Bacteria: A Missing Link in Irritable Bowel Syndrome?

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The 2005 Nobel Prize in Physiology or Medicine was awarded to Barry J. Marshall and J. Robin Warren for their contribution to elucidating a primary role of bacteria in peptic ulcer disease. *Helicobacter pylorus* is now considered an established cause of more than 90% of duodenal ulcers and up to 80% of gastric ulcers. A role of bacteria in other diseases previously not commonly associated with microbes, including cancer and cardiovascular disease, has also been demonstrated. Recently, bacteria have been proposed to be important in the pathophysiology of irritable bowel syndrome (IBS). In fact, the putative microbial contribution to IBS provides a theory for understanding many aspects of IBS that until now were confounded by multiple, and often competing, hypothesized mechanisms.

Irritable bowel syndrome is a chronic gastrointestinal condition that can have substantial impact on patients’ quality of life. Symptoms of IBS, such as bloating, abdominal pain, and flatulence, are usually associated with a primary disruption in bowel habits (i.e., constipation or diarrhea). Given the wide range of symptoms associated with IBS, it is not surprising that the underlying pathophysiologic mechanisms may involve complex interactions among various biologic systems. Also not surprising is the variety of treatment options prescribed for this condition, which range from symptom-directed fiber therapies to agents that alter the effects of neurotransmitters. However, for many patients, therapeutic management of IBS symptoms can be challenging due to lack of efficacy or adverse effects.

Increasing evidence suggests that intestinal bacteria may be involved in the pathophysiologic mechanisms underlying IBS, thus providing a rationale for exploring the potential efficacy of antibiotic therapies for the treatment of IBS. In September 2005, a group of gastroenterologists from the United States convened in Irving, Texas, to develop a shared understanding of data suggesting the involvement of intestinal bacteria in the pathophysiology of IBS and to consider the implications of these findings for the management of the condition. During that meeting, discussion focused on IBS as a sequela of acute bacterial gastroenteritis (postinfectious IBS), the presence of small intestinal bacterial overgrowth (SIBO) in IBS, and potential applications of antibiotics for prevention and treatment of IBS. This supplement is based on the proceedings of that meeting.

The first article, “The Clinical and Economic Burden of Irritable Bowel Syndrome,” describes the complex, heterogeneous clinical and physiologic manifestations of IBS; the negative impact of IBS on health-related quality of life, healthcare utilization,
and workplace productivity; and the direct and indirect costs of the illness. The negative impact of IBS translates into substantial economic costs in the United States. The review emphasizes the need for multidimensional patient management strategies to reduce the economic burden of IBS on the patient, employer, and healthcare system.

A second article, “Current Diagnostic Strategies and Pharmacologic Treatment Options for Irritable Bowel Syndrome,” details approaches to diagnosing IBS and evaluates current treatment options, asserting that the complexity of IBS pathophysiology makes the accurate diagnosis and optimal management of this disorder challenging. The review discusses the strengths and weaknesses of the symptom-based criteria for IBS diagnosis and contends that application of the new Rome III criteria may help provide physicians with a more valid diagnostic tool and increase the likelihood that individuals who may have IBS will be diagnosed in clinical practice. The article also details current treatment options for IBS, including the potential benefits of antibiotic therapy in improving global symptoms of IBS. The author concludes that additional high-quality studies are necessary to establish the role of emerging therapies for treatment of IBS.

Dr Herbert L. DuPont discusses bacterial involvement in the development of postinfectious illness in the article, “Postinfectious Irritable Bowel Syndrome: Clinical Aspects, Pathophysiology, and Treatment.” Dr DuPont asserts that IBS may result from an acute episode of bacterial gastroenteritis in some patients. In clinical studies, up to 32% of individuals evaluated for 1 year following an acute episode of bacterial gastroenteritis developed postinfectious IBS (PI-IBS). Dr DuPont reviews clinical findings supporting that acute bacterial infection can cause chronic mucosal inflammation and alterations in the host response that may underlie persistent bowel symptoms in patients with PI-IBS. Dr DuPont contends that effective management of acute bacterial gastroenteritis with prophylaxis or treatment may be an important strategy for reducing the risk of PI-IBS. He suggests several potential applications for antibiotic therapy, including the following: 1) antibiotic prophylaxis for acute bacterial gastroenteritis to prevent development of PI-IBS by removing a precipitating cause; 2) antibiotic treatment of acute bacterial gastroenteritis to prevent the development of PI-IBS by reducing the length and severity of acute bacterial illness and associated inflammation and immune activation; and 3) antibiotic treatment of SIBO or IBS postinfection to eradicate bacteria that cause or exacerbate functional bowel symptoms.

As discussed by Dr DuPont in the review on PI-IBS and by Dr Mark Pimentel in the review, “Bacteria and the Role of Antibiotics in Irritable Bowel Syndrome,” the nonabsorbed antibiotic rifaximin has potential utility in each of the aforementioned conditions. In discussing the potential role of antibiotics in the treatment of SIBO and IBS, Dr Pimentel details the putative contribution of SIBO to the pathophysiology of IBS. He also reviews data demonstrating that antibiotics, including the nonabsorbed antibiotic rifaximin, effectively relieve symptoms and eradicate bacteria in patients with SIBO (with or without a diagnosis of IBS), reduce bloating and gas in patients with functional gastrointestinal disorders, and improve symptoms of IBS diagnosed according to Rome criteria. Dr Pimentel asserts that, considering its broad-spectrum activity against enteric bacteria, robust efficacy in eradicating SIBO, favorable tolerability profile, and lack of clinically relevant antibiotic resistance with 20 years of prescribing in Europe, rifaximin may be an appropriate treatment option for some patients with IBS.

Dr Pimentel and Dr DuPont’s discussion of clinical data is complemented in the final review, “Antibiotics for the Treatment of Functional Gastrointestinal Symptoms: A Case Series,” describing several cases in which various antibiotics were administered to treat functional gastrointestinal symptoms in “real-world” clinical practice. Conclusions about the efficacy of antibiotics for functional gastrointestinal symptoms cannot be drawn on the basis of these reports alone; however, the cases illustrate potential applications of antibiotics for functional gastrointestinal disorders and suggest areas for further investigation.

The contributions of bacteria to IBS pathophysiology and of antibiotics to disease management have only begun to be fully appreciated. As with peptic ulcer disease, understanding the potential pathogenic role of bacteria in IBS will help improve treatment strategies and reduce the humanistic and economic burden of this illness.