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RS HISTOLOGY

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The Respiratory System

It is composed of a conducting portion and a respiratory one and a transitional zone in between.

Conducting portion:

- Provides passage of air.
- It begins from the nose then we go through the larynx, trachea, primary bronchi, secondary bronchi, tertiary bronchi and bronchioles. The bronchi are formed from cartilage and this helps them in remaining open to allow the passage of air.
- No gaseous exchange occurs through it.

Respiratory portion:

- Where gas exchange takes place.
- It includes the respiratory bronchiole, alveolar ducts and the alveoli.



- We have terminal bronchioles (part of the conducting portion) and respiratory bronchioles (Part of the respiratory portion) that differ in their cellular structure; the terminal bronchiole is formed by ciliated and non-ciliated simple columnar/cuboidal epithelium, but the respiratory bronchiole is formed by simple squamous epithelium which is very thin to allow for gas exchange.
 - P.S: Bronchiole \rightarrow No cartilage.
 - Asthma happens because of a problem in the bronchioles, especially in the terminal ones.

Now we'll study both portions in more details...

Conducting portion

- 1. Nose.
- 2. Nasopharyngeal cavity.
- 3. Larynx.
- 4. Trachea.
- 5. Bronchi: (1ry, 2ndry, 3ry).
- 6. Large Bronchioles.
- 7. Terminal bronchioles.



- Regarding the bronchi: The primary refers to the main bronchi that it outside the lungs, the secondary bronchi -AKA lobar bronchi- go to the lobes of the lungs (2 lobes in the left lung and 3 in the right one) and as for the tertiary bronchi, they're called bronchopulmonary segments that are distributed as 10 segments in each lung.
- The type of epithelium changes as we move distally in the conducting portion; we begin with pseudostratified ciliated columnar epithelium and when we reach the terminal bronchiole it becomes simple columnar then simple cuboidal -ciliated or non- ciliated for both of them.
 - Further clarification: As we move distally in the terminal bronchiole, the epithelium changes from simple columnar to simple cuboidal *it becomes lower* and from ciliated to non-ciliated.
- The following figure shows a cross-section of the trachea; it shows multiple layers, the first one being the mucosa and it's composed of 3 layers; lining epithelium, lamina propria and muscularis



mucosa, these are similar to the ones of the GI tract, but the difference lies in the lining epithelium which is *'pseudostratified ciliated columnar epithelium and goblet cells'* and this is generally the lining epithelium in the respiratory tract , however, there is a transition in the terminal bronchioles as mentioned previously.

 $\circ~$ The number of goblet cells decreases as we move distally.

- The lamina propria is a loose connective tissue and it contains a gland 'seromucous gland'.
- The second layer is the submucosa that is considered dense connective tissue containing blood vessels, nerves and some seromucous glands as well.
- Following the submucosa, we have the supportive layer, this layer is hyaline cartilage and it is present in the respiratory tract in order for it to remain open allowing the passage of air.
 - This hyaline cartilage is C- shaped in the trachea (absent posteriorly) because the oesophagus lies posterior to it and the presence of cartilage there compresses the oesophagus so it is substituted with trachealis muscle (A smooth muscle).
 - In the left and right main bronchi, the C-shaped hyaline cartilage becomes plates of cartilage surrounding the whole bronchus.
 - > The last layer is connective tissue- for support.
 - Major function of the conducting portion is to condition the inspired air.
 - Additionally, before it enters the lungs, inspired air is cleansed, moistened, and warmed.
 - Numerous mucous and serous glands as well as a rich superficial vascular network in the lamina propria.

Respiratory portion

Respiratory bronchioles (region of transition; weak area, more prone to become cancerous tissue).

- 1. Alveolar ducts.
- 2. Alveolar sacs (the end part of alveoli).
- 3. Alveoli: main sites for the principal function of the lungs that is the exchange of O2 and CO2 between inspired air and blood.



- In the respiratory bronchiole, the epithelium becomes simple squamous and the goblet cells become very few, also you'll find more smooth muscles.
- The epithelium of the alveoli and their surrounding capillaries is simple squamous as well.
- The change in the type of epithelium is quite logical since it serves the function of the tissue.



- The exchange of gases (O2 & CO2) between the alveoli & the blood occurs by passive diffusion.
- The alveoli contain type 1 alveolar cells; squamous cells for gas exchange, and type 2 alveolar cells; cuboidal cells that are surfactant-secreting.
- Surfactants decrease the alveoli's surface tension allowing their inflation and their secretion begins in the 8th or 9th month of gestation.



- The fetus gets his O2 supply from the placenta, then right after delivery, the doctor pats on the newborn's back thus stimulating the respiratory centers in the brain and accordingly the phrenic nerve sends a message to the diaphragm making it contract then the baby cries and the lungs inflate giving the newborn to breathe by his own.
- Many infants are born with respiratory distress syndrome so they're put in incubators until their lungs secrete enough surfactants.
- When blood first arrives at the pulmonary capillary at its arteriole end, the partial pressures of carbon dioxide and oxygen are: PCO2 = 45 mm Hg PO2 = 40 mm Hg
- In the alveoli: PO2 = 105 mmHg PCO2 = 45 mmHg
- O2 is taken up by RBCs and CO2 is released due to difference in pressure.
- After the net diffusion of oxygen PO2 in the venous end equals 95mmHg.
- Oxygen is then taken by tissue cells for metabolic activity (tissue PO2 = 40 mmHg).
- In short, blood flows from the arteriole end (high PCO2; exchange occurs) reaching capillaries (now blood high in oxygen content) then venules (with low PCO2 and high O2, which impedes further exchange).
- When taking a blood specimen to assess blood gases, it should be taken from the artery.

Carbon-dioxide in the blood:

- ➤ 7% dissolved in plasma.
- 23% combine with hemoglobin to form carbaminohemglobin.
- 70% converted to protons by carbonic anhydrase and combines to hemoglobin (reversible reaction).





Respiratory Epithelium

- Lined with ciliated pseudostratified columnar epithelium.
- Contains 5 types of cells (other than the pseudostratified ciliated ones).
- All of them resting on basement membrane, but not all of them reach the surface.
- The most common cells to be seen in the lining epithelium under the LM are the pseudostratified ciliated cells and goblet cells; others are seen under the EM.



- According to the figure above, the 5 types of cells are:
 - (Diffuse neuroendocrine system cells) that are related to the neural cells, 2) Brush cells with microvilli, 3) seromucous cells, 4) Goblet cells, 5) Basal or stem cells that are precursor cells.
- Each type of cell present in the lining epithelium has its own character and function.

Ciliated columnar cells

- Most abundant type
- Each cell has about 300 cilia on its apical surface
- Basal bodies:
 - Where cilia are inserted in the apical part of the cell.
 - Apical mitochondria (large number).
 - Supply adenosine triphosphate (ATP) for ciliary beating.



Cilliary movements

- Dynein, a protein normally participates in the ciliary movement (an outward movement in the respiratory tract; to expel foreign bodies).
- Nicotin prevents formation of dynein, which leads to improper movement of cilia.
- Immotile cilia syndrome (Kartagner Syndrome): caused by nicotine.
 - o caused by immobility of cilia and flagella.
 - induced, in some cases, by deficiency of Dynein.



 Causes infertility in men and chronic Respiratory tract infections in both sexes.



Mucous goblet cells

- > Apical mucous Droplets.
- Composed of Glycoproteins and Contains Polysaccharides.
- Secretes mucin which trapes the foreign bodies.

Brush cells

- > Numerous microvilli on their apical Surface.
- Sensory receptors (afferent nerve Endings on their Basal surfaces).





Basal (short) cells

- Small rounded cells.
- Believed to be Generative stem cells.
- Differentiate by mitosis into the other cell types (reserve cells).
- The basement membrane in the respiratory tract is relatively thick and all cells of the respiratory tissue must reach it and not necessarily to the apical surface (hence, *pseudo*-stratified), as basal cells do not reach the apical surface.



Small granule cell

- Cells of the DNES (diffuse Neuroendocrine system).
- Regulates locally the Excretions or secretions of Mucous and serous glands in the respiratory tract.
- > Also called *Kulchitsky Cells*.



Layers of the respiratory tube

- 1. Mucosa:
 - a. Epithelium resting on a thick basement Membrane and goblet cells.
 - b. lamina propria: contains an important gland.
 - c. muscularis mucosa (smooth muscle).
- 2. Submucosa: that houses mucous and Seromucous glands
- 3. Supportive layer: Smooth muscle and hyaline cartilage.
- 4. Adventitia: Connective tissue coverings.
 - Generally, hyaline cartilage decreases towards the alveoli, from C shaped cartilage to cartilage plates to no cartilage in the bronchioles.
 - While the smooth muscle cells are the exact opposite, at the beginning, they are scarce, at the bronchioles, they increase gradually forming a spiral layer surrounding the lumen.

- Eventually, these muscles will form knobs around the alveoli.
- These muscles can contract, narrowing the lumen, causing wheezing and asthma.
- It can be treated with bronchodilator like adrenaline
- You should know how the lining epithelial, goblet cells (decrease), diameter (decrease), cilia (decrease), cartilage (decrease), Smooth muscle (increase), elastic fibers (increase) and reticular fibers (increase) change as we are moving distally.
- Elastic fibers and reticular fibers are important for lung inflation.

Nasal Cavity

- Subdivided into
 - The vestibule
 - o The respiratory area
 - o Olfactory region



The vestibule

- Most anterior and dilated portion of the nasal cavity
- Lined by modified skin.
- Contains sebaceous and sweat Gland.
- Thick short hairs, or vibrissae.
- Trap and filters out large particles from the inspired air.



Epithelium loses its keratinized nature and undergoes a transition into typical respiratory epithelium before entering the nasal fossae



The respiratory area

- Covered with pseudostratified columnar and goblet cells.
- The sub. Epithelial connective tissue is rich with blood vessels and seromucous glands.

Olfactory region

- Present in the roof and Upper parts of the nasal Cavity
- Covered by pseudostratified columnar with olfactory Mucosa which contains:
 - Olfactory epithelium
 - o Corium (lamina propria)
 - Bowman's gland: are found in the submucousa, they have a duct that opens directly to the apical surface. It dissolves the odor so it can be converted to impulses.





Olfactory epithelium

- It is a pseudostratified columnar Epithelium composed of three types of cells:
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 - 1. Supporting Columnar (sustentacular) cells
 - broad, cylindrical apexes and Narrower bases
 - o microvilli submerged in a fluid layer
 - o contain a light-yellow pigment
 - o around the bipolar cells
 - 2. Basal cells: single layer at the base of the epithelium
 - o spherical or cone shaped
 - $\circ\;$ divide by mitosis to replace other cells.
 - 3. Olfactory cells: Bipolar neurons
 - Their nuclei lie below the Nuclei of the supporting cells
 - Cilia (nonmotile) rise from their apexes (dendrites, hairlets) these cilia receive the odor.







- Respond to odoriferous Substances by generating a Receptor potential, smell impulses, which will be transmitted by the axons of olfactory nerves.
- Afferent axons of these Bipolar neurons unite in small Bundles, and synapse with the Olfactory lobe (the center).

Olfactory epithelium

Olfactory cells



Lamina propria

- Corium (lamina propria) Is rich in blood vessels.
- Contains Bowman's Gland that secrete watery Mucous
- Facilitating the access of New odoriferous Substances.

Nasal Sinuses

- Lined with a thinner respiratory
 Epithelium (similar composition but thinner).
- > Contains few goblet cells.
- The lamina propria contains Only a few small glands.
- Continuous with the Underlying periosteum.
- Contain air, and its duct opens in the lateral wall of the nose.
- Contain few glands.







The Bronchial Tree

Structural changes in the bronchial Tree

- The trachea extends from the level of C6 to T4 (bifurcation point), angle of louis.
- It bifurcates into two bronchi (right and left).
- The right is shorter more vertical and wider while the left is longer, narrower and more horizontal. That's why foreign materials usually dislodge in the right bronchus.
- Each bronchus is surrounded by *circular* plates of hyaline cartilage which diminishes distally.
- Only The trachea and the 1ry (main) bronchus are Extra-pulmonary.
- We have three Lobar (2ndry) bronchi in the right and two in the Left lung.
- There are 10 bronchopulmonary tertiary, segmental- bronchi on each side.
- The diameter decreases distally.
- Segmental (tertiary) Bronchus is almost 5mm or less in diameter.
- Each bronchiole enters a Pulmonary lobule.
- Each large bronchiole (1 mm) gives 5-7 terminal ones.
- Terminal bronchioles (0.5 mm) contain clara cells (simple cuboidal no cilia) and Neuroepithelial bodies (chemoreceptor).

Trachea

- lined with a typical respiratory mucosa
- C-shaped rings of hyaline cartilage that Keep the tracheal lumen open (in the Lamina propria)
- Fibroelastic ligament and bundle of Smooth muscle (Trachealis) bind to the Perichondrium and close the rings Posteriorly







- Some longitudinal muscles may be Found behind the trachealis in the Submucosa or lamina propria.
- Numerous Seromucous glands That produce a more Fluid mucus
- Contain the same 5 Types of cells in the Mucosa, but we mainly see pseudostratified and goblet cells.
- The ligament prevents Overdistention of the lumen
- > The muscle allows regulation of the lumen
- Contraction of the Trachealis Muscle and the resultant Narrowing of the tracheal Lumen are involved in the Cough reflex.





Bronchi

Divided into:

- Extrapulmonary (primary Bronchus):
 - Resembles trachea in structure
 - Have plates of hyaline cartilage, which circulate the entire wall forming rings to keep the lumen open, but it is no longer C Shaped, however, they decrease distally.
- Intrapulmonary (2ndry and Tertiary):
 - They have complete muscular Layer, which increases distally causing folding of the lumen.
 - Cartilaginous plates instead of Rings (fewer plates)
 - Goblet cells decrease distally



> Now, let's wrap up the whole lecture..

Differences between the trachea and Bronchi

1. Narrower lumen (small Bronchus 5mm or less)

2. Irregular bronchial cartilage Plates

3. Smooth muscle layer Consisting of spirally arranged Bundles between the lamina p. And submucosa

 Contraction of this muscle layer Is responsible for the folded Appearance of the bronchial Mucosa Differences between the trachea and Bronchi

4. Lamina propria is Rich in elastic fibers and contains an Abundance of mucous and serous glands

5. Respiratory Epithelium with fewer Goblet cells 6. Numerous Lymphocytes and Lymphatic Nodules (BALT) are Present (infiltrated by the adventitia), increase distally until the bronchioles, then they are replaced by dust cells (macrophage cells)







Structural changes in the conducting Portion of the respiratory tract

Extra-pulmonary bronchi

- Pseudostratified ciliated Columnar epithelium with goblet Cells.
- Prominent basement membrane.
- Relatively thin lamina propria (elastic layer at base)
- Submucosa with seromucous Glands
- "C" shaped hyaline cartilage rings w/ smooth muscle between ends of cartilage



Intrapulmonary bronchi

- Pseudostratified ciliated Columnar changing to ciliated Simple columnar in smaller Branches. Goblet cells at all Levels.
- Below lamina propria are Interlacing spirals of smooth Muscle
- Seromucous glands decrease as Bronchi get smaller.
- Plates of cartilage gradually Disappear

Bronchioles (1 mm or less - important -)

- Simple Ciliated columnar to simple ciliated cuboidal
- Goblet cells decrease and Clara cells Appear
- Spirals of smooth muscle relatively Heavier than elsewhere (gradually Decrease in amount)
- No seromucous glands
- No cartilage

Respiratory bronchioles

- Cuboidal epithelium with Some cilia. Then they form Clara cells and No goblet cells. Then simple squamous epithelial.
- Thin supporting wall of C.T. And an incomplete layer of Smooth muscle.
- Outpocketings of alveoli, Numbers increase at lower Levels.







Bronchioles

- Clara cells
- devoid of cilia
- secrete proteins that protect the bronchiolar lining Against oxidative pollutants and inflammation.
- Neuroepithelial bodies
- contain secretory granules and receive cholinergic nerve endings
- chemoreceptors that react to changes in gas Composition within the airway

Elastic Fibers

- Longitudinal elastic fibers are present in all the segments of the bronchial system (in the L.propria), especially around the alveoli to allow inflation and deflation of the lung
- The smaller the bronchiole the higher Proportions of elastic fibers.

"لاَ يَغُرَّنَّكَ تَقَلُّبُ الَّذِينَ كَفَرُواْ فِي الْبِلَادِ، مَتَاعٌ قَلِيلٌ ثُمَّ مَأْوَاهُمْ جَهَنَّمُ وَبِئسَ الْمِهَادُ".