Anatomy and Histology of the Respiratory System

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Introduction

The complex process of gas exchange, the cornerstone of respiratory physiology, is fundamentally rooted in the architectural design and microscopic composition of the respiratory system. To fully appreciate the physiological mechanisms governing ventilation, diffusion, and perfusion, a thorough understanding of respiratory anatomy and histology is paramount.

This chapter will delve into the structural organization of the respiratory tract, from the macroscopic to the microscopic level, illuminating how form dictates function.

By bridging the gap between structure and function, this foundation will provide the essential context for subsequent discussions on the physiological processes that enable life-sustaining respiration.

Nose

Function

The function of the nasal cavity is breathing and airflow, but even more specifically filtering, warming, and moisturizing the air in this process before traveling through the rest of the respiratory system. Vascular networks existing within the connective tissue of nose contributing to the warming of air that is inspired. Glands are also present in the submucosa, contributing secretions that keep the nasal cavity and mucosal surfaces wet, allowing for the humidification of air. The nose also is used for olfaction, or smell. The nasal cavity also consists of hairs, referred to as vibrissae, which aid in filtering out particulate matter from atmospheric air inhaled.

Anatomy

The external nose is composed of paired nasal bones, consisting of 2 small bones at the ridge of the nose. The alar cartilage forms the tip and side of the nose, while the lateral cartilage forms the bridge of the nose. The nasal septum is comprised of multiple parts, including the vomer, the perpendicular plate of the ethmoid, and the septal cartilage. The vomer makes up the inferior and posterior portions of the septum. The perpendicular plate of the ethmoid bone contributes to the superior and posterior septum. The septal cartilage forms the anterior most portion of the septum alongside the vomer and perpendicular plate of the ethmoid.

The nasal cavity is composed of the lateral and inferior bones. The lateral nasal wall includes multiple bones such as the maxilla, palatine, sphenoid, nasal, frontal, inferior concha, middle concha, and superior concha of the ethmoid bone. The hard palate is the inferior limit that is formed from portions of both the maxilla and palatine bones. The lateral nasal wall is made up of the superior, middle, and inferior nasal conchae/turbinates. The superior, middle, and inferior meatuses are the spaces that exist in between the turbinates.

The nasal cavity is innervated by the trigeminal nerve (cranial nerve V). Specifically, sensation of the nose comes from CN V1 (the ophthalmic division) and CN V2 (the maxillary division). CN V1 provides sensation of the external nose, in addition to the anterosuperior lateral wall and nasal septum. The anterior and posterior ethmoidal nerves stemming from the nasociliary nerve provide this innervation. CN V2 provides sensation of the nostrils. The nasopalatine nerve innervates the posteroinferior nasal septum and

the greater palatine nerve supplies the posteroinferior lateral wall. Smell comes from the olfactory nerve, or cranial nerve I. Receptors of the nerve are present on the superior, lateral, and septal walls of the nose.

The nasal cavity receives its blood supply from various arteries, including the ophthalmic, maxillary, and facial arteries. The ophthalmic artery comes off of the internal carotid artery, branching into anterior and posterior ethmoidal arteries which supply the lateral and septal walls. The maxillary artery stems from the external carotid artery, branching into the greater palatine artery and terminating with the sphenopalatine artery. The greater palatine artery supplies the hard palate, traveling through the incisive canal. The greater palatine and sohenopalatine arteries form an anastamosis in the nasal cavity. The facial artery is another branch of the external carotid artery and supplies the septum via septal branches of the superior labial artery. Two arterial plexuses exist in the nasal cavity– Kiesselbach's plexus (also known as Little's area) and Woodruff's plexus. Kiesselbach's plexus is formed from branches of both the anterior and posterior ethmoidal arteries, the sphenopalatine artery, and the greater palatine artery. Thus, there are branches from contributions of the both the internal and external carotid arteries. It is located in the anterior, inferior portion of the nasal septum and is the source of a majority of nosebleeds. Woodruff's plexus is located in the posterior, lateral nasal wall. Its major contributions come from the sphenopalatine and greater palatine arteries.

Histology

The nose marks the beginning of the conducting zone, responsible for moving atmospheric air into the lungs (respiratory zone) for gas exchange.

The nasal cavity consists of ciliated columnar cells, basal cells, goblet cells, and . Ciliated columnar cells contain cilia, which beat to move particulates towards the pharynx. The basal cells of the nasal cavity are stem cells, which do not extend to the surface of the epithelial sheet. The nasal cavity also has Goblet cells, which are responsible for the production of mucinogen that is hydrated to produce mucin.
Brush cells are largely responsible for the sensation experienced in the nasal cavity, due to their contact with afferent nerve endings. Brush cells are columnar cells with blunt microvilli. Paracrine and endocrine functions are also accomplished in the nose via small-granule cells, which release secretory granules into the surrounding connective tissue.

Depending on the specific location, the lamina propria overlies either bone or cartilage. The lamina propria is highly vascularized containing many large blood vessels. The function of this is to bring warm blood near the epithelial surface in order to warm atmospheric air entering the nose. Seromucous glands

also exist in the lamina propria, which provide a supportive function to goblet cells. The lamina propria also provides a protective function via the presence of lymphocytes, mast cells, and plasma cells.

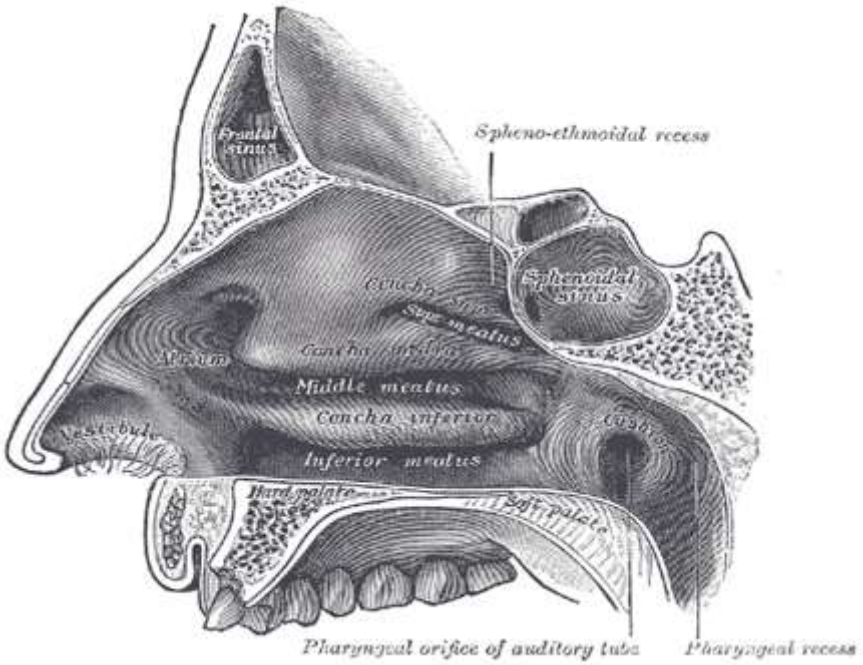


Figure 1: Sagittal plane of the nose. From reference 1

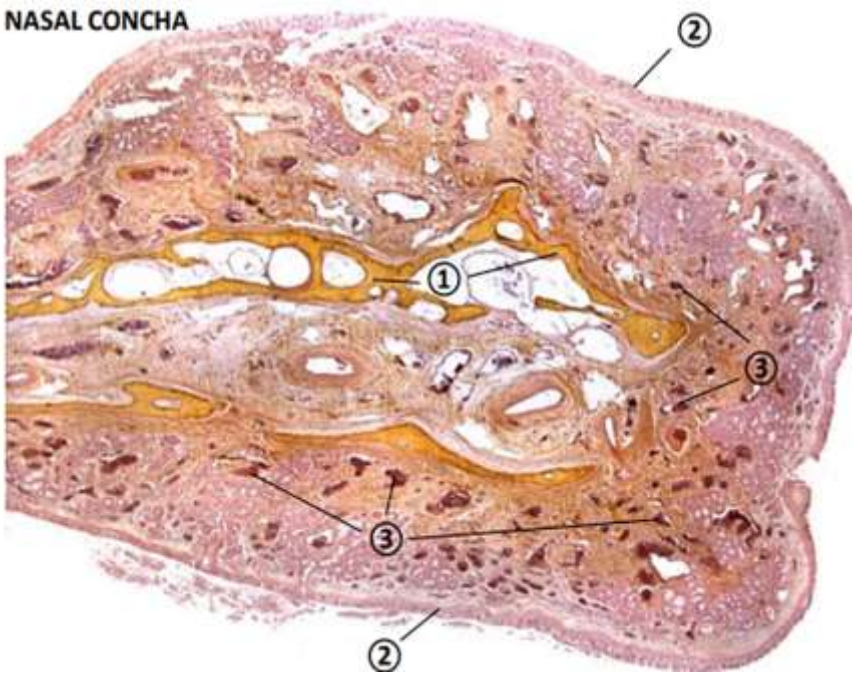


Figure 2: Low microscopic power of the nasal conchae. 1.turbinate spongy bone, 2. pseudostratified columnar ciliated e. with abundant goblet cells, 3.thin, cavernous, venous plexuses. Reference 6

Mouth

Function

The mouth includes the oral cavity, teeth, gingivae, tongue, palate, and palatine tonsils. The boundaries of the mouth are the oral fissure anteriorly, the floor of the mouth inferiorly, the posterior tonsillar pillar posteriorly, and the hard and soft palates superiorly. The hard palate consists of maxillary bones anteriorly and palatine bones posteriorly. The soft palate is composed of muscle and mucus membrane. The tonsillar fossa serves as the boundary between the oral cavity and the oropharynx. Within the mouth, there are 32 permanent teeth, which lie in sockets known as alveoli. Children have 20 deciduous teeth. The mouth serves both digestive and respiratory functions.

Anatomy

The maxillary artery provides blood supply to the oral cavity via multiple branches. The tongue is supplied by the lingual artery, the mandibular dentition by the inferior alveolar artery, and the maxillary dentition by the superior alveolar branches of the infraorbital artery. Arterial supply to the palate comes from the greater and lesser palatine arteries (branches of the maxillary artery), in addition to the ascending palatine artery (branch of the facial artery). Venous drainage of the oral cavity follows alongside respective arteries, via the greater and lesser palatine veins, the sphenopalatine vein, and the lingual vein.

Nerve supply to the mouth primarily comes from branches of the trigeminal nerve (CN V). Sensory innervation to the palate is from CN V2, the maxillary branch of the trigeminal nerve. The gingivae, mucous membranes, and glands of most of the hard palate are innervated by the greater palatine nerve branch off CN V2. The mucous membrane of the anterior hard palate is innervated by the nasopalatine nerve. The soft palate is innervated by the lesser palatine nerve. CN V3 supplies sensory innervation to the lower lip, gingivae, and mandibular dentition. This occurs via the buccal, mental, and inferior alveolar nerves. Motor innervation to muscles of mastication is supplied by CN V3, while muscles of facial expression are supplied by CN VII. General sensation to the anterior 2/3 of the tongue is supplied by the lingual nerve (CN V3), with the posterior 1/3 of the tongue being supplied by the glossopharyngeal nerve (CN IX). Taste to the anterior 2/3 of the tongue is supplied by the chorda tympani (CN VII), while CN IX supplies the posterior 1/3 of the tongue. All intrinsic and extrinsic muscles of the tongue, with the exception of the palatoglossus, receive motor innervation from the hypoglossal nerve (CN XII).

Histology

The mouth is lined by stratified squamous epithelium, which is keratinized in high-friction areas and non-keratinized in areas of lower stress. Keratinized areas include the hard palate, gingiva, and dorsum of the tongue. Areas made of non-keratinized epithelium are the soft palate and floor of the mouth.

Certain areas of the oral cavity contain specific histological features that distinguish them from others and contribute to their respective functions. The lips are rich in capillaries, sebaceous, and sweat glands. The cheeks contain a buccal fat pad and contain salivary glands within their submucosa. The hard palate lacks submucosa centrally. The soft palate has skeletal muscles and mucous glands. The tongue has taste buds, papilla, and lingual glands.

The histology of the oral cavity is otherwise consistent with its stratified squamous epithelium overlying a lamina propria and submucosa.

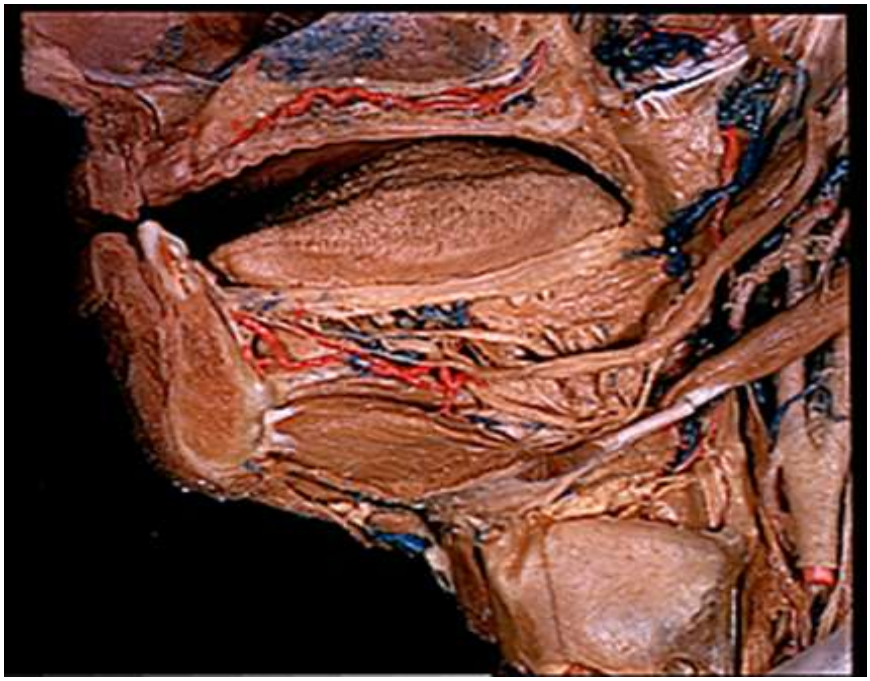


Figure 3: Sagittal cut of the oral cavity. From reference 2

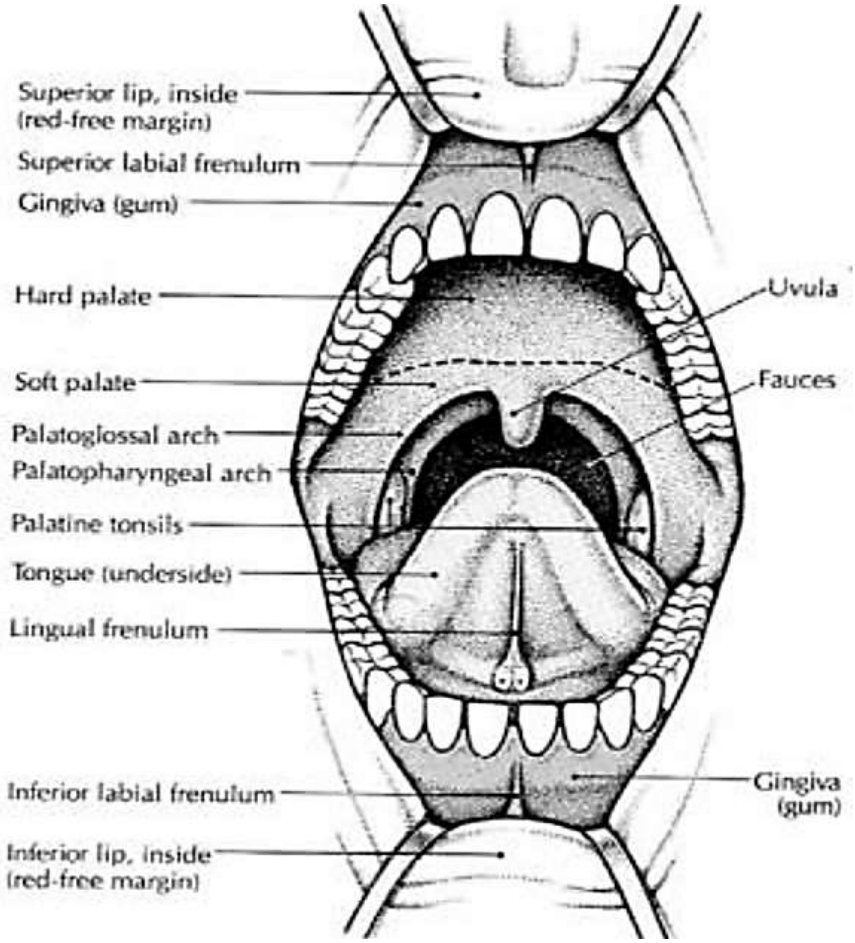


Figure 4: Illustration of the oral cavity. From reference 1

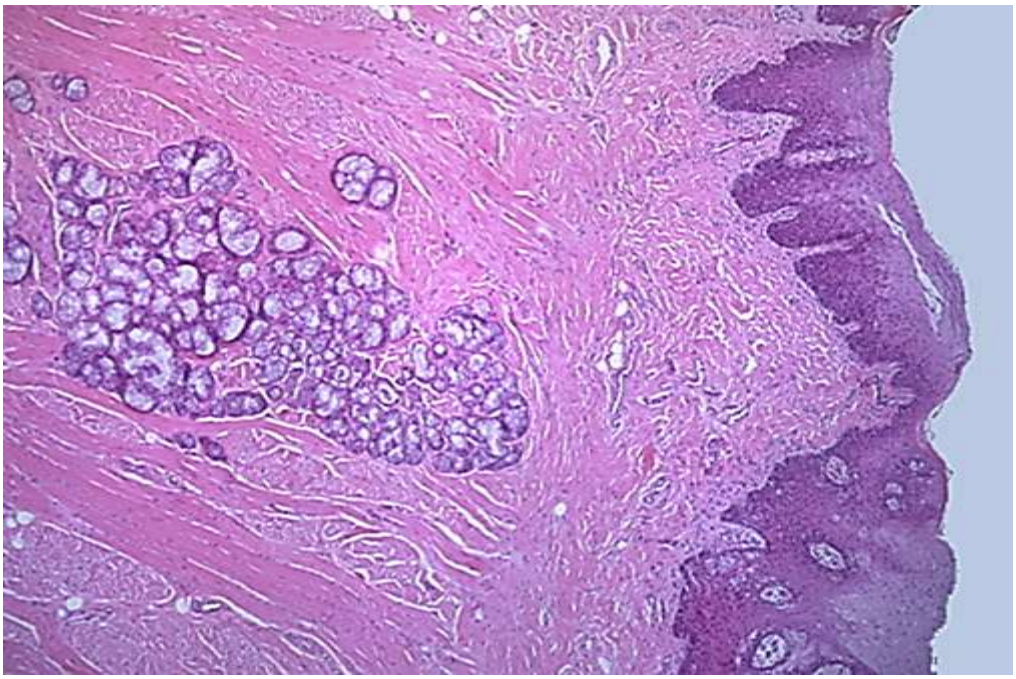


Figure 5: Tongue: low microscopic power, the normal tongue has an overlying squamous epithelium beneath which is a lamina propria. The bulk of the tongue is composed of skeletal muscle. Scattered throughout the tongue, but more prominent toward the back of the tongue, are minor salivary glands. Reference 5

Pharynx

Function

The pharynx is the continuation of the nasal and oral cavities, descending until it becomes the esophagus and larynx. Its main function is swallowing, contributing to the pharyngeal phase as a bolus of food comes into contact with the posterior 1/3 of the tongue and the palatoglossal arches.

Anatomy

It is divided into 3 regions: the nasopharynx, oropharynx, and laryngopharynx. These regions respectively communicate with the nasal cavity, oral cavity, and larynx. The retropharyngeal space lies behind the pharynx, serving as a potential space of loose connective tissue, lymph vessels, lymph nodes, and other small vasculature. It is located between the buccopharyngeal and prevertebral fascia, extending from the base of the skull to the posterior mediastinum.

The pharynx receives sensory innervation from various nerves. The nasopharynx anterior to the auditory tube is innervated by the mandibular branch of the trigeminal nerve (CN V2), the nasopharynx posterior to the auditory tube and the oropharynx by the glossopharyngeal nerve (CN IX), and the laryngopharynx by the vagus nerve (CN X). Efferent innervation to the muscles of the pharynx is done by CN X.

The pharynx obtains its blood supply via arterial branches stemming from the external carotid artery, including the facial, maxillary, and lingual branches. The external and internal venous pharyngeal plexus are responsible for venous supply to the pharynx, ultimately draining into the internal jugular vein.
The pharynx also contains Waldeyer's ring, a lymphatic space in between the palatine, pharyngeal, lingual, and tubal tonsils. This ring is filled in by mucosa associated lymphatic tissue, also known as MALT.

Histology

Similar to the oral cavity, the histology of the pharynx varies slightly by region and function. The epithelium of the nasopharynx is a pseudostratified columnar epithelium with goblet cells, whereas that of the oropharynx and laryngopharynx is non-keratinized stratified squamous epithelium. Its lamina propria contains lymphoid tissue, i.e. MALT mentioned previously. The submucosa is made up of blood vessels, nerves, and mucus-secreting glands that are particularly prominent in the nasopharynx. The muscular layer contains an inner longitudinal layer (stylopharyngeus, salpingopharyngeus, and palatopharyngeus

muscles) and an outer circular layer (pharyngeal constrictor muscles). The adventitia then makes up the outer connective tissue layer.

Larynx

Function

The larynx is the inferior continuation of the pharynx, located in between the pharynx and the trachea. The function of the larynx is sound production and a source of protection for the respiratory system against foreign particles.

Anatomy

It consists of both cartilage and ligament/membrane, including the thyroid cartilage, cricoid cartilage, epiglottic cartilage, right and left arytenoid cartilage, right and left corniculate cartilage, right and left cuneiform cartilage, thyrohyoid ligament/membrane, and cricothyroid ligament/membrane.

The intrinsic muscles of the larynx are responsible for vocalization and phonation as they alter the tension and length of the vocal cords. These muscles also close the laryngeal inlet. Innervation to all muscles of the larynx occurs via the recurrent laryngeal nerve, which branches off of the inferior laryngeal nerve. The exception to this is the cricothyroid, which is innervated by the external laryngeal nerve, a branch of the superior laryngeal nerve.

The larynx also has extrinsic muscles, responsible for either elevating or depressing both the hyoid and larynx while speaking and swallowing. The suprahyoid muscles are responsible for elevation, while the infrahyoid muscles are responsible for depressing the larynx and hyoid.

The internal and external branches of the laryngeal nerve provide innervation to the larynx, with the internal branch providing sensory innervation above the vocal folds and the external branch providing sensory innervation to the cricothyroid and inferior pharyngeal constrictor muscles. The recurrent laryngeal nerve provides motor innervation to all intrinsic muscles of the larynx aside from the cricothyroid muscle and sensory innervation to the larynx at and inferior to the vocal folds.

Blood is supplied to the internal laryngeal muscles and the internal superior larynx by the superior thyroid artery, branching off the external carotid artery. The internal inferior larynx receives blood supply from the inferior thyroid artery, branching off the thyrocervical trunk. Venous drainage of the larynx occurs through the superior, middle, and inferior laryngeal veins. Drainage of the superior laryngeal vein goes to the internal jugular vein, while the inferior laryngeal vein drains into the brachiocephalic vein.

Histology

The supraglottic region of the pharynx (superior to the vocal cords) is made of pseudostratified ciliated columnar epithelium with goblet cells. The true vocal cords have stratified squamous non-keratinized epithelium. The infraglottic space is made primarily of pseudostratified ciliated columnar epithelium, which is continuous with tracheal epithelium. The larynx also contains a lamina propria and submucosa, with mucus and seromucous glands being most prominent in this space within the supraglottic and subglottic regions. Beneath this lies cartilage, such as the thyroid, cricoid, and arytenoid cartilages. Intrinsic muscles lie beneath this, which contribute to voluntary movement.

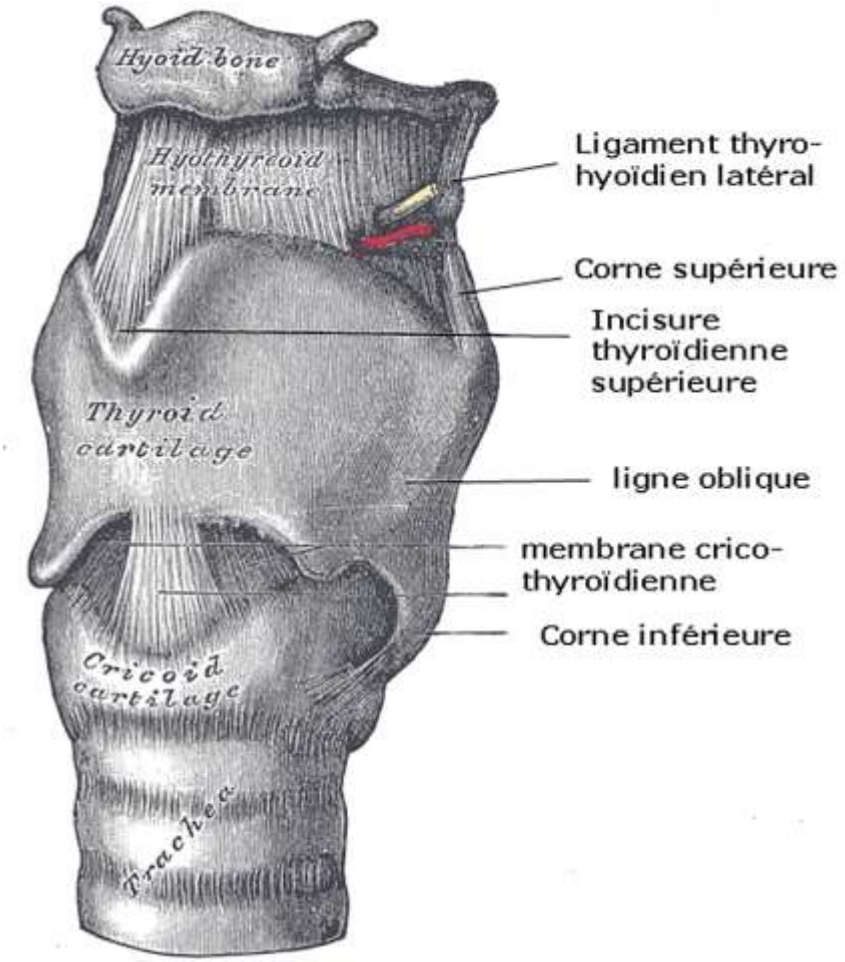


Figure 6: Anatomical structure of the larynx. From reference 1.

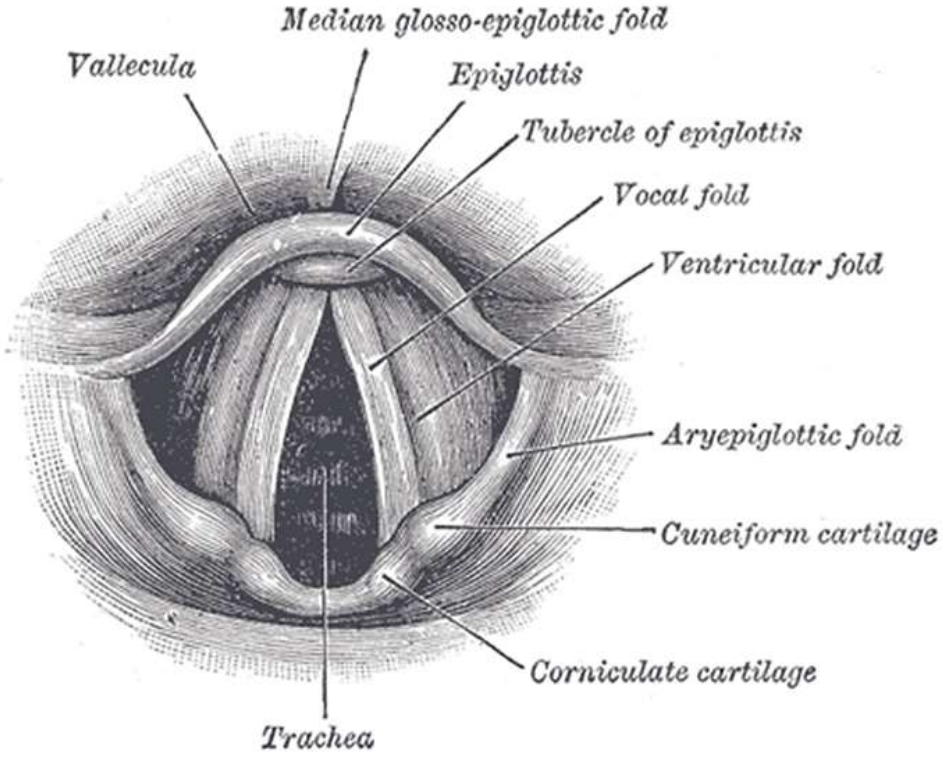


Figure 7: Illustration of the vocal cords top view. From reference 1.

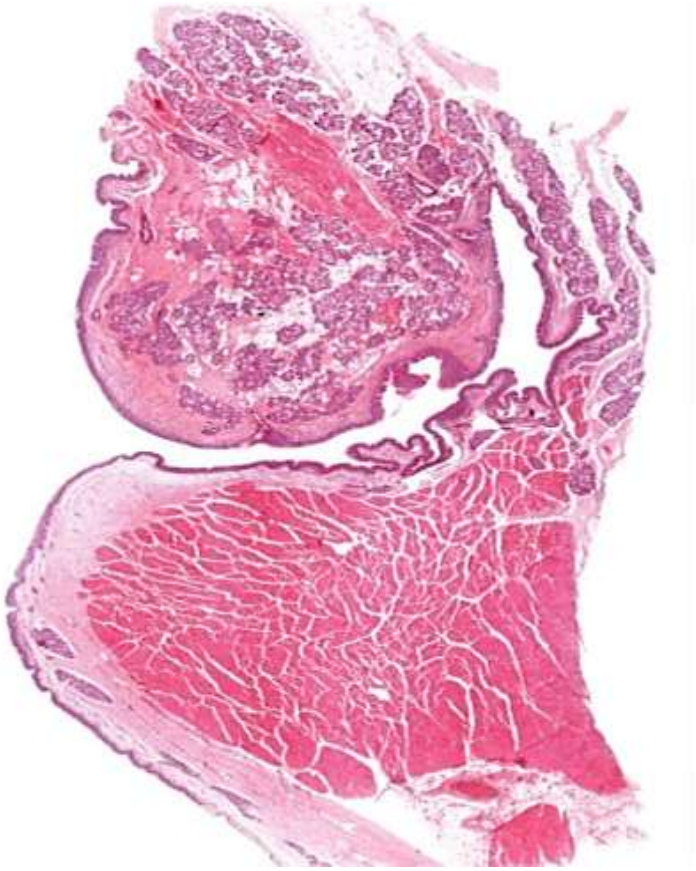


Figure 8: Low microscopic power of the larynx. Reference 6

Tracheo-Bronchial Tree

Function

The tracheobronchial tree's main functions are air conduction, filtration, warming, and humidification, moving air from the trachea through branching bronchi and bronchioles deep into the lungs. Its specialized lining traps particles with mucus, which is then swept upwards by cilia (the mucociliary escalator) for expulsion, protecting the delicate alveoli where gas exchange occurs. Cartilage keeps larger airways open, while smooth muscle in smaller bronchioles allows for airflow regulation.

Anatomy

The trachea consists of multiple ringed cartilages, extending from the larynx before dividing at the carina into right and left main bronchi. The main bronchi subsequently divide into between 23 and 24 subdivisions, which also contain cartilage up to the 11th order division. These subdivisions gradually decrease in size, with smaller bronchi eventually leading to the terminal bronchioles which have a diameter of 0.5 mm. Terminal bronchioles then divide into respiratory bronchioles and alveolar ducts, which are directly responsible for gas exchange. Respiratory bronchioles are made up of approximately 300 million alveolar air sacs.

Histology

The tracheo-bronchial tree gradually loses cartilage and mucus glands as the tree descends into smaller structures.

The trachea is made of pseudostratified columnar epithelium with goblet cells, containing C-shaped cartilage rings, seromucous glands, and smooth muscle. While the bronchi share the same type of epithelium with the trachea, they contain irregular cartilage plates, in addition to seromucous glands and smooth muscle. Distal to this, bronchioles are made of simple ciliated columnar/cuboidal epithelium with a smaller proportion of goblet cells, smooth muscle, and no cartilage or seromucous glands. Terminal bronchioles have a simple cuboidal epithelium with smooth muscle and club cells. Club cells are specialized, non-ciliated columnar epithelial cells. Respiratory bronchioles have a similar histology with a simple cuboidal to squamous epithelium. Lastly, alveoli have a simple squamous epithelium made up of Type I pneumocytes which are responsible for gas exchange in the lungs. These contain no cartilage, seromucous glands, or muscle.

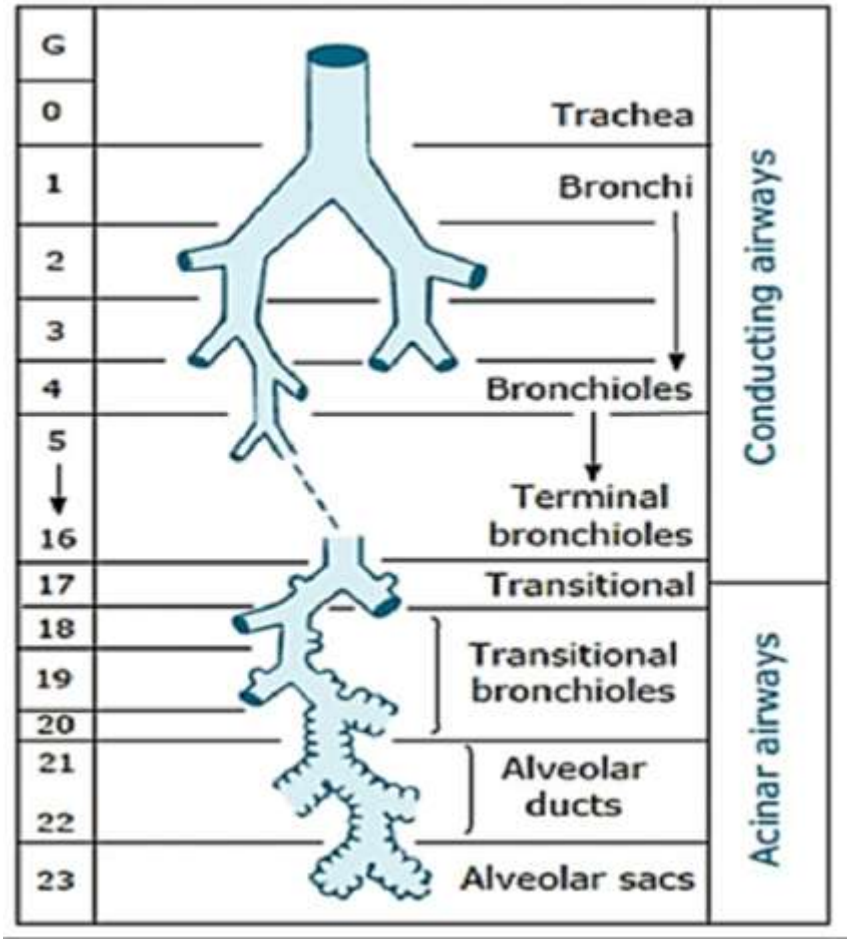


Figure 9: Illustration of the Tracheo-Bronchial tree. From reference 4

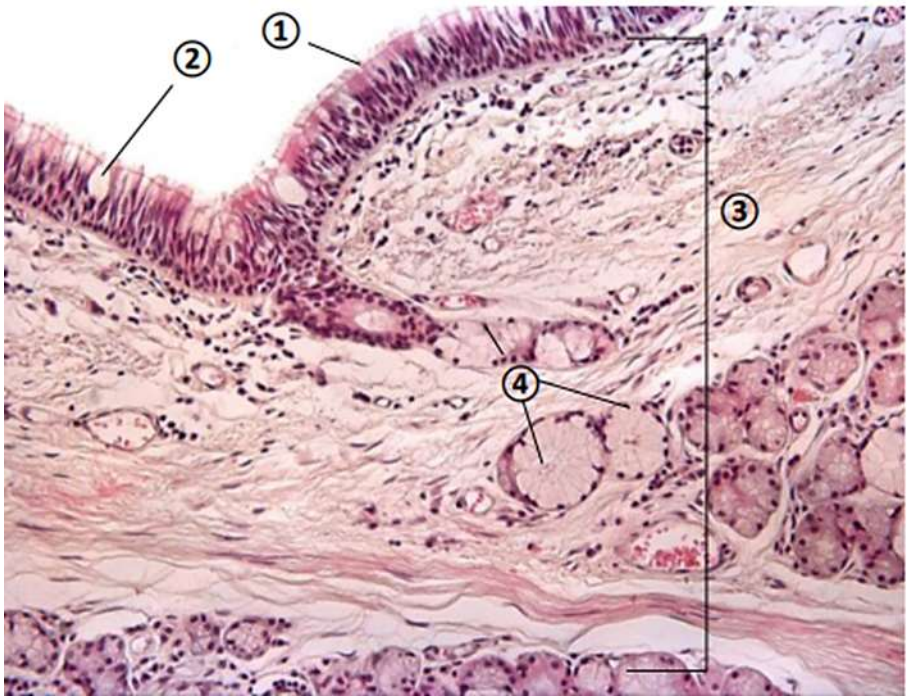


Figure 10: Low microscopic power of the Trachea. 1. ciliated columnar cells, 2. Goblet cells, 3.lamina propria, 4.collagen connective tissue, lymphocyte infiltrations, tuboalveolar seromucous glands. From reference 6

Lungs

Function

The overarching purpose of the lungs are to oxygenate the blood, remove carbon dioxide, and filter the blood, assist in the maintenance of acid-base balance, body temperature, along other immunity and hormonal role.

Anatomy

The right lung consists of 3 lobes– the upper lobe, middle lobe, and lower lobe. The left lung, however, has only an upper and lower lobe. The lingula stems off of the left upper lobe, wrapping around the heart and occupying a space analogous to the location of the right middle lobe.

The lung receives dual blood supply from both pulmonary and bronchial circulations. The pulmonary circulation brings deoxygenated blood from the right ventricle of the heart into the lungs for oxygenation, allowing the lungs to return oxygenated blood to the left atrium via pulmonary veins. Pulmonary arteries run parallel to the bronchi. Bronchial circulation supplies oxygenated blood to the lungs from the thoracic aorta, providing nourishment to lung tissue. Bronchial veins drain deoxygenated blood from lung tissue, draining into the azygos vein and hemiazygos vein on the right and left side, respectively. They also partially drain into the pulmonary veins, therefore creating a physiological right-to-left shunt.

The lungs receive innervation solely from the autonomic nervous system. Parasympathetic innervation to the lungs occurs via the vagus nerve (CN X), leading to bronchoconstriction, increased mucus production, and vasodilation. Sympathetic innervation to the lungs is done by the sympathetic trunk (T1-T5), causing bronchodilation, decreased mucus production, and vasoconstriction.

Histology

The lung matrix is the non-cellular, three-dimensional scaffold of proteins, proteoglycans, and glycoproteins that provides structural support and elasticity to the lung, which is essential for proper function. It also provides vital biochemical and biomechanical signals to the resident cells, influencing their behavior, differentiation, and the lung's repair processes. The lung matrix is broadly organized into two main types of structures:

Basement membranes: Thin, dense sheets of specialized proteins that sit beneath the epithelial and endothelial cell layers of the airways, alveoli, and blood vessels, acting as a barrier and anchoring point for cells.
Interstitial matrix: A looser, fibril-like meshwork that fills the space between cells in the lung parenchyma and large airway walls.

The alveoli, are lined by an exceedingly thin simple squamous epithelium that forms the air-blood barrier. This barrier primarily consists of flattened Type I pneumocytes, which cover about 95% of the surface area to facilitate rapid gas diffusion, and cuboidal Type II pneumocytes, which secrete a substance called surfactant to reduce surface tension and prevent alveolar collapse. Immune cells, known as alveolar macrophages or "dust cells," are also present to engulf any remaining debris.

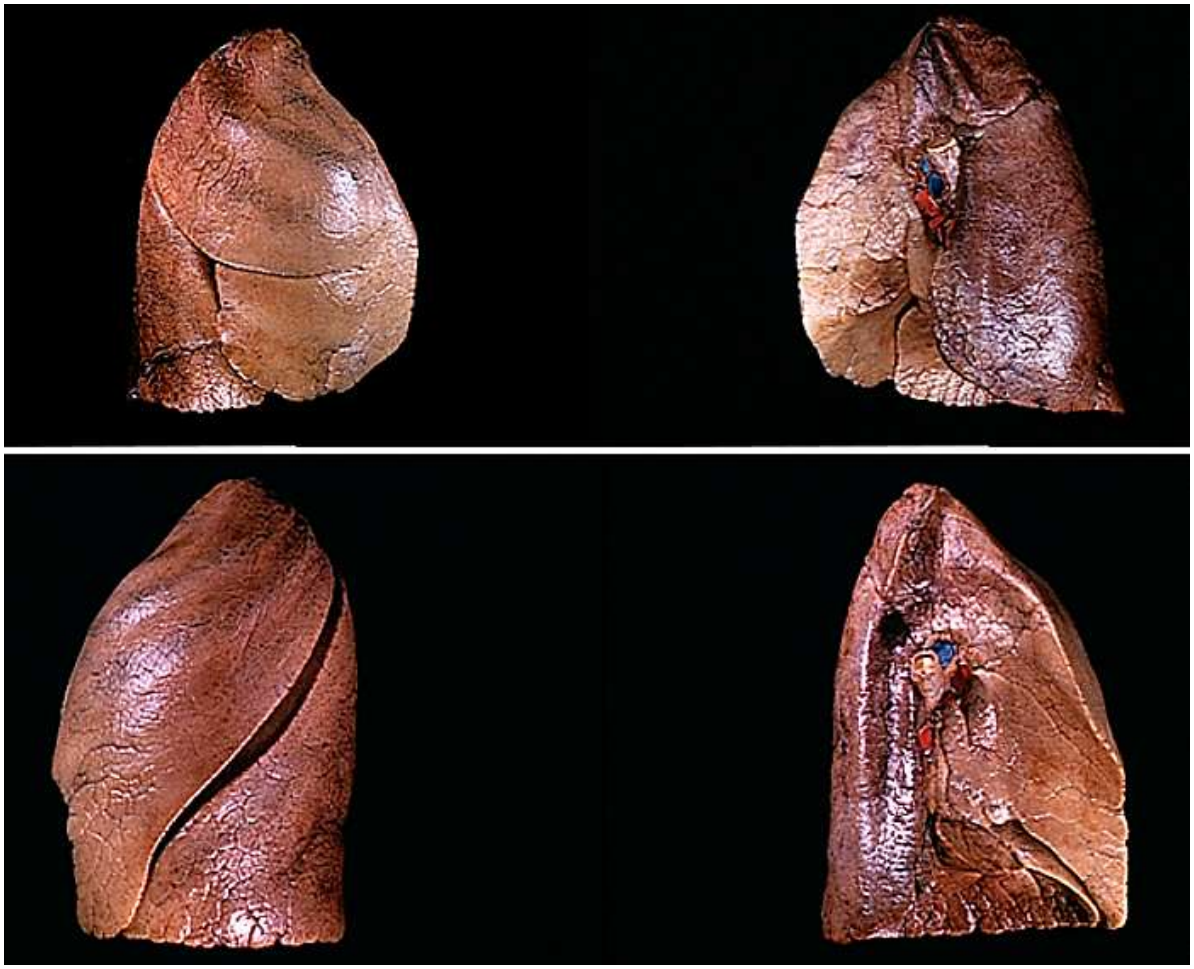


Figure 11: Lateral and medial aspects of the Right lung (top) and Left lung (bottom). From reference 2

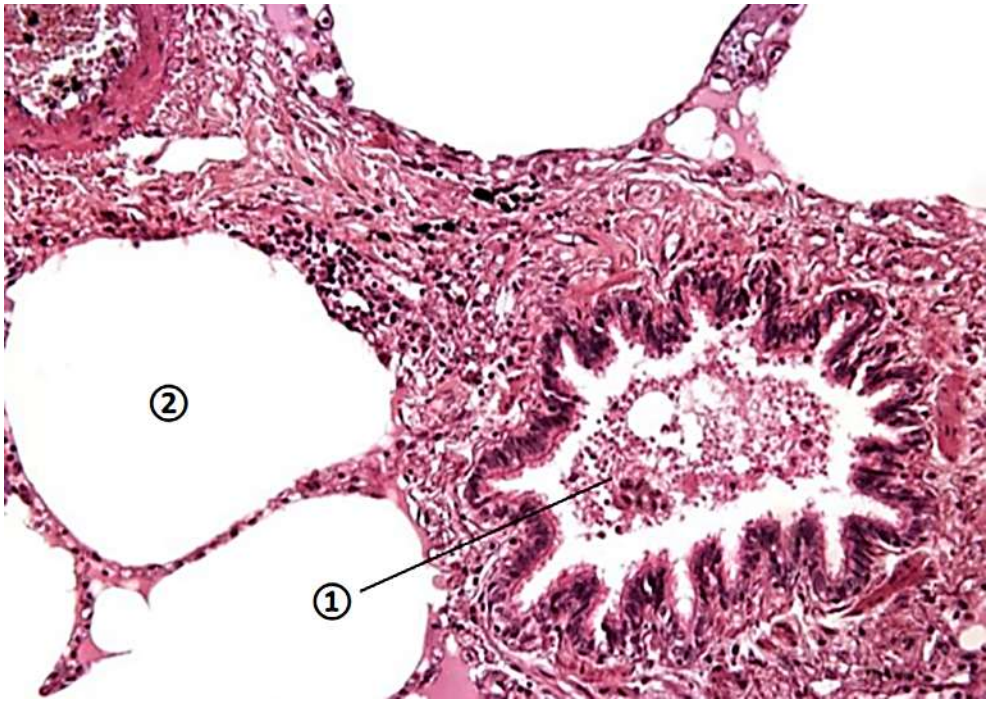


Figure 12: Lung low magnification. 1. Terminal Bronchioli. 2. Alveoli have thin walls, less than 1 micron. From reference 6

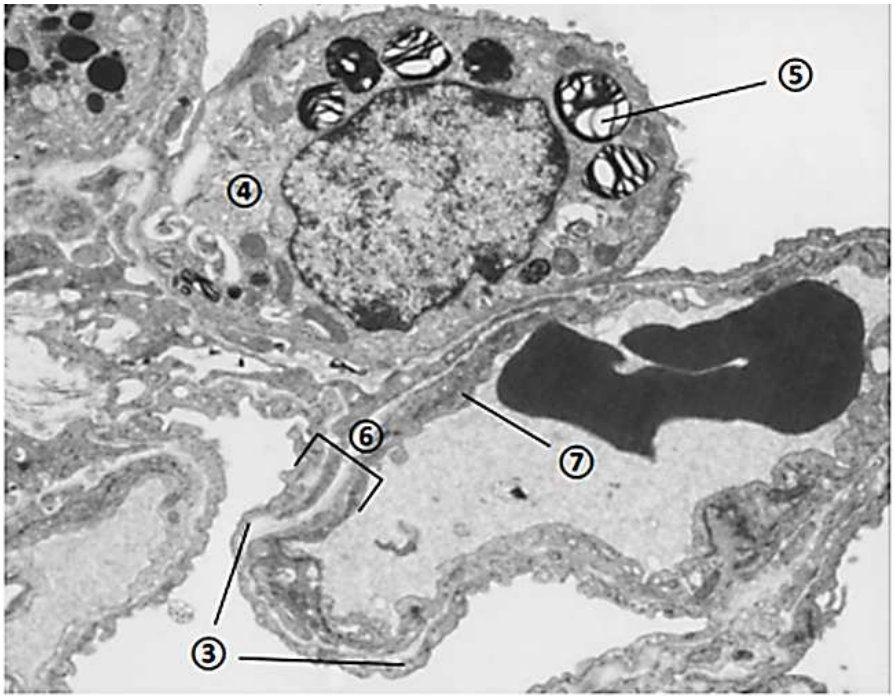


Figure 13: 3. Type 1 Pneumocytes, 4. Type 2 Pneumocytes, 5. Lamellar bodies, 6. Blood-air barrier, 7. Capillary endothelium. From reference 6

Muscles

Functions

The primary function of the respiratory muscles is to change the shape and volume of the thoracic cavity to move air into and out of the lungs.

There are multiple muscles that contribute to inspiration and expiration, including the diaphragm, external intercostal muscles, internal intercostal muscles, sternocleidomastoid (SCM), scalene muscles, and abdominals.

Anatomy

The diaphragm is the primary muscles of respiration. It receives innervation from the phrenic nerves (C3-C5), blood supply from the internal thoracic and inferior phrenic arteries, and venous drainage via the brachiocephalic veins and inferior vena cava.

The external intercostal muscles function to aid in inspiration. They are innervated by the intercostal nerves, receive blood from the intercostal arteries, and drain into the intercostal veins which empty into the azygos vein.

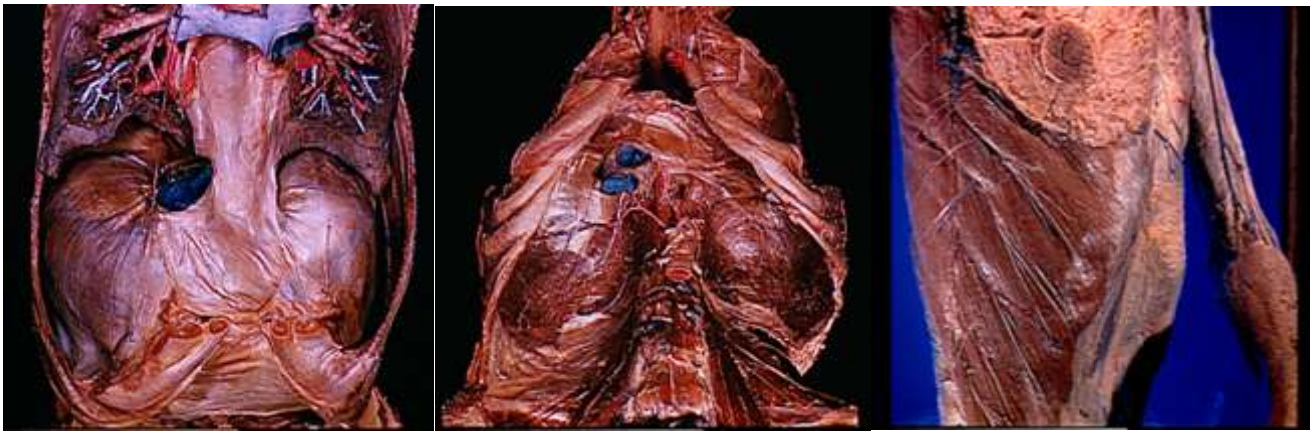
The internal intercostal muscles function in expiration. Similar to the external intercostal muscles, they are innervated by the intercostal nerves, receive blood from the intercostal arteries, and drain into the intercostal veins.

Both the sternocleidomastoid (SCM) and scalene muscles serve as accessory muscles for inspiration. The SCM is innervated by the spinal accessory nerve (CN XI) and the scalene muscles are innervated by the cervical spinal nerves (C3-C8). The SCM receives blood supply from the occipital artery, and the scalene muscles receive blood from the cervical arteries. These muscles drain into the jugular and subclavian veins.

The abdominal muscles consist of the rectus abdominis, internal and external obliques, and transversus abdominis. They serve the purpose of forced expiration, as they increase intrathoracic pressure and hence push the diaphragm up. These muscles are supplied by the thoracoabdominal nerves (T7-L1). They receive their blood supply from the epigastric and lumbar arteries and drain into corresponding veins.

Histology

The diaphragm is a mixed muscle made up of approximately 55% fatigue-resistant slow oxidative (SO or Type I) fibers, 21% fast oxidative glycolytic (FOG or Type IIa) fibers, and 24% fast glycolytic (FG or Type IIx/IIb) fibers.



A **B** **C**

Figure 14: A. Diaphragm viewed from above, B, Diaphragm viewed from below, C. Antero-lateral thoracic wall showing the Latissimus dorsi muscle, Serratus anterior muscle, External abdominal oblique muscle. From reference 2

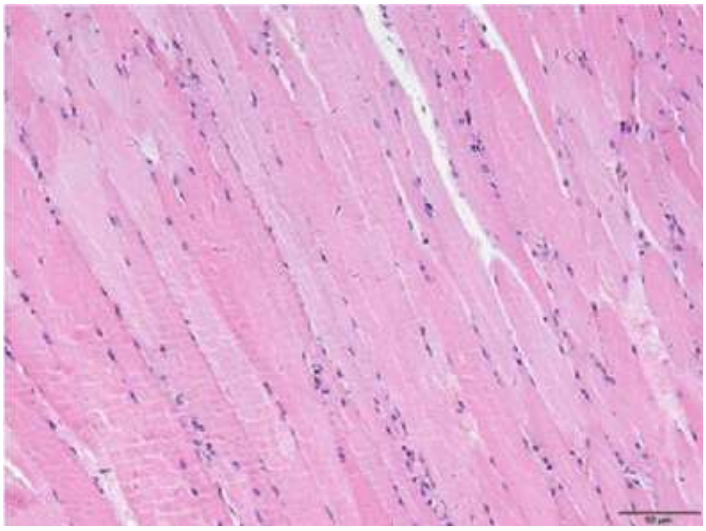


Figure 15: Light microscopy of striated muscles of diaphragm from. From reference 6

Conclusion

Altitude exposes the human cardiopulmonary system to stressors similar to a natural stress test: lower oxygen pressure, changes in intrathoracic pressure, sympathetic activation, and environmental extremes. Here, we explored how fundamental respiratory physiology (gas exchange, oxyhemoglobin affinity, ventilation–perfusion matching) and heart–lung interactions are altered across altitudes. Key principles include the drop in ambient pressure leading to hypoxemia and hyperventilation, the resulting hemodynamic changes, and the remarkable acclimatization process that partially compensates over time. We discussed how these changes impact patients with heart failure, lung diseases, and other conditions – often heightening risks of decompensation – and reviewed clinical strategies to mitigate those risks.

Ultimately, the heart–lung unit is a team, and altitude challenges that team in unique ways. A healthy person's cardiovascular and respiratory systems usually adapt well. But in someone with an underlying disease, the margin for error is thin. Clinicians must be aware of altitude physiology to provide sound advice and recommendations. Altitude-related illnesses further underscore the importance of recognizing symptom patterns and intervening early.

In conclusion, altitude medicine is an intricate interplay of foundational physiology and clinical medicine. By applying principles like gas laws and heart–lung interactions, we can predict how a given person might respond to 3000 m before they ever get there. Similarly, by leveraging modern interventions and timely interventions, we can often circumvent problems or treat them effectively. As travel and living at high altitude become more common, this knowledge becomes increasingly relevant. The human body is adaptable, but not invincible: understanding its limits at altitude allows us to test those limits safely. This chapter highlights the resilience of the cardiopulmonary system and the importance of supporting it, especially when the Earth's environment demands more than usual.

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