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PART 1

Pathobiology of the
Esophagus and
Stomach

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Anatomy, Embryology, and Congenital Malformations of the Esophagus and Stomach

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Summary

Understanding the anatomy and embryology of the esophagus and stomach is necessary for dealing with clinically important congenital malformations. The esophagus acts as a conduit for the transport of food from the oral cavity to the stomach which, as a J-shaped dilation of the alimentary canal, connects with the duodenum distally. Sphincters at the upper esophagus, distal esophagus/proximal stomach, and distal stomach have strategic functions. Formation of the esophagus (primitive foregut) begins at 6 weeks and the stomach is recognizable in the fourth week of gestation as a dilation of the distal foregut. Congenital abnormalities of the esophagus are common and of the stomach are rare.

Case

A 7-year-old male developed dysphagia while attending a birthday party. A hot dog did not pass despite retching and giving the boy carbonated beverages. He was seen in the emergency room where an esophagram was performed. A contrast radiograph outlined a 1-cm length of hot dog above a 10-cm stricture in the mid-esophagus. There was no associated tracheal–esophageal fistula. With anesthesia, an endoscopy was performed and the hot dog was removed. The patient was seen in follow-up evaluation and causes for mid-esophageal stricture were explored. No etiology was found and the clinical findings were attributed to congenital esophageal stenosis. At a later time, endoscopy was repeated and dilation was carried out with bougies. Further dilations were undertaken and surgery was being discussed.

Anatomy

The esophagus is a conduit for the transport of food from the oral cavity to the stomach. It is an 18 to 22-cm long, hollow, muscular tube with an inner “skin-like” lining of stratified squamous epithelium. The esophagus is collapsed and airless at rest but, during swallowing, is distended by the food bolus. When the bolus is delivered to the stomach, it is stored in the gastric fundus, then mixed with acid and ground in the gastric body and antrum. Finally, it is propelled through the pylorus and into the duodenum.

Structurally, the esophageal wall is composed of four layers: innermost mucosa, submucosa, muscularis propria, and outermost adventitia; unlike the remainder of the gastrointestinal tract, the esophagus has no serosa [1,2]. The esophageal musculature is comprised of skeletal muscle in the upper third and smooth muscle in the lower two-thirds. Both skeletal and smooth muscle are innervated by the Vagus nerve with nuclei located within the central medullary swallowing center. The stomach is also innervated by the Vagus nerve, which splits into two

branches—the left which innervates the dorsal wall (greater curvature) and the right which innervates the ventral wall (lesser curvature).

Upper Esophageal Sphincter

Proximally, the esophagus begins where the inferior pharyngeal constrictor merges with the cricopharyngeus, an area of skeletal muscle known as the upper esophageal sphincter (UES). The UES is contracted at rest, creating a high-pressure zone that prevents inspired air from entering the esophagus. UES contraction is mediated by intrinsic muscle tone and vagal acetylcholine release, while relaxation is mediated by inhibition of acetylcholine release [3].

Esophageal Body

The esophageal body lies within the posterior mediastinum behind the trachea and left mainstem bronchus [1]. At the T10 vertebral level the esophageal body leaves the thorax through a hiatus within the right crus of the diaphragm. Within the hiatus the esophageal body ends in a 2 to 4-cm asymmetrically thickened, circular smooth muscle known as the lower esophageal sphincter [4]. Pain within the esophagus is mediated by stimulation of chemoreceptors in the esophageal mucosa or submucosa and mechanoreceptors in the esophageal musculature [5].

Lower Esophageal Sphincter (LES)

The LES is contracted at rest due to intrinsic smooth muscle tone and vagal acetylcholine release. This contraction creates a high-pressure zone that prevents gastric contents from entering the esophagus. The high-pressure zone is also aided by contraction of the diaphragm and weakened in the presence of a hiatal hernia. During swallowing, LES relaxation occurs by vagal release of nitric oxide (and vasoactive intestinal peptide), enabling peristalsis to push the bolus from the esophagus into the stomach [4]. The same mechanism initiates receptive relaxation of the gastric fundus to accommodate a meal without a concomitant increase in intragastric pressure.

Mucosa

On endoscopy, the esophageal stratified squamous-lined mucosa appears smooth and pink while the stomach's simple columnar mucosa is red. Their junction is recog-

nized by an irregular, white, “Z-shaped” line (ora serrata). Squamous cells have no secretory capacity while gastric cells can secrete both into the lumen (acid, pepsin, and a variety of other products) and the blood (gastrin). Below the epithelium is the lamina propria, a loose network of connective tissue with blood vessels and scattered white cells. A thin layer of smooth muscle, the muscularis mucosae, separates the lamina propria from the submucosa, a network of dense connective tissue comprised of blood vessels, lymphatic channels, Meissner neuronal plexus and, in the esophagus, submucosal glands. The esophageal glands secrete mucus and bicarbonate into collecting ducts that deliver the fluid to the esophageal lumen. Between the inner circular and outer longitudinal layers of the muscularis propria is Auerbach neuronal plexus.

Embryology

In the developing fetus, the gastrointestinal tract and the respiratory tract develop from a common tube of endoderm. Between weeks 7 and 10, a ventral diverticulum is formed, which subsequently develops into the respiratory tract; the remaining dorsal part of the tube becomes the primitive foregut. The foregut is initially lined by ciliated columnar epithelium, but begins to transform into stratified squamous epithelium by week 16. This epithelial transition is complete by birth. At embryonic week 4, the stomach is discernable as a dilation of the distal foregut. As the stomach grows, it rotates 90° around its longitudinal axis so that the greater curvature is located dorsally and the lesser curvature ventrally.

Congenital Malformations of the Esophagus and Stomach

Congenital anomalies of the esophagus are relatively common (1 in 3000 to 1 in 4500 live births) and are due to either transmission of genetic defects or intrauterine stress that impedes fetal maturation [6–8]. A clinical overview is presented in Table 1.1. In premature infants about 50% of esophageal anomalies are also associated with anomalies at other sites; this has given rise to the term VACTERL. The letters in VACTERL represent a mnemonic depicting these anomalies which include:

Table 1.1 Clinical aspects of esophageal developmental anomalies. (Reproduced with permission from Long JD, Orlando RC. Anatomy, histology, embryology, and developmental anomalies of the esophagus. In: Feldman M, Friedman LS, Sleisenger MH, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease; Pathophysiology/Diagnosis/Management*, 7th edn. Philadelphia: Saunders (an imprint of Elsevier Science); 2002: 556.)

Anomaly	Age at presentation	Predominant symptoms	Diagnosis	Treatment
Atresia alone	Newborns	Regurgitation of feedings Aspiration	Esophagogram* Radiograph—gasless abdomen	Surgery
Atresia + distal fistula	Newborns	Regurgitation of feedings Aspiration	Esophagogram* Radiograph—gasless abdomen	Surgery
H-type fistula	Infants to adults	Recurrent aspiration pneumonia Bronchiectasis	Esophagogram* Bronchoscopy	Surgery
Esophageal stenosis	Infants to adults	Dysphagia Food impaction	Esophagogram* Endoscopy†	Bougienage‡ Surgery§
Duplication cysts	Infants to adults	Dyspnea, stridor, cough (infants) Dysphagia, chest pain (adults)	EUS* MRI/CT† Esophagogram	Surgery
Vascular anomalies	Infants to adults	Dyspnea, stridor, cough (infants) Dysphagia (adults)	Esophagogram* Angiography† MRI/CT/EUS	Diet modification‡ Surgery§
Esophageal rings	Children to adults	Dysphagia Food impaction	Esophagogram* Endoscopy†	Bougienage
Esophageal webs	Children to adults	Dysphagia	Esophagogram* Endoscopy†	Bougienage

*Diagnostic test of choice.

†Confirmatory test.

‡Primary therapeutic approach.

§Secondary therapeutic approach.

CT, computed tomography; EUS; endoscopic ultrasonography; MRI, magnetic resonance imaging.

Vertebral, Anal, Cardiac, Tracheal, Esophageal, Renal, and Limb systems. Specific defects within this group are the patent ductus arteriosus, cardiac septal deformity, and imperforate anus.

Esophageal Atresia and Tracheoesophageal (TE) Fistula

Esophageal atresia, a failure of the primitive foregut to re-canalize, occurs as an isolated anomaly in 7% and in conjunction with a TE fistula in 93%. In the isolated type of esophageal atresia the upper esophagus ends in a blind pouch and the lower esophagus connects to the stomach. The condition is suspected at birth by the occurrence of choking, coughing, and regurgitation on first feeding in combination with a scaphoid gasless abdomen. The diag-

nosis can be confirmed by failure to pass a nasogastric tube into the stomach and air in the upper esophagus on chest radiograph following air insufflation via a nasoesophageal tube.

When esophageal atresia is associated with a TE fistula, the majority of the cases are accompanied by the distal type in which the upper esophagus ends in a blind pouch and the distal esophagus connects to the trachea. The clinical presentation of the distal type is similar to isolated esophageal atresia, with the addition of recurrent aspiration pneumonia and increased abdominal air. Both of these are attributed to the communication between the esophagus and trachea, permitting reflux of gastric contents into the trachea and air into the esophagus and stomach (which can be seen on plain radiographs) [7].

There are three less common types of TE fistula. The first is when both upper and lower segments of the atretic esophagus communicate with the trachea; the second is when just the upper segment communicates with the trachea; and the third or “H-type fistula” is when the esophagus is *not* atretic, but still communicates with the trachea. All TE fistula types present with recurrent aspiration pneumonia due to the communication between the esophagus and trachea; however, they can be differentiated by other clinical features. The first two types present in infancy and are distinguished from each other by the presence or absence of bowel gas on a plain radiograph (gas present when there is an accompanying distal TE fistula). In contrast, diagnosis of the H-type TE fistula may be delayed until childhood or young adulthood [8]. The diagnosis of an H-type fistula is usually made either on bronchoscopy after ingestion of methylene blue to stain the fistula site or on esophagography.

The treatment of almost all esophageal anomalies is surgical. Success rates depend upon the type and severity of accompanying genetic abnormalities. For isolated atresias, surgical success is about 90%; however, there is an increased risk of gastroesophageal reflux disease after correction due to abnormalities of both esophageal motility and luminal acid clearance.

Congenital Stenosis

Esophageal stenosis, which varies in length from 2 to 20 cm is rare and typically occurs in males [9]. The precise cause is unknown and most present with solid-food dysphagia and regurgitation in infancy or childhood. Diagnosis is made by either esophagography or endoscopy. Treatment is by endoscopic-guided bougienage, which has variable efficacy depending upon the length and the complexity of the stricture. It is possible that some, perhaps many, of the cases once considered congenital stenosis actually are involved with eosinophilic esophagitis (see Chapter 34).

Esophageal Duplications

Congenital duplications of the esophagus are rare and arise as epithelial-lined outpouchings off the primitive foregut. There are two types: cystic and tubular. Cysts account for 80% of the duplications and are usually single, fluid-filled structures. They do not communicate with the lumen and when large are often associated with compression of the adjacent tracheobronchial tree,

resulting in cough, stridor, wheezing, cyanosis, or chest pain. When asymptomatic they may be detected as mediastinal masses on chest radiography or submucosal lesions on esophagogram. The diagnosis is confirmed by computed tomography (CT), magnetic resonance imaging (MRI) or endoscopic ultrasonography (EUS). Surgical excision is usually required to exclude a cystic neoplasm [10].

Tubular esophageal duplications are less common and, unlike the cystic type, *do* communicate with the true lumen [10]. They usually cause chest pain, dysphagia, or regurgitation in infancy, and the diagnosis is established by esophagography or endoscopy. Reconstructive surgery is indicated for those patients who are symptomatic [10–12].

Vascular Anomalies

Intrathoracic vascular anomalies are present in 2–3% of the population. Most are asymptomatic, however some may develop symptoms from esophageal compression (dysphagia and regurgitation) in childhood or adulthood. Dysphagia lusoria, the most common vascular compression of the esophagus, is due to an aberrant right subclavian artery, arising off the left side of the aortic arch [13]. Diagnosis is made by a pencil-like extrinsic esophageal compression at the level of the third to fourth thoracic vertebrae on barium esophagogram [13]. Confirmation is made by CT, MRI or EUS [13,14]. Initial treatment is dietary modification (mechanical soft diet) for symptom control with surgery reserved for refractory cases.

Esophageal Rings

The distal esophagus may contain up to two “rings”, the muscular A ring and the mucosal B or Schatzki ring. The A ring is 4–5 mm thick and represents an enlargement of the upper end of the LES [15,16]. It is both uncommon and rarely symptomatic. The B ring, which is 2 mm thick, represents the squamocolumnar junction [15,16]. It is common and usually asymptomatic, unless the lumen size is compressed to less than 15 mm, at which point intermittent solid-food dysphagia or acute impaction may occur [15,16].

Esophageal Webs

Esophageal webs are thin mucosal protrusions extending from the anterior wall of the esophagus in the cervical

region. They are thus best visualized on a lateral view of an esophagram. Unlike rings, webs rarely encircle the lumen [17]. Nonetheless, cervical webs can cause solid-food dysphagia. The triad of cervical webs, dysphagia, and iron-deficiency anemia is referred to as the Plummer–Vinson or Paterson–Brown–Kelly syndrome [17]. The syndrome is significant as it increases the risk of squamous cell carcinoma of the pharynx and esophagus and may also be associated with celiac sprue [17,18]. Treatment with iron has been reported to not only correct the iron deficiency but to also induce resolution of the web. Isolated cervical webs are treated by esophageal bougienage.

Heterotopic Gastric Mucosa

Heterotopic gastric mucosa is also known as the “inlet patch”. It is seen on 10% of endoscopies as a small, red island of mucosa just below the UES. Typically, inlet patches are asymptomatic though rarely they secrete acid and cause strictures or ulcers [19] and even more rarely evolve into adenocarcinoma [20].

Congenital Malformations of the Stomach

Congenital malformations of the stomach are very uncommon and include: gastric atresia, microgastria, gastric volvulus, gastric diverticulum, and gastric duplications. When symptomatic, these lesions typically present with epigastric pain, nausea, and vomiting, reflecting the degree of gastric outlet obstruction. Gastric atresia may be associated with both Down syndrome and epidermolysis bullosa. Unlike esophageal duplications, gastric duplications rarely communicate with the lumen and therefore develop into masses within the stomach wall. Congenital laxity of ligaments attaching stomach to duodenum, spleen, liver, and diaphragm are contributing causes of gastric volvulus, which are either mesenteroaxial or organoaxial in type based on the axis of rotation. Mesenteroaxial gastric volvulus may be asymptomatic or symptomatic with chronic, intermittent, upper gastrointestinal symptoms [21]. Organoaxial gastric volvulus is typically acute, presenting with abdominal pain, retching, and inability to pass a nasogastric tube (Borchardt triad). It is commonly associated with a diaphragmatic hernia and a gas-filled viscus in the thorax may be seen on chest radiography. Diagnosis is confirmed by upper gastrointestinal series.

Take-home points

Anatomy:

- The upper esophageal sphincter (UES) is a skeletal-muscle structure that prevents inhaled air from entering the esophagus. The lower esophageal sphincter (LES) is a smooth-muscle structure that prevents gastric contents from refluxing into the esophagus.
- The distal end of the LES demarcates the anatomic gastroesophageal junction. This muscular junction on endoscopy is approximated by the proximal (oral) end of the gastric folds.
- The squamocolumnar junction on endoscopy is denoted by a white, irregular, “Z-shaped” line that is the transition between esophageal and gastric epithelia.
- The stomach is comprised of a cardia, fundus, body, antrum, and pylorus and is completely invested by peritoneum except at the gastroesophageal junction.

Embryology:

- The formation of the esophagus (primitive foregut) begins at 6 weeks in the embryo; it is initially lined by a ciliated columnar epithelium but this is completely replaced by stratified squamous epithelium by birth.
- The stomach is identifiable by week 4 in the embryo as a dilation of the distal foregut. As it grows it rotates 90° around its longitudinal axis so that the greater curvature lies to the left and lesser curvature to the right.

Congenital malformations of the esophagus and stomach:

- Congenital anomalies of the esophagus are common and gastric anomalies are rare.
- Most esophageal atresias are accompanied by a distal-type TE fistula.
- The only TE fistula that may go undetected until adulthood is known as the H type.
- The inlet patch is usually an incidental finding on endoscopy, appearing as a small island of red-appearing gastric mucosa just below the UES.
- The B or Schatzki ring is a 2-mm thick mucosal indentation located at the squamocolumnar junction. When reducing the esophageal lumen to <15 mm, it commonly causes intermittent solid-food dysphagia or acute solid-food impaction.
- Cervical webs, dysphagia, and iron-deficiency anemia are a triad known as the Plummer–Vinson or Paterson–Brown–Kelly syndrome.
- Gastric volvulus can be mesenteroaxial or organoaxial in type, the latter typically an acute event producing abdominal pain, retching an inability to pass a nasogastric tube (Borchardt triad).

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