

# Preface

Gastroparesis has become a well-recognized gastrointestinal disorder. Patients with gastroparesis can be particularly challenging; the disorder has limited treatments that are effective in reducing symptoms and/or are FDA approved for use in this condition. There also appears to be an increasing number of patients being diagnosed with this condition, either due to increased recognition of this disorder, or possibly due to an increased prevalence of the disorder. One contribution to this observation is due to the increase of diabetes in the general population. There are often many areas of treatment to address with these patients. Many types of health care providers may need to care for these patients, including gastroenterologists, nutritionists, endocrinologists, internists, pain management specialists, psychiatrists, and surgeons. Fortunately, gastroparesis is being increasingly studied over the last decade from a variety of areas with a marked increase in information on gastric motility and gastroparesis. This is an ideal time to develop a book on the many aspects of gastroparesis.

This book reviews the epidemiology, pathophysiology, symptomatic presentation, diagnosis, and treatments for gastroparesis. This book discusses what is currently known about this disorder, pointing out areas of controversy, discussing unmet needs, and areas for future research to help improve our understanding of gastroparesis.

Despite the high prevalence of gastroparesis, the etiology and pathophysiology of this heterogeneous disorder remain incompletely understood. Why does this disorder occur more often in women – not only for idiopathic gastroparesis, but also for diabetic and postsurgical gastroparesis? Symptoms can be varied in this condition – some present with abdominal fullness, some with nausea, and others with abdominal discomfort or pain. Why do some patients have abdominal discomfort, or even pain? How should abdominal pain be treated in these patients in whom one wants to avoid medications that can affect gastric emptying or cause new symptoms as side effects. Our knowledge and understanding of what is known, as well as the challenges in treatment, are thoroughly brought to light by the authors who address these aspects of gastroparesis in this book.

Diagnosis of gastroparesis entails demonstrating delayed gastric emptying. Symptoms of gastroparesis can be mildly correlated with gastric retention. Three tests are clinically available for demonstrating delayed gastric emptying: gastric emptying scintigraphy, wireless motility capsule, and gastric emptying breath testing. Gastric emptying scintigraphy has become standardized into a 4 h imaging test. However, many centers are reluctant to perform a 4 h scintigraphy study due to the investment in manpower and use of dedicated imaging facilities. How a shorter test impacts on diagnosis and treatment of patients is not clear. Gastric emptying occurs with proximal gastric accommodation followed by antral contractility and pyloric relaxation. Does assessment of regional gastric motility improve the evaluation and management of the patients? Wireless motility capsule measures gastric emptying of an indigestible capsule. The test provides information also on gastric contractility and information on whole gut transit. In some patients with gastroparesis, there are abnormalities in whole gut transit, suggesting a more diffuse process. Finally, gastric emptying breath testing has been used in many clinical research studies, and is undergoing the FDA approval process for use as an office-based clinical test. All these diagnostic options, the pros and cons, are extensively and objectively presented and discussed in this book by expert contributors.

Treatment of gastroparesis is generally with dietary modification, prokinetic agents to gastric emptying, and antiemetic agents to reduce nausea and vomiting. Unfortunately, at the present time, there is a paucity of agents to treat gastroparesis. Metoclopramide has been used for several decades. Side effects, primarily involving the central nervous system, can occur in patients, necessitating to stop this treatment. Recently, the FDA issued a warning about the long-term side effects of metoclopramide, particularly tardive dyskinesia. The antibiotic erythromycin, which is also a motilin receptor agonist, has been shown to increase gastric emptying. However, the prokinetic effects of erythromycin reduce over time due to receptor tolerance. The serotonin 5-HT<sub>4</sub> receptor agonists, cisapride and tegaserod, were used off label to treat gastroparesis until they were pulled from the market. It is apparent that new prokinetic agents are needed to treat gastroparesis. However, it has been difficult to establish symptomatic benefit with prokinetic drugs in gastroparesis, possibly because of the pathophysiological heterogeneity of the patients, the inconsistent relationships between changes in motor function measured by variable and often nonstandardized methods and symptomatic outcome, and a lack of well-accepted symptom endpoints for clinical trials. Many experienced clinicians are using domperidone for gastroparesis, an agent approved in many countries but not the USA, through the FDA IND process. Therapeutic options, as well as surgical solutions, are extensively reviewed by experts who are practicing gastroenterologists facing the challenges of managing gastroparesis every day in their practices as well as performing cutting edge clinical research.

There have been several organizations behind advancing the field of gastroparesis, for which the authors appreciate their role in increasing our understanding of gastroparesis: the American Neurogastroenterology and Motility Society (ANMS) and the NIH Gastroparesis Clinical Research Consortium.

The ANMS has been particularly active in the field of gastroparesis since it is a relatively common disorder of gastrointestinal motility. The ANMS has had a series

of conferences and consensus manuscripts on gastroparesis. A clinical review was published in 2006 on the treatment of patients with gastroparesis. This was a multidisciplinary effort led by the ANMS with input from gastroenterologists and other specialists who are involved in the care of patients with gastroparesis. A consensus document was developed by members of the ANMS and the Society of Nuclear Medicine recommending a standardized method for measuring gastric emptying by scintigraphy using a low-fat, egg white meal with imaging at 0, 1, 2, 4 h after meal ingestion, which provides standardized information about normal, rapid, and delayed gastric emptying. Adoption of this standardized protocol will help resolve the lack of uniformity of testing, add reliability and credibility to the results, and improve the clinical utility of the gastric emptying test. The proceedings from a 2009 conference sponsored by the American Gastroenterological Association and the ANMS reviewed the advances in the understanding of the epidemiology, pathophysiology, diagnosis, and treatment of gastroparesis and functional dyspepsia. The ANMS also developed a task force for gastroparesis endpoints for clinical trials. In this initiative, the ANMS helped convert a symptom questionnaire for gastroparesis into a daily diary version, which appears to be a useful outcome endpoint for gastroparesis clinical trials. This validation has become necessary as a prelude for new drug applications to the Food and Drug Administration.

The NIH Gastroparesis Clinical Research Consortium (GpCRC) is a cooperative network of seven clinical centers and a Data Coordinating Center funded through the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health. The mission of the GpCRC is to improve the understanding of gastroparesis by conducting multicenter, observational studies on well-characterized patients with gastroparesis. The studies emanating from the consortium involve a large number of patients, which will better define the disorders. Studies have been developed for idiopathic gastroparesis, diabetic gastroparesis, and the comparison between the two types of gastroparesis. Pathologic studies have recently been published showing reductions in the interstitial cells of Cajal and an inflammatory infiltrate in the myenteric plexus. A wealth of information is being evaluated on the clinical course of patients with gastroparesis.

This book, the first to focus on the many aspects of gastroparesis that has been published over the recent years, provides a comprehensive review and in depth critical distilling of our knowledge, covering important areas for physicians, nutritionists, nurses, and paramedical staff as well as clinical investigators and basic scientists interested in this disorder. Each chapter has been written by an expert in the area, specifically selected because they are recognized as national and international leaders. This exhaustive text will place the reader at the cutting edge of the field and prepare them for future advances while permitting this knowledge to be directly applied to their patients suffering with gastroparesis.

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