

CURRENT
GASTROENTEROLOGY

GARY GITNICK

VOLUME 5

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Edited by

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Dedication

THIS BOOK is dedicated to my colleagues. Those who write the chapters cannot be adequately compensated for the time and effort they have contributed to this educational undertaking. Those who review the chapters in an effort to improve the quality of the volume are inadequately rewarded and go generally unrecognized. The staff in my office, which, for many years, has struggled under the pressure of deadlines, and my wife Cherna and my children—Tracy, Jill, Kim, and Neil—who have not complained in spite of the many hours taken away from the family all deserve credit for this text, as well as past and present volumes. It is through the efforts of all of these individuals that the quality of this book has been ensured on an annual basis.

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Preface

PREFACES ARE MORE OFTEN written for the benefit of the writers than for that of the readers. This may be because readers judge a volume on the basis of its content and quality without regarding the content of the preface (just as the lover of fine wines judges the wine and not the label). A preface does, however, provide an opportunity for an editor or an author to prepare the reader for what lies ahead. Although it does not dissuade critics from criticizing nor encourage readers to read on, it may pave the way for these to take place.

This book represents the basic belief of the editor and the authors that the volume of literature published each year in the field of gastroenterology exceeds the ability of individuals to adequately read, digest, explore, and understand. Nevertheless, in spite of the impossibility of staying abreast of all that is developing in the field, it is important that physicians remain constantly aware of new advances and new trends. This volume tries to satisfy that need.

Authors who are eminent in their field of expertise have been asked to review the previous year's literature in their area and to describe those studies that seem most significant. New areas of development are emphasized, while those apparently less important are not mentioned. Major areas of progress or groups of studies that indicate new trends are assessed. With each edition, the editor and authors have strived to achieve coherence by integrating new areas of interest and recruiting new authors, while rotating approximately one third of the previous authors. This continual influx brings to each volume a fresh approach to areas of importance and interpretations of medical progress.

This book provides a compilation of all information believed to be important. We apologize if some studies have not been included because of our lack of appreciation of their possible significance. To avoid inappropriate omissions or unnecessary emphasis, and to lessen the risk of prejudice of individual authors

in the selection of material for each chapter, I submitted each completed chapter to one or more experts in the field who were asked to review the chapter and determine if emphasis was equitably and appropriately placed, misinterpretation was avoided, and all those studies that seemed most significant during the review year were included.

I am indebted to those reviewers who worked with me this year in preparing this text. They are Eugene DiMagno, M.D.; David Gocke, M.D.; Jon Isenberg, M.D.; Ronald Katon, M.D.; Bernard Levin, M.D.; Charles Pope, II, M.D.; William Snape, M.D.; and Tadataka Yamada, M.D. I am also indebted to Mrs. Susan Dashe for the many hours of work she spent in bringing this volume to completion. My colleagues who wrote the chapters and are to the greatest extent responsible for the success of this series receive my greatest thanks. I am also grateful to my associates at Year Book Medical Publishers, Inc., for their dedicated efforts in expeditiously publishing this text so that the contents are indeed current.

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CHAPTER 1

The Esophagus

Morris Traube

Richard W. McCallum

AS IN other areas of medicine, there has been an ever-increasing literature on the esophagus. This chapter is not intended to serve as an encyclopedic recitation of all the papers that have appeared in the past year. Rather, it is designed to review what we consider the highlights of new information advancing knowledge of the esophagus in health and disease states.

PHYSIOLOGY

A knowledge of normal physiology is welcome not only on its own merit but also for its value in enhancing an understanding of pathologic states and the subsequent development of rational approaches to therapy.

Upper Esophageal Sphincter

The upper esophageal sphincter (UES) serves to prevent air from entering the esophagus during inspiration. It is also known that the UES responds to intraluminal esophageal perfusion with liquid by increasing its tone. This response is even greater with acid perfusion of the esophagus. These observations form a basis for the proposal that the UES may also function to prevent reflux of esophageal contents into the pharynx and tracheobronchial tree. Accordingly, Sondheimer¹ recently studied pharyngeal and UES function in 16 infants with

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gastroesophageal reflux (GER), of whom five had had pulmonary aspiration, and in 11 age-matched controls. UES and pharyngeal motor function were found to be similar in both groups. Thus, although there has been increasing awareness in the pediatric literature of pulmonary complications of GER, the UES has not been identified as a conspirator. Moreover, the acid perfusion experiments do not by themselves show a physiologic role for the UES in preventing reflux in the normal state.²

Esophageal Body

Over the years, the literature on the pathophysiology of GER disease has shifted away from basal lower esophageal sphincter (LES) pressure per se, and some of the new emphasis has been placed on the presence of abnormal esophageal acid clearance in patients with GER disease. Several recent papers were of interest because they addressed the issue of control of acid clearance in the normal state. In eight normal volunteers, Madsen et al.³ performed 12-hour continuous pH and pressure recordings in the esophagus in the basal state and after the intraesophageal instillation of 0.1N hydrochloric acid in various volumes. These investigators found that the number of peristaltic sequences required to return the esophageal pH to 5 after spontaneous reflux episodes or imitated (acid-instillation) reflux episodes correlated with the degree of fall in pH accompanying the episodes. The clearing efficiency was 0.37 pH units per peristaltic contraction. The number of peristaltic contractions required to raise the pH was independent of the volume of instillation in the range of 2.5–15 ml; however, there was large variability among individuals, so this conclusion from observations in eight subjects may not be warranted. Similar conclusions regarding the role of esophageal peristalsis in acid clearance were reported by Helm et al.⁴ Volunteers were given boluses of acid intraesophageally, while manometry and pH monitoring were performed. Stepwise increases in pH were associated with sequential swallow-induced peristaltic waves. Furthermore, these investigators studied the role of saliva in esophageal acid clearance. Stimulation of saliva production by lozenges greatly improved acid clearance time, whereas oral aspiration of saliva markedly delayed acid clearance time. Replacement of the aspirated saliva by bicarbonate, but not by water, restored acid clearance toward normal. Thus, in normal subjects, neutralization of acid by saliva carried into the esophagus with each swallow accounts for esophageal acid clearance. The precise role of delayed esophageal clearance in relation to abnormalities of saliva production or peristalsis in GER disease remains to be studied. Certainly there has been no predictable observation that patients with Sjögren's syndrome and decreased salivation have an increased severity or frequency of heartburn, although this aspect could conceivably contribute to the problems seen in scleroderma patients.

Lower Esophageal Sphincter

Despite some insults and protests lodged against it in recent years, the LES seems to remain pivotal in the prevention of GER. Although it had previously been shown in dogs that the interdigestive migrating motor complex affected the LES,⁵ data in humans were not available until recently. Dent et al.⁶ studied overnight manometric tracings of upper gastrointestinal (GI) tract motility in normal volunteers. LES contractions occurred in association with the gastric interdigestive contractions, thus maintaining a pressure gradient between the stomach and the esophageal body. This coupling of the migrating motor complex activity of the LES and the stomach may be an important physiologic mechanism for preventing GER during interdigestive motor activity of the stomach. Although GER patients studied had normal intact coupling, abnormalities could perhaps be suspected in scleroderma patients. More importantly, this concept will need to be considered when prolonged monitoring of the LES is undertaken. Fluctuations in LES pressure can best be interpreted when gastric pressure is also monitored. Increases in LES pressure after administration of pharmacologic agents can only be considered significant if they are greater or separable from changes that may be simultaneously induced in gastric pressure.

ESOPHAGEAL FUNCTION TESTS

Potential Difference

Measurement of esophageal potential difference (PD) has been used in the past to locate the squamocolumnar junction. Recently, Orlando et al.,⁷ using a manometric catheter perfused with Ringer's solution as a PD probe, extended the technique and studied PD in 103 patients (mostly with GER) who had also undergone esophagoscopy and biopsy and in 26 patients with achalasia or diffuse esophageal spasm. The PD was abnormal in 90 of the 103 patients, as well as in seven of the achalasics. Generally, the GER patients had a low PD, whereas patients with Barrett's epithelium had a high PD. The practical value of these interesting findings remains to be defined. However, the authors have suggested that identification of a high PD might be useful in alerting the endoscopist that Barrett's epithelium may be present. Perhaps studies will show that the PD may have some value in detecting GER in the absence of endoscopic esophagitis.

Electrical Activity

Measurements of electrical activity in animals have contributed much to our understanding of esophageal function. Application of this technique to the

in vivo human esophagus is of particular interest because of physiologic variation among species and the lack of appropriate animal models for the classic human esophageal motility disorders. Ouyang et al.⁸ reported results of experiments with platinum ring electrodes attached to a manometric catheter. In five normal subjects no slow wave activity was seen in the esophageal body but spike activity was seen with swallow-induced contractions. The resting pressure of the LES was also not associated with spike activity. In ten patients with diffuse esophageal spasm, the majority of the spontaneous contractions were not associated with spike activity. Thus, this method may allow correlation of electrical and mechanical activity in the human esophagus and may permit study of the complex esophageal contractile system at one step earlier than is currently done with manometric techniques. It may also raise such questions as whether certain pharmacologic agents may be active against spike-dependent contractions as opposed to spike-independent contractions, and vice versa.

Manometry

While we await further results of experiments with electrical activity, care of patients continues! Does esophageal motility have a place in the *clinical* laboratory? Meshkinpour et al.⁹ reported that in their experience with 363 patients who underwent motility studies, the clinical diagnosis was changed by the procedure in only 6%, with the cost of studies being \$3,945 per alteration of diagnosis. Manometry, however, was beneficial in specific subgroups, such as achalasia—four of 27 patients with suspected achalasia did not have the diagnosis confirmed by manometry, and eight additional patients were so diagnosed by manometry. As Castell¹⁰ points out in his accompanying editorial, esophageal motility is beneficial but patient selection must be appropriate. If, for example, the 121 patients examined for chronic heartburn were excluded, the cost of the studies per alteration of a diagnosis would be reduced to \$2,630. It would be fair to conclude that motility is not generally useful in the routine clinical assessment of heartburn but may be beneficial and should be performed in selected patients with dysphagia in whom motility disorders are sought. Most recently, however, motility laboratories have increasingly been called on to evaluate patients with unexplained chest pain, and a generally rewarding number of manometric disorders have been unmasked in such patients.^{9,11,12} A detailed cost analysis, including evaluation of cost per change in diagnosis or treatment, in a large series of such patients would be worthwhile.

Radionuclide Studies

Even in the absence of detailed cost analysis, manometry clearly has its disadvantages—cost and discomfort to the patient and lack of availability at

many medical centers. Are there any tests on the horizon which may in some cases be useful in place of manometry? Recent work with esophageal radionuclide transit studies suggest such a possibility. Blackwell et al.¹³ used a technique similar to that of Russell et al.¹⁴—a bolus of water and technetium sulfur colloid was given to the subject in the supine position and transit time from cricoid to stomach was determined by use of a γ -ray counter. Blackwell's 16 control subjects had a transit time of mean 7 seconds. Sixteen of 19 patients with a previously diagnosed esophageal motility disorder had delayed transit times. Fifty patients were prospectively evaluated with manometry for symptoms suggestive of dysmotility (mostly with chest pain or dysphagia). Twenty-six of the 31 patients with normal manometric findings had normal transit times, and 16 of the 19 patients with abnormal manometry had delayed transit times. The results of this study show that radionuclide transit may be as sensitive as manometry in the detection of esophageal motility disorders. However, further studies are necessary to determine the sensitivity of radionuclide transit time in various subsets of patients, including those evaluated for chest pain in the absence of dysphagia. In addition, the ability of radionuclide transit to demonstrate abnormality in patients with high amplitude peristaltic contractions^{11,12} would need to be demonstrated before transit could be more widely accepted. An additional question is whether a solid bolus might be more beneficial than a liquid-tagged one. If studies over the next few years give favorable results, radionuclide transit might be useful as an initial screening method, with manometry being used in those with delayed transit times to obtain further information and classification of the abnormality present, as suggested by Russell et al.¹⁴

Transit studies notwithstanding, nuclear medicine has played a role in the esophagus, such as in the evaluation for GER or in the assessment of drug therapy, as reviewed by McCallum.¹⁵ Holloway et al.¹⁶ recently utilized an isotope-labeled solid meal to measure esophageal emptying in patients with achalasia before and after therapy with either pneumatic dilatation or myotomy. The percent change in LES pressure and percent change in esophageal emptying were significantly correlated. Symptom score also correlated with percent change in both LES pressure and esophageal emptying. The authors concluded that radionuclide esophageal emptying may be a practical alternative to esophageal manometry in the assessment of treatment. However, since results correlate with symptom score, the test is not essential in a clinical setting in the follow-up of achalasia therapy. Currently, the role of esophageal emptying is greatest in the clinical research setting in the evaluation of drug or invasive therapy.

GASTROESOPHAGEAL REFLUX DISEASE

Gastroesophageal reflux is one of the commonest problems faced by patients and physicians. Appropriately, it is a topic that has been frequently reviewed