Trachea: Anatomy and Physiology

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KEYWORDS

• Macroscopic and microscopic anatomy • Morphogenesis • Tracheal stem cells • Physiology • Function

KEY POINTS

- The trachea is a tube made up of cartilage, connective tissue, smooth muscle, and a mucosal layer connecting the larynx to the principal bronchi and finally to the lungs.
- The tracheal mucosa consists of a pseudostratified columnar epithelium with kinocilia and goblet cells, supported by a lamina propria containing tracheal glands.
- Morphogenesis of the trachea depends on epithelial-mesenchymal interactions of the endodermal trachea and the mesoderm-derived mesenchyme surrounding it.
- The mucosal epithelium and the ducts of the tracheal glands contain different types of stem cells.
- The main functions of the trachea comprise air flow into the lungs, mucociliary clearance, and humidification and warming of the air.

ANATOMIC OVERVIEW OF THE TRACHEA

The trachea (windpipe) is a semiflexible tube of 1.5 to 2 cm in width and 10 to 13 cm in length, reaching from the lower portion of the larynx approximately at the level of the sixth to seventh cervical vertebra to the fourth to fifth thoracic vertebra, where it bifurcates to form the two bronchi for the lungs. The tracheal wall consists of up to 20 incomplete rings of hyaline cartilage forming the anterior and lateral circumference, and smooth muscle at the posterior side, which are both embedded into a fibrous membrane of elastic connective tissue (**Fig. 1**). The muscle contains transverse and longitudinal fibers; the transverse fibers connect the ends of the cartilaginous rings posteriorly and are termed m. trachealis. Seromucinous tracheal glands are located in the connective tissue between the epithelial layer and the cartilage, sometimes also on the outer side, and are found abundantly exterior to the tracheal muscle. The function of the glands that open via ducts on the inner surface of the trachea is to lubricate the inner lining of the trachea. The epithelium consists of a pseudostratified columnar epithelium with kinocilia and goblet cells that also produce a mucous film (**Fig. 2**). The direction of the beat of the kinocilia toward the larynx results in the transport of particulates and cell detritus away from the lungs and its elimination from the body.

MORPHOGENESIS OF THE TRACHEA

During the fourth week of development, the trachea develops initially from the ventral foregut epithelium forming the tracheobronchial diverticulum, and grows caudally before branching into the lung buds that will later elongate to form the principal bronchi. The inner lining of the trachea is thus of endodermal origin. However, it is an excellent example of epithelial-mesenchymal interactions that occur commonly during organogenesis, because the endodermal tube undergoes morphogenetic movements such as growth and branching

The authors have nothing to disclose.
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Thorac Surg Clin 24 (2014) 1–5
http://dx.doi.org/10.1016/j.thorsurg.2013.09.004
1547-4127/14/$ – see front matter

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Fig. 1. Transverse section of a human trachea with fibromuscular portion (paries membranaceus; 1) and tracheal cartilage (3); the seromucinous tracheal glands (2) are located in the connective tissue subjacent to the inner lining. The tunica mucosa (4) consists of the pseudostratified columnar epithelium shown in Fig. 2, and the lamina propria. The tunica adventitia is labeled as 5. (Azan staining, original magnification × 40).

only under the influence of the surrounding splanchnic mesoderm (Fig. 3). The interactions are based on signals from the major signaling pathways such as fibroblast growth factor 10, Sprouty, epidermal growth factor, insulin-like growth factor, hepatocyte growth factor, and transcription factors.[1] During the fourth week of development, the trachea branches to form the right and the left lung bud. The development of the trachea thus forms the prerequisite for the formation of the lungs by repeated rounds of bifurcation events (Fig. 4).

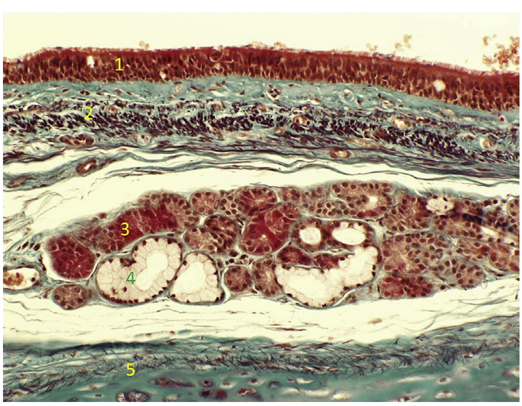

Fig. 2. Detail of the tracheal wall showing (1) the ciliated pseudostratified columnar epithelium, (2) elastic fibers of the lamina propria, tracheal glands with serous (3) and mucinous (4) acini, and (5) hyaline tracheal cartilage. (Goldner staining, original magnification × 200).

RECENT HISTOLOGIC FINDINGS

A detailed analysis of the pseudostratified mucosal epithelium of the trachea has revealed the presence of several highly specialized and less well-defined cell types. The most common distinction is made between the "brush cells" and the neuroendocrine cells resembling the enteroendocrine cells of the gastrointestinal tract, neuroendocrine cells being dispersed in the respiratory epithelium. The function of the neuroendocrine cells in the respiratory tract is currently under debate; mechanosensitive functions and O_2-sensing functions[2] have been suggested. In contrast to the enteroendocrine cells, the chemosensory function of the neuroendocrine cells in the respiratory tract has not yet been proved. The non-neuroendocrine cells of the respiratory tract have been termed brush cells, and are solitary chemosensory cells in the upper airways. Surprisingly, cells expressing the molecular components of the taste transduction pathway display the ultrastructural morphology of the brush cells.[3] The term brush cell reflects the presence of apical microvilli containing villin and fimbrin.[4] Recently, cholinergic chemosensory cells have been described in the trachea[5–7] by expression of relevant receptors and components of the bitter taste transduction pathway. These cells are connected to afferent fibers of the vagal nerve via nicotinic acetylcholine receptors. These cholinergic brush cells were demonstrated to affect the control of breathing,[5] and are thus functional in safeguarding the lower airways by sensing the composition of the luminal fluid inside the trachea and the bronchi.

TRACHEAL STEM CELLS

As the epithelium of the airways is exposed to the environment with the risk of injury, it must be able to physiologically regenerate. During this process, a subpopulation of the basal cells in the pseudostratified columnar epithelium is activated, and replaces the sloughed or injured surface cells.[8–10] The stem/progenitor cells can be characterized by the presence of transcription factor Trp-63 (p63) and cytokeratins 5 and 14.[11] Trp-63 is involved in the development of the respiratory and other epithelia, in particular the establishment of the basal cells.[12] In contrast to rodents in which these stem/progenitor cells are only present in the trachea, in humans they occur throughout the respiratory tract, including the small bronchi. Basal cells can develop into ciliated surface cells and Clara cells which, as Clara cells give rise to goblet cells, can be considered multipotent.