HISTOLOGY OF THE RESPIRATORY SYSTEM

Respiration is a process by which the structures responsible for this function ensure gas exchange necessary for maintaining cellular activity.

The respiratory system functions to exchange carbon dioxide for oxygen, which is subsequently distributed to all tissues of the organism. To fulfill this function, air must be conveyed to the region of the respiratory system where gas exchange occurs.

I. General Overview

The respiratory system ensures gas exchange between the blood and ambient air (hematosis). It conducts air toward the alveoli, where these gas exchanges necessary for blood reoxygenation take place. Thus, through the bloodstream, it ensures cellular respiration.

In mammals, the respiratory system includes

- The upper respiratory cavities: consisting of the external nose, nasal cavities, paranasal sinuses, and the rhinopharynx (nasopharynx).
- The conducting airways: consisting of the larynx, trachea, and bronchi.
- The lungs: which are the site of hematosis between blood and alveolar air.

The respiratory system comprises two distinct regions: a **conducting zone** and a **respiratory zone**, which is the site of gas exchange.

I.1 Conducting Airways

The conducting airways of larger diameter are extrapulmonary, whereas those of smaller diameter are intrapulmonary. The respiratory zone is entirely intrapulmonary.

The diameter of the airway lumen is modified by the presence of smooth muscle cells distributed along their entire length.

The conducting airways are subdivided into upper airways and lower (deep) airways.

I.1.1 Upper Airways

The upper airways are represented by the nasal cavities, the nasopharynx, and the larynx.

I.1.2 Lower Airways

They are subdivided into two groups:

I.1.2.1 Conducting pathways

- Trachea
- Bronchi
- Bronchioles

I.1.2.2 Gas exchange zones

- Respiratory bronchioles
- Alveolar ducts
- Alveoli

I.2 Gas Exchange Territories (Respiratory Zone)

The lungs, a spongy mass, are the site where exchanges between blood and air occur at the level of the pulmonary alveoli. The lungs are housed within the thoracic cavity and are mechanically linked to thoracic movements through the opposition of the two pleural layers.

II. Histological Architecture of the Respiratory System

II.1 Upper Airways

The upper airways are represented by the nasal cavities, the nasopharynx, and the larynx.

II.1.1 Nasal Cavities

These consist of two cavities separated by a median septum. Each cavity communicates on one side with the pharynx and on the other with the exterior through the nostrils.

The nasal cavities can be divided into four regions: the nasal vestibule, the nasal cavities proper, the paranasal sinuses, and the olfactory organ.

II.1.1.1 Nasal Vestibule

It is lined by keratinized stratified squamous epithelium continuous with the epidermis of the external surface of the nose. This region is rich in sebaceous glands and contains hairs (vibrissae).

II.1.1.2 Nasal Cavities Proper

This is the respiratory region, also referred to as the Schneiderian membrane. It is lined by a mucosa composed of an epithelium resting, via a basement membrane, on a chorion (lamina propria).

II.1.1.2.1 Epithelium

The epithelium is of the respiratory type (pseudostratified ciliated), composed of two main cell types: ciliated columnar cells and goblet cells secreting mucus. Between these two cell types, basal cells responsible for renewal are also present.

II.1.1.2.2 Chorion (Lamina Propria)

It is attached to the bony periosteum by a thin dense fibrous layer. It contains seromucous glands, which are branched tubuloacinar glands, as well as a highly developed vascular network responsible for warming the inspired air. The air is subsequently humidified by the glands and then filtered by the mucociliary layer.

II.1.1.3 Paranasal Sinuses

These are small air-filled cavities located within the bones of the face (frontal, maxillary, ethmoid, and sphenoid bones).

These cavities communicate with the nasal cavities through a narrow opening. They are lined by a respiratory-type epithelium that is much thinner than that of the nasal mucosa.

II.1.1.4 Olfactory Organ

The olfactory organ occupies the upper part of the nasal cavities. It is lined by olfactory mucosa, whose lining epithelium has a specific structure and function.

II.1.2 Pharynx

The pharynx partially belongs to the digestive tract. Its wall is described as comprising a mucosa, an inconsistent submucosa, and a muscular layer.

The mucosa is lined, depending on the region, by either respiratory epithelium or stratified squamous epithelium.

The submucosa consists of dense connective tissue, and the muscular layer is composed of striated muscles organized into an inner longitudinal layer and an outer oblique or circular layer. Numerous elastic fibers are present between the muscle bundles.

The pharynx is the crossroads of the respiratory and digestive pathways. In its three regions—nasopharynx, oropharynx, and laryngopharynx—the mucosal epithelium differs.

II.1.2.1 Nasopharynx

The nasopharynx represents the upper part of the junction between the respiratory and digestive tracts. It continues from the nasal cavities.

Like the nasal cavities, it is lined by pseudostratified respiratory epithelium, with some isolated areas of non-keratinized stratified squamous epithelium on its posterior surface. It contains lymphoid formations constituting the tonsils.

II.1.2.2 Oropharynx

The oropharynx extends the oral cavity and, like it, is lined with stratified squamous epithelium.

II.1.2.3 Laryngopharynx

It is lined with the same type of epithelium as the esophagus, namely non-keratinized stratified squamous epithelium.

II.1.3 Larynx

The larynx is a rigid tubular structure (cartilaginous) located anterior to the esophagus and forming the junction between the pharynx and the trachea.

It consists of a cartilaginous skeleton, a fibroelastic layer, and a laryngeal mucosa formed by an epithelium that varies according to location:

- Stratified non-keratinized squamous epithelium (anterior surface and upper third or half of the posterior surface of the epiglottis)
- Pseudostratified epithelium with goblet cells (in the remainder of the larynx)
- Stratified ciliated columnar epithelium (above the vocal cords), with some areas of squamous epithelium

Laryngeal glands, like those of the trachea and bronchi, are mixed (seromucous) and generally classified as tubular glands. Both mucous and serous tubules are present, and their distribution is highly variable. The serous and mucous cells are surrounded by myoepithelial cells.

II.2 Lower Airways

II.2.1 Trachea

The trachea is a flexible tube that descends vertically into the mediastinum. Its length varies depending on the species, ranging from 10 to 22 cm.

Its upper end is attached to the cricoid cartilage, and it terminates inferiorly at the tracheal bifurcation.

Its shape is cylindrical, maintained by a framework of 16 to 20 incomplete cartilaginous rings shaped like a horseshoe, open posteriorly and closed by a fibro-muscular band.

The trachea consists of:

- A mucosa
- A fibrocartilaginous submucosa
- An external connective adventitia

II.2.1.1 Tracheal Mucosa

The respiratory mucosa consists of an epithelium and a chorion (lamina propria).

II.2.1.1.1 Tracheal Epithelium

It is pseudostratified ciliated epithelium composed mainly of ciliated cells and goblet cells.

Ciliated Cells

These cells beat toward the larynx. Their movements transport upward any material destined to be eliminated through the upper respiratory tract and the larynx, along with the mucus secreted by goblet cells. This forms the mucociliary apparatus, whose role is essential in pulmonary clearance.

Goblet Cells

These are mucus-secreting cells producing mucoproteins.

Basal Cells

These constitute a reserve cell population capable of renewal.

Argentaffin (Chromaffin) Cells

These cells are isolated or grouped in pairs or small clusters. They are located in the deep portion near the epithelial basement membrane and belong to the APUD system.

Glands

These are associated with the epithelium and are tubuloacinar, seromucous glands, identical to those found in the larynx.

II.2.1.1.2 Chorion (Lamina Propria)

The chorion is composed of loose connective tissue containing blood vessels, fibroblasts, and lymphocytes.

In its superficial part, it contains collagen and elastic fibers. In the deeper part, elastic fibers condense into a continuous layer, while cells and vessels become less numerous.

II.2.1.2 Submucosa

The cartilaginous elements consist of hyaline cartilage in young individuals and fibro-hyaline cartilage in adults. They are embedded in a fibrous perichondrium, which is denser superficially.

The tracheal muscle occupies the posterior non-cartilaginous space and connects the ends of the cartilage rings.

II.2.1.3 Adventitia

This is a loose connective-adipose layer containing nerves, arteries, veins, and lymphatic vessels specific to the trachea.

II.2.2 Primary Bronchi

The division of the trachea gives rise to the right and left primary bronchi, which are extrapulmonary.

After entering the lungs, the primary bronchi divide into:

- Two branches on the left
- Three branches on the right

Their histological structure is similar to that of the trachea.

II.2.3 Bronchi

II.2.3.1 General Organization

The trachea divides into right and left primary bronchi, which are extrapulmonary. Each bronchus is directed toward the corresponding lung.

The lobar bronchi enter the lungs, closely associated with connective tissue sheaths containing arteries, veins, and lymphatics.

II.2.3.2 Histological Structure

Extrapulmonary bronchi have a structure similar to that of the trachea but are smaller.

Intrapulmonary bronchi gradually develop a cartilaginous framework in the form of irregular plates distributed along the circumference.

II.2.3.2.1 Mucosa

The mucosa is composed of pseudostratified ciliated epithelium with three types of cells:

- Ciliated columnar cells
- Goblet cells
- Basal cells

The epithelium rests on a chorion made of loose connective tissue rich in lymphocytes and highly vascularized.

Two main features characterize this chorion:

- Numerous elastic laminae that fold the mucosa
- Circular smooth muscle fibers forming the **Reissessen muscle**

II.2.3.2.2 Submucosa

Contains bronchial glands, most of which are serous. These glands extend between the cartilaginous plates.

II.2.3.2.3 Fibrocartilaginous Layer

Formed by irregular plates of hyaline cartilage.

II.2.3.2.4 Perichondrium / Bronchovascular Sheath

A loose connective tissue sheath common to the bronchus and its corresponding pulmonary artery. It contains vascular and lymphatic structures as well as lymphoid aggregates.

II.2.4 Bronchioles

By definition, intrapulmonary bronchi are referred to as bronchioles and are devoid of cartilage and glands.

Under light microscopy at high magnification, three types of bronchioles can be distinguished.

II.2.4.1 Proper Bronchioles

Their diameter ranges between 1 and 1.5 mm.

They are lined by a simple epithelium composed of:

- Ciliated columnar cells
- Goblet cells
- Clara (club) cells (non-ciliated)

This epithelium rests on a connective-elastic chorion with a well-developed Reissessen muscle.

II.2.4.2 Terminal Bronchioles

Their diameter ranges between 0.5 and 1 mm.

They are lined by a simple cuboidal ciliated epithelium with rare mucous (goblet) cells. This epithelium rests on a chorion limited by the Reissessen muscle.

II.2.4.3 Respiratory Bronchioles

They open into alveolar ducts and have a diameter of less than 0.5 mm.

They differ from terminal bronchioles by the presence of openings bounded by alveolar walls, interrupting the bronchiolar epithelium and giving it a discontinuous appearance.

The epithelium is simple, ciliated, sometimes very flattened (endothelium-like), and devoid of mucous cells. It rests on a connective-elastic chorion containing some muscle fibers.

Bronchioles are airways with a diameter less than 1 mm and lack cartilage.

Their lumen, star-shaped at rest, is lined by simple ciliated columnar epithelium. Beyond the bronchioles, goblet cells are absent.

The smooth muscle layer is arranged in a spiral manner.

The total surface area of all bronchioles is much greater than that of the rest of the conducting zone. The tone of smooth muscle effectively regulates intrapulmonary airway resistance.

The terminal portion of the conducting airways is the terminal bronchiole.

It divides into short branches called respiratory bronchioles, whose walls contain alveoli.

Each respiratory bronchiole divides into segments called alveolar ducts, into which alveolar sacs and alveoli open.

The terminal bronchiole has a ciliated columnar epithelium lacking goblet cells and containing a few non-ciliated Clara cells, which constitute the predominant cell type in the epithelium of respiratory bronchioles.

II.2.5 Respiratory Tissue

The lungs, which constitute the respiratory tissue, are composed of two structures located laterally in the thoracic cavity, separated by the mediastinum.

They rest on the diaphragm, which separates the thoracic cavity from the abdominal cavity.

Respiratory (pulmonary) tissue consists of alveolar ducts and pulmonary alveoli.

II.2.5.1 Alveolar Ducts

Alveolar ducts follow respiratory bronchioles.

They are formed by a discontinuous wall into which numerous alveoli open.

They are lined by simple squamous epithelium resting on a thin connective-elastic tissue.

They also contain some smooth muscle fibers at the openings between adjacent alveoli, forming alveolar sphincters.

At their dilated terminal portion, called the atrium, several alveolar sacs open.

II.2.5.2 Pulmonary Alveoli

Alveoli consist of a wall and a cavity.

The wall is formed by alveolar lining epithelium, while the cavity contains air.

The alveolar epithelium is not in direct contact with air, as it is separated by an intra-alveolar fluid film.

Alveoli are separated from each other by connective-elastic tissue forming interalveolar septa.

II.2.5.2.1 Alveolar Epithelium

This is a simple squamous epithelium composed of three cell types:

- Type I pneumocytes
- Type II pneumocytes
- Type III (brush) pneumocytes

Type I Pneumocytes

These are small alveolar cells with:

- A thicker region (1–3 μm) containing the nucleus and organelles
- A very thin cytoplasmic extension (~0.2 μm)

This extension contains numerous pinocytotic vesicles involved in macromolecule transport between the alveolar cavity and the septal space.

They form part of the alveolar-capillary membrane through which gas diffusion occurs.

Type I pneumocytes are connected to each other and to type II pneumocytes by tight junctions (zonula occludens), ensuring cohesion of the alveolar wall.

Type II Pneumocytes

These are large, rounded or pyramidal cells partially covered by type I pneumocytes. Only their apical surface is exposed to the alveolar lumen.

Their plasma membrane bears numerous short microvilli connected to the cytoskeleton.

The ratio in alveolar epithelium is approximately:

- 4 type I pneumocytes
- 6 type II pneumocytes

Type III Pneumocytes (Brush Cells)

Characterized by numerous apical microvilli. Their function remains unclear.

II.2.5.2.1.4 Intra Alveolar Septa

These are connective spaces separating adjacent alveoli, forming the pulmonary interstitium through which interstitial cells and fluid (lymph) circulate.

They contain:

- Fibers: collagen, reticular, and elastic fibers
- Cells: connective and blood-derived cells, highly polymorphic
- Capillaries

II.2.5.3 Alveolar Cavity

Contains two main structural elements:

II.2.5.3.1 Surfactant

A superficial phospholipid film produced by type II pneumocytes.

It is located between the air phase and the alveolar liquid surface.

Thickness: ~30 nm
Composition:

- 75% lipoproteins
- 25% phospholipids

Function:

- Reduces surface tension
- Facilitates reopening of collapsed alveoli
- Reduces interalveolar tension
- Improves respiratory mechanics

II.2.5.3.2 Alveolar Macrophages

These cells appear free within alveolar cavities but attach to the surfactant layer via cytoplasmic extensions.

They are rich in:

- Lysosomes
- Phagolysosomes
- Residual bodies

They exhibit intense phagocytic activity and are of bone marrow origin.

II.2.5.4 Interalveolar Communications

Specialized structures allowing direct communication between alveoli:

- **Pores of Kohn**: openings in alveolar walls enabling air passage between alveoli
- **Canals of Lambert**: connections between bronchioles and adjacent alveoli

II.2.5.5 Connective-Elastic Framework

Includes:

- Peribronchial and periarterial sheaths
- Septa dividing anatomical regions
- Intra Alveolar septa

This interstitium provides pathways for:

- Blood vessels
- Lymphatics
- Nerves

Functions:

- Mechanical support
- Protection of alveoli
- Elastic recoil facilitating passive expiration

II.2.6 Pleura

The pleura is a serous membrane enveloping each lung.

It consists of two layers:

- Visceral pleura (in contact with the lung)
- Parietal pleura (in contact with the thoracic wall)

Between them lies a virtual space, the pleural cavity, containing a small amount of fluid allowing smooth sliding between layers.

II.2.6.1 Structure of the Pleura

Each pleural layer consists of three components:

II.2.6.1.1 Pleural Mesothelium

A simple squamous epithelium.

Cells measure approximately:

- 30–50 μm in length
- 5–8 μm in thickness

They may desquamate into pleural fluid.

II.2.6.1.2 Submesothelial Layer

Composed of loose connective tissue containing few cells.

This layer is devoid of blood and lymphatic vessels.

II.2.6.1.3 Superficial Fibroelastic Layer

A thick layer of collagen and elastic fibers.

Each pleural layer is attached:

- Parietally to the thoracic wall
- Viscerally to the lung via subpleural connective tissue

II.2.6.2 Pleural Cavity

A very thin real space between the two pleural layers.

It contains pleural fluid forming a film approximately 20 μm thick, composed of low-viscosity interstitial lymph rich in potassium and albumin, and containing desquamated mesothelial cells.