

SITARAMAN AND FRIEDMAN'S

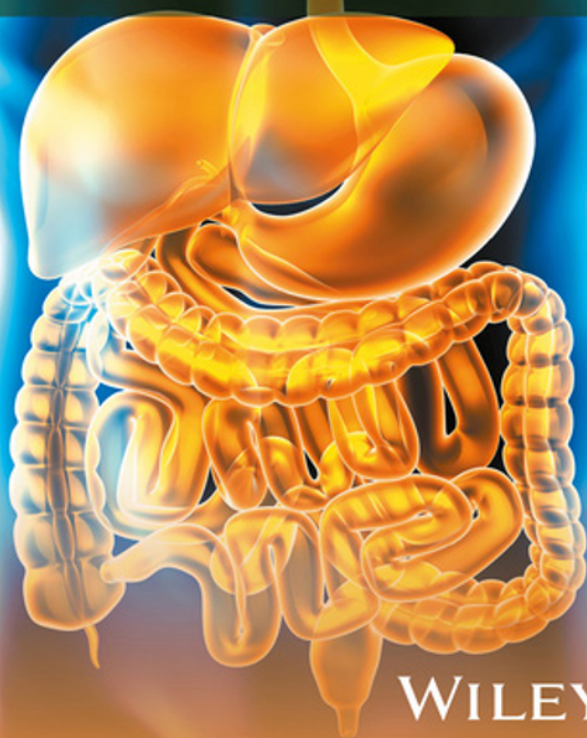
Essentials of Gastroenterology

Second Edition

Edited by

Shanthi Srinivasan

& Lawrence S. Friedman



WILEY Blackwell

**Sitaraman and Friedman's
Essentials of Gastroenterology**

Sitaraman and Friedman's Essentials of Gastroenterology

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Second Edition

WILEY Blackwell

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In Memory of Shanthi V. Sitaraman, MD, PhD

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Foreword

The practice of gastroenterology and hepatology continues to evolve at a seemingly revolutionary pace. Since the First Edition of *Essentials of Gastroenterology* was published in 2012, we have witnessed the advent of powerful new biologic agents for the treatment of inflammatory bowel disease. And who could have imagined then that we could cure over 90% of patients with chronic hepatitis C virus infection with direct-acting antiviral therapies? Despite these (and other) important advances, the clinical foundation of the field of gastroenterology that has been the basis of such important treatment strategies remains the same. Understanding the pathophysiology and clinical features of gastrointestinal and liver diseases is a critical aspect of every medical student's education in human diseases.

The First Edition of this textbook was developed and co-edited by the late Shanthi V. Sitaraman, MD, PhD, Professor of Medicine and Pathology at Emory University School of Medicine who, sadly, did not live to see her work published. Shanthi was an exceptional teacher, physician and scientist who died far too young in April 2011. Lawrence S. Friedman, MD, Professor of Medicine at Harvard Medical School and Tufts University School of Medicine, co-edited the first edition with Shanthi and suggested to me that we update the text as a Second Edition, and I am truly grateful that Shanthi Srinivasan, MD, Professor of Medicine and Chief of Gastroenterology at the Atlanta Veterans' Affairs Medical Center and a colleague and close friend of Shanthi Sitaraman, agreed to serve as co-editor with Dr Friedman of this Second Edition.

As in the First Edition of *Essentials of Gastroenterology*, each chapter of the Second Edition begins with a clinical vignette after which the fundamental aspects of pathophysiology, clinical features, and approach to treatment are presented. This technique in education is used in many medical schools, including Emory University School of Medicine, in which first-year medical students are immersed in patient-related case histories when studying each organ system. The chapters are written concisely to give the trainee the ability to take away key points ('Pearls') that are critical to the development of skills in differential diagnosis, assessment, and treatment planning. Furthermore,

easy-to-understand diagrams and tables, as well as exceptionally clear illustrations, endoscopic photographs, and radiologic images, make this book particularly useful not only as a guidebook for medical students, but also as a quick reference for medical house officers who are confronted with patients with gastrointestinal and liver disease.

The success of the First Edition of this textbook and its design is not fortuitous. Dr Friedman, one of the foremost master clinicians of gastroenterology and hepatology in Boston – and a former mentor of the late Dr Sitaraman – has once again, along with Dr Srinivasan, devoted a great amount of time to carefully editing each chapter. The result is a brilliantly crafted, concise, and enjoyable book to read. The questions and answers presented at the end of each chapter are timely and integrative in design, giving trainees the ability to sharpen the depth of their conceptual knowledge about the approach to the natural history of diseases seen in the practice of gastroenterology. Impressively, Drs Srinivasan, Friedman, and the contributing authors of the updated text provide new information on treatment approaches for the major diseases covered in this book.

Finally, the editors and authors owe a tremendous debt of gratitude to Carla Fairclough and Alison Sholock, who incorporated the numerous editorial changes made by Drs Srinivasan and Friedman. They meticulously transformed handwritten edits sent to them on the original and revised manuscripts into polished final versions. Their organization has made the work of the editors immensely easier. I am also deeply grateful to our faculty (including some former faculty) in the Division of Digestive Diseases at Emory University School of Medicine who wrote and revised all of the chapters in this text. Many of them are teachers in the first-year medical student curriculum ‘Foundations of Medicine’ course, which was initially organized by Dr Sitaraman. To paraphrase a sentiment expressed by Dr Daniel K. Podolsky in the Foreword to the First Edition of *Essentials of Gastroenterology*, “...though we have been deprived of Shanthi Sitaraman’s distinguished career as a teacher, mentor, physician, and investigator,” the Second Edition of this textbook “...once again serves as an important hallmark of Shanthi’s enduring legacy” to our discipline.

Frank A. Anania, MD, FACP, AGAF, FAASLD
Emory University School of Medicine

Preface

This Second Edition of *Essentials of Gastroenterology* is the first for which Shanthi V. Sitaraman has not served as a co-editor, because of her untimely death as the First Edition was published in 2012. A tribute to Shanthi Sitaraman follows this Preface and the Acknowledgments. Succeeding Shanthi Sitaraman as co-editor is her colleague and friend, Shanthi Srinivasan, an accomplished editor, gastroenterologist, and professor at the Emory University School of Medicine with an interest in basic enteric neuroscience and gastrointestinal motility. The title of the book has been revised to include Shanthi Sitaraman's name to reflect her enduring contribution.

The field of gastroenterology and hepatology has progressed at a rapid pace, and *Sitaraman and Friedman's Essentials of Gastroenterology, Second Edition*, reflects this progress with an updated content five years after the First Edition of the book was published. In editing this book, we have kept the format similar to that of the First Edition, which was well received, but have updated the content. Throughout the book, we have continued to emphasize fundamental clinical points in a clear, organized, and concise manner. Our goal remains for the book to provide up-to-date, foundational knowledge of gastrointestinal medicine and of the most important and common clinical problems encountered in the field. Among the areas in which remarkable changes have occurred since publication of the First Edition are new treatment regimens for hepatitis C, improved management of portal hypertension, and expanded drug therapy for inflammatory bowel disease. Primary biliary cirrhosis is now called primary biliary cholangitis. In the chapter on peptic ulcer disease, treatment protocols for *Helicobacter pylori* and the indications for confirming the eradication of *H. pylori* have been updated. Other major changes include updated methodology for the diagnosis of motility disorders, including the wireless motility capsule and three-dimensional high-resolution manometry, a new section on eosinophilic esophagitis, and updated criteria for the diagnosis of irritable bowel syndrome.

The book represents contributions from faculty and fellows in the Division of Digestive Diseases and the Departments of Pathology, Radiology, and Surgery

at the Emory University School of Medicine, and is geared toward medical students studying gastroenterology in an introductory course on clinical medicine or on a clinical rotation in medicine or gastroenterology. Many of the contributors have been recipients of awards for outstanding contributions to medical education. New authors include faculty who have recently come to Emory. Each has helped to revitalize and refresh the book.

The format of the Second Edition remains unchanged. The book has 28 chapters that are organized into five sections. Each chapter covers a key clinical issue in the practice of gastroenterology, and the Picture Gallery provides the proverbial ‘textbook’ examples of dermatology, radiology, and pathology findings in gastroenterology. The chapters are written in an easy-to-read outline format that covers the basics of pathophysiology, clinical features, diagnosis, natural history, prognosis, and treatment of the common disorders seen in the practice of gastroenterology. Figures and tables illustrate and highlight key information. Shaded boxes draw attention to important practice points, and a concluding segment in each chapter in the first four sections provides a list of ‘pearls’ useful in clinical practice. Illustrative cases begin each chapter in the first four sections, and multiple-choice questions pertaining to these clinical vignettes and to the content of the chapter provide an opportunity for the reader to test his or her knowledge of the subject matter after reading a chapter. A few key references and web links are provided. The aim is to make the information as clear, concise, and ‘digestible’ as possible. Medical students will find the information relevant and readily understandable, while more senior trainees can use the book to obtain a quick and practical review of the field in a short amount of time. Readers should find the book useful and focused, without being overwhelming.

We are excited to present this Second Edition and hope that it will continue to be an enduring tribute to Shanthi Sitaraman’s dream of fostering excellence in medical education.

*Shanthi Srinivasan, MD
and Lawrence S. Friedman, MD*

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*Shanthi Srinivasan, MD
and Lawrence S. Friedman, MD*

Tribute to Shanthi V. Sitaraman

Essentials of Gastroenterology, First Edition, was conceived, developed, and co-edited by Shanthi V. Sitaraman, MD, PhD, who tragically passed away after a long illness as the book was nearing completion. The book reflects Shanthi's dream and vision to create a textbook of gastroenterology targeted specifically to medical students but useful as well to residents rotating on a gastroenterology service and fellows and practitioners preparing for certification examinations and desiring a quick, focused review of the state-of-the-art of the field.

The opportunity to work with Shanthi Sitaraman on the First Edition of this book was a once-in-a-lifetime experience that we will always treasure. We have both had the privilege and honor of working with Shanthi. To Shanthi Srinivasan, Shanthi was a best friend, mentor, colleague, and confidante. To Lawrence Friedman, Shanthi was a star trainee, superb clinician, and accomplished researcher. As we edited each chapter, we remember the discussions we had with Shanthi about the book and the passion she infused in us to make it as perfect as possible. She loved students, and the book was her long-lasting gift to them and an enduring legacy to the field of gastroenterology. Her love of gastroenterology and passion for teaching were evident throughout the entire project, and shine in this book.

Shanthi was a brilliant and dedicated physician-scientist who, as a faculty member at Emory, made numerous contributions to education, research, and clinical practice. Her work in inflammatory bowel diseases resulted in over 200 publications that advanced our understanding of basic mechanisms of inflammation and led to novel approaches to therapy. Her devotion to patients was legendary, and in 2011 she received the Crohn's and Colitis Foundation of America Premier Physician Award in Georgia. She mentored and taught countless medical students, residents, fellows, and junior faculty, and her humanitarian service to the greater Atlanta community was inspiring.

Essentials of Gastroenterology is both a fitting tribute to, and a wonderful legacy of, an exceptional educator, colleague, and friend. Shanthi herself was an award-winning teacher who was beloved by the students, residents, fellows, and faculty at Emory. She was a recipient of the Silver Pear Mentoring Award

from the Department of Medicine, the Student Association Teaching Award and Dean's Teaching Award from the School of Medicine, and the Attending of the Year designation and the Mentor Award from the Division of Digestive Diseases at Emory, among numerous other honors. She is sorely missed, and we are proud to dedicate the Second Edition of the retitled *Sitaraman and Friedman's Essentials of Gastroenterology* to her.

*Shanthi Srinivasan, MD
and Lawrence S. Friedman, MD*

Luminal Gastrointestinal Tract

Shreya Raja and Melanie S. Harrison

1

Gastroesophageal Reflux Disease

Shani Woolard and Jennifer Christie

Clinical Vignette

A 50-year-old man with a history of hypertension and hyperlipidemia presents with a 4-month history of chest discomfort. He describes the discomfort as a burning and occasionally a pressure sensation in the mid-sternal area. The discomfort often occurs 45 minutes after eating a meal and lasts for about 3 hours, gradually improving thereafter. He occasionally awakens in the morning with a sore throat, cough, and bitter taste in his mouth. He has tried over-the-counter ranitidine, with only minimal relief. He was recently seen in the emergency department for an episode of severe chest pain. A cardiac work-up, including an electrocardiogram, cardiac enzymes, and a stress echocardiogram, was negative. Physical examination reveals a well-built, well-nourished man in no apparent distress. The blood pressure is 137/84 mmHg, pulse rate 72 per minute, respiratory rate 14 per minute, and body mass index 30. The physical examination is otherwise unremarkable.

General

- Gastroesophageal reflux disease (GERD) is defined as symptoms or tissue damage caused by the reflux of gastric contents into the esophagus.
- GERD is a common disorder, affecting almost half of the US population, with varying severity. Some 40% of the US population experiences reflux symptoms about once per month, 20% complain of symptoms once per week, and 7–10% report daily symptoms.
- GERD affects 10–20% of western populations. It is less common in Asian and African countries.
- It is estimated that GERD costs the US nearly \$2 billion each week in lost productivity.

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The most common symptoms of GERD are heartburn and regurgitation. GERD is the most common cause of noncardiac chest pain.

Risk Factors

- Advancing age (>65 years)
- Obesity
- Genetic factors
- Alcohol use
- Pregnancy
- Smoking

Spectrum of GERD

- The clinical spectrum of GERD ranges from nonerosive reflux disease (NERD) to erosive esophagitis (Figure 1.1). NERD is defined as symptoms of acid reflux without evidence of esophageal damage, such as mucosal erosions or breaks on esophagogastroduodenoscopy (EGD) in patients who are not on acid-suppressive therapy.
- A small proportion of patients will develop metaplasia of the squamous esophageal epithelium to columnar epithelium (Barrett's esophagus). Barrett's esophagus is a risk factor for adenocarcinoma.
- Some patients who present with heartburn have 'functional' heartburn. This is defined as a burning retrosternal discomfort in the absence of

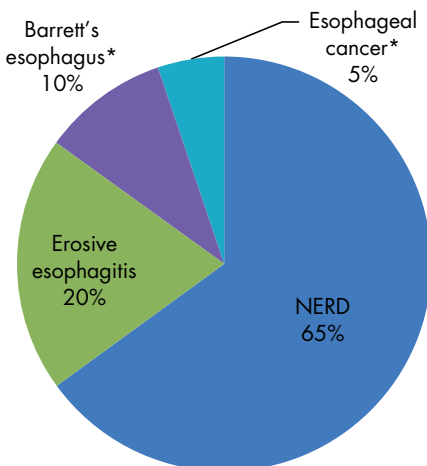


Figure 1.1 Clinical spectrum of GERD.
(*May be associated with erosive esophagitis; NERD, nonerosive esophageal reflux disease.)

gastroesophageal reflux or an esophageal motor disorder. Ambulatory pH testing may be useful to differentiate NERD from functional heartburn.

Pathophysiology

- Transient lower esophageal sphincter relaxations (TLESRs):
 - The etiology of GERD is multifactorial; however, ‘aberrant’ TLESRs are the major pathophysiologic factors in many patients with GERD.
 - A TLESR is defined as relaxation of the lower esophageal sphincter in response to gastric distension. In healthy persons, TLESRs occur in the absence of a swallow, last 10–30 seconds, and result in physiologic gastroesophageal reflux.
 - TLESRs are regulated by the neurotransmitter γ -aminobutyric acid (GABA) acting on GABA type B receptors located in the peripheral nervous system, as well as in the brainstem.
 - In many cases, GERD is thought to be caused by an increased number or a prolonged duration of TLESRs.
- Gastric factors:
 - Increased gastric acid production as well as delayed gastric emptying with distention may trigger TLESRs.
- Diminished esophageal clearance:
 - Poor esophageal clearance due to defects in primary or secondary esophageal peristalsis allows prolonged exposure of the esophageal mucosa to acid.
- Diet and medications:
 - Dietary factors such as acidic foods, caffeine, alcohol, peppermint, and chocolate may reduce lower esophageal sphincter (LES) tone or increase gastric acid production.
 - Medications such as calcium channel blockers, hormones (e.g., progesterone, cholecystokinins, secretin), beta-adrenergic agonists (albuterol), nitrates, and barbiturates can decrease LES tone, thereby predisposing to gastroesophageal reflux.
 - Smoking has also been associated with a predisposition to gastroesophageal reflux.
- Hiatal hernia:
 - A hiatal hernia usually occurs when there is a defect in the diaphragmatic hiatus that allows the proximal stomach to herniate above the diaphragm and into the thorax. It is unclear how this predisposes to gastroesophageal reflux. The barrier function of the LES to prevent the reflux of gastric contents into the esophagus is thought to be disrupted. Large hiatal hernias also lead to increased acid dwell times in the distal esophagus.

Clinical Features

- Thorough history-taking detailing the onset and duration of symptoms and the association of symptoms with meals and diet should be conducted. ‘Alarm symptoms’ such as vomiting, gastrointestinal bleeding, weight loss, dysphagia, early satiety, and symptoms of cardiac disease should be elicited.
- Patients may present with typical (classic) or atypical symptoms.
- Typical symptoms:
 - **Heartburn** is described as a burning sensation in the substernal area that may radiate to the neck and/or back.
 - **Regurgitation** is the feeling of stomach contents traveling retrograde from the stomach up to the chest and often into the mouth.
 - **Dysphagia** (difficulty swallowing) is reported in about 30% of patients with GERD, even in the absence of esophageal inflammation or a stricture.
 - Less common symptoms associated with GERD include water brash, burping, hiccups, nausea, and vomiting. Water brash is the sudden appearance of a sour or salty fluid in the mouth, and represents secretions from the salivary glands in response to acid reflux. Odynophagia (painful swallowing) occurs when there is severe esophagitis.
 - The sensitivity of typical symptoms for detecting GERD is poor.
- Atypical symptoms:
 - Patients may present with chest pain, chronic cough, difficult-to-treat asthma, and laryngeal symptoms such as hoarseness, throat clearing, or throat pain.
 - Patients with atypical symptoms are less likely than patients with typical symptoms to have endoscopic evidence of esophagitis or Barrett’s esophagus. They also have a less predictable response to therapy. Ambulatory esophageal pH testing (see later) is not as sensitive for diagnosing GERD in patients with atypical symptoms as it is in patients with typical symptoms.
- In uncomplicated GERD, physical findings are minimal or absent.

GERD as the etiology of chest pain should be pursued only after potentially life-threatening cardiac etiologies have been excluded.

Diagnosis

Trial of Proton Pump Inhibitor (PPI) Therapy

- A PPI trial is the simplest approach for diagnosing GERD and evaluating symptom response to treatment.