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GASTROENTEROLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Gastroenterology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in gastroenterology. Each quarterly manual reviews a topic essential to the current practice of gastroenterology.

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Treatment of Inflammatory Bowel Disease

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Treatment of Inflammatory Bowel Disease

Jeffrey A. Tuvlin, MD, Miles Sparrow, MD, and Stephen B. Hanauer, MD

INTRODUCTION

Ulcerative colitis and Crohn's disease are two similar but overlapping types of inflammatory bowel disease (IBD). IBD is thought to be the result of overactivation of the immune system directed at luminal antigens of the gastrointestinal tract. Whereas a certain degree of chronic inflammation in the intestines is normal, there is failure of down-regulation in IBD, resulting in acute inflammation. In ulcerative colitis, this inflammation is limited to the colon. In Crohn's disease, the inflammation may affect any portion of the gastrointestinal tract from the mouth to the anus. In ulcerative colitis, the colonic inflammation tends to be superficial, affecting the mucosal layer of the bowel and resulting in the clinical manifestations of hematochezia, diarrhea, cramping, and urgency. In Crohn's disease, the inflammation may be transmural within the colon or small bowel, leading to symptoms of abdominal pain, diarrhea, anemia, and the formation of strictures and enterocutaneous or entero-enteric fistulae. To diagnose IBD accurately, physicians rely on a combination of endoscopic, radiologic, serologic, and histologic tests.

In North America and Europe, the prevalence of Crohn's disease is 26.0 to 198.5 and that of ulcerative colitis is 37.5 to 229 per 100,000.¹ Once thought to be mostly a disease of Caucasians, the incidence of IBD among African Americans seems to be higher than previously thought,² and IBD is seen in members of populations at low risk when they move to Westernized cultures.

The importance of shared genetic and environmental influences on IBD are reflected by its familial association. Twin studies have revealed a concordance of 42%–58% and 6%–17% for Crohn's disease and ulcerative colitis, respectively.^{3,4} First-degree relatives of patients with either disease have a relative risk of 10 to 15 of developing the same disease.^{5,6} The recently discovered NOD2/CARD15 gene is a cytosolic protein with 3 major polymorphisms that appears to be associated with Crohn's disease but not with ulcerative colitis.^{7–9} Persons who are heterozygous for mutated genes carry a 2- to 4-fold increase in disease development. Double-dose or compound heterozygous carriage car-

ries a 20- to 40-fold increase in risk. Carriage of this risk allele seems to be associated with ileal disease location.^{10,11} An understanding of how genetics are associated with increased or earlier risk of IBD complications may allow for the initiation of earlier or more aggressive therapy for individual patients.

INDUCTION AND MAINTENANCE OF REMISSION

GOALS OF THERAPY

When evaluating and treating a patient with IBD, the major management goals are (1) to determine the disease extent and severity (**Table 1**), (2) to induce clinical remission, and (3) to maintain clinical remission. It is important to determine which areas of the gastrointestinal tract are involved and how severely each area is affected. This information has implications for the choice of therapy because different medications target specific areas of the gastrointestinal tract, and certain surgical procedures are appropriate for certain locations of disease activity. Medications vary in their effectiveness in treating ulcerative colitis and Crohn's disease, and thus a clear diagnosis is paramount.

It is important to recognize that treatments used to establish a remission may or may not be effective in the long term in *keeping* patients well. For example, mesalamine preparations, often used to induce a remission in ulcerative colitis, also are effective in maintaining remission. Corticosteroids, on the other hand, work well in inducing remissions in ulcerative colitis and Crohn's disease but are neither effective nor acceptable in maintaining remissions because of their long-term side effect profile. Several options are available for treating a patient with IBD. The choice is based on patient factors (eg, diagnosis, disease location, severity, special circumstances) as well as medication factors (eg, pharmacokinetics, pharmacodynamics, safety, cost, tolerability).

AMINOSALICYLATES

The 5-aminosalicylates (5-ASAs) have been the mainstay of treatment for mild-to-moderate ulcerative colitis for more than 50 years and are successful in both the