

New Developments in the Treatment of Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a common chronic functional bowel disorder. Not only does it have a significant impact on a patient's quality of life, but this sometimes debilitating condition has a significant impact on society as well. IBS is second only to the common cold as a cause of absenteeism from work and school and it costs the US healthcare system at least \$8 billion annually.¹ Unfortunately, existing pharmacotherapeutic options are limited in treating the multiple symptoms associated with the disorder.

Compelling findings relevant to new approaches in the management of IBS were explored in a symposium sponsored by the Johns Hopkins University School of Medicine, held May 23, 2000, in San Diego, California. Titled "Irritable Bowel Syndrome: Examining New Findings and Treatments," the symposium presented the most recent data on the pathophysiology and treatment of IBS. The goals of the meeting were 3-fold: to familiarize the attendees with the distinctive diagnostic markers for the identification and classification of patients with IBS; to examine the role of serotonin in the pathophysiology of IBS; and to examine emerging treatment options for patients with IBS.

This supplement to *The American Journal of Managed Care* features the proceedings of this symposium. The symposium was moderated by Marvin M. Schuster, MD, Professor of Medicine and Psychiatry at the Johns Hopkins

University School of Medicine and Director of the Division of Digestive Diseases of the Marvin M. Schuster Center for Digestive and Motility Disorders at the Johns Hopkins Bayview Medical Center in Baltimore.

Dr. Schuster's article provides data regarding the epidemiology of IBS. It is interesting to note although patients experience significant limitations in various aspects of their personal lives, the physician perspective of the disease is often dismissive of its severity. Dr. Schuster discusses the definitive criteria for IBS, which include 2 out of 3 features of altered bowel habits, and provides a brief review of the pathophysiology of the disorder. Recommended laboratory investigations are identified, as well as criteria that do not support a diagnosis of IBS.

In the second article, the role of serotonin (5-hydroxytryptamine, or 5-HT) in the pathophysiology of IBS is described by Michael D. Crowell, PhD, Associate Professor of Medicine at the Johns Hopkins University School of Medicine. Dr. Crowell also serves as Director of GI Physiology and Motility and Associate Director of the Marvin M. Schuster Center for Digestive and Motility Disorders. Dr. Crowell describes the coordinated actions of the central, autonomic, and enteric nervous systems and how they modulate intestinal motor, sensory, and secretory activities. These integrated actions help explain the triad of dysfunction seen in IBS, namely

altered motility, altered sensation, and psychosocial factors. Of the various modulators involved in the brain-gut interaction, serotonin has received the most attention. It has been theorized that the activation of pain pathways and gastrointestinal motor activity may be facilitated or inhibited in IBS by serotonin or its associated receptors, thus suggesting the utility of these agents in this disorder.

In the third article, Nicholas J. Talley, MD, PhD, Professor of Medicine at the University of Sydney in Australia and head of the Division of Medicine at the Nepean Hospital in Penrith, Australia, describes current and investigational treatments for IBS. Of particular interest are the efficacy data for the serotonin agents: the 5-HT₄ receptor partial agonist tegaserod and the 5-HT₃ antagonist alosetron (which was removed from the market in November 2000 and is being

considered for reintroduction to the market). Other investigational agents that act via another mechanism, such as prucalopride and 5-HT₁ agonists, may also be useful therapies for IBS.

The last article, by Robert Martin et al, examines the economic implications of current IBS management practices and formulates recommendations based on these implications. Because IBS is a condition with high direct and indirect costs, the authors believe that management strategies should be evaluated both on their clinical efficacy and on their cost effectiveness.

... REFERENCE ...

1. Longstreth GF. Irritable bowel syndrome: A multibillion-dollar problem. *Gastroenterology* 1995;109:2029-2031.

Update: Status of Tegaserod*

In February 2000, Novartis submitted a New Drug Application for its irritable bowel syndrome drug, tegaserod. On June 15, 2001, the Food and Drug Administration (FDA) issued a "not approvable" letter to Novartis as a result of tegaserod trial data showing incidences of gall bladder surgery in patients receiving the drug. At the time this supplement went to press, Novartis had indicated they would file an appeal with the FDA by the end of July 2001. Novartis maintains there is no statistical difference with regard to the incidence of abdominal surgery between the placebo and treatment groups in their clinical trial.

**The Pink Sheet*. Chevy Chase, MD: F-D-C Reports, Inc; June 25, 2001.