurately predicted the need for colectomy in 90.3% of cases. However, it has not been validated in an external prospective cohort (OG4).13

**Discussion**

The early and accurate identification of patients with adult-onset UC who are at highest risk for a poor outcome remains a clinical challenge (OG5).82 Nevertheless, effective management of these patients requires early recognition and close monitoring during early treatment so that more progressive steps can be taken in a timely fashion if initial treatment is not effective (OG2).50,83 We present 2 hypothetical cases of patients with UC to illustrate the challenge. The patients had similar symptoms on initial presentation, yet their predicted outcomes differed based on characteristics such as age and smoking status, laboratory results, and endoscopy results.

Data from the epidemiologic and clinical studies that we reviewed indicated that patients with UC at highest risk for poor outcome tended to be young nonsmokers who were hospitalized soon after diagnosis, those who had high CRP levels and ESRs, those who had low levels of hemoglobin, and those who had extensive colitis with deeper ulcerations. Application of these factors to the case examples presented shows a process that can help identify the patients most likely to have poor outcomes who require rapid step-up therapy.

Identification of new markers or testing strategies could increase our ability to rapidly identify high-risk patients. A promising area of research is the testing of a new point-of-care FCP test to distinguish patients with IBD from those with non-IBD (OG4).84 Rapid point-of-care FCP testing may have prognostic value in the inpatient setting. Further prospective studies are needed
to validate these prognostic factors and to evaluate whether early introduction of biologic or immunosuppressive therapy in high-risk patients slows disease progression (OG5).83

References
82. Travis S, Satsangi, Lemann M. Predicting the need for colectomy in severe ulcerative colitis: a critical appraisal of clinical parameters and currently available biomarkers. Gut 2011;60:3–9.

Reprint requests
Address requests for reprints to: Walter Reinisch, MD, Department of Medicine, McMaster University, 1280 Main Street West, Hamilton, L8S 4L8 Ontario, Canada. e-mail: reinisw@mcmaster.ca; fax: (484) 434-2801.

Conflicts of interest
These authors disclose the following: Walter Reinisch has served as a speaker, consultant, and/or advisory board member for Abbott Laboratories, AbbVie, Aesca, Amgen, Astellas, Astra Zeneca, Biogen IDEC, Bristol-Myers Squibb, Cellerix, ChemoCentryx, Celgene, Centocor, Danone Austria, Elian, Ferring, Galapagos, Genentech, Grünenthal, Johnson & Johnson, Kyowa Hakko Kirin Pharma, Lipid Therapeutics, Millenium, Mitsubishi Tanabe Pharma Corporation, MSD, Novartis, Otsuka, PDL, Pharmacosmos, Pfizer, Procter & Gamble, Prometheus, Roberts Clinical Trial, Schering-Plough, Setpoint Medical, Shire, Takeda, Therakos, Tigenix, UCB, Vifor, Yakult, Zynegien, Austria, and 4SC; and Peter Higgins has served as a consultant for AbbVie, Amgen, Genentech, JBR Pharma, and Lycera. The remaining author discloses no conflicts.

Funding
Supported by Merck Sharp & Dohme, Corp, a subsidiary of Merck & Co, Inc (Whitehouse Station, NJ), which provided medical writing and editing services from Angela Cimmino, PharmD, and Ellen Stoltzts, PhD, of JK Communications, Conshohocken, PA, during the development of this manuscript. The authors are solely responsible for the content of the article.

1. The need for emergency colectomy is most common in which of the following groups
   a) long-standing disease refractory to therapy
   b) UC diagnosed in the inpatient setting
   c) Recent diagnosis of UC
   d) Refractory left-sided colitis

2. Elevation of which of the following tests is associated with a worse prognosis in UC
   a) CRP
   b) Fecal calprotectin
   c) hemoglobin
   d) pANCA

True or False

3. UC tends to have a milder course in females compared to males

4. Younger age at initial diagnosis of UC is associated with a more aggressive course of the disease

5. Non-smokers or recent ex-smokers have a higher risk for more virulent UC course

6. Endoscopic findings at time of initial diagnosis do not correlate with future disease outcome