The Esophageal Wall

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KEYWORDS

• Mucosa • Submucosa • Muscularis propria
• Adventitia • Lymphatics

The sole function of the esophagus is transport of solid and liquid nourishment from the pharynx to the stomach and, rarely, venting of the stomach with retrograde passage of gastric contents into the pharynx. What appears to be a simple task is provided by a complex and not completely understood organ. To investigate, diagnose, and treat both benign and malignant esophageal diseases, an in-depth understanding of the esophageal wall is required.

THE ESOPHAGEAL WALL

The esophageal wall is a four-layer structure with a mucosa, submucosa, muscularis propria, and adventitia (**Fig. 1**).

Mucosa

The mucosa is composed of the epithelium and its basement membrane, the lamina propria, and the muscularis mucosae.

Epithelium and basement membrane

The esophagus is lined by stratified nonkeratinizing squamous epithelium (**Fig. 2**). Unlike the skin, it is a moist surface and lacks appendages other than the ducts of submucosal glands. Its role is to protect the underlying esophageal wall from mechanical damage, microorganisms, and toxic materials. However, it is not keratinizing as in mammals that eat coarse food. The esophageal epithelium is continuous with pharyngeal epithelium. It ends abruptly at the squamocolumnar junction, which resides in the distal 2 to 3 cm of the tubular esophagus in normal individuals, a region also known as the lower esophageal sphincter. The normal squamocolumnar mucosal junction does not necessarily align with the gastroesophageal junction, the anatomic junction of the tubular esophagus, and the saccular stomach. The gastroesophageal junction is the site at which the proximal-most radiating gastric folds terminate. Thus, the normal squamocolumnar mucosal junction can be located anywhere from the gastroesophageal anatomic junction to 2 to 3 cm above it. The mucosa distal to the squamocolumnar junction, also known as the z-line, is gastric cardiac and fundic glandular epithelium (**Fig. 3**).

The epithelium has three layers: basal cell, prickle cell, and functional cell. The basal cell layer (stratum basale or stratum germinativum) is 1 to 3 cells thick and is the source of epithelial regeneration. It occupies 10% to 15% of the epithelium, except in the distal esophagus, where a thickness of more than 15% may still be normal. Progressive maturation with flattening of cells occurs within the epithelium as it extends onto the epithelial surface. The boundary between the basal cell and prickle cell layers is arbitrarily defined as the point at which nuclei are separated by a distance no greater than their diameter. The prickle cell (stratum spinosum) is so named because of the shrinkage artifact that exposes the adhesion between cells at their desmosomal junctions. The cells in the functional layer maintain their nuclei, and although they do not keratinize, they may

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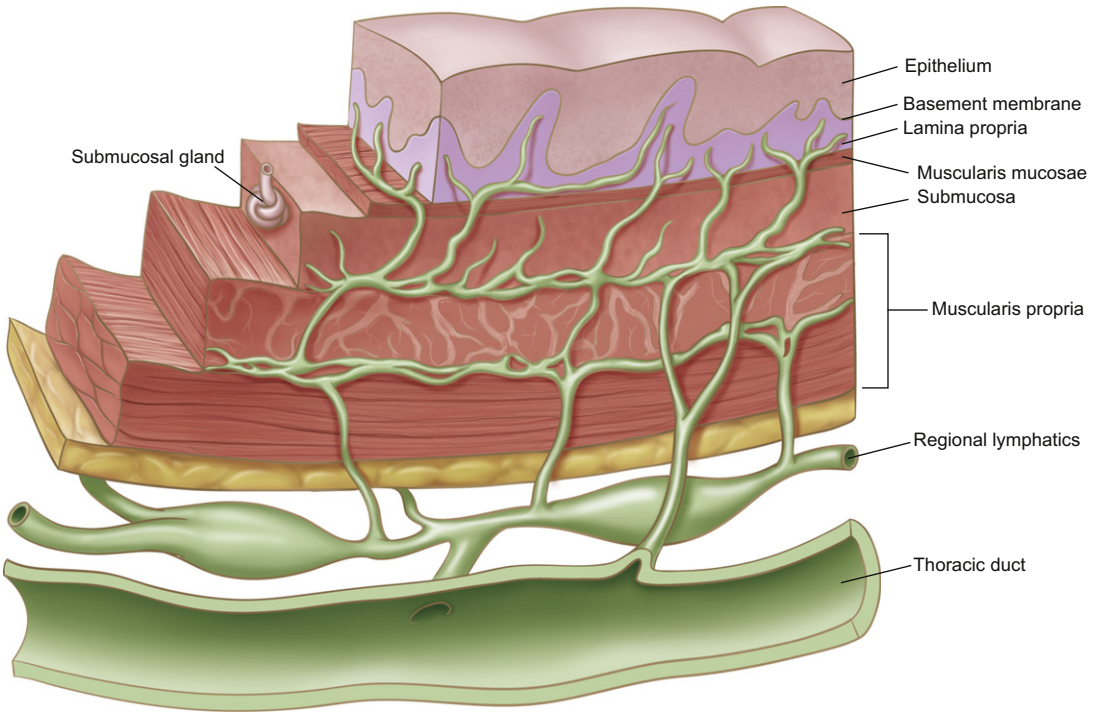

Fig. 1. The esophageal wall is a four-layer structure, with a mucosa, submucosa, muscularis propria, and adventitia. The mucosa is a three-layer structure, with an epithelium and its basement membrane, lamina propria, and muscularis mucosae. (*Adapted from* Cleveland Clinic Foundation, 1999; with permission.)

occasionally demonstrate keratohyalin granules. In humans, esophageal epithelium turnover is approximately 21 days.[1]

Lymphocytes are normally found above the basal cell layer. The conformational changes necessary for their intracellular position between progressively flattening epithelial cells give them an appearance termed a "squiggle cell." This can mimic the segmented nucleus of a granulocyte, except that lymphocytic squiggle cells lack the cytoplasmic granules of either a neutrophil or an eosinophil. Argyrophil-positive endocrine cells[2] and rare melanocytes[3] are also found in normal basal cell layers and are the cells of origin for neuroendocrine carcinomas, including small-cell carcinoma, of the esophagus and primary esophageal melanoma, respectively.

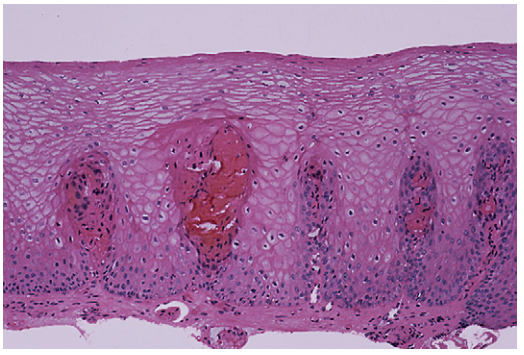

Fig. 2. Stratified nonkeratinizing squamous epithelium of normal esophageal mucosa, demonstrating the 1- to 2-cell-thick basal layer occupying no more than 15% of the mucosal thickness and the gradual flattening of the squamous cells as the epithelium matures to the mucosal surface. Note also that the subepithelial papillae of lamina propria extend no higher than two-thirds of the epithelial thickness (hematoxylin and eosin).

The findings of squamous hyperplasia, regeneration, and intraepithelial inflammation (**Fig. 4**) are nonspecific signs of esophagitis most typically, but not necessarily, resulting from gastroesophageal reflux disease. Epithelial hyperplasia is defined by basal cell hyperplasia (more than 15% of the mucosal thickness occupied by basal cells) or papillomatosis (elongation of the subepithelial papillae of lamina propria to more than two-thirds of the mucosal thickness). Intraepithelial inflammatory cells comprise neutrophils, eosinophils, and lymphocytes.

Glandular epithelium in the tubular esophagus may derive from congenital ectopic columnar epithelium (inlet-patch within the proximal esophagus) or an acquired columnar lining (Barrett esophagus), a metaplastic response to chronic gastroduodenal reflux into the distal esophagus.