The Little GI Book

An Easily Digestible Guide to Understanding Gastroenterology

Douglas G. Adler

SLACK INCORPORATED

The Little GI Book

An Easily
Digestible Guide
to Understanding
Gastroenterology

The Little GI Book

An Easily Digestible Guide to Understanding Gastroenterology

Douglas G. Adler, MD, FACG, AGAF, FASGE
Associate Professor of Medicine
Director of Therapeutic Endoscopy
University of Utah School of Medicine
Salt Lake City, Utah

SLACK INCORPORATED

www.Healio.com/books

ISBN: 978-1-61711-072-6

Illustrations done by Jeff Moore.

Dr. Douglas G. Adler has no financial or proprietary interest in the materials presented herein.

The procedures and practices described in this publication should be implemented in a manner consistent with the professional standards set for the circumstances that apply in each specific situation. Every effort has been made to confirm the accuracy of the information presented and to correctly relate generally accepted practices. The authors, editors, and publisher cannot accept responsibility for errors or exclusions or for the outcome of the material presented herein. There is no expressed or implied warranty of this book or information imparted by it. Care has been taken to ensure that drug selection and dosages are in accordance with currently accepted/recommended practice. Off-label uses of drugs may be discussed. Due to continuing research, changes in government policy and regulations, and various effects of drug reactions and interactions, it is recommended that the reader carefully review all materials and literature provided for each drug, especially those that are new or not frequently used. Some drugs or devices in this publication have clearance for use in a restricted research setting by the Food and Drug and Administration or FDA. Each professional should determine the FDA status of any drug or device prior to use in their practice.

Any review or mention of specific companies or products is not intended as an endorsement by the author or publisher.

SLACK Incorporated uses a review process to evaluate submitted material. Prior to publication, educators or clinicians provide important feedback on the content that we publish. We welcome feedback on this work.

Published by: SLACK Incorporated
6900 Grove Road
Thorofare, NJ 08086 USA
Telephone: 856-848-1000
Fax: 856-848-6091
www.Healio.com/books

Contact SLACK Incorporated for more information about other books in this field or about the availability of our books from distributors outside the United States.

Library of Congress Cataloging-in-Publication Data

Adler, Douglas G., 1969- author.
The little GI book : an easily digestible guide to understanding gastroenterology / Douglas G. Adler.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-61711-072-6 (alk. paper)
I. Title.
[DNLM: 1. Gastrointestinal Diseases--therapy. 2. Gastrointestinal Diseases--diagnosis. WI 140]
RC801
616.3'3--dc23

2013008247

Dedication

For my mother, and all that she does.

Contents

Acknowledgments

As always, I am deeply indebted to my wife and children for all of their love and support. I would also like to thank Carrie Kotlar, John Bond, and Ryan Brophy from SLACK Incorporated for their enthusiasm and assistance with this project.

About the Author

Douglas G. Adler, MD, FACG, AGAF, FASGE received his medical degree from Cornell University Medical College in New York, NY. He completed his residency in internal medicine at Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA. Dr. Adler completed both a general GI fellowship and a therapeutic endoscopy/ERCP fellowship at the Mayo Clinic in Rochester, MN. He then returned to the Beth Israel Deaconess Medical Center for a fellowship in endoscopic ultrasound. Dr. Adler is currently an Associate Professor of Medicine and Director of Therapeutic Endoscopy at the University of Utah School of Medicine in Salt Lake City. Working primarily at the University of Utah School of Medicine's Huntsman Cancer Institute, Dr. Adler's clinical, educational, and research efforts focus on the diagnosis and management of patients with gastrointestinal cancers and complex gastrointestinal disease, with an emphasis on therapeutic endoscopy. He is the author of more than 200 scientific publications, articles, and book chapters and is editor of the previously published books, *Curbside Consultation in GI Cancers for the Gastroenterologist: 49 Clinical Questions* and *Self-Expanding Stents in Gastrointestinal Endoscopy*.

Preface

Gastroenterology is an exciting and fascinating field.

No, really, it is.

This statement may come as a shock to many people; most individuals don't think that their digestive tract is exciting in any way. In all honesty, they are correct (the blood and guts of blood and guts is not exactly party talk). Most of us who practice gastroenterology and related fields didn't go into this business for the glamour.

Nonetheless, I stand by my original statement. Modern gastroenterology has evolved from a diagnostic discipline into a field that allows its practitioners to perform some of the most innovative therapeutic interventions in all of medicine on a daily basis. Gastroenterology incorporates a tremendous range of benign and malignant illnesses, includes patients from the very young to the elderly, involves many organs (as opposed to some specialties that just focus on one organ), and allows those who practice it to treat and cure many maladies from the common to the obscure. We get to see and do amazing things all the time in this profession.

As you begin your study of gastroenterology, you will quickly find that there are many new concepts and terms to be absorbed in a rapid manner. Most of this can sound like incomprehensible jibber-jabber. People will hurl all manner of medical and surgical jargon your way and will assume that you understand exactly what they mean (when you may not understand them at all!). It can be overwhelming to try to wrap your brain around all of this, especially if you've never heard it before, and many questions will cross your mind. What's the difference between a subtotal colectomy and a total proctocolectomy? How are colon and rectal cancers different (or are they really not different at all)? How can you tell if a patient has cirrhosis? What do you do next if he or she

does have cirrhosis? If the patient is jaundiced, should you order an ultrasound, an MRI scan, or an ERCP (and what the heck is an ERCP, anyway?)?

This is not a 1000-page, hardcover textbook of gastroenterology. In this book, which you can easily toss into your backpack or carry in the pocket of your white coat, I have attempted to provide the reader with a sort of "field guide" to gastroenterology. You should feel free to dog-ear the corners of the pages and highlight key passages as you see fit. Using an organ-based approach, we start at the top (the esophagus) and work our way down through the entire gastrointestinal tract to the very end (the colon and rectum). Don't be fooled: despite the small size of this book, there's a lot of valuable information here. I've worked hard to emphasize key concepts across all of gastroenterology for you. The chapters are designed to be easy to read, giving you a straightforward and practical understanding of gastrointestinal anatomy, physiology, disease states, and treatment. I have also included a wide range of images and figures to reinforce many of the core concepts in the text.

I wrote this book for a wide audience—medical assistants, nursing students, nurses and nurse practitioners, physicians' assistants, medical students, residents in medicine and surgery, and anybody else who wants a solid foundation for learning about gastroenterology will benefit from this book.

I hope that it is the first of many gastroenterology books you delve into during your career.

Douglas G. Adler, MD, FACG, AGAF, FASGE
Salt Lake City, Utah

Chapter 1

Esophagus

Basic Esophageal Anatomy and Physiology

Most people think the esophagus is simply a tube to carry food from the mouth to the stomach and never give it a second thought. In fact, the esophagus is a complex organ that performs a variety of functions, all of which we rely on to get us through each and every meal, drink, snack, and overindulgence.

The esophagus begins just below the upper esophageal sphincter, extends down through the chest, and ends at the level of the lower esophageal sphincter (LES), beyond which lies the stomach. Like all hollow gastrointestinal organs, the esophagus is composed of many layers and is

Adler DG. *The Little GI Book: An Easily Digestible Guide to Understanding Gastroenterology (pp 1-32).*

not just a cylindrical piece of meat. The innermost lining of the esophagus is referred to as the *mucosa*. Below the mucosa lies the submucosa, and below that lies the muscularis propria, which allows the esophagus to contract. Beyond the muscularis propria lies the adventitia, which forms the outer coating of the organ.

The muscle in the esophagus is different at the top than it is at the bottom of the esophagus, and this is worth a few words of discussion. The muscle at the top is striated muscle, and the muscle at the bottom of the esophagus is smooth muscle. The muscle in the middle of the esophagus is somewhere between striated and smooth—a transition between the two. This is important because we can control striated muscle voluntarily but we cannot control smooth muscle. What this really means is that we can initiate a swallow, but once the swallow starts, it proceeds automatically without conscious control. In other words, you cannot consciously stop a swallow once it is started.

When you are at rest, the esophageal sphincter, for the most part, stays closed (so that food and other unpleasant things do not come up out of your stomach and into your mouth!), and the esophagus does not contract. Between meals, you swallow saliva from time to time. Occasionally, the sphincters will have brief episodes of relaxation, and this is important for certain diseases like gastroesophageal reflux disease (GERD), which we will cover a little later.

During a normal, healthy swallow, the upper esophageal sphincter relaxes and food moves into the top of the esophagus (propelled by the tongue and the pharynx). The esophageal muscles contract in a coordinated and stepwise manner to push the food down through the esophagus toward the stomach. When the food gets to the bottom of the esophagus, the LES relaxes on schedule, and the food passes through into the stomach, where digestion can begin. Most of us swallow hundreds

of times a day and never give it a second thought; the system works extremely well most of the time. When the system doesn't work well (ie, if the esophagus is diseased or there is a problem swallowing), people tend to notice it immediately. As a general rule, people with swallowing problems are said to have dysphagia.

Dysphagia

Dysphagia can be caused by either mechanical problems (a tumor blocking the esophagus stricture, scar tissue, etc), motility problems (ie, something is either wrong with the way the esophagus is contracting or with how the sphincters are functioning, and food is not being moved forward the way it should), or a combination of both.

Mechanical problems are, as a rule, easy to identify, although they may not be easy to treat. People with mechanical problems as a cause of their dysphagia tend to have more difficulty swallowing solids as opposed to liquids. This is because a chunk of meat will most likely get stuck, but a sip of juice can get through a narrow or partially blocked esophagus. Most people with mechanical problems will present to a gastroenterologist for evaluation at some point because solid food dysphagia is a very concerning symptom. Some of the most common mechanical problems that lead to dysphagia include esophageal cancer (which can occur anywhere in the esophagus), rings that can narrow the esophageal lumen (often referred to as *Schatzki rings*), webs (which can block the esophagus), scar tissue from prior surgery, and inflammatory strictures from GERD. In some cases, the esophagus itself may be completely normal but it is being compressed by an abnormal structure that is just next to it, such as a tumor in the lungs (imagine a foot stepping on a garden hose—there is nothing wrong with the hose

itself except for the foot that is squashing it). Last, sometimes, people have pockets in their esophageal walls that can trap food and make it hard to swallow. These pockets are usually referred to as *diverticula*.

Motility problems, in contrast, usually result in people having trouble swallowing both solids and liquids. In some patients with motility troubles, the esophagus looks normal when viewed via endoscopy but just doesn't work (contract) properly. Sometimes the problem can be with esophageal peristalsis; other times, the sphincters don't work right; and sometimes both peristalsis and sphincter function are impaired. The upshot is that you need both a working esophagus and working sphincters to have a normal swallow.

The classic esophageal motility problem, and the one you are most likely to be asked questions about, is known as *achalasia*. Achalasia combines an LES that doesn't relax (even during a swallow when there is food in the esophagus) with a noncontractile, aperistaltic esophagus. This is really a double whammy—when people with achalasia swallow, the food goes into an esophagus that cannot contract and move it forward properly. When the food finally gets down to the distal esophagus, the sphincter doesn't relax to let the food into the stomach. People with achalasia have severe swallowing difficulties; they trap food in their esophagus where it goes bad (and smells terrible) and are at high risk for developing a type of esophageal cancer known as *squamous cell cancer* as a consequence of the disease. The exact cause of achalasia is unclear, but in some cases, it may be related to a type of parasitic infection known as *Chagas disease* (from the parasite *Trypanosoma cruzi*). Treatments for achalasia include a surgical myotomy (to physically cut the LES muscle so that it can stay open) performed with or without a fundoplication (where the top of the stomach is wrapped around itself to prevent acid reflux), injection of the neurotoxin/acetylcholine blocker known as

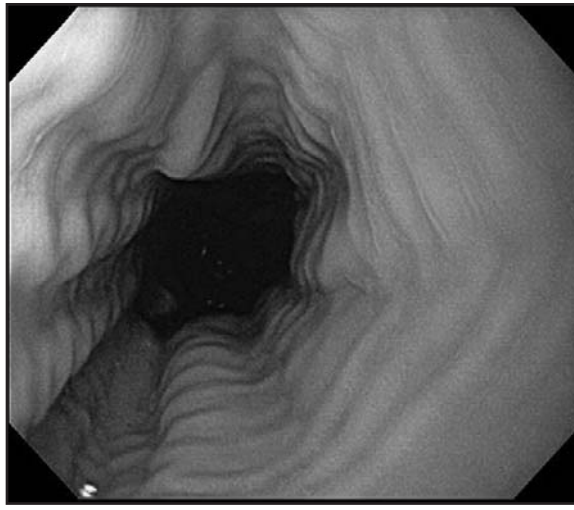

Figure 1-1. Endoscopic image of a patient with dysphagia and eosinophilic esophagitis. Note the ringed appearance of the esophagus, the linear furrows, and the narrowed lumen.

botulinum toxin (Botox) into the LES (again so that it stays open), or dilation of the LES with very large balloons to stretch and partially tear muscle fibers in the LES (so that it stays open) so that food can get into the stomach.

Another common motility problem that you may encounter is referred to as *eosinophilic esophagitis*. Eosinophilic esophagitis is a very common cause of dysphagia and is often seen in young people. People with eosinophilic esophagitis have an esophagus that looks normal or may have a ringed appearance (like a cat's esophagus). These patients may have an esophagus with deep furrows or white plaques on the surface as well (Figure 1-1). When biopsied, the esophagus of a patient with eosinophilic esophagitis is rich in a kind of

white blood cell called eosinophils (which often mediate allergic reactions). Patients with eosinophilic esophagitis often have a history of asthma, eczema, food allergies, and related problems. Eosinophilic esophagitis may also be related to acid reflux. Treatments for eosinophilic esophagitis usually include acid blockers (proton pump inhibitors [PPIs]), swallowed steroids, or other medications to decrease the number of eosinophils in the esophageal wall. Most patients respond well to medical therapy. You should think about eosinophilic esophagitis if you see a young person coming to the hospital for a food impaction (food, usually meat, stuck in his or her throat that has to be removed with an endoscope). These patients often have a narrow caliber esophagus that is prone to trapping foods and can be easily traumatized with an endoscope during endoscopy.

Other esophageal motility problems that cause dysphagia include scleroderma (also sometimes referred to as *progressive systemic sclerosis*), where patients have poor esophageal contractility combined with an LES that stays open all the time and they develop chronic acid reflux that scars the esophagus, and spastic disorders of the esophagus, such as diffuse esophageal spasm and/or nutcracker esophagus. These last two disorders can produce severe pain as well as dysphagia. These diseases are often treated with PPIs, nitrates, and calcium channel blockers, but it can be very difficult to control these symptoms.

Gastroesophageal Reflux Disease

Pathophysiology

Gastroesophageal reflux disease, also known as *GERD*, represents one of the most common indications for a patient to be evaluated by a gastroenterologist. If you are reading this as a young person and have never

experienced reflux or heartburn symptoms, you may wonder why there are so many television commercials for antireflux medications. If you are reading this and you are over 30 years old, you have very likely experienced reflux and/or heartburn at least once and know that the pain from this condition can be severe, can be extremely uncomfortable, and can last for hours at a time.

GERD is somewhat difficult to define, but a definition that most would agree on involves the reflux of gastric contents (that includes stomach acids as well as other substances, such as bile from the intestines and/or food) into the esophagus with the production of associated reflux symptoms, such as chest pain, heartburn, regurgitation, nausea, dysphagia, globus (a sensation of fullness in the neck), and water brash (hyper-salivation), among others. Typical heartburn pain is retrosternal and is often severe. Patients may have difficulty concentrating, eating, or sleeping due to heartburn pain.

GERD can develop for a variety of reasons. Transient LES relaxations are thought to be the most common mechanism causing GERD in patients with normal LES resting pressures. Many patients also develop a hypotensive LES that serves as an inadequate barrier to keep gastric contents out of the esophagus. A variety of conditions, foods, and medications can lead to a hypotensive LES. Alcohol, caffeine, peppermint, and chocolate are among the most common causes of a hypotensive LES. It is often *very difficult* to convince patients to stop eating these foods, even if they are having significant symptoms of heartburn or reflux. (Would you want to stop eating chocolate or drinking alcohol if a doctor told you to?)

Gastric distention, commonly seen after eating a large meal, is associated with a hypotensive LES as well. The presence of a hiatal hernia, a condition where some of the acid-producing stomach slips through the diaphragm and into the chest, is also a common etiology for a hypotensive LES. Obesity is also associated with

a hypotensive LES. Many patients, unfortunately, have a variety of potential etiologies simultaneously (ie, a 55-year-old obese woman with a large hiatal hernia who drinks 4 cups of coffee per day is very likely to experience heartburn symptoms).

Beyond being painful and uncomfortable, GERD is a particular cause of concern as it is a commonly recognized cause of a condition known as *Barrett's esophagus*. Barrett's esophagus involves the transition of the normal squamous mucosal lining of the distal esophagus into columnar cells (making the esophagus in some ways mimic the appearance of the small bowel when viewed under a microscope). Patients with Barrett's esophagus are at increased risk of developing esophageal adenocarcinoma during their lifetime; thus, the presence of reflux is directly related to the development of esophageal cancer in many patients. We'll discuss Barrett's esophagus in more detail a little later on.

It's worth noting that we do have some defenses against GERD. Saliva contains significant amounts of the alkali bicarbonate, which can help to neutralize gastric acid that makes it into the esophagus. A healthy LES prevents most acid and gastric contents from spilling back into the esophagus as well. In addition, an upright posture promotes the flow of any refluxed contents back down into the stomach. Thus, patients with decreased saliva production (smokers) are at increased risk for developing reflux, and many patients develop nocturnal reflux when lying flat in bed.

Diagnosis

Many patients will correctly diagnose themselves with esophageal reflux based on symptoms. If a formal diagnosis of reflux (with or without esophagitis) is desired, this can be achieved via several means. The most common way that we diagnose patients with reflux is by directly visualizing an inflamed and/or ulcerated distal

esophagus during an upper endoscopy (esophagogastroduodenoscopy). Reflux esophagitis can have a range of appearances that most gastroenterologists should be very comfortable identifying. These can include mild redness (erythema) in the distal esophagus, superficial ulcers, deep ulcers, frank bleeding, and acid-related esophageal strictures. Patients can have one or more of these features simultaneously. Some patients have a normal upper endoscopy in the setting of reflux or heartburn symptoms. These patients may have what is known as *nonerosive reflux disease* (NERD).

I should also point out that esophagitis can come from other causes besides GERD, so think of other possible etiologies when you see a patient with esophagitis. Fungal infections (usually from *Candida* species), viral infections (herpes simplex virus and cytomegalovirus), and medications (bisphosphonates, tetracycline, etc) can lead to esophagitis as well. Patients undergoing radiation therapy (for esophageal cancer, lung cancer, or other malignancies) can develop radiation esophagitis. Radiation esophagitis can be severe and can lead to chronic strictures of the esophagus that can be very difficult to treat. Pill esophagitis can occur when a medication in pill form that is itself caustic lodges in the esophagus and causes a direct chemical burn (Figure 1-2).

If endoscopy cannot be performed or is unrevealing and a diagnosis of reflux is still suspected, patients can undergo ambulatory esophageal pH monitoring. This can be performed using either a nasal esophageal catheter (which patients tend to dislike) or a wireless device that can be clipped into the distal esophagus (which is more comfortable but requires endoscopy to place). Both devices work equally well and can record the esophageal exposure to acid over a protracted period of time. In general, esophageal pH monitoring is performed for at least 24 hours, although sometimes longer studies are needed. Episodes of acid exposure may not directly correlate to symptoms of reflux or heartburn, of note.

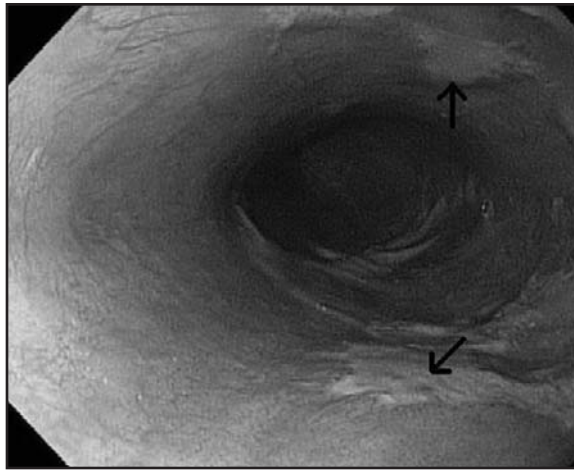

Figure 1-2. Endoscopic image of pill esophagitis in a patient taking tetracycline. There are focal "kissing" ulcers on opposite walls of the esophagus (arrows) from the edges of the pill itself.

Esophageal manometry is a helpful test in patients in whom reflux (or dysphagia for that matter) is suspected to arise from an abnormal esophageal motility disorder. In this test, a catheter is placed into the esophagus that can measure upper and lower esophageal sphincter pressure as well as peristaltic contractions. Conditions associated with reflux, such as scleroderma, can easily be diagnosed via esophageal manometry. Other tests that can sometimes be used to diagnose acid reflux include the Bernstein test, which involves instilling acid into the patient's esophagus to see if it replicates his or her reflux symptoms (I promise I'm not making that one up!), or an x-ray study where the patient drinks contrast material and the radiologist looks to see if the contrast material flows back into the esophagus after it reaches the stomach. These last two tests are uncommonly used in the modern era.

Medical Treatment of GERD

Most patients with symptomatic acid reflux respond well to treatment. Before prescribing medications, it's always a good idea to see if the patient can respond to nonpharmacologic therapy in the form of lifestyle modifications. Some lifestyle modifications that we typically recommend that patients try include stopping the consumption of trigger foods (caffeine, chocolate, etc) and/or alcohol (a relatively unpopular suggestion), weight loss, avoiding wearing tight clothing or tight pants, avoiding eating within several hours of going to sleep to allow the stomach to empty, chewing gum to promote salivation, stopping smoking, and elevating the head of the bed 6 to 8 inches to reduce nocturnal reflux events.

While all of these lifestyle modifications are known to be highly effective in treating patients with symptomatic acid reflux, they are, in practice, poorly received by patients, and medical therapy is generally required. It is often extremely difficult to modify behaviors that may have been present for decades, and simply telling patients to change their lifestyle often has no impact on their actual behavior. Patients will often readily agree to change their lifestyle when confronted by an earnest physician wearing a white coat with a stethoscope around his or her neck, but the minute they return to their natural habitat, old habits generally resume.

Antacids are the oldest and least expensive medications available to treat acid reflux. These drugs are inexpensive, available over the counter, and safe during pregnancy (for the most part); can help heal gastric and esophageal ulcers; and work well at preventing and controlling symptoms. Downsides to antacids include a relatively short duration of action and the need for frequent repeated doses.

H2 receptor antagonists (eg, cimetidine, ranitidine) represent a potent class of medications that block acid

secretion from the gastric parietal cell by blocking H2 histamine receptors. These agents are also available over the counter, inexpensive, and much more effective at treating symptoms and healing ulcers than simple antacids. These drugs are removed via hepatic and renal clearance and are relatively safe and well tolerated. Patients may develop tolerance to these drugs over time (known as *tachyphylaxis*) and may need drug holidays (a period of time where they have to stop taking the drug) to recover useful benefit from these agents.

PPIs work by reversibly binding to the hydrogen-potassium ATPase found on the luminal surface of gastric parietal cells. Many PPIs are approved for use in the United States: omeprazole/esomeprazole, lansoprazole/dexlansoprazole, rabeprazole, and pantoprazole. PPIs represent the most powerful antisecretory medications in widespread use around the world. Some PPIs are available via prescription only, and other PPIs are available over the counter. PPIs cost more than other antisecretory agents, but patients do not develop tolerance to them and they have a long duration of action (special long-acting PPIs are also available).

Other acid-blocking or antisecretory medications are available but are much less widely used than antacids, H2 blockers, and PPIs.

If the patient has typical symptoms in the presence of risk factors and the absence of alarm features in his or her history (bleeding, weight loss, dysphagia), it is not unreasonable to simply try an empiric trial of medication in an attempt to reduce or relieve symptoms. In addition, many patients desire or require medications alongside lifestyle modifications to reduce their reflux symptoms. Some physicians like to try a "step-up" protocol to treat acid reflux (ie, start lifestyle modifications, begin antacids or H2 receptor blockers, and use PPIs as the last resort). Others like to go right to PPI therapy to get the patient the maximal symptomatic relief in the shortest time, albeit with the highest cost (this is known as a *"top-down"*

approach). It's hard to say that one approach is better than the other, but if you experience reflux anytime soon, don't be surprised if you reach for a PPI before anything else because you are so miserable!

Other agents less commonly used to treat GERD include promotility agents, such as bethanechol and metoclopramide.

Barrett's Esophagus

Barrett's esophagus is an extremely common esophageal condition. It's hard for a gastroenterologist to go more than a few days without seeing a patient with Barrett's esophagus, and we talk about this disease all the time.

A normal, healthy esophagus is lined by a flat squamous epithelium. Patients with Barrett's esophagus, in contrast, have a distal esophagus that is lined with metaplastic columnar epithelium. This columnar epithelium has an atypical appearance that is usually easy to recognize endoscopically. The normal esophagus has a light, pale pink appearance. Barrett's esophagus, in contrast, has a richer salmon-colored appearance. Barrett's esophagus also often has "tongues" of mucosa that can reach quite proximally in the esophagus.

Barrett's esophagus is a big deal. Why is a change in the lining of the esophagus such a big deal? Simply put, Barrett's esophagus is a precancerous condition. Patients with Barrett's esophagus are at increased lifetime risk of developing esophageal adenocarcinoma, which is usually a fatal condition. These patients have about a 30-fold increased risk of developing esophageal adenocarcinoma during their lifetime (Figure 1-3). That having been said, most patients with Barrett's esophagus will never develop esophageal cancer, but when looked at as a special subset of patients, their risk of cancer is quite high.

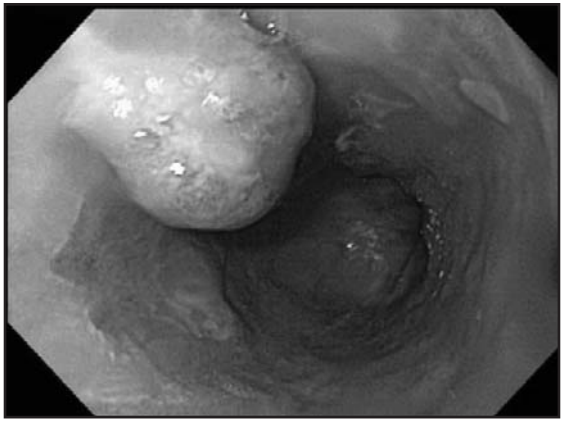

Figure 1-3. Early esophageal adenocarcinoma arising in a patient with Barrett's esophagus. Note the different appearance of the Barrett's mucosa in the distal esophagus.

Diagnosis

In general, two things are required to diagnose a patient with Barrett's esophagus. First, an appearance suggestive of Barrett's esophagus (salmon pink distal esophagus) must be detected by endoscopy. Second, a biopsy must be obtained showing intestinal metaplasia (the formal term for the columnar cell-lined esophagus seen in Barrett's esophagus). The biopsy is critical for several reasons: it allows histologic confirmation of the presence of Barrett's esophagus, and it also allows evaluation for any dysplasia and the severity of that dysplasia. Dysplasia specifically refers to precancerous change in the Barrett's esophagus itself. It's important to know if there is dysplastic change in the Barrett's esophagus when deciding on management (either medical or surgical) and surveillance regimens. Most of the time, a gastroenterologist can be reasonably sure that he or she is seeing Barrett's esophagus simply based on the appearance of

the esophagus, but we still biopsy anyway to be sure. Even experienced gastroenterologists can be wrong about the presence or absence of Barrett's esophagus based on appearance, and no matter how hard you try, you really can't see dysplasia with a standard endoscope; you need a pathologist to tell you whether it is present or absent and to what level of severity. Most gastroenterologists perform 4 quadrant biopsies every 2 cm for the entire length of the Barrett's esophagus to adequately sample tissue.

Long- and Short-Segment Barrett's Esophagus

The squamocolumnar junction (known as the *z-line*) occurs at the bottom of the tubular esophagus. The gastroesophageal junction (GEJ) also occurs in the distal esophagus and marks where the esophagus ends and the proximal stomach begins. In a normal healthy patient, the squamocolumnar junction and the GEJ coincide (ie, the entire esophagus is lined by squamous epithelium). In patients with Barrett's esophagus, the squamocolumnar junction is proximal to the GEJ. If the squamocolumnar junction is less than 3 cm above the GEJ and the patient has Barrett's esophagus confirmed by biopsy, this is considered to be *short-segment* Barrett's esophagus. If the squamocolumnar junction is more than 3 cm above the GEJ in a patient with Barrett's esophagus confirmed on biopsy, this is considered to be *long-segment* Barrett's esophagus. This distinction is important: patients with short-segment Barrett's esophagus may have less severe GERD or may have no GERD symptoms at all. Patients with long-segment Barrett's esophagus tend to have more severe GERD symptoms, including proximal esophageal acid exposure and nocturnal symptoms. Of greater importance, dysplasia and esophageal adenocarcinoma are much more common in patients with long-segment Barrett's esophagus when compared to short-segment Barrett's esophagus.

Management

Management of patients with Barrett's esophagus generally runs along 3 separate lines: surveillance, ablation or resection of the Barrett's mucosa, and acid suppression.

Once the presence of Barrett's esophagus is established, all patients with the disease should undergo endoscopic surveillance with biopsies periodically. Most people use the guidelines on surveillance of Barrett's esophagus published by the American College of Gastroenterology. For patients with Barrett's esophagus and no dysplasia seen on two separate endoscopies within 1 year, follow-up endoscopy should be performed every 3 years, as long as no dysplasia is detected. Patients with low-grade dysplasia should have a repeat endoscopy within 6 months and then annually thereafter unless more worrisome findings are detected. Patients with high-grade dysplasia (the last stop on the train before it pulls into "Cancer Station") confirmed by an expert pathologist have several options. One option is to undergo frequent surveillance by endoscopy with biopsies every 3 months unless cancer is detected. Another option would include referring the patient to a surgeon for a formal esophagectomy. A third option would be to undergo endoscopic treatment for the high-grade dysplasia in an attempt to eradicate it.

It's worth noting here that an esophagectomy is a major undertaking. An esophagectomy involves removal of almost the entire esophagus and having the stomach pulled up vertically into the chest (where it is sewn into the very top of the remnant esophagus) to create a conduit for food to go from the mouth into the digestive system. An esophagectomy is one of the most complex, invasive, and unpleasant surgeries for a patient to undergo. Patients who are operated on by very experienced surgeons may still develop complications that can be severe, such as strictures at the site where the top of the esophagus is sewn onto the stomach. Many

patients with Barrett's esophagus are elderly with other significant medical problems and may not be ideal candidates for surgery, especially major surgery. Given these facts, it might seem unlikely that anybody would choose esophagectomy in the setting of Barrett's esophagus with high-grade dysplasia, but in practice, some patients do select this option. People sometimes pick to undergo an esophagectomy because we know that high-grade dysplasia in a patient with Barrett's esophagus does not rule out the presence of a synchronous (ie, simultaneous) esophageal cancer, perhaps at a site in the Barrett's mucosa that was not sampled on recent biopsies. Our standard regimen of 4 quadrant biopsies every 2 cm per surveillance endoscopy is a good idea, but it is far from perfect, and if the patient is young and healthy enough to undergo esophagectomy, this is the most definitive answer to avoid esophageal cancer.

Endoscopic techniques to treat patients with Barrett's esophagus and high-grade dysplasia all use destructive methods to eliminate the Barrett's mucosa. Currently available endoscopic techniques involve the use of radio waves (radiofrequency ablation), heat (argon plasma coagulation), cold (cryotherapy), or destructive drugs that are activated by specific wavelengths of light delivered by a laser catheter (photodynamic therapy). Radiofrequency ablation is currently the most widely employed technique. These approaches all work to varying extents, but each carries its own procedure-related risks, including the risk of inadequate treatment with persistence of precancerous or frankly cancerous tissue in the Barrett's mucosa. If patients have nodules in the setting of their Barrett's esophagus, these are especially worrisome and are removed separately, but with other endoscopic techniques such as endoscopic mucosal resection (EMR). EMR comes with risks such as perforation and bleeding, but it can be done safely by experienced endoscopists.

Last, we always want to treat the underlying problem in patients with Barrett's esophagus and GERD. All patients with Barrett's esophagus should be placed on an aggressive antacid regimen of PPIs, almost always used in a twice-a-day formulation. The use of aggressive acid suppression probably has several benefits. First, it may promote regression of Barrett's esophagus with restoration of the normal squamous epithelium. Second, it may slow or prevent progression of Barrett's esophagus either in size (ie, the amount of esophagus involved) or in regard to the presence or severity of dysplasia. Third, it helps to control symptoms of GERD, which is very important to the patient. It may be worth considering a fundoplication as well because many patients with Barrett's esophagus have an underlying hiatal hernia, but this is not universally agreed on.

Esophageal Varices

Overview

Esophageal varices, simply put, represent dilated esophageal veins that put patients at high risk of gastrointestinal bleeding. Patients with esophageal varices almost always have underlying portal hypertension, usually in the context of cirrhosis. Cirrhosis of any kind can lead to portal hypertension, and portal hypertension from any cause can lead to varices. We'll cover esophageal varices in other chapters of this book as well, but it seems prudent to first discuss them here in the esophageal section so you can see them in the context of other diseases of the esophagus.

Pathophysiology

The portal vein is a large venous structure that runs through the liver. Patients with cirrhosis often develop

outflow obstruction of the portal vein to varying degrees. When the pressure gradient between the portal vein and the hepatic veins gets too high (usually >12 mm Hg), backflow in the venous system causes veins in the esophageal wall, which are usually collapsed, to distend with blood. These distended veins are then referred to as *varices*. Because these veins are not typically supposed to have flow in them, and because patients with underlying liver disease often have a tendency toward bleeding, it is very common for these patients to develop variceal hemorrhage at some point in their lives. All patients with cirrhosis are typically screened periodically for esophageal varices, and those who are found to have them undergo treatment to try to eradicate the varices before they can bleed. If a patient develops a variceal bleed and was not known to have varices before this event, the varices can still be treated by a variety of methods. Variceal hemorrhage is often sudden in onset as well as severe and life-threatening, so a great deal of energy is put into avoiding variceal bleeds when at all possible.

Endoscopic Evaluation

Most patients with known or suspected cirrhosis undergo periodic endoscopic evaluation to look for the presence or absence of varices (Figure 1-4). If varices are present, the gastroenterologist will evaluate them for their size (larger varices are more likely to bleed than smaller varices) and for other signs that suggest the varices are at high risk for bleeding. High-risk signs that can be seen during an endoscopic examination include the red wale sign (red lines on the surface of the varices), red spots, signs of recent hemorrhage like fresh or old blood in the esophagus, fibrin plugs on the varices, and tortuosity to the overall shape of the esophageal varices. Varices that flatten with air insufflation into the esophagus are at lower risk for bleeding than varices that do not collapse. It's also important to take into account things such as the

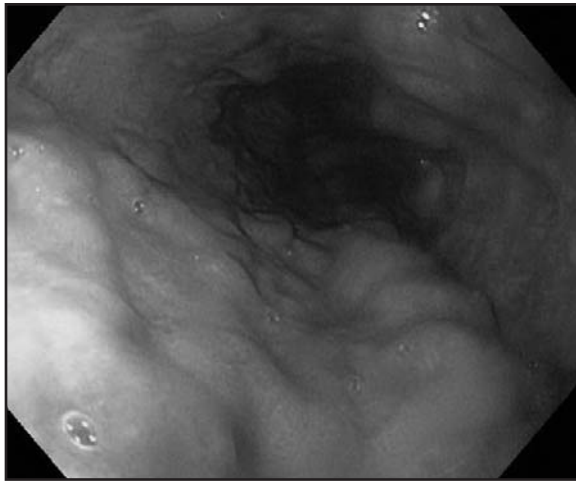

Figure 1-4. Endoscopic image of esophageal varices bulging into the esophageal lumen.

severity of the underlying cirrhosis, any history of variceal bleeding, and other factors when deciding how likely a patient is to experience a variceal bleed in the future.

Primary Prevention of Esophageal Variceal Bleeding Using Medications

If the patient is found to have esophageal varices and is at risk for variceal hemorrhage, steps to avoid the occurrence of a gastrointestinal bleed are warranted.

The first line of treatment to prevent a first episode of variceal bleeding in patients with portal hypertension is the use of nonselective beta-blockers. These agents work by decreasing portal venous flow and can help decompress esophageal varices. Several nonselective beta-blockers are currently available in the United States, with propranolol and nadolol being the two most commonly used. These drugs can cause a significant

reduction in the risk of a first episode of esophageal variceal bleeding. These drugs also decrease the patient's heart rate and are typically titrated to the point where the patient's heart rate is between 55 and 60 bpm. Giving more drug above this level may result in the patient developing an unacceptably low heart rate, which can lead to other complications, such as episodes of syncope (fainting). Other agents are used as primary prevention of esophageal variceal bleeding (either alone or in combination with other drugs), but none are as widely used as the nonselective beta-blockers.

Endoscopic Therapy for Esophageal Varices

Several endoscopic techniques are used to treat esophageal varices. These techniques can be used as primary prevention (in patients who have never bled) or as a secondary treatment (in patients who have recently bled or who are actively bleeding).

Endoscopic band ligation represents the most widely used technique to treat esophageal varices in any situation. The technique is remarkably simple: a cap is fitted to the end of the endoscope, and the endoscope is advanced into the esophagus. When varices are identified, they are sucked into the cap on the tip of the endoscope, and what is essentially a very small and very strong rubber band is deployed around the varix. This rubber band cuts off all blood flow in the varix and also produces inflammation and thrombosis. Once banded, the varix itself will typically scar down, and the band will slough off at a later date. In contrast to early band ligators, which could only deploy one band at a time, modern endoscopic band ligators can deploy multiple bands without having to be removed from the patient. It's not uncommon to deploy 5 to 10 bands in a single procedure in a patient with multiple esophageal variceal trunks, often using multiple bands on the same variceal trunk at different distances from the incisors (Figure 1-5).

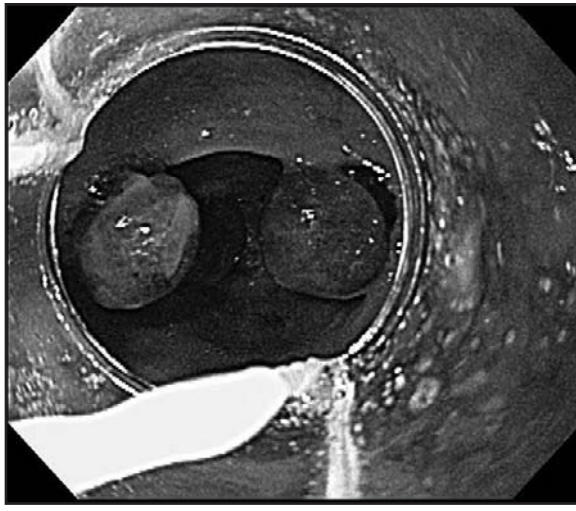

Figure 1-5. Two banded esophageal varices viewed endoscopically through a cap fitted to the end of an endoscope.

Endoscopic band ligation can be used in patients who have never bled (but who have high-risk stigmata as described above) as well as patients with a history of past or active bleeding; the technique used is exactly the same. Once patients have had bands deployed, they generally need periodic re-examination to ensure complete eradication of all their esophageal varices. Patients who have had multiple episodes of banding of their varices often have an esophagus full of stellate scars, each one showing the location of a previously deployed band.

As fair warning to the reader, I should probably let you know that esophageal variceal banding can be quite painful for the patient. It is not uncommon to see patients grimacing and rubbing their hand over their chest in the recovery room following the procedure. This is not really

surprising given the nature of the procedure overall. Most patients who undergo esophageal variceal banding will request some sort of pain medication to control the pain. The pain usually lasts for several days and then fades away. After esophageal banding is performed, it is generally a good idea to place patients on a liquid diet for a day or two as their swallowing may be impaired by the presence of all the banded varices in the esophagus. Once in a blue moon, you will read or hear about a patient who developed esophageal obstruction following banding of esophageal varices, but this is a very rare event.

Another treatment for esophageal varices about which you should be aware is known as *sclerotherapy*. Sclerotherapy involves injecting sclerosing agents into the varices to promote inflammation and clot formation as well as scarring. A variety of sclerosing agents are commercially available. For many years, sclerotherapy was the gold standard approach to the endoscopic treatment of esophageal varices, but, given the rise of endoscopic band ligation over the past 25 years, sclerotherapy is much less commonly used. Most physicians use sclerotherapy when endoscopic band ligation has been attempted and is unsuccessful in treating a patient with active variceal bleeding. The sclerosing agents used in sclerotherapy are also quite toxic and have to be handled with extreme care. Exposure of these agents to the eye, for example, can result in serious injury.

If endoscopic therapy with bands or sclerotherapy fails to treat a patient with active variceal hemorrhage, other techniques can be used in an attempt to save the patient's life, such as the creation of a decompressing portosystemic shunt (which is performed by interventional radiologists and not gastroenterologists). Another option is the use of an esophageal balloon to compress and tamponade the varices (known as a *Blakemore tube* or a *Sengstaken-Blakemore tube* if there is an additional balloon to compress gastric varices).

Esophageal Cancer

The term *esophageal cancer* refers to tumors of the esophagus that arise from its most superficial lining, the mucosa. The overwhelming majority of esophageal cancers are either squamous cell cancers or adenocarcinomas. Historically, squamous cell cancers were very commonly seen, and adenocarcinomas were rare entities. This trend has reversed over the past several decades, with a significant rise in the incidence of esophageal adenocarcinoma. Currently, esophageal adenocarcinomas outnumber squamous cell carcinomas. Esophageal squamous cell cancers typically develop in the upper and middle portions of the esophagus, while adenocarcinomas almost always involve the distal esophagus. Tumors that involve the distal esophagus and the proximal stomach are often referred to as *junctional tumors* because they span the esophagogastric junction. These tumors are also virtually always adenocarcinomas.

Etiology

The main risk factors for esophageal squamous cell cancer include tobacco use, alcohol consumption, prior head and neck cancer, lye ingestion, and achalasia. Lye, typically found in over-the-counter household cleaning products, is often ingested during suicide attempts. Lye ingestion typically leads to severe inflammation and stricture formation in the esophagus, and can give rise to squamous cell cancer many years later.

The number one risk factor for the development of esophageal adenocarcinoma is Barrett's esophagus. GERD is commonly associated with Barrett's esophagus, as we discussed previously, and GERD itself is independently linked to the development of esophageal adenocarcinoma. Obesity is also an independent risk factor for esophageal adenocarcinoma, probably because obese

patients are at increased risk for GERD and, in turn, Barrett's esophagus.

A prior history of esophageal cancer is also a risk factor for the future development of esophageal cancer. Patients who undergo an esophagectomy can still develop recurrent esophageal cancer, most notably adenocarcinoma.

Clinical Presentation and Pretreatment Evaluation

A few lucky patients have their esophageal cancers discovered incidentally during upper endoscopy either for unrelated causes or during the surveillance of Barrett's esophagus. Patients with early-stage esophageal cancer can often undergo endoscopic removal of the tumor or an esophagectomy with a very high chance of complete curative resection.

Unfortunately, most patients with esophageal cancer present with relatively advanced disease (Figure 1-6). The reason that most patients present with late-stage disease is that most early tumors are asymptomatic. Surprisingly, patients can have a relatively large esophageal lesion and still not develop dysphagia (hence the common delay in diagnosis of these cancers). The presence of dysphagia to solid foods, weight loss, episodes of food impaction, and other alarming features typically drives patients to see their physicians, which ultimately leads to some sort of imaging study or endoscopy that discloses the presence of the tumor. Historically, esophageal cancers were typically diagnosed via barium swallow or other radiographic studies, but currently, the overwhelming majority of esophageal cancers are diagnosed during an upper endoscopy in which a biopsy is obtained.

Once a patient has been diagnosed with esophageal cancer of any type, the next best test to obtain is a computed tomography (CT) scan of the chest, abdomen, and pelvis to look for spread of the tumor to other organs. These satellite tumors are referred to as *metastases*. If the

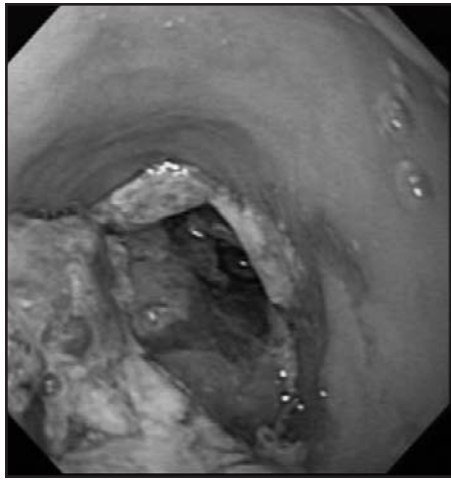

Figure 1-6. An obstructing esophageal cancer causing malignant dysphagia.

CT scan discloses metastatic disease, the patient has stage IV disease, and his or her disease is unresectable and, for all intents and purposes, incurable.

If the patient does not have evidence of spread to other organs on CT scanning, the patient should undergo an endoscopic ultrasound (EUS) examination. EUS refers to endoscopic examination with special endoscopes that not only have a light and a camera built into them, but an ultrasound transducer as well. EUS allows the endoscopist to not only see the tumor, but to see through the tumor and into the surrounding thoracic and abdominal structures (Figure 1-7). Regular endoscopes can only biopsy tissue that they can see directly. EUS scopes have the advantage of being able to biopsy tissue that cannot be seen endoscopically, but rather only on ultrasound. EUS scopes have the capacity to perform fine-needle aspiration through the esophageal wall and

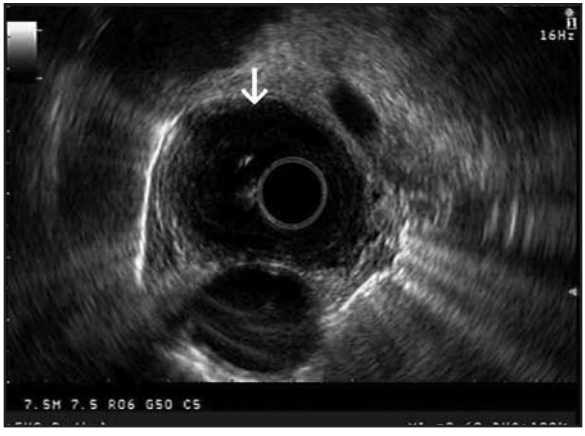

Figure 1-7. EUS image of the same patient in Figure 1-6. The esophageal cancer has obliterated all esophageal wall layers. The tumor is the irregularly shaped dark lesion (arrow) surrounding the endoscope that lies at the center of the screen. The dark circle at the bottom of the image is the aorta.

into suspicious peritumoral lymph nodes to definitively assess for the presence or absence of cancer in those lymph nodes.

We discussed earlier that the esophageal wall is made up of many layers. Esophageal cancer staging is dependent on the assessment of what layers of the esophageal wall the tumor has invaded. Tumors that only invade the mucosa and the submucosa are potentially removable by endoscopic techniques only, such as EMR. Tumors that are too big to be removed endoscopically but still only invade the mucosa and the submucosa can be removed by proceeding directly to surgery in the form of esophagectomy. Tumors that invade the deeper layers of the esophagus, such as the muscularis propria or the adventitia, or tumors of any depth of invasion that

have associated malignant lymph nodes require additional treatments prior to surgery, known as *neoadjuvant therapy*.

Neoadjuvant Therapy and Subsequent Esophagectomy

Neoadjuvant therapy typically consists of a combination of chemotherapy and radiation therapy, delivered over the course of several months. Neoadjuvant therapy is administered to the patient by a medical oncologist and a radiation oncologist who deliver the chemotherapy and radiation therapy treatments, respectively. Neoadjuvant therapy can melt away lymph nodes, reduce tumor size and metabolic activity, and generally make patients better candidates for esophagectomy by decreasing their overall tumor burden. A small subset of patients will have a complete response to chemoradiation therapy alone (ie, they will have no detectable tumor when evaluated by endoscopy, CT scan, or other methods to look for cancer).

Many patients with esophageal cancer will ultimately proceed to esophagectomy. Esophagectomy should be performed by an experienced surgical oncologist, hopefully at a high-volume cancer center. As we mentioned earlier, the surgery is a major undertaking and is not without risks, even in the hands of an expert surgeon.

Endoscopic Treatments for Dysphagia in Esophageal Cancer

Most patients with esophageal cancer will develop dysphagia at some point during their disease. If the patient proceeds directly to surgery, usually no additional treatments for his or her dysphagia are needed as the tumor will simply be removed during the operation (unless he or she develops a postoperative stricture!). If the patient has unresectable disease and a large tumor

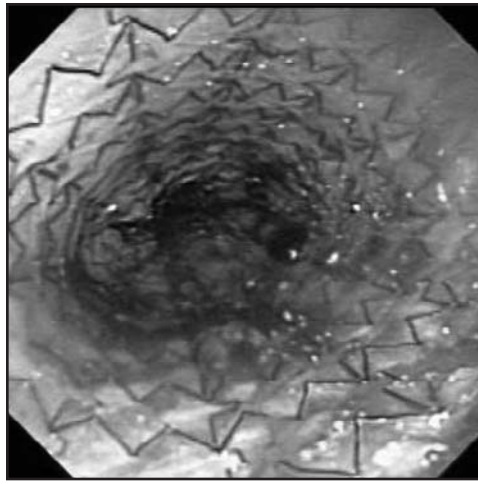

Figure 1-8. Same patient in Figure 1-6 following placement of an esophageal stent to relieve the obstruction.

that causes dysphagia or has a potentially resectable tumor but must undergo neoadjuvant therapy prior to surgery first, treatment for dysphagia is usually desired. Treating a patient's dysphagia has several benefits—it allows patients to take nutrition and hydration by mouth, and it also allows patients to take medications by mouth. In addition, most patients simply feel better when they can eat and drink without the fear of food becoming stuck in their esophagus.

The most common treatment for dysphagia in patients with preoperative or nonoperative esophageal cancer is a self-expanding stent (Figure 1-8). These stents can either be made of metal or plastic and are inserted endoscopically. The stents are supplied from their manufacturers on thin delivery catheters, and when placed across the

tumor and deployed in the esophagus, they shorten in terms of length and expand in terms of width. The stents hold the esophagus open and allow the patient to have improvement in his or her symptoms of dysphagia.

Esophageal stents are available in 2 varieties: fully covered or partially covered. Fully covered stents are constructed of a metal mesh or a plastic mesh coated with silicone or other thin plastic materials. Fully covered stents have the advantage of being potentially removable at some later date as their coating prevents them from permanently embedding into the surrounding esophageal wall. The drawback of these devices is that fully covered stents are more prone to migration as the coating reduces their ability to anchor their position in the esophagus. Partially coated stents (in which a portion of the metal mesh that makes up the stent is not coated and the bare wires of the stent are exposed) are generally used in patients with unresectable disease in whom there is no plan to ever remove the stent. It is very uncommon for a partially covered esophageal stent to migrate, as tumor tissue can grow through the uncovered portion of the stent, helping to anchor them into position.

Self-expanding stents are widely used to treat dysphagia from esophageal cancer. These devices also have a role in the treatment of benign strictures of the esophagus, as well as a variety of other difficulties. Some patients with esophageal cancer (or lung cancers that invade the esophagus) can develop a hole between their airway and the esophagus, known as a *tracheoesophageal fistula* (TEF). A TEF can be a medical emergency because whenever the patient tries to swallow, he or she can pass swallowed solids or liquids into his or her lungs. This can lead to shortness of breath, pneumonia, and other severe difficulties. Esophageal stents are often used to cover up the TEF and allow patients to swallow safely. Esophageal stents can also be used to cover up holes in the esophagus that occur spontaneously (Boerhaave's syndrome), from

iatrogenic causes (endoscopy with perforation of the esophagus), or from trauma in selected patients.

While stents can provide the patients with significant improvement in their level of dysphagia, it's important to remember that they are far from perfect devices. Esophageal stents typically don't allow patients to eat anything they want as soon as they are deployed. This is not surprising, as esophageal stents have no ability to produce peristaltic contractions like the normal esophagus does to help food move along and into the stomach. Most patients with an esophageal stent can return to a diet of soft foods and are usually able to drink any liquid without difficulty. Very few patients with an esophageal stent can eat a completely normal diet. In addition, the stents carry risks of complications, including pain, esophageal perforation, bleeding, and migration of the stent out of the esophagus and into the stomach (where it can no longer help treat the patient's dysphagia). Most patients tolerate stents well, but if complications arise, they can be serious.

Other endoscopic treatments for dysphagia include ablative techniques such as laser therapy or argon plasma coagulation that simply burn away obstructing esophageal tumor tissue. Cryotherapy can be used to freeze tumor tissue and destroy it. If patients are not felt to be candidates for stenting or do not want an esophageal stent, they can have a feeding tube placed. Feeding tubes allow medications, nutrition, and hydration to be delivered to the patient's digestive system, but they do not allow a return to eating by mouth. Nasogastric tubes (that go from the nose through the esophagus and into the stomach), gastrostomy tubes (that go through the abdominal wall and into the stomach), and jejunostomy tubes (that go through the abdominal wall and directly into the small bowel) are all commonly used in esophageal cancer patients. The selection of a particular type of tube is often individualized depending on the patient's overall situation.

Bibliography

Adler DG, Romero Y. Primary esophageal motility disorders. *Mayo Clin Proc.* 2001;76(2):195-200.

Almansa C, Devault KR, Achem SR. A comprehensive review of eosinophilic esophagitis in adults. *J Clin Gastroenterol.* 2011;45(8):658-664.

Brimhall B, Adler DG. Esophageal stents for the treatment of malignant dysphagia in patients with esophageal cancer. *Hosp Pract (Minneap).* 2010;38(5):94-102.

Patti MG, Pellegrini CA. Esophageal achalasia 2011: pneumatic dilatation or laparoscopic myotomy? *J Gastrointest Surg.* 2012;16(4):870-873. Epub 2011 Oct 4.

Qureshi W, Adler DG, Davila R, et al; Standards of Practice Committee. ASGE Guideline: the role of endoscopy in the management of variceal hemorrhage, updated July 2005. *Gastrointest Endosc.* 2005;62(5):651-655. Erratum in: *Gastrointest Endosc.* 2006;63(1):198.

Siddiqui AA, Sarkar A, Beltz S, et al. Placement of fully covered self-expandable metal stents in patients with locally advanced esophageal cancer before neoadjuvant therapy. *Gastrointest Endosc.* 2012;76(1):44-51.