Edited by Frank P. Brooks

Gastrointestinal Pathophysiology

Second Edition

Gastrointestinal Pathophysiology

SECOND EDITION

edited by FRANK P. BROOKS, M.D. Sc.D. (Med)
Professor of Medicine and Physiology
School of Medicine, University of Pennsylvania

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To
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Founder of The Gastrointestinal Section,
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Preface to the Second Edition

We have been gratified by the reception accorded to the first edition of this book. The pace of advances in the study of gastrointestinal diseases has continued to be rapid, and we have undertaken a second edition in an attempt to incorporate new information and to respond to the valuable critiques of the first. In general, the points of concern fell into two categories: the omission of areas such as acute and chronic hepatitis and the disorders following gastrointestinal surgery, and the unevenness from one chapter to another. We have remedied the omissions by adding new chapters in these areas, by taking advantage of new members of our staff to add new sections on the irritable bowel syndrome and diverticular disease (Dr. Snape), and by selecting new authors for several chapters: Dr. Levine on diarrhea and constipation and malabsorption and maldigestion syndromes, Dr. Long on pancreatic disease, Dr. Senior on celiac sprue, Dr. Holtzapple on Hirschsprung's disease, Dr. Wagner on cirrhosis, and Dr. Soloway on gastrointestinal bleeding. Drs. Cohen, Shiau, and Glick have joined Dr. Brooks as co-authors of some chapters to bring their experience to these sections. Dr. Trotman has accepted the responsibility for updating the sections on ascites and encephalopathy. Our goal remains the same: to present to the reader concepts of gastrointestinal and hepatic diseases as disturbances of normal function and to apply them to diagnosis and treatment. We believe that this edition comes nearer to attaining it. We note with regret the death of Dr. Edwin O. Polish, one of the contributors, on January 29, 1977.

March 1978

F.P.B.

Preface to the First Edition

Current trends in medical education include an early introduction of the student to the patient and an emphasis on clinically relevant aspects of the basic medical sciences. Courses have been reorganized to integrate the basic and clinical sciences. The memorization of facts is minimized and instead an interdisciplinary, problem-solving approach has become the order of the day for students and house staff. At the University of Pennsylvania, as in most other medical schools, we have experienced a series of curriculum changes designed to incorporate these trends. Students begin to see patients from their first day in school, and preclinical disciplines emphasize material relevant to clinical matters. This is an attempt to integrate the teaching of anatomy, physiology, pathology, and clinical diagnosis in the first semester. After a basic eight-week course in clinical medicine, usually taken early in the second year, students are free to elect four- to six-week periods in the subspecialties, including gastroenterology. The problem-oriented record is the standard form for students and house staff at our hospitals.

In our attempts to evaluate these curricular reforms, one of the most revealing exercises was to compose a list of what we, as faculty, expected our students to learn during their medical school experience. With few exceptions, such as specialized techniques for the management of medical emergencies, the items listed turned out to be the time-honored basic clinical tools physicians have always required to take intelligent care of their patients. Emphasis was placed on incorporating current knowledge, presenting it in a form that can

be readily used by the physician in his or her contact with patients, and keeping it brief, since our students require training as generalists upon which those who wish can build a career in the specialties.

Our experience in postgraduate teaching led us to believe that family physicians, internists, and pediatricians share much the same interest. Like students, their time for reading is limited.

This book has grown out of our teaching experience. We have chosen to focus on a relatively small number of diseases, some seen regularly in the practice of gastroenterology. Enough is known about the mechanisms of all these diseases to contribute to a practical approach to their diagnosis and treatment.

The book begins with a brief overview of gastrointestinal function and the consequences of its disruption that is meant to serve as a guide in approaching patients with gastrointestinal disease. Once the symptoms and signs of gastrointestinal disease have been discussed in general, we proceed to the consideration of specific diseases. The format is standardized: definition, symptoms and signs, etiology, pathophysiological significance, diagnostic considerations, and therapeutic considerations. Although eleven different authors have contributed sections to the book, the unifying influence of working together at the University of Pennsylvania and liberal editorial revision should be apparent. Sections with no author(s) listed were written by the editor; references are listed by section.

School of Medicine F.P.B.
University of Pennsylvania
Philadelphia
March 1974

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1 Introduction

FRANK P. BROOKS

This chapter will serve both as an introduction and a summary of the textbook. Pedagogically, we are committed to teaching based upon an understanding of mechanisms rather than a memorizing of a list of appropriate actions in response to particular symptoms and signs. We suggest that after reading the text, the reader return to reread the introduction. If the reader then finds this rather terse statement more meaningful, we will have achieved much of what we set out to do.

Patients with diseases of the digestive tract present a broad spectrum of signs and symptoms. Chief complaints vary from "gallstones" to "gas." Each patient relates his history in language appropriate to his or her experience and culture. The approach that will most likely lead to accurate diagnosis and therapy is to guide patients toward a reasonably precise description of what they feel or sense and then to relate them to the major events occurring in gastrointestinal function. Thus, a chief complaint of "gallstones" as reported by the patient becomes, under gentle but persistent questioning, acute severe epigastric pain, and "gas" becomes belching and a feeling of fullness in the abdomen after meals.

If one keeps in mind the normal course of physiological events as food enters the digestive tract, it is much easier to interpret the patient's symptoms logically. The control of food and water intake is the first major physiological system encountered as food enters the gastrointestinal tract. Obesity may reflect hypothalamic dysfunction, psychological problems, or hypoglycemia due to an islet-cell tumor of the pancreas. Weight loss, on the contrary, is a dramatic feature of the psychological disturbance known as anorexia nervosa and a host of inflammatory and neoplastic lesions of the gastrointestinal tract as well. Rapid changes in weight usually reflect retention of water or diuresis rather than a change in body mass. Gain in weight on an appropriate diet under close observation is a reassuring sign to physicians fearing the diagnosis of cancer.

As food enters the esophagus, an obstructive lesion can produce dysphagia. Reflux esophagitis can lead to heartburn. Symptoms of gastric and duodenal disease are usually affected either favorably or adversely by eating. As food enters the stomach, nervous stimuli produce receptive relaxation in preparation for the arrival of the food bolus. Failure of relaxation due to denervation or stiffening from inflammation or malignant infiltration leads to increased resistance to distention, early satiety, and pain. Coincidentally with food entering the stomach, changes in colonic motility may dominate the patient's complaints and confuse the differentiation of gastric from colonic lesions.

With gastric emptying, the chyme enters the duodenum and stimulates secretion of pancreatic juice and emptying of the gallbladder. The buffering effect of the chyme, and the neutralizing and diluting effect of bile and pancreatic juice, reduces the hydrogen ion concentration of the duodenal content and relieves the pain of duodenal ulcer. However, pain from a diseased gallbladder or chronic pancreatitis will become worse. Obstruction of gastric emptying leads to vomiting, usually of undigested food.

The liver is the chief offender as a "silent" organ, and it may be the site of significant disease in the absence of symptoms as food passes through the digestive tract. In the absence of a gallbladder to act as a reservoir for bile, jaundice develops more rapidly in the presence of obstruction in the biliary tree. Once liver failure occurs, jaundice, ascites, and semicoma follow. These symptoms result from failure of the liver cells to transport and excrete bilirubin from por-

tal hypertension and hypoalbuminemia, and from exposure of the brain to such metabolic inhibitors as ammonia.

During the passage of food through the small intestine, digestion and absorption are accomplished through the action of intraluminal and mucosal surface events aided by a constant to-and-fro motion of the intestinal stream, with a net movement toward the anus.

Failure of bile acid secretion due to hepatic, or biliary disease, or interruption of the enterohepatic circulation of bile acids, results in reduced digestion and absorption of fat and, probably, in reduced water and electrolyte absorption and consequent diarrhea. Similarly, reduced pancreatic secretion due to pancreatic disease or impaired release of secretin and cholecystokinin-pancreozymin (CCK-PZ) leads to deficient lipolysis, proteolysis, steatorrhea, and azotorrhea (excess nitrogen in the stool). Manifestations of fat-soluble vitamin deficiencies follow. Factors contributing to the formation of a lithogenic bile and the formation of gallstones may include the composition of the diet.

The major factors determining digestion and absorption of food, once the intraluminal phase of digestion is complete, are the action of brush border enzymes and the transport processes by which the products of digestion enter the cells of the intestinal mucosa. Clearly, mucosal atrophy, as seen in celiac sprue, will profoundly impair all these functions.

Of interest is the specialization of intestinal function. To a degree, jejunal and ileal function can compensate for defective duodenal digestion and absorption of fat, protein, and carbohydrates. At least two absorptive processes, however, involving bile acids and vitamin B_{12} are unique to the ileum. In the presence of ileal disease in regional enteritis or after excision of the terminal ileum, symptoms of vitamin B_{12} deficiency and of interruption of the enterohepatic circulation of bile acids can be expected.

The presence of normal colonic function is essential to normal defecation, and the consequences of colonic disease are diarrhea and constipation. In most instances, these symptoms are related to poorly understood dysfunction of colonic motility. However, cancer of the colon, the second most common cancer in males in the United States, produces a change in bowel function primarily by altering bowel habit toward either constipation or diarrhea or a combination of both. The symptoms of colonic disease are almost always re-

lated to defecation. In diverticulitis, the pain becomes more severe upon defecation. In partial intestinal obstruction, the pain may be relieved by defecating or passing flatus. The pain of the irritable bowel syndrome is either relieved or made worse by defecation. Sometimes events in the colon reflect events more proximal in the alimentary tract. The gastrocolic response to food may trigger the onset of pain from a colonic lesion. Deficiency of the brush border enzyme lactase leads to passage of undigested lactose into the colon, where bacterial fermentation produces an osmotic diarrhea. The presence of an aganglionic segment of colon produces a functional obstruction to the passage of intestinal content and a greatly dilated proximal colon in Hirschsprung's disease.

Thus, the consequences of gastrointestinal disease of various portions of the bowel and its solid organ derivatives can be related to the passage of a meal through the alimentary tract. Frequently, disease of one area has consequences that lead to symptoms and signs of a general nature or symptoms and signs identified with the function of other portions of the tract. Anorexia and weight loss may occur with almost any gastrointestinal disease. Nausea and vomiting, gastrointestinal bleeding, belching, and flatulence are equally nonspecific, although the character of the bleeding usually distinguishes the source as the upper or the lower digestive tract. Diarrhea and constipation are usually the result of small or large bowel disease. Psychosomatic factors enter into the manifestations of almost all gastrointestinal disorders. In many patients, after excluding other causes, we must concentrate our therapeutic efforts on the psychophysiological approach. In other diseases, such as peptic ulcer and ulcerative colitis, the etiological significance of psychosomatic factors remains unknown. In all chronic disease of the alimentary tract, thoughtful attention by the physician to the psychological impact of the disease will be appreciated by the patient.