MICROSCOPIC ANATOMY SLIDE REVIEW
RESPIRATORY SYSTEM

I. RESPIRATORY SYSTEM
UPPER VS. LOWER RESPIRATORY TRACT
Upper respiratory = Vestibule of the nose through the laryngopharynx
Lower respiratory = Larynx through alveolar sacs & alveoli

CONDUCTING VS. RESPIRATORY PORTIONS
Conducting Portion:
Consists of airways with no alveolar epithelium in their walls:
Includes everything from nasal cavities & sinuses down to & including terminal bronchioles
Functions include:
- Carries air to respiratory portion of the tract
- Warms & moistens the air
- Mucus traps particulate matter, & ciliated cells propel mucus toward larynx (the muco-ciliary escalator) where it elicits a cough reflex
- Larynx functions in sound production (phonation)

Respiratory Portion:
Includes all airways where alveolar epithelium makes up at least part of the wall, i.e., respiratory bronchioles, alveolar ducts, alveolar sacs, & alveoli
Functions include:
- Gas exchange between air & blood across the alveolar epithelium
- Surfactant production

THE FOUR MAJOR TYPES OF EPITHELIUM IN THE RESPIRATORY TRACT
"The respiratory" epithelium
Olfactory epithelium
Bronchiolar epithelium
Alveolar epithelium
1. "The Respiratory" Epithelium
   Pseudostratified ciliated columnar with goblet cells
   Found in most of the nasal cavity, most of nasopharynx, most of larynx, & in trachea, bronchi & the largest bronchioles
   Also contains minor cell types that you are not responsible for identifying:
   Brush cells (regarded as sensory receptors)
- apical end has blunt microvilli
- basal end is associated with nerve terminals

**Small granule cells (Kulchitsky cells)**
- a type of diffuse neuroendocrine system (DNES) cell
- have secretory granules in basal cytoplasm
- secrete into lamina propria
- different types exist; they secrete different hormones such as serotonin, bombesin, catecholamines

2. Olfactory Epithelium

Lines part of the roof of nasal cavity, superior part of nasal septum, & superior conchae (part of lateral wall of nasal cavity)

Is a pseudostratified columnar epithelium

Lacks goblet cells

Thicker (taller) than the respiratory epithelium that surrounds it

Contains 3 major cell types:
- **supporting (sustentacular) cells** (have microvilli)
- **basal cells** (are stem cells for the other two types)
- **olfactory receptor cells** (detect odors)

There is a characteristic positioning of nuclei within the olfactory epithelium:
- nuclei of supporting cells usually lie closest to the free surface
- nuclei of basal cells lie closest to basement membrane
- nuclei of olfactory receptor cells lie at an intermediate level

Olfactory receptor cells are true bipolar neurons
- basal end of each cell gives rise to an **axon**
- axons form bundles in the lamina propria that eventually form the **olfactory nerve (cranial nerve I)**
- nerve bundles penetrate the cribiform plate of the ethmoid bone, enter cranium, & synapse in the olfactory bulb of the brain
- have long **cilia** arising from an apical enlargement called the **olfactory vesicle**
- plasma membrane of cilia carries receptors for odors

**Bowman’s glands** lie in lamina propria & empty into nasal cavity

Are serous glands; often paler-staining than the mixed mucoserous glands associated with the respiratory epithelium

3. "Bronchiolar" Epithelium

Simple columnar or cuboidal epithelium that is found in:

**Conducting bronchioles** except for the largest (which still have respiratory epithelium)
**Respiratory bronchioles**, which by definition also have alveolar epithelium lining some part of their walls

Cell types include:

**Clara cells (bronchiolar cells)**
- are unique to bronchiolar epithelium
- often have a dome-shaped or pointed apical end that extends further into the lumen than the other epithelial cell types (like a tongue or flame)
- have some short microvilli, but no cilia
- are the stem cells for the bronchiolar epithelium
- have apical secretory granules that are released into the lumen
- secrete some of the proteins of surfactant (proteins A, B & D)
- do not secrete the phospholipids that decrease alveolar surface tension
  - therefore Clara cell secretion by itself cannot substitute for the surfactant produced by alveolar Type II cells

**Ciliated cells**

**Goblet cells** (absent from healthy terminal bronchioles)

4. Alveolar Epithelium

Lines alveoli wherever they are found (in **respiratory bronchioles**, **alveolar ducts**, or **alveolar sacs**)

Contains **Type I & Type II alveolar cells** in approximately equal numbers

But Type I cells (squamous) cover ~ 95% of alveolar surface area

Therefore alveolar epithelium looks like a simple squamous epithelium by LM

**Type I cells** (Type I pneumocytes, squamous alveolar cells)

Form tight junctions with one another and with Type II cells

Difficult to distinguish from capillary endothelial cells

- Type I tend to bulge slightly into alveolar lumen
- endothelial cells tend to bulge slightly into the capillary lumen

**Type II cells** (Type II pneumocytes, great alveolar cells, septal cells)

Are stem cells that give rise to Type I & II cells

Rounded cells; often located at the angles where alveolar walls meet

Usually found as scattered individual cells rather than in groups

Cytoplasm may appear pale & foamy by LM due to extraction of surfactant

Produce **surfactant in lamellar bodies** that are derived from Golgi

**NOTE:** **Alveolar macrophages (dust cells)** are not part of the epithelium

Found on the surface of alveolar epithelium (in the aqueous hypophase of the surfactant layer) & within the CT of the interalveolar septum (see below)

- in sections they may artifactually seem to be floating free in the alveolar lumen
Phagocytize particles including bacteria
Phagocytize surfactant (i.e., play a role in turnover of surfactant)

TYPES OF AIRWAYS

LARYNX

Responsible for phonation (true vocal folds) & preventing entrance of food into trachea (vestibular or false vocal folds, plus epiglottis)
Lined mainly by respiratory epithelium
Contains:
- Hyaline cartilages (e.g., the thyroid cartilage & cricoid cartilage)
- Elastic cartilages (e.g., epiglottis)
- Skeletal muscles that move the cartilages and vocal folds
Has 2 pairs of folds, both oriented in an anterior-posterior direction:

**Vestibular folds (= ventricular folds, false vocal folds)**
- located superior to the true vocal folds
- usually covered by respiratory epithelium
- contain many seromucous glands
- no skeletal muscle within the fold

**Vocal folds (true vocal folds)**
- usually have a minimally keratinized stratified squamous epithelium
- contain the **vocalis muscle** (skeletal), which is a part of the thyroarytenoid muscle
- contain the **vocal ligament (= vocal cord)**; composed of dense regular elastic tissue
- have “no” glands (at least not near the vocal ligament)

The folds divide the lumen of the larynx into three regions:

**Vestibule** (superior to false folds)
**Ventricle** (between false & true vocal folds)
**Infraglottic region** (inferior to true vocal folds)

TRACHEA

 Begins inferior to cricoid cartilage of the larynx
 Ends at its bifurcation into primary bronchi (at the sternal angle)
Has a mucosa, submucosa, cartilage layer, & adventitia
Mucosa
- Has a tall respiratory epithelium
- Unusually thick basement membrane often visible with H&E stain
- Thin lamina propria that is more cellular than the submucosa
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Elastic fibers (instead of a muscularis mucosae) form the boundary between lamina propria and submucosa

Submucosa
- Contains mixed mucoserous glands
- Contains larger blood vessels than lamina propria

C-shaped rings of hyaline cartilage
- Are deficient posteriorly (allows a bolus of food to pass more easily down the esophagus)

Dense CT and the trachealis muscle (smooth muscle) bridge the gap between the ends of each cartilage
- Dense CT unites each cartilage ring with the ones superior & inferior to it
- Adventitia is the CT that lies exterior to cartilage

BRONCHI
- At their origins, the right & left primary bronchi (= extrapulmonary bronchi, main bronchi) initially have same histology as trachea
- At about the point where they enter lung tissue & become intrapulmonary bronchi their histology changes
- Intrapulmonary bronchi (secondary or lobar, tertiary or segmental, and smaller) have:
  - Irregular cartilage plates (not C-shaped) that may overlap
  - A muscularis mucosae instead of a layer of elastic fibers between lamina propria & submucosa
  - Fewer glands (mucoserous)
- All bronchi have a respiratory epithelium

BRONCHIOLES
- By definition, contain no cartilage
- Muscularis mucosae (smooth muscle) is prominent
- Have “no” glands
- Types of bronchioles:
  - **Conducting Bronchiole**
    - Definition: A bronchiole that has no alveolar epithelium in its walls
    - The epithelium is:
      - respiratory epithelium in the largest conducting bronchioles
      - bronchiolar epithelium with goblet cells in most smaller conducting bronchioles
      - bronchiolar epithelium without goblet cells in normal terminal bronchioles
  - **Terminal Bronchiole**
    - Definition: The smallest type of conducting bronchiole. It branches to form one or more respiratory bronchioles.
    - Can be identified in two ways:
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- in longitudinal section, where you can see that it directly gives rise to respiratory bronchioles
- at high enough magnification so that you can see that it has neither goblet cells nor patches of alveolar epithelium

**Respiratory Bronchiole**

Definition: An airway whose bronchiolar epithelium is interrupted by patches of alveolar epithelium

Is the most proximal part of the respiratory portion of the respiratory system (the part in which efficient gas exchange can occur)

**ALVEOLAR DUCTS**

- Tubular airways whose walls are made up of alveoli
- Lumen lined by alveolar epithelium
- Smooth muscle encircles mouth of each alveolus in an alveolar duct
  - Acts like a sphincter around the opening of the alveolus
  - Forms a “knob” at end of interalveolar septum

**ALVEOLAR SACS**

- Each sac consists of a spherical cluster of alveoli that open onto a common central space (the atrium)
- Found as terminal enlargements at the end of an alveolar duct or scattered along its length
- Very difficult to identify in sections
- Alveoli of alveolar sacs have elastic and reticular fibers encircling their openings instead of smooth muscle

**INTERALVEOLAR SEPTA (WALLS)**

- Separate adjacent alveoli from one another
- Are lined on both free surfaces by alveolar epithelium
- Contain a rich network of continuous (nonfenestrated) alveolar capillaries

**Alveolar pores (of Kohn)** are openings through the interalveolar septum that connect the air spaces of neighboring alveoli

- Often connect alveoli that arise from different airways (i.e., alveoli that abut one another “back-to-back”)
- Help to equilibrate air pressure within a bronchopulmonary segment
- Can serve as alternate (collateral) pathways by which air from unobstructed airways can reach alveoli normally supplied by the blocked airways
- Can also be a route for spread of disease
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AIR-BLOOD BARRIER

Represents the structures across which gasses must diffuse in order to exchange between blood in an alveolar capillary and air in an alveolus.

**Minimum air-blood barrier** consists of:

- Surfactant layer
- Alveolar Type I cell cytoplasm
- Fused basal laminae of the alveolar epithelium & the endothelium
- Endothelium of alveolar capillary

Barrier is thicker in many places due to the presence of Type II cells in the epithelium, &/or CT cells and fibers in the interalveolar septum.

NOTE: The minimum barrier is not the same thing as an interalveolar septum.

Minimum barrier separates alveolar air space from capillary lumen.

Interalveolar septum separates the air spaces of 2 adjacent alveoli.

PULMONARY BLOOD SUPPLY

Pulmonary arteries:
- Wall is thinner than other arteries of comparable diameter because it is a low-pressure system.
- Branches of pulmonary arteries in the lung follow the airways closely, branching as the airways branch.
- Carry oxygen-poor blood to the alveolar capillary network.

Pulmonary veins:
- Most are located in connective tissue septa between lung lobules, not near the large airways and arteries.
- As they approach the hilum they run closer to the airways and arteries.
- Have a thinner wall than the pulmonary artery.
- Carry oxygen-rich blood back to the left atrium.

Bronchial arteries:
- Much smaller than pulmonary arteries.
- Arise from the aorta.
- Carry oxygen-rich blood to supply the walls of bronchi & bronchioles.
- Located within the airway wall.
- Deoxygenated blood leaving the bronchial artery capillary bed drains:
  - mainly into alveolar capillaries for re-oxygenation.
  - some drains directly into pulmonary veins at the venous end of the alveolar capillary beds.
- some drain into **bronchial veins**, which are found only near the root of the lung

### KEY FEATURES OF THE RESPIRATORY SYSTEM

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<th>GLANDS</th>
<th>WALL</th>
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<tr>
<td>Trachea &amp; extrapulmonary bronchi</td>
<td>Respiratory epithelium</td>
<td>Mucoserous</td>
<td>C-shaped hyaline cartilages; elastic fiber layer between mucosa &amp; submucosa</td>
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<td>Respiratory epithelium</td>
<td>Mucoserous</td>
<td>Irregular hyaline cartilage plates; muscularis mucosae</td>
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<tr>
<td>Largest bronchioles</td>
<td>Respiratory epithelium</td>
<td>“None”</td>
<td>Muscularis mucosae; no cartilage</td>
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<tr>
<td>Smaller conducting bronchioles</td>
<td>Bronchiolar epithelium</td>
<td>None</td>
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<td>Alveolar ducts</td>
<td>Alveolar epithelium</td>
<td>None</td>
<td>Alveoli with smooth muscle sphincters</td>
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<td>Alveolar sac</td>
<td>Alveolar epithelium</td>
<td>None</td>
<td>Alveoli with elastic fibers around their mouths</td>
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