Respiratory System
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Learning objectives

Students should be able to:

1. Identify, in order, the structures comprising the respiratory system.
2. Describe the histology of "typical" respiratory passageways.
3. Identify and describe the histology of the extrapulmonary components of the conducting portion.
4. Identify and describe the histology of the intrapulmonary components of the conducting portion.
5. Identify and describe the histology of the components of the respiratory portion of respiratory system.
6. Correlate the histology of all these structures with their functions

Overview

I. Functions of the respiratory system

A. Conduct air to lungs
B. Oxygen-carbon dioxide exchange
C. Regulate air temperature
D. Humidify air
E. Reduce air speed
F. Maintain patency
G. Remove foreign matter
H. Provide the special sense of smell
I. Provide for phonation

II. Components of the respiratory system

A. In relationship to lungs (listed in order from exterior to interior), i.e., the path of inspired air

**EXTRAPULMONARY**

1. Nasal cavity
2. Pharynx
3. Larynx
4. Trachea
5. Primary bronchi

**INTRAPULMONARY**

1. Secondary bronchi
2. Bronchioles
3. Terminal bronchioles
4. Respiratory bronchioles
5. Alveolar ducts
6. Alveoli – where gas exchange occurs

B. According to function (listed in order from exterior to interior)

**CONDUCTING PORTION** - Transports air from exterior to lungs

1. Nasal cavity
2. Pharynx
3. Larynx
4. Trachea
5. Primary bronchi
6. Secondary bronchi
7. Bronchioles
8. Terminal bronchioles
RESPIRATORY PORTION - Involved with gas exchange

1. Respiratory bronchioles
2. Alveolar ducts
3. Alveoli – where gas exchange occurs

Respiratory Portion of Respiratory System

III. Histological overview of respiratory passageways

A. Composition of “typical” passageway in the conducting portion of the respiratory system
1. **Mucosa** (mucous membrane)

   a. Respiratory epithelium:
      - **pseudostratified columnar** with **cilia**; sometimes basement membrane is quite prominent.

   **MUCOSA**

   ![Diagram of Mucosa](image)

   1.) **Goblet cells**
   2.) Brush cells with numerous microvilli: sensory receptors
   3.) Neuroendocrine cells (diffuse neuroendocrine system, DNES)
      b. Lamina propria – well vascularized, usually with many longitudinally arranged elastic fibers
      c. Deepest layer of mucosa consists of one of the following:
         1.) **Elastic lamina**–longitudinally arranged elastic fibers
         2.) **Muscularis mucosae** of smooth muscle
         3.) This layer may be lacking
         2. **Submucosa**–well vascularized; contains mucous and serous (mixed) glands
         3. **Cartilage** or **bone**
         4. **Adventitia**
B. Structural transitions in walls and layers of the passageways from extrapulmonary passageways to alveoli:

1. **Layers** becoming thinner as passageways decrease in diameter.
2. **Epithelial** modifications
   a. Epithelium decreases in height from pseudostratified columnar to simple columnar to simple squamous at the alveolar level.
   b. Cilia are present through the beginning of the respiratory bronchioles.
3. Mixed glands stop relatively abruptly at the junction of a secondary bronchus with a bronchiole. Goblet cells are present in the larger bronchioles, but not in the smaller.
4. Cartilage decreases in size, breaks up into plates and stops relatively abruptly at the junction of a secondary bronchus with a bronchiole.
C. Results in the formation of the wall of an alveolus, where gas exchange occurs

1. Simple squamous epithelium lines each alveolus
2. Connective tissue core is composed of reticular and elastic fibers and numerous capillaries.

CONDUCTING PORTION

I. Nasal cavities

A. Non-olfactory region
   1. Vestibules: epithelium undergoes a transition from epidermis of skin with hairs to pseudostratified, respiratory epithelium.
   2. Nasal fossae
      a. "Typical" with abundant blood vessels; muscularis mucosae is lacking.
      b. Bones and cartilage maintain patency.

B. Olfactory region
   1. Upside down, U-shaped area in posterior, superior regions of nasal fossae that extends over superior conchae and about 1 cm down nasal septum
   2. Composition of wall
      a. Mucosa
         1.) Thick, pseudostratified columnar epithelium with nonmotile cilia.
            a.) Olfactory cells (neurons) are bipolar neurons that respond
to odors. Each neuron possesses a single dendrite that projects to the surface and terminates in a swelling, an **olfactory vesicle**. Non-motile cilia extend over the epithelial surface to increase surface area and respond to odors.
b.) Support cells span the epithelium and support the olfactory cells.
c.) Basal cells are located on the basal lamina and serve as reserve cells for the other cell types

2.) Muscularis mucosa is not present, so the lamina propria blends with the submucosa to form a single layer. This connective tissue contains **Bowman's glands** - serous glands whose watery secretions flush odorants from the epithelial surface.

b. Bones maintain patency

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**OLFACTORY EPITHELIUM**

![Diagram of Olfactory Epithelium](image)

To CN I

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**II. Larynx**

A. Mucosa

a. Epithelium:

1.) Pseudostratified with cilia and goblet cells in most areas

2.) Stratified squamous moist over true vocal fold and much of epiglottis due to large amount of friction incurred in these areas.

b. No muscularis mucosae or elastic lamina so lamina propria blends into submucosa.
B. Submucosa with mixed glands (except in the true focal fold)

C. Cartilages that maintain patency and support the vocal apparatus are numerous, uniquely shaped and are usually hyaline; the epiglottis and other, smaller cartilages are elastic. The larger cartilages are the epiglottis, thyroid and cricoid.

D. Vocal apparatus is a modification in the larynx composed of two pairs of horizontally positioned mucosal folds located on the lateral walls of the larynx.
   1. False vocal folds - more superior in location. Resemble the wall of a “typical” respiratory passageway except the deepest layer of the mucosa is absent (no muscularis mucosae nor elastic lamina).
   2. The ventricle, a space, separates the false from the true vocal folds.
   3. True vocal folds
      a. Lined by a stratified squamous moist epithelium and its lamina propria
      b. A vocal ligament of dense regular elastic connective tissue is located at the edge of the fold, keeping the rim of the fold taut.
      c. Vocalis muscle, skeletal muscle, lies beneath each true vocal fold. This muscle alters the shape of the vocal fold and aids in phonation.
III. **Trachea** and **primary bronchi** (one to each lung) are identical in structure and will be considered together.

A. **Mucosa**

   1. **Epithelium**—pseudostratified with cilia and goblet cells with a very prominent basement membrane

   2. Lamina propria

   3. **Elastic lamina** of longitudinally-arranged elastic fibers

B. Submucosa with **mixed glands** and abundant blood vessels

C. C-shaped **cartilage rings** maintain patency; **trachealis muscle** (smooth) interconnects open ends of tracheal rings.
IV. **Secondary bronchi** (intrapulmonary)
   
   A. **Introduction**
   
   1. The first intrapulmonary structures and; therefore, are the first of the remaining passageways that are all **surrounded** by alveoli.
   
   2. A secondary bronchus supplies each of the three lobes of the right lung and two lobes of the left lung.
   
   3. Are similar to, but diminish in size from the primary bronchus.

   B. **Mucosa**

   1. **Epithelium** – pseudostratified with cilia and goblet cells

   2. Lamina propria contains numerous, longitudinally arranged elastic fibers

   3. **Muscularis mucosae**–composed of smooth muscle fibers arranged in criss-crossing bands

   C. Submucosa with **mixed glands**

   D. Patency maintained by **plates of hyaline cartilage**

   E. Adventitia is present

V. **Bronchioles** (intrapulmonary)

   A. Walls of **bronchioles** continue to decrease in size. The greatest changes in histology occur in the walls of the bronchioles as glands and cartilage are eliminated.
B. Mucosa

1. **Epitheliium**

   a. Pseudostratified columnar with cilia and goblet cells in the largest bronchioles that decreases to:

   b. Simple columnar with cilia in the smallest bronchioles (*terminal bronchioles*), but no goblet cells persist.

   c. **Clara cells** are present in the terminal bronchioles.

      1.) Tall, dome-shaped, non-ciliated cells.

      2.) Possess numerous secretory granules whose contents probably aid in lowering surface tension of the terminal bronchioles, thus aiding in inspiration.

2. Lamina propria contains numerous, longitudinally arranged elastic fibers.

3. **Muscularis mucosae** reaches its greatest development of smooth muscle (criss-crossing bands) in relationship to thickness of the wall of all passageways.

C. Submucosa contains no glands.

D. **NO Cartilages** or bones support bronchioles; therefore, submucosa and adventitia form a single connective tissue layer.

![Figure 12](image-url)
## Summary of conducting portion or respiratory system:

<table>
<thead>
<tr>
<th>Passageway</th>
<th>Epith</th>
<th>Cilia</th>
<th>Goblet cells</th>
<th>Mixed glands</th>
<th>Elstc Fbrs Where?</th>
<th>SM M</th>
<th>Cart</th>
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<tbody>
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<td>Trachea/Primary bronchus</td>
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## RESPIRATORY PORTION

I. Primary function: gaseous exchange occurs at the level of the **alveolus**. Therefore, an alveolus must be an integral part of ALL of the passageways of the respiratory part of the respiratory system.
II. Respiratory bronchiole

A. Continue to decrease in diameter and in thickness of their walls.

B. Mucosa
   1. **Simple cuboidal epithelium** with a few sparsely scattered cilia and Clara cells
   2. Elastic fibers in lamina propria
   3. **Muscularis mucosae** of smooth muscle

C. **Alveoli** bulge off from wall, i.e., lumen of alveolus is continuous with lumen of respiratory bronchiole

III. Alveolar ducts

A. An **alveolar duct** is formed as the alveoli in a respiratory bronchiole increase in number, thereby decreasing the amount of wall that is present.

B. At the level of the alveolar duct, the "wall" is reduced to a series of rings framing the entrance to an alveolus or a group of alveoli (alveolar sac).

C. When sectioned, these rings resemble knobs to which the alveoli are attached.

   1. Wall
      a. **Simple cuboidal epithelium**
      b. Elastic fibers and smooth muscle in "knobs"
      c. Alveoli bulge from the framework formed by the knobs.
IV. **Alveolar sacs**—two or more alveoli arising from a single pair of knobs

V. **Alveoli**

A. Thin-walled, hollow compartments where gaseous exchange occurs. Approximately 200 µm in diameter.

B. **Interalveolar septum** - connective tissue core separating two alveolar spaces
   1. Connective tissue core
      a. **Elastic fibers** predominate with reticular fibers also.
      b. **Alveolar macrophages**, in CT here as well as through CT supporting all the passageways, engulf dust and carbon particles (dust cells).
      c. LARGE **capillary network** bulges from septum into alveolar space, forming approximately 80% of alveolar surface.
   2. Epithelium lining alveolus
      a. **Pulmonary epithelial, small alveolar, or type I cell** is a simple squamous epithelial cell that lines 95% of alveolar surface area.
      b. **Septal, great alveolar, or type II cell** – regenerates type I and II cells
         i. Spherical cell with microvilli that bulges into alveolar space
         ii. Possess mitochondria, RER and a well–developed Golgi complex
         iii. Vacuolated, foamy cytoplasm caused by presence of lamellar bodies containing phospholipids, glycosaminoglycans, and proteins
         iv. Produces surfactant which lowers surface tension of alveoli
D. Additional components

1. Pulmonary surfactant
   a. Definition: extracellular fluid layer lining alveoli that lowers alveolar surface tension, aiding in inflation of alveoli during inspiration, and preventing collapse of alveoli during expiration.
   b. Composition – monomolecular surface film of phospholipids (palmitoyl lecithin) that covers an underlying aqueous hypophase
   c. Appears during the last weeks of gestation. Absence or insufficiency of surfactant may result in respiratory distress syndrome or hyaline membrane disease in infants born prematurely.
2. Additional alveolar macrophages lie free in alveolar space within the surfactant layer. With congestive heart failure, RBCs pass into alveolar spaces and are phagocytized by the macrophages that are then called "heart failure" cells.
3. Small openings (alveolar or Kohn's pores) in the interalveolar septa between neighboring alveoli aid in equalizing interalveolar pressure. Unfortunately, they also facilitate the transport of bacteria between alveoli too.
VI. **Air-blood barrier**

A. Barrier through which gases pass; separating alveolar space from capillary lumen

B. Composition

1. Pulmonary epithelial cell and its
2. Basement membrane which is fused with:
3. Basement membrane of the:
4. Capillary endothelial cell

VII. **Pleura**—serous membrane (serosa) covering lungs

A. Composition
1. Simple squamous epithelium (mesothelium)

2. Underlying connective tissue layer with elastic fibers

B. Subdivisions (continuous at hilum of lung)

1. Visceral – covers lung tissue proper

2. Parietal–line inner surface of thoracic cavity

C. Function – produces a film of fluid that lubricates the lung surface

VIII. Vascular supply to lungs

A. Functional circulation to/from alveoli, i.e., supplies deoxygenated blood to alveolar capillaries where gaseous exchange occurs

1. **Pulmonary artery** and its branches – travel adjacent to bronchial tree, supplying deoxygenated blood to:

2. **Capillary plexus** in interalveolar septa; capillaries bulge into alveolar space. Capillaries anastomose to form:

3. **Pulmonary veins** – travel singly in parenchyma away from airways. After leaving a lung lobule, veins join the bronchial tree near hilum; carry oxygenated blood

B. Nutrient vessels: bronchial arteries small vessels lie within walls of bronchial tree (and, therefore, are smaller than any layer of the wall) throughout conducting portion of respiratory system, supply oxygen and nutrients to the passageways themselves.

IX. Correlation between respiratory histology and disease/aging

A. Under trauma, respiratory epithelium can undergo metaplasia to become stratified squamous moist
epithelium with NO cilia. A concomitant increase in mixed glands (and their secretions) is also seen, resulting in increased intraluminal secretory products without the ability to clear these secretions. Examples: chronic bronchitis or smoker’s cough.

B. Loss of elasticity in elastic fibers naturally occurs with aging and decreases the ability of the passageways and alveoli to recoil, resulting in senile emphysema.

C. Hypertrophy of smooth muscle occurs in asthma, decreasing the diameter of respiratory passageways and impeding respiration.

D. Pulmonary edema, caused by pneumonia or congestive heart failure, results in fluid–filled alveolar spaces and a concomitant compromise in respiration.

E. Respiratory distress syndrome or hyaline membrane disease (see “Surfactant”).

F. Alveolar pores aid in equalizing interalveolar pressure but also facilitate spread of infection between alveoli.

G. Inflammation of the pleura, pleurisy, can result in an abundant transudate in the pleural space and adhesions between visceral and parietal layers.

![Normal Bronchiole](image)

**Normal Bronchiole**

![Cross section of a normal bronchiole](image)

**CHRONIC BRONCHITIS**
Air tubes narrowed due to thickened mucous membrane; surrounding tissue inflamed. Mucus and pus impede action of respiratory cilia. Characterized by cough

**BRONCHIAL ASTHMA**
Swelling of air passages and surrounding tissue. Muscles of air tubes become spastic, causing narrowing. Thick mucus fills air tubes and sacs, breathing becomes labored, expiration difficult

**EMPHYSEMA**
Walls of individual alveoli torn; repair impossible. Small air tubes collapse, trapping air; expiration difficult. Lung tissue becomes inelastic; lungs enlarge, resulting in Inspiratory–expansile appearance

**BRONCHIEC/ASIS**
Small air tubes widened abnormally and irregularly. Bronchial mucous membrane d suppurating tissue infected. Air ducts contain thick secretions. Destruction of wall muscles, elastic tissue and cartilage of bronchial wall in varying degrees

Figure 19
<table>
<thead>
<tr>
<th>Passageway</th>
<th>Epithelium</th>
<th>GC</th>
<th>Cilia</th>
<th>Glands</th>
<th>SM M/Elst Lam</th>
<th>Bone Cart</th>
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**Image references:**

Figures 1, 2, 3, 7: Sources unknown


Figures 8 and 13: Ragnit Geeraets, Ph.D.


Figures 11, 16: Caroline G. Jackson, Ph.D.

Figures 6 and 20: Alice S. Pakurar, Ph.D.

Figure 18: A. Stevens and J. Lowe, Human Histology, p. 170, Mosby, 1997


Figure 20: B.L. Baker, et al., Laboratory Guide for Microscopic Anatomy, The University of Michigan, p. 59, 1965, modified by A.S. Pakurar
Laboratory terminology

You are responsible for identifying the following structures in the CD-ROM images. While additional features may be mentioned in the legend or indicated on the images, you are not required to identify them at this time. The practical exam for these CD-ROM-based laboratories will use either the same or similar images to those included in the package.

Nasal cavity/septum

- Olfactory region
- Respiratory regions
- Hyaline cartilage or bony framework
- Olfactory epithelium
- Bowman's glands
- Pseudostratified columnar epithelium with cilia and goblet cells
- Mixed glands

Larynx

- Thyroid, cricoid and epiglottal cartilages
- Ventricles
- False and true vocal folds
- Vocalis muscle
- Vocal ligament
- Stratified squamous moist epithelium
- Pseudostratified columnar epithelium with cilia and goblet cells
- Mixed glands

Trachea and primary bronchi

- Pseudostratified columnar epithelium with cilia and goblet cells
- Elastic lamina
- Mixed glands
- C-shaped cartilage ring
- Trachealis (smooth) muscle

Lung tissue proper

Secondary bronchi

- Pseudostratified columnar epithelium with cilia, goblet cells
- Muscularis mucosae
- Cartilage plates

Bronchioles

- Simple columnar epithelium with cilia
- Clara cells
Muscularis mucosae

Respiratory bronchioles

Simple cuboidal epithelium with and without cilia
Muscularis mucosae

Alveolar ducts

Alveoli

Type I cells—simple squamous epithelium
Type II cells—septal cells
Macrophages in wall of alveoli and other passageways Macrophages lying free in alveolar spaces

Branches of pulmonary artery and vein
Branches of bronchial artery
Pulmonary capillaries
Air-blood barrier
Pleura

VIRTUAL SLIDE LINKS

Trachea 1
Trachea 2
Lung