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THE SCIENCE AND PRACTICE OF CLINICAL MEDICINE

Jay P. Sanford

Editor-in-Chief

Disorders of the Gastrointestinal Tract
Disorders of the Liver
Nutritional Disorders

Edited by

John M. Dietschy

Disorders of the Gastrointestinal Tract Disorders of the Liver Nutritional Disorders

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Preface

As they undertook the writing of a new textbook of medicine, the editors felt that there was a need for a book that approached clinical problems from the standpoint of general symptom complexes as well as specific diseases. That general format has been utilized in this, the textbook's first volume, which deals with diseases of the gastrointestinal tract and of the liver and nutritional disorders. The major portions of this volume begin with a review of the normal physiologic and biochemical functions of the organ; this review is followed by a discussion of the specific diagnostic procedures available for studying dysfunction of that system. The subsections deal with the clinical manifestations of diseases which affect that organ system. These sections utilize two

entirely different approaches: The chapters in the first subsection discuss the sick patient from the standpoint of the differential diagnosis of major symptom complexes, such as upper gastrointestinal bleeding, obstructive jaundice, or fat malabsorption. The chapters in the second subsection provide detailed discussions of specific diseases.

We hope that this dual approach to problems of clinical medicine, based upon sound knowledge of basic physiologic and biochemical principles, will provide the student, house officer, and practicing physician with the most useful kind of reference textbook.

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Contents

ESOPHAGUS

Anatomy and Normal Functional Physiology of the Esophagus and Pharynx 1

Anatomy, Blood Flow, and Innervation of the Esophagus and Pharynx *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 1

Normal Functional Physiology of the Esophagus *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 2

Procedures for the Diagnosis of Diseases of the Esophagus 4

X-Ray *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 4

Esophageal Motility Studies *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 4

Esophageal Acid Perfusion Test (The Bernstein Test) *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 5

Esophagoscopy *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 5

Cytology *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 5

Differential Approach to the Major Clinical Syndromes of Diseases of the Esophagus 6

Dysphagia *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 6

Pain of Esophageal Origin *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 7

Specific Diseases of the Esophagus 8

Achalasia *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 8

Systemic Sclerosis (Scleroderma) *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 10

Symptomatic Diffuse Esophageal Spasm *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 12

Miscellaneous Disorders of Esophageal Motility *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 12

Lower Esophageal Ring *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 12

Neoplasms of the Esophagus *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 14

Dysphagia Lusoria *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 14

Esophageal Webs (Plummer-Vinson Syndrome,

Patterson-Kelly Syndrome) *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 14

Gastroesophageal Reflux and Its Complications *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 15

Congenital Anomalies of the Esophagus *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 17

Esophageal Diverticula *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 17

Lacerations and Perforations of the Esophagus *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 18

Infections (Moniliasis) *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 18

Hiatus Hernia *Sidney Cohen, M.D., and Lauran D. Harris, M.D.* 19

STOMACH AND SMALL AND LARGE INTESTINE

Anatomy of the Gastrointestinal Tract 20

Anatomy, Blood Supply, and Innervation of the Stomach and Small and Large Intestine *Arvey I. Rogers, M.D.* 20

Normal Functional Physiology of the Gastrointestinal Tract 27

Motility of the Gastrointestinal Tract *J. J. Misiewicz, B.Sc., M.B., F.R.C.P.* 27

Secretory Mechanisms in the Stomach *Byron E. Kolts, M.D.* 30

Bacteriology of the Gastrointestinal Tract *Sherwood Gorbach, M.D.* 32

Normal Mechanisms of Water and Electrolyte Absorption by the Gastrointestinal Tract *Frederick A. Bieberdorf, M.D.* 33

Normal Mechanisms of Carbohydrate Absorption *Flavio O. Nervi, M.D.* 35

Normal Mechanisms of Protein Absorption *Flavio O. Nervi, M.D.* 38

Normal Mechanisms of Lipid Absorption *Henrik Westergaard, M.D.* 38

Normal Mechanisms of Fat- and Water-Soluble Vitamin Absorption *Henrik Westergaard, M.D.* 39

Procedures for the Diagnosis of Diseases of the Gastrointestinal Tract 40

Tests of Gastric Secretory Capacity *Byron E. Kolts, M.D.* 40

Radioimmunoassay of Gastrointestinal Hormones <i>Byron E. Kolts, M.D.</i>	42	Eosinophilic Gastroenteritis <i>Theodore M. Bayless, M.D.</i>	118
Tests of Intestinal Absorption <i>Frederick A. Wilson, M.D.</i>	42	Chronic Ulcerative (Nongranulomatous) Jejuno-Ileitis <i>Theodore M. Bayless, M.D.</i>	119
Collection and Handling of Fecal Specimens for Bacteriologic and Parasitological Examination <i>Jay P. Sanford, M.D.</i>	44	Whipple's Disease <i>Theodore M. Bayless, M.D.</i>	120
Examination of Rectal Smears <i>Stuart H. Danovitch, M.D., F.A.C.P.</i>	45	Lymphangiectasia <i>David H. Alpers, M.D.</i>	123
Biopsy Procedures of the Stomach, Small Bowel, and Rectum <i>William O. Dobbins III, M.D.</i>	46	Vascular Anomalies of the Gastrointestinal Tract <i>Arvey I. Rogers, M.D., and Steven Bernstein, M.D.</i>	124
Cytology Procedures in the Gastrointestinal Tract <i>William O. Dobbins III, M.D.</i>	47	Diseases Associated with Defects in Sugar Absorption <i>Sheldon E. Schwartz, M.D.</i>	127
Endoscopy of the Gastrointestinal Tract <i>Stuart H. Danovitch, M.D., F.A.C.P.</i>	47	Diverticula of the Gastrointestinal Tract <i>J. J. Misiewicz, B.Sc., M.B., F.R.C.P.</i>	129
Radiographic Examination of the Alimentary Tract <i>Edward E. Christensen, M.D.</i>	49	Familial Polyposis Syndromes <i>Sheldon E. Schwartz, M.D.</i>	133
Turnover Time and Pool Size of Bile Acid <i>David H. Alpers, M.D.</i>	52	Bacterial Overgrowth and the Blind Loop Syndrome <i>Sherwood Gorbach, M.D.</i>	137
Quantitation of Protein Loss by the Gastrointestinal Tract <i>David H. Alpers, M.D.</i>	53	Regional Enteritis <i>Alfred J. Wall, M.D. (M.E.L.B., M.R.A.C.P.), and Sumner C. Kraft, M.D., F.A.C.P.</i>	138
Differential Approach to the Major Clinical Syndromes of Gastrointestinal Disease	54	Ulcerative Colitis and Crohn's Colitis <i>Sumner C. Kraft, M.D., F.A.C.P., and Alfred J. Wall, M.D. (M.E.L.B., M.R.A.C.P.)</i>	144
Differential Approach to Gastrointestinal Bleeding <i>John A. Balint, M.D., M.R.C.P.</i>	54	Motor Abnormalities of the Bowel <i>J. J. Misiewicz, B.Sc., M.B., F.R.C.P.</i>	151
Differential Approach to Major Syndromes of Abdominal Pain <i>John B. Rodgers, Jr., M.D.</i>	58	Bezoars of the Gastrointestinal Tract <i>Patricia Brannan, M.D.</i>	155
Differential Approach to Intestinal Obstruction and Ileus <i>I. James Sarfeh, M.D.</i>	63	Pneumatosis Cystoides Intestinalis <i>Flavio O. Nervi, M.D.</i>	157
Differential Approach to Protein-Losing Enteropathy <i>David H. Alpers, M.D.</i>	66	Acute Appendicitis <i>Flavio O. Nervi, M.D.</i>	158
Differential Approach to Acute Diarrheal Syndromes <i>Frederick A. Bieberdorf, M.D.</i>	68	Intestinal Function Following Resection of Fistula Formation <i>David H. Alpers, M.D.</i>	159
Differential Approach to Chronic Diarrheal Syndromes <i>Frederick A. Bieberdorf, M.D.</i>	73	The Intestine in Systemic Disease <i>Frederick A. Wilson, M.D.</i>	163
Differential Approach to Steatorrhea <i>Henrik Westergaard, M.D.</i>	76	Tumors of the Stomach, Small Intestine, and Colon <i>Paul Sherlock, M.D., F.A.C.P., and Sidney J. Winawer, M.D., F.A.C.P.</i>	170
Differential Approach to Selective Carbohydrate Malabsorption <i>Sheldon E. Schwartz, M.D.</i>	80		
Differential Approach to Anemia Associated with Gastrointestinal Disease <i>Eugene P. Frenkel, M.D.</i>	83	PANCREAS	
Specific Diseases of the Gastrointestinal Tract	86	Anatomy of the Pancreas	190
Congenital Anomalies of the Gastrointestinal Tract <i>Henrik Westergaard, M.D.</i>	86	Structure and Function of the Exocrine Pancreatic Cell <i>James D. Jamieson, M.D., Ph.D.</i>	190
Peptic Ulcer Disease <i>James E. McGuigan, M.D.</i>	88	Normal Functional Physiology of the Pancreas	193
Surgical Treatment of Peptic Ulcer and Post-gastrectomy Complications <i>Robert N. McClelland, M.D., F.A.C.S.</i>	102	Mechanisms of Control of Pancreatic Secretion <i>Henry D. Janowitz, M.D., and Peter A. Banks, M.D.</i>	193
Gastritis <i>Stuart H. Danovitch, M.D., F.A.C.P.</i>	111	Electrolyte Compositions of Pancreatic Juice <i>Henry D. Janowitz, M.D., and Peter A. Banks, M.D.</i>	194
Idiopathic Sprue and Tropical Sprue <i>Walter Rubin, M.D.</i>	114	Pancreatic Enzymes in the Pancreatic Secretions <i>Henry D. Janowitz, M.D., and Peter A. Banks, M.D.</i>	195

Procedures for the Diagnosis of Diseases of the Pancreas 196

- Pancreatic Enzymes in the Blood and Body Fluids
Henry D. Janowitz, M.D., and Peter A. Banks, M.D. 196
- Urinary Enzyme Studies *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 196
- Diagnosis of Macroamylasemia *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 196
- Duodenal Drainage *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 197

Specific Diseases of the Pancreas 199

- Congenital Anomalies *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 199
- Acute Pancreatitis *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 199
- Recurrent Pancreatitis *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 207
- Chronic Pancreatitis *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 208
- Cysts of the Pancreas *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 210
- Cystic Fibrosis *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 210
- Tumors of the Pancreas *Henry D. Janowitz, M.D., and Peter A. Banks, M.D.* 211

LIVER AND BILIARY TRACT

Anatomy of the Liver and Biliary System 217

- Anatomy, Blood Flow, and Innervation of the Liver and Gallbladder *J. W. Grisham, M.D.* 217

Normal Functional Physiology of the Liver and Gallbladder 222

- Bile Formation and Secretion
James L. Boyer, M.D. 222
- Bilirubin Metabolism *James L. Boyer, M.D.* 223
- Protein Synthesis by the Liver
James L. Boyer, M.D. 226
- Carbohydrate Metabolism by the Liver
Charles S. Lieber, M.D. 226
- Lipid Metabolism by the Liver
Charles S. Lieber, M.D. 227
- Ethanol Oxidation by the Liver
Charles S. Lieber, M.D. 228

Procedures for the Diagnosis of Diseases of the Liver and Biliary System 230

- Liver Function Studies
Steven Schenker, M.D. 230
- Methods for Measuring Portal Pressures
Athol Ware, M.B.B.S., M.R.A.C.P. 232
- Liver Biopsy
Athol Ware, M.B.B.S., M.R.A.C.P. 233
- X-Ray Examination of the Hepatobiliary System
Edward E. Christensen, M.D. 234

Differential Approach to Major Clinical Syndromes of Diseases of the Liver and Biliary Tract 247

- Differential Diagnosis of Liver Dysfunction
Steven Schenker, M.D. 247
- Differential Diagnosis of Patterns of Abnormal Histology in Liver Biopsies
James L. Boyer, M.D. 254
- Clinical Manifestations and Differential Diagnosis of Portal Hypertension *Harold O. Conn, M.D.* 259
- Differential Diagnosis of Ascites
Harold O. Conn, M.D. 261
- Differential Diagnosis of Coma in Patients with Liver Disease *Steven Schenker, M.D.* 263
- Differential Diagnosis of Renal Failure in Patients with Liver Disease *Alan R. Hull, M.D.* 265
- Hematologic Manifestations of Liver Disease
Marvin J. Stone, M.D., F.A.C.P. 267

Specific Diseases of the Liver and Gallbladder 271

- Congenital and Neonatal Liver Disease
Athol Ware, M.B.B.S., M.R.A.C.P. 271
- Alcoholic Liver Disease
Harold J. Fallon, M.D. 273
- Cirrhosis of Obscure Origin
Harold J. Fallon, M.D. 280
- Wilson's Disease (Hepatolenticular Degeneration)
Irmin Sternlieb, M.D. 287
- Hemochromatosis *Eugene R. Schiff, M.D.* 289
- Cardiac Cirrhosis *Eugene R. Schiff, M.D.* 291
- Viral Hepatitis *James Shorey, M.D.* 291
- Involvement of the Liver in Other Infectious Diseases
James P. Nolan, M.D. 302
- Involvement of the Liver in Various Systemic Diseases *James P. Nolan, M.D.* 307
- Liver Disease Associated with Toxins and Drugs
James P. Nolan, M.D. 316
- Liver Disease in Pregnancy
Steven Schenker, M.D. 319
- Portal and Hepatic Vein Thrombosis
Athol Ware, M.B.B.S., M.R.A.C.P. 320
- Familial Hyperbilirubinemic Syndromes
Gerald M. Fleischer, M.D., and Ralph E. Kirsch, M.B.Ch.B., M.D., F.C.P.(S.A.) 324
- Tumors of the Liver *Elliot Alpert, M.D.* 328
- The Pathophysiology of Cholesterol Gallstone Formation
Bryan E. Lukie, M.D., F.R.C.P. (C.) 333
- Cholelithiasis *Kerrison Juniper, Jr., M.D.* 335
- Cholecystitis *Kerrison Juniper, Jr., M.D.* 338
- Diverticula of the Gallbladder
Kerrison Juniper, Jr., M.D. 340
- Cholangitis *Kerrison Juniper, Jr., M.D.* 340
- Bile Duct Stricture
Kerrison Juniper, Jr., M.D. 341

Postcholecystectomy Syndrome	
<i>Kerrison Juniper, Jr., M.D.</i>	341
Biliary Dyskinesia	
<i>Kerrison Juniper, Jr., M.D.</i>	341
Biliary Tract Ascariasis	
<i>Kerrison Juniper, Jr., M.D.</i>	342
Biliary Anomalies	
<i>Kerrison Juniper, Jr., M.D.</i>	342
Sclerosing Cholangitis	
<i>Eugene R. Schiff, M.D.</i>	342
Fistula between the Biliary System and the Bowel	
<i>Eugene R. Schiff, M.D.</i>	343
Tumors of the Gallbladder and Bile Ducts	
<i>Elliot Alpert, M.D.</i>	345

DIAPHRAGM, PERITONEUM, MESENTERY, AND OMENTUM

Specific Diseases of the Diaphragm	<i>Steven A. Bernstein, M.D., and Arvey I. Rogers, M.D.</i>	347
Specific Diseases of the Omentum	<i>Steven A. Bernstein, M.D., and Arvey I. Rogers, M.D.</i>	350
Specific Diseases of the Mesentery	<i>Steven A. Bernstein, M.D., and Arvey I. Rogers, M.D.</i>	351
Specific Diseases of the Peritoneum	<i>Steven A. Bernstein, M.D., and Arvey I. Rogers, M.D.</i>	352

NUTRITIONAL DISEASES

Obesity and Anorexia Nervosa	355
Obesity	<i>Albert Stunkard, M.D., and Jules Hirsch, M.D.</i> 355
Anorexia Nervosa	<i>Albert Stunkard, M.D.</i> 361
Vitamin-Deficient States and Other Related Diseases	364
Protein Malnutrition States	<i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i> 364
General Considerations in Vitamin Deficiency	

<i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	366
Ascorbic Acid and Ascorbic Acid Deficiency (Scurvy) <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	372
Biotin and Biotin Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	374
Cyanocobalamin (Vitamin B ₁₂) and Cyanocobalamin Deficiency (Pernicious Anemia) <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	376
Folic Acid and Folic Acid Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	380
Nicotinic Acid and Nicotinic Acid Deficiency (Pellagra) <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	384
Pantothenic Acid and Pantothenic Acid Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	386
Pyridoxine (Vitamin B ₆) and Pyridoxine Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	387
Riboflavin (Vitamin B ₂) and Riboflavin Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	389
Thiamine (Vitamin B ₁ , Aneurine) and Thiamine Deficiency (Beriberi) <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	390
Vitamin A and Vitamin A Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	393
Vitamin E (Tocopherol) and Vitamin E Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	395
Vitamin K and Vitamin K Deficiency <i>Robert H. Herman, M.D., Fred B. Stifel, Ph.D., and Harry L. Greene, M.D.</i>	396

ESOPHAGUS

Anatomy and Normal Functional Physiology of the Esophagus and Pharynx

ANATOMY, BLOOD FLOW, AND INNERVATION OF THE ESOPHAGUS AND PHARYNX

Sidney Cohen
and
Lauran D. Harris

The swallowing apparatus consists of the pharynx, the upper esophageal sphincter, the esophagus, and the lower esophageal sphincter. The pharynx extends from the base of the skull to the cricoid cartilage anterior. It communicates with the nasal cavities and auditory canals, larynx, and esophagus. The upper esophageal sphincter forms the junction of pharynx and esophagus. This sphincter is composed of the middle constrictor fibers of the cricopharyngeal muscle. The essential anatomic features of the esophagus and its sphincters are shown in Fig. 1 (see page 2).

The esophagus is a muscular tube about 25 cm long, extending from the pharynx to the stomach and fixed only at its proximal and distal ends. It extends through the superior and posterior portions of the mediastinum. Along its course, the cervical portion comes in close proximity to the thyroid gland, trachea, and carotid arteries, while the thoracic portion is adjacent to the aorta, left bronchus, and left atrium. The esophagus passes through the esophageal hiatus of the diaphragm and terminates by joining the cardiac portion of the stomach.

The pharynx, upper esophageal sphincter, and the upper one-third of the esophagus are composed of striated muscle; the distal two-thirds of esophagus and the lower esophageal sphincter are smooth muscle. The lower esophageal sphincter has no distinguishing anatomic characteristics, but does have highly specialized physiologic characteristics.

The innervation of the pharynx is through the pharyngeal plexus, laryngeal nerves, and ninth cranial nerve. The esophagus is innervated by the vagus and by sympathetic nerves which form the esophageal plexus.

The blood supply of the esophagus is from the

descending aorta, bronchial arteries, and left gastric artery. Veins terminate in the azygous and gastric veins. The gastric veins form a connection between the portal and systemic systems. This connection may be of considerable functional significance when normal portal blood flow is compromised. As pressure in the portal system increases, flow in the gastric veins reverses, and the portal system begins to drain into the systemic system via the azygous vein. As this occurs, the anastomatic venous channels in the distal esophagus become distended to form esophageal varices.

NORMAL FUNCTIONAL PHYSIOLOGY OF THE ESOPHAGUS AND PHARYNX

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The act of swallowing is a smoothly functioning process that requires integration of skeletal muscle components of the mouth and pharynx with smooth muscle components of the esophagus. The entire process requires coordination of propulsive forces in the pharynx and esophagus with inhibition of the resting tone within the upper and lower esophageal sphincters.

ORAL AND PHARYNGEAL COMPONENTS

It is far easier to swallow than it is to describe the act of swallowing. Essentially, openings to the outside and to adjoining cavities must first be closed. Openings to the outside are sealed by closing the lips, raising the soft palate, and approximating the posterior pillars—all by contraction of the appropriate muscles. The larynx is isolated from the pharynx by elevation of the larynx with closure of the glottis and retroversion of the epiglottis over the laryngeal orifice.

Once an oropharyngeal cavity has been formed, the bolus is transported into the pharynx by movement of the tongue. Sequential pharyngeal contractions then rapidly move the bolus distally into the expectant esophagus.

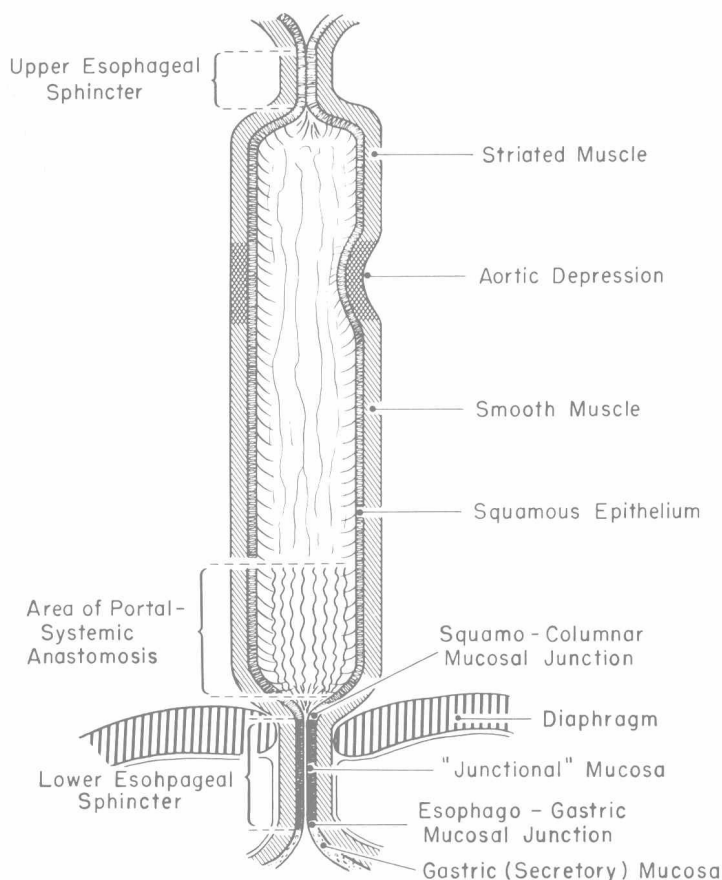


Fig. 1. Anatomic features of the esophagus and its sphincters.

Separating the pharynx and the esophagus is a specialized area some 3–4 cm long which is normally closed—the cricopharyngeus or upper esophageal sphincter. With the onset of swallowing, the upper esophageal sphincter relaxes to allow the bolus ready access to the esophagus.

ESOPHAGEAL COMPONENTS

The functions of the esophagus are quite simple—transporting material from mouth to stomach and preventing reflux of gastric contents. All derangements of normal physiological behavior, therefore, interfere with either transport or the prevention of gastroesophageal reflux.

Esophageal transport requires the integration of peristalsis with relaxation of the lower esophageal sphincter. Peristalsis is defined as a distally progressive band of circular muscle contraction some 3–4 cm axial extent that begins as an extension of upper esophageal sphincter closure. This band of contraction sweeps distally at a rate of 3–5 cm/sec, obliterating the esophageal lumen and effectively transporting material into the stomach. Distally, the peristaltic wave blends into the relaxed lower esophageal sphincter and serves to close it, thus returning the esophagus to its normal resting state. If initiated by a swallow, the entire process is called primary peristalsis. However, local stimulation of the esophageal mucosa (material left behind by insufficient primary peristalsis, refluxed gastric contents) can initiate

an apparently identical sequence. In this instance, however, it is called secondary peristalsis. Local nonpropulsive, nonintegrated esophageal contractions are frequently misnamed tertiary peristalsis. The term “peristalsis” (as applied to the esophagus) should be reserved for the entire integrated process of sphincteric relaxation and distally progressive contraction.

Usually, each swallow is followed by primary peristalsis. A series of swallows in rapid succession, however, may result in inhibition of all esophageal motor activity, converting the esophagus into a flaccid conduit from pharynx to stomach—thus the ability possessed by some individuals to “chug-a-lug” an entire bottle of beer. Following the last swallow, peristalsis restores the esophagus to its normal resting state.

The normal resting pressure within the thorax (and therefore within the resting esophageal lumen) is slightly negative as compared to atmospheric pressure. On the other hand, resting intraabdominal (and hence intragastric) pressure is slightly positive. It is obvious that gastroesophageal reflux (from positive to negative pressures) would occur almost continuously without a mechanism preventing it. A specialized 3–5 cm segment of distal esophagus—the lower esophageal sphincter—is this barrier mechanism. This sphincter is normally closed by circular muscle contraction sufficient to maintain an intraluminal pressure some 15–30 mm Hg above intraab-

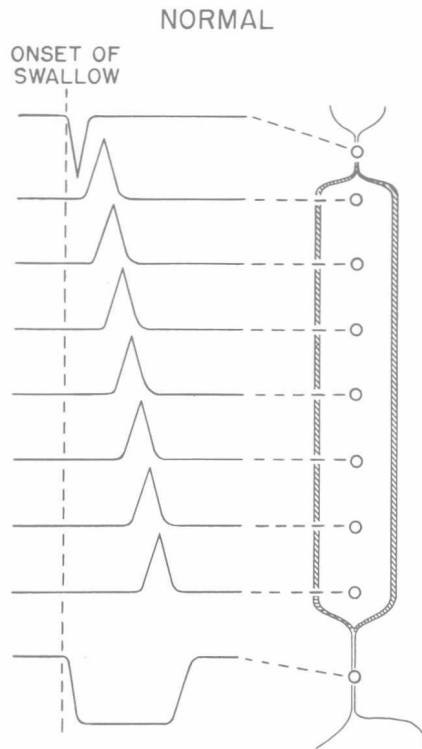


Fig. 1. Normal sequence of primary peristalsis, initiated by a swallow at the vertical dotted line. With the onset of a swallow, both the upper esophageal sphincter and the lower esophageal sphincter relax.

dominal pressure. While this contracted sphincter segment prevents gastroesophageal reflux, it must also allow transport of swallowed material into the stomach. How the lower esophageal sphincter accomplishes both aims is diagrammed in Fig. 1. As the peristaltic wave begins proximally by closing the upper esophageal sphincter, pressure in the lower esophageal sphincter abruptly drops and approximates gastric pressure. While the lower esophageal sphincter is not then "open," it cannot act as a barrier to transport material in either direction at that moment. Fortunately, the distally progressive peristaltic wave ensures that flow is distal—not proximal. As the peristaltic wave reaches the lower esophageal sphincter, sphincter tone is restored—often with a slight temporary overshoot.

In the past, it had been thought that mechanical factors such as various acute angulations or compression by surrounding pressures or the diaphragm helped prevent reflux. However, recent evidence leaves little doubt that the lower esophageal sphincter's ability to maintain its tone is the sole determinant of gastroesophageal competence.

The lower esophageal sphincter does not have a fixed

strength, but its strength can be adapted to meet changing need. For example, it is not at all unusual for intraabdominal pressure to increase by 50–75 mm Hg while coughing, straining at stool, lifting an object, or even during deep inspiration. This should be enough to overcome easily the advantage the lower esophageal sphincter has of some 15–30 mm Hg intraluminal pressure over resting intraabdominal pressure. Fortunately, however, as intraabdominal pressure increases, lower esophageal sphincter pressure also increases and maintains a pressure gradient. In fact, the normal lower esophageal sphincter does more than just maintain its resting pressure advantage of 15–30 mm Hg. As intraabdominal pressure increases, this increment in pressure is matched by approximately a 2:1 increment in lower esophageal pressure. The degree to which the lower esophageal sphincter responds to the stimulus of increased intraabdominal pressure (i.e., 1:1, 2:1, 3:1, etc.) seems to be determined by the resting lower esophageal sphincter strength—the stronger the lower esophageal sphincter initially, the greater its response to a given increase in intraabdominal pressure. While the mechanism of this response is not as yet completely understood, it has been postulated to be a reflex arc mediated by the vagus. It should be emphasized that this presumed reflex arc is not affected by the sphincter's location in abdomen or chest or by other purely mechanical factors.

It is clear from the above that resting lower esophageal sphincter strength is of prime importance in the maintenance of gastroesophageal competence since it determines not only the ability to prevent gastroesophageal reflux under average resting conditions but also governs the degree to which the sphincter responds to the challenge of an increase in intraabdominal pressure. Therefore, recent studies showing resting tone of the lower esophageal sphincter to be largely or even completely controlled by endogenous secretion of the gastrointestinal hormones are of considerable interest. Although work in this fascinating area is still in its infancy, the hormones, gastrin, cholecystokinin-pancreozymin, secretion, and glucagon have all been found to affect the lower esophageal sphincter. Of these, only gastrin increases lower esophageal sphincter strength—the others seem to be inhibitory. Since eating serves as a potent physiologic stimulus for gastrin release from the gastric antrum, the important function of increasing lower esophageal sphincter strength at a time when it is most important to prevent reflux of the acid gastric contents would seem to be served quite nicely. The hormones inhibiting lower esophageal sphincter strength—all released from the small intestine—would seem to counteract this gastrin response when it is presumably no longer required. Our understanding of gastrointestinal physiology should be increased rapidly by this recently opened field of investigation.

Procedures for the Diagnosis of Diseases of the Esophagus

X-RAY

Sidney Cohen

and

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The single procedure most helpful in the evaluation of esophageal disease is a properly done radiographic examination. Although the details or mechanics of the procedure will vary depending on what is seen or suspected, barium sulfate is by far the most commonly employed radiopaque contrast medium. The viscosity or concentration of the barium sulfate suspension is often varied—again, depending on what is seen or suspected. On occasions, solids or semisolids may be employed, particularly when evaluating a suspected disorder of esophageal transport. These materials may be radiolucent (bread or a whole marshmallow “washed down” with liquid barium sulfate) or radiopaque (barium sulfate in a capsule or compressed into a “wafer” or pill).

In the course of obtaining the conventional films, the radiologist usually evaluates the esophagus fluoroscopically. Many centers have recently begun to employ cine-radiography routinely in suspected disorders of esophageal transport. The resultant cine is particularly useful for detailed studies of esophageal motor disorders.

Although the position of the patient during the examination may depend to some extent upon the lesion suspected, in general the supine position is standard and preferable. In this position, the esophagus does not have the advantage of gravity and must be emptied by its own initiative. The effect of gravity may also be utilized to test the integrity of the lower esophageal sphincter—by tilting the patient to a slightly head-down position and observing whether or not contrast material flows retrograde from stomach to esophagus. It is common practice to provide the added stress of increased intraabdominal pressure (by simple manual compression of the abdomen, a Valsalva

maneuver, etc.) when lower esophageal sphincter integrity is evaluated. While the instances of gastroesophageal reflux are increased by these maneuvers, the reliability of these observations is still questionable. The incidence of both false-positives and false-negatives is sufficiently high that this test of gastroesophageal reflux correlates only poorly with clinical evidence of gastroesophageal reflux.

Table 1 attempts to show the relative usefulness of procedures usually employed to diagnose common esophageal abnormalities.

ESOPHAGEAL MOTILITY STUDIES

Sidney Cohen

and

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The recording of intraluminal pressure has become widely used in the investigation and diagnosis of abnormalities of the esophagus and its sphincters. Pressure may be measured or expressed in many ways, but the method most often used at present requires that pressure be transmitted through fluid-filled, open-tipped catheters to external transducers. Three catheters having a total outside diameter about 4.5 mm are assembled into a single unit. The orifices through which pressure is transmitted are 5 cm apart, and their relative positions are usually indicated by a radiopaque marker. The catheters are then filled with fluid and continuously infused by a syringe pump to ensure that a sufficient volume of fluid is available for displacement to the transducers. The output from these transducers is then graphed on a multichannel recorder. The recording tubes are passed through the nose or mouth, and the patient is usually studied in the supine position. The recording orifices are first advanced into the stomach and then slowly withdrawn at cen-

Table 1
Procedures for the Diagnosis of Diseases of the Esophagus

	X-RAY	ESOPHAGOSCOPY	BIOPSY	CYTOLOGY	MANOMETRY
Achalasia	XXX	XX		X	XXXX
Diffuse Esophageal Spasm	XXX	X			XXXX
Scleroderma	XXX	XX	XX		XXXX
Lower Esophageal Ring	XXXX	XXXX	XX		
Neoplasm	XXX	XXXX	XXXX	XXXX	X
Benign Stricture	XXX	XXX	XXX	X	X
Incompetent LES	XXX	XXX			XXXX
Esophagitis	XX	XXXX	XXXX		XX

XXXX—May be diagnostic;

XXX—May strongly suggest diagnosis;

XX—May be useful by helping to confirm diagnosis;

X—May be useful by helping to rule out another lesion.

timeter or half-centimeter intervals, continuously recording pressure throughout the length of the esophagus and pharynx. At each interval, the patient is asked to swallow—either a “dry” swallow (the small amount of saliva present in the mouth) or a “wet” swallow (2–5 ml of water). Swallowing and respirations are monitored by changes in pressure recorded from small pneumatic bellows placed over the larynx and chest respectively.

The study briefly outlined above allows measurement of both resting strengths of the two sphincters as well as these sphincters’ response to swallowing. In addition, responses to swallowing of the body of the esophagus and the pharynx can be evaluated.

ESOPHAGEAL ACID PERFUSION TEST (THE BERNSTEIN TEST)

**Sidney Cohen
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The purpose of this test is to simulate gastroesophageal reflux by instilling 0.1 normal HCl into the esophagus. A comparison can then be made between any resultant symptoms and a given patient’s naturally occurring symptoms. 0.1 normal HCl and 0.9 percent sodium chloride are alternately perfused at a rate of approximately 7 ml/min into the upper one-third of the esophagus. Each solution is usually instilled for 30 min (unless symptoms occur earlier). The patient should not be aware of the nature of the solution infused—better yet, the solution should be prepared and labeled (A and B, 1 and 2, etc.) by a third person and the procedure performed in double-blind fashion.

The test is considered negative if no symptoms occur during the course of a 30-min acid perfusion, positive if acid perfusion (and only acid perfusion) is uniformly accompanied by the patient’s spontaneously occurring symptoms.

Opinions vary about the reliability and usefulness of this test. It is our opinion that this test contributes relatively little to a careful, detailed history.

ESOPHAGOSCOPY

**Sidney Cohen
and
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Direct visualization of the esophageal lumen and mucosa may be of considerable diagnostic value—particularly in evaluation of upper gastrointestinal hemorrhage, an

obstructing lesion of the esophagus, or esophagitis. In addition, mucosal biopsies may be obtained under direct vision. Since the recently perfected flexible fiberoptic instruments have made the procedure both simpler to perform and less hazardous for the patient, the indications for esophagoscopy are presently being expanded. At present, rigid scopes are generally used only for special procedures such as removal of foreign bodies from the esophagus.

The procedure is done using topical anesthesia and sedative premedication. Although patients are usually hospitalized, there seems to be a growing tendency for esophagoscopy to be done on an outpatient basis. Other than infrequent reactions to the premedication and anesthetic agents, the chief complication is perforation—occurring most commonly at the cricopharynx. With the fiberoptic scopes, the incidence of perforation is about 0.01 percent, with a considerably lower mortality rate. Contraindications to esophagoscopy include (1) an uncooperative patient; (2) severe bony abnormalities of the cervical spine; (3) large aortic aneurysms; and (4) pharyngeal diverticula or strictures.

CYTOLOGY

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The high degree of accuracy with which esophageal neoplasia may be diagnosed has made exfoliative cytology one of the more useful procedures employed in the diagnosis of esophageal lesions. In the hands of experts, a positive cytologic diagnosis may be made in over 90 percent of patients having a carcinoma of the esophagus, while false-positive diagnoses are under 1 percent. Not unexpectedly, the accuracy of the procedure is directly related to the skill of both the cytologist and the person obtaining the specimen. The specimen is obtained by centrifugation of material acquired either by lavage or by direct brushing of a lesion. These procedures may be done either during endoscopy or by radiologic localization of a tube at the appropriate area. There are no contraindications to or complications from exfoliative cytology itself—only those of the associated endoscopy or intraluminal tube.