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Preface ix

Miguel Regueiro and Arthur M. Barrie III

**Evolving Inflammatory Bowel Disease Treatment Paradigms:
Top-Down Versus Step-Up** 577

Shane M. Devlin and Remo Panaccione

Crohn disease (CD) and ulcerative colitis (UC) comprise a group of inflammatory disorders of the gastrointestinal tract that can vary in severity of disease, anatomic extent of inflammation, presence and nature of extraintestinal manifestations, and response to therapeutic approaches. There have been attempts to classify CD based on the location and behavior of disease. Advances in understanding of genetic susceptibility to inflammatory bowel disease (IBD) suggest that CD and UC may represent a continuum of overlapping disorders. This has led to an attempt to classify IBD on clinical, molecular, and serologic grounds. Differences in clinical, genetic, and immunologic profiles may require more targeted, refined treatment approaches to help clinicians make decisions regarding recently introduced biologic agents. This article provides an overview of the current approaches to therapy for CD and UC and focuses on the evidence supporting the rationale for changing paradigms in the management of IBD, including mucosal healing as an end point and earlier use of immunosuppressive and biologic agents, particularly in CD (so-called top-down therapy).

Treatment of Fistulizing Inflammatory Bowel Disease 595

David A. Schwartz and Brad E. Maltz

Fistulas manifest frequently in Crohn disease and can result in significant morbidity and often lead to the need for surgical intervention. Historically, it has been more difficult to obtain complete fistula closure in patients with perianal Crohn disease. Anti-tumor necrosis factor- α agents and the use of more accurate imaging modalities such as magnetic resonance imaging and rectal endoscopic ultrasound have enhanced the ability to manage fistulizing Crohn disease. A combined medical and surgical approach usually presents the best option for most patients.

Pediatric Inflammatory Bowel Disease: Highlighting Pediatric Differences in IBD 611

Cary G. Sauer and Subra Kugathasan

Inflammatory bowel disease (IBD) includes Crohn disease and ulcerative colitis, and is often diagnosed in late childhood and early adulthood. What determines the age of onset remains unexplained. Early onset may represent the “pure” form of the disease process and hence may hold secrets of the initiating events of IBD pathogenesis. Clinical scientists continue to focus on pediatric IBD because it may shed light on the cause and prevention of this lifelong disease. Over the last decade, data in

pediatric IBD studies have demonstrated many similarities and differences between pediatric and adult onset, which continue to add pieces to an increasingly complex IBD puzzle. The mechanism responsible for these similarities and differences remains unanswered. This article discusses clinically relevant epidemiology and treatment aspects of pediatric IBD, with special focus on similarities and differences in pediatric and adult IBD. Evidence-based treatment algorithms, with special focus on pediatric studies and care for children, are also highlighted.

Pregnancy and Inflammatory Bowel Disease

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Uma Mahadevan

This review covers important questions that arise for physicians caring for women with inflammatory bowel disease. Fertility, pregnancy outcomes and the safety of medications in pregnancy and lactation are discussed.

Pouchitis and Pouch Dysfunction

651

Hao Wu and Bo Shen

Restorative proctocolectomy with ileal pouch-anal anastomosis has become the surgical treatment of choice for most patients with ulcerative colitis who require surgery. Although the surgical procedure offers a cure in some patients, postoperative inflammatory and noninflammatory complications are common. Pouchitis is the most common long-term complication of the procedure. Pouchitis represents a spectrum of disease processes with heterogeneous risk factors, clinical phenotypes, natural history, and prognosis. Accurate diagnosis and classification are important for proper treatment and prognosis.

Safety Profile of IBD: Lymphoma Risks

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Meenakshi Bewtra and James D. Lewis

This article describes the cancer risks of commonly used inflammatory bowel disease (IBD) medications, with an emphasis on hematologic malignancy risks. The increasing use of immunosuppressant therapies in the treatment of IBD has raised this question to an even greater importance. Studies evaluating these medications are complicated due to varying disease severity and concomitant use of other immunosuppressant medication. The potential risks of all therapies must be weighed against the benefits these therapies can offer these patients.

Safety Profile of IBD Therapeutics: Infectious Risks

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Waqas Afif and Edward V. Loftus Jr

Over the last decade, the medical treatment of inflammatory bowel disease (IBD) has been revolutionized, with increasing use of both immunomodulatory and biologic medications. Corticosteroids have increasingly been associated with an elevated risk of serious and opportunistic infections, both independently and in combination with immunomodulator and biologic agents. There are limited data on the infectious risk of immunomodulators. It is unclear if anti-tumor necrosis factor agents increase

overall infectious risk in patients with IBD, but the available literature has demonstrated an increased risk of opportunistic infections, particularly in terms of tuberculosis and histoplasmosis. Combination therapy likely increases the risk of opportunistic infections in patients with IBD but this has not yet been conclusively proved.

***Clostridium Difficile* and Inflammatory Bowel Disease**

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Ashwin N. Ananthkrishnan, Mazen Issa, and David G. Binion

The past decade has seen an alarming increase in the burden of disease associated with *Clostridium difficile*. Several studies have now demonstrated an increasing incidence of *C difficile* infection in patients with inflammatory bowel disease (IBD) with a more severe course of disease compared with the non-IBD population. This article summarizes the available literature on the impact of *C difficile* infection on IBD and discusses the various diagnostic testing and treatment options available. Also reviewed are clinical situations specific to patients with IBD that are important for the treating physician to recognize.

Novel Diagnostic and Prognostic Modalities in Inflammatory Bowel Disease

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Timothy L. Zisman and David T. Rubin

Inflammatory bowel disease remains a complex disease with variable clinical presentations and often nonspecific symptoms. Physicians must rely on diagnostic tools for clarification of disease diagnosis and for guiding management of patients with established disease. Advances in radiologic imaging modalities facilitate early and accurate detection of luminal disease and extraluminal complications. The introduction and dissemination of small bowel capsule endoscopy and double-balloon enteroscopy permit detailed visualization and sampling of the mucosa throughout the entire bowel. Serologic biomarkers are evolving as a valuable tool to clarify diagnosis and stratify patients by disease phenotypes and patterns of behavior. Neutrophil-derived fecal biomarkers are emerging as useful surrogate markers of intestinal inflammation with the potential for a variety of clinical applications, but their application to clinical management has not yet been clarified.

Postoperative Management of Crohn Disease

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Su Min Cho, Sung W. Cho, and Miguel Regueiro

Crohn disease often recurs after surgical resection. Despite extensive research in the prevention of postoperative Crohn disease, optimal management strategies have yet to be defined. Risk of disease recurrence needs to be carefully balanced against potential risks associated with treatment. Patients with low risk of postoperative recurrence may not require medication, whereas those at moderate risk may benefit from antibiotics or immunomodulators. Those at highest risk of recurrence may benefit from biologic therapy for maintenance of surgical remission. Postoperative colonoscopy within 1 year of resective surgery is important for identification of disease recurrence and modification of medications.