RESPIRATORY SYSTEM

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Plan of lecture

1. General characteristics and functions of the respiratory system.

2. Embryogenesis of the respiratory system.

3. Structural and functional organization of the conductive portion of respiratory system.

4. Lungs. Structural units of the lungs.

5. Respiratory department. Structural elements of lung acinus.

6. Aerohematic barrier.

7. Blood supply and innervation of organ of the respiratory system.
Systema Respiratorium
(The Respiratory System)

The complex of organs and tissue which are necessary to exchange blood carbon dioxide (CO$_2$) with air oxygen (O$_2$)

1. conductive portion;
2. respiratory portion;
3. pleura & ventilation mechanism.
Conductive Portion

- Nasal cavity;
- Nasopharynx;
- Larynx;
- Trachea;
- Arbor bronchialis:
  - main bronchi (primary);
  - large bronchi (secondary);
  - medium bronchi;
  - small bronchi;
  - bronchioles;
  - terminal bronchioles.

- directed passage & conditioning of air (warming/cooling, filtration, humidification);
- vocalization;
- smell (olfaction).
Functions of the conducting portion

- are to provide a route for the air to reach the lungs and also for conditioning the air
- Air-conditioning during its passage through the conducting portion includes:
  - filtration (by hairs)
  - cleansing (by mucus and ciliary action)
  - moistening (by mucus)
  - warming or cooling (by heat exchange via blood vessels)
Embryogenesis of the respiratory system

FETAL STAGE

Embroinary: (3-7 weeks)
  - Trachea (day 24)
  - Source bronchii (day 28)
  - Lobe bronchii (day 37)
  - Segmentary bronchii (day 42)

Pseudoglandular: (7-17 weeks)
  - Bronchioli (12-16 weeks)
  - Terminal bronchioli (16-17 weeks)

Canalicular: (17-27 weeks)
  - Respiratory bronchioli (18-25 weeks)

Saccular: (28-36 weeks)
  - Alveolar ducts (25 weeks to 1 year)

Alveolar: (36-40 weeks)
  - Alveoli (36 weeks to 3 years)

AIRWAY

Extrapulmonary arteries (day 34)
  - Lobe arteries (day 44)
  - Pre-acinar arteries (7-17 weeks): 11 to 23 generations

ARTERIAL DEVELOPMENT

Intra-acinar arteries (18-25 weeks): 3 to 5 generations
  - Alveolar ducts arteries (25 weeks – 18 months): 2-3 generations
  - Capillary alveoli (30 weeks – 18 years) 11 to 23 generations
Embryogenesis of the respiratory system
Respiratory Epithelium
(ciliated pseudostratified columnar)

- **Ciliated columnar cells** (~300 cilia - mucus transport)
- **Mucus goblet cells** (glycoprotein mucus production)
- **Brush cells** (microvilli, nerve endings – sensory receptors)
- **Basal (short) cells** (stem cells, regeneration)
- **Small granule cell** (APUD cells – serotonin, calcitonin, ...)
- **M-cells** (mesenchimal macrophage-like antigen-presenting cells)
- **Secretory Clara cells** (secrete defensive proteins in terminal bronchioles)
Nasal Cavity

- **Vestibule (vestibulum nasi)**
  - epithelium - skin → respiratory;
  - numerous sebaceous and sweat glands;
  - vibrissae.

- **Nasal fossae**
  The nose is divided by the nasal septum into two chambers. Three incomplete plates of bone (conchae or turbinates) divide each chamber into three smaller chambers (superior, middle and inferior). The surface of these chambers is lined with respiratory epithelium, apart from the superior chamber, which is lined by a specialized olfactory (smell) receptor (Regio olfactoria).
Respiratory Region of the Nasal Cavity

Ciliated, pseudostratified columnar epithelium of the respiratory mucosa is composed of five cell types:

• **Ciliated cells**, tall columnar cells with cilia that project into the mucus covering the surface of the epithelium

• **Goblet cells** that synthesize and secrete mucus

• **Brush cells**, a general name for those cells in the respiratory tract that bear short, blunt microvilli

**Small granule cells (Kulchitsky cells)** that resemble basal cells but contain secretory granules. These are endocrine cells of the diffuse neuroendocrine system (DNES)

• **Basal cells**, stem cells from which the other cell types arise

The **lamina propria** of the respiratory mucosa has a rich, vascular network that includes a complex set of capillary loops.
Smell (Olfaction)
olfactory epithelium

Pseudostratified columnar epithelium:

- supporting (sustentacular) cells;
- basal cells (stem cells);
- olfactory cells (bipolar neurons, that regenerates, with long non-motile cilia).

Bowman’s glands.
- **Olfactory cells.** These are bipolar neurons. The apical part of the neuron is a modified dendrite, which has a terminal globular vesicle (olfactory vesicle) with 6-8 nonmotile cilia, which are very long (150-200mm). The perikaryon is located in the middle of the "epithelium" and leads to the axon, which enters the underlying connective tissue. The axons in this connective tissue are present in small bundles (fila olfactoria) surrounded by an envelope of dense connective tissue. These axons are non-myelinated, lack endoneurial sheaths, and belong to the central nervous system.

- **Supporting cells.** These are columnar cells (really glia) and contain a yellow pigment in their cytoplasm.

- **Basal cells.** These are small cells situated close to the basal lamina. It is possible that these are replacement cells for the supporting cells.

- The lamina propria, in addition to the fila olfactoria, possesses epithelial tubuloalveolar glands of Bowman. These produce secretions that are conveyed to the free surface of the epithelium via secretory ducts. These secretions are believed to function to moisten and refresh the sensory surface of the chemoreceptors.
Nasopharynx & Larynx

- The nose leads to the nasopharynx, the first part of the pharynx. The development of the palate in evolution was of utmost biological significance as it enabled the separation of the route for air (nasopharynx) from the route for feeding (oropharynx). People with incomplete palates (cleft palate) suffer from many clinical problems and palate malformations need to be surgically corrected as soon as possible.

- Ciliated pseudostratified (respiratory) epithelium except of epiglottis and true vocal cords, covered by *stratified squamous epithelium*.

- Lamina propria & submucosa – mucus & serous glands, lymphoid tissues.
  
  MALT – mucosa-associated lymphoid tissue, including tonsillae pharyngea et tubaria.
  
  Auditory (Eustachean) tubes – connect middle ear with pharynx.
The larynx is an irregular tube connecting the pharynx to the trachea. The larynx has two functions: phonation (creation of sounds for speech) and control of the air pathway so that only air (and not food or foreign objects) reaches the lower respiratory passages. During swallowing the larynx moves upwards and directs the food to the esophagus. If anything other than air enters the larynx there is a cough reflex (to prevent fluids or food entering the trachea). In cases of drowning, the cough reflex may cause uncontrolled laryngeal spasm, preventing oxygen reaching the lungs and death by asphyxiation. Autopsies of bodies after drowning commonly reveal lungs that are virtually free of water.

The mucosa of the larynx has two pairs of folds. The false vocal cords (upper folds) are separated from the true vocal cords (lower folds) by the laryngeal ventricle. The true vocal cords, by modifying the slit-like opening (rima glottidis) enable us to produce sounds.
The **true vocal cords** consist of:

- stratified squamous epithelium
- vocal ligament (connective tissue, which is mainly elastic bundles)
- vocal muscle (skeletal muscle, which regulates the tension of the folds).

The **false vocal cords** consist of:

- respiratory epithelium
- lamina propria with many exocrine glands

Irregular plates of hyaline cartilage provide support and protection for the larynx.

Lymphatic nodules are common in the lamina propria of the larynx, especially in the area of the false vocal cords.
Trachea

- **Mucosa** (respiratory epithelium with laminia propria);
  - vascular (venous) plexus,
  - lymphoid tissue (MALT).

- **Submucosa** (SM);
  - seromucous glands

- **Fibrosa** (F) or *tunica fibromusculocartilaginea*;
  - C-shaped hyaline cartilage with smooth muscle bundle.

- **Adventitia** (not shown, - lose connective tissue).
Tracheal Epithelium

**Ciliated cells**, the most numerous of the tracheal cell types, extend through the full thickness of the epithelium. Cilia appear in histologic sections as short, hairlike profiles projecting from the apical surface. Each cell has approximately 250 cilia. Immediately below the cilia is a dark line formed by the aggregated ciliary basal bodies. The cilia provide a coordinated sweeping motion of the mucous coat from the farthest reaches of the air passages toward the pharynx. In effect, the ciliated cells function as a “mucociliary escalator” that serves as an important protective mechanism for removing small inhaled particles from the lungs.

• **Mucous cells** are similar in appearance to intestinal goblet cells and are thus often referred to by the same name. They are interspersed among the ciliated cells and also extend through the full thickness of the epithelium. They are readily seen in the light microscope after they have accumulated mucinogen granules in their cytoplasm. Although the mucinogen is typically washed out in hematoxylin and eosin (H&E) preparations, the identity of the cell is made apparent by the remaining clear area in the cytoplasm and the lack of cilia at the apical surface. In contrast to ciliated cells, the number of mucous cells increases during chronic irritation of the air passages.
Tracheal Epithelium

**Brush cells** have the same general features as those described for the respiratory epithelium of the nasal cavity. They are columnar cells that bear blunt microvilli. The basal surface of the cells is in synaptic contact with an afferent nerve ending (epitheliodendritic synapse). Thus, the brush cell is regarded as a receptor cell.

**Small granule cells** (Kulchitsky cells) are respiratory representatives of the general class of enteroendocrine cells of the gut and gut derivatives. Small granule cells usually occur singly in the trachea and are sparsely dispersed among the other cell types. They are difficult to distinguish from basal cells in the light microscope without special techniques such as silver staining, which reacts with the granules. The nucleus is located near the basement membrane; the cytoplasm is somewhat more extensive than that of the smaller basal cells. With the transmission electron microscope (TEM), a thin, tapering cytoplasmic process is sometimes observed extending to the lumen. Also, with the TEM, the cytoplasm exhibits numerous, membranebounded, dense-core granules. In one type of small granule cell, the secretion is a catecholamine. A second cell type produces polypeptide hormones such as serotonin, calcitonin, and gastrin-releasing peptide (bombesin). Some are present in groups in association with nerve fibers, forming neuroepithelial bodies, which are thought to function in reflexes regulating the airway or vascular caliber.
Tracheal Epithelium

- **Basal cells** serve as a reserve cell population that maintains individual cell replacement in the epithelium. Basal cells tend to be prominent because their nuclei form a row in close proximity to the basal lamina. Although nuclei of other cells reside at this same general level within the epithelium, they are relatively sparse. Thus, most of the nuclei near the basement membrane belong to basal cells.
The trachea divides into the two primary bronchi, which enter the lung at the hilum.

These primary bronchi divide into smaller secondary bronchi (3 in the right lung, 2 in the left lung). The extrapulmonary bronchi have a similar histological appearance to that of the trachea.

The intrapulmonary bronchi (lobar bronchi) have irregular plates of hyaline cartilage (instead of C-shaped rings). In transverse section these appear as small oval or crescent-shaped plates or islands of cartilage. As the bronchi become smaller, the bands of smooth muscle in the wall become more prominent. Contraction of this smooth muscle after death typically causes the mucous membrane of the bronchi to appear to have longitudinal folds. The lamina propria of the bronchi has abundant elastic fibers.
Main (primary, left & right) bronchi

Ø ~ 6-8 mm

- Mucosa (respiratory epithelium with laminia propria);
  - lymphoid tissue (BALT);
  - lamina muscularis mucosae

- Submucosa (SM);
  - seromucous glands

- Fibrosa (F);
  - rings of hyaline cartilage

- Adventitia (not shown).
Large and middle (secondary and tertiary) bronchi

- Ø ~ 4-5 mm
- **Mucosa**
  - (respiratory epithelium with laminia propria);
  - lymphoid tissue (BALT);
  - lamina muscularis mucosae;
  - elastic fibers;
  - longitudinal folds of mucosa.
- **Submucosa (SM);**
  - few seromucous glands
- **Fibrosa (F);**
  - hyaline cartilages irregular (isolated plates or islands)
- **Adventitia** (loose connective tissue, with lymphatic nodules and vessels).
Terminal bronchioles

The first and larger bronchioles are the terminal bronchioles. These have a diameter less than 1mm and lack cartilage in their walls. They lack glands in the mucosa. Goblet cells are virtually absent and if present are only found in very small numbers in the initial segments. A simple ciliated columnar or cuboidal epithelium lines the terminal bronchioles. (In the initial segments of the largest bronchioles, it may be pseudostratified). Clara cells (non-ciliated secretory cells) are dome-like cells located between the ciliated cells. The function of Clara cells is still unknown. They secrete glycosaminoglycans in response to chemical irritation (xenobiotics).

- The lamina propria of the terminal bronchioles contains relative large amounts of smooth muscle and elastic fibers. These smooth muscles contract and severely restrict air-flow during asthmatic attacks. Asthmatics use drugs that stimulate the sympathetic innervation of the smooth muscle and cause their relaxation resulting in distention of the bronchiolar diameter.
Small bronchi & bronchioles

- **Mucosa**
  - (simplified respiratory epithelium with lamina propria);
  - only scattered goblet cells;
  - lymphoid tissue (BALT);
  - lamina muscularis mucosae;
  - elastic fibers;
  - no glands, no cartilages.

- **In terminal bronchioles**:  
  - cuboidal epithelium with rare ciliated and goblet cells;
  - secretory Clara cells (help to utilize surfactant remnants and synthesize defensive proteins);
  - M-cells (antigen-presenting cells);
  - APUD cells of Kulchitsky (serotonin, bombesin, calcitonin, norepinephrin).

- **Adventitia**
  - lose connective tissue, with rare lymphatic nodules and macrophage cells of Langherhans).
Respiratory bronchioles

These are short tubes regarded as areas of transition between the conducting and respiratory portions of the respiratory system. The diameter of the respiratory bronchioles is about 0.5mm. The lining epithelium is simple cuboidal and non-ciliated. They have no cartilage in their walls. They lack goblet cells.
Respiratory portion
divisions of one terminal bronchiole – pulmonary acinus

Acinus consists of:

- Respiratory bronchioles;
- Alveolar ducts;
- Alveolar sacs with alveoli.

Interalveolar septum:

- Type I cells - squamous alveolar cells, respiratory;
- Type II cells - rounded alveolar cells, produce (as well as utilize) compounds of pulmonary surfactant;
- Fibroblasts;
- Lung macrophages (dust cells and cells of Langherghans).
Blood-Air (aerohematic) Barrier

1. Surfactant (surface lining);
2. Squamous alveolar cells (type I);
3. Fused basal laminae;
4. Capillary endothelial cells
Pleura

- Pleura – serous membrane covering the lung. Consists of visceral and parietal layers.

- Both membranes are composed of mesothelial squamous cells resting on fine connective tissue layer.
Aerohematic barrier

- Nucleus of endothelial cell
- Alveolar lumen
- Capillary lumen
- Surfactant (surface lining)
- Alveolar epithelium
- Fused basal laminae
- Endothelium
- Erythrocyte
- CO₂
- O₂

0.1–1.5 μm
Blood supply

- The bronchi, the connective tissue of the lung, and the visceral pleura receive their blood supply from the bronchial arteries.
- The bronchial veins drain into the azygos and hemiazygos veins.
- The alveoli receive deoxygenated blood from the terminal branches of the pulmonary arteries.
The innervation of the respiratory system

- The trachea, bronchial tree, and lungs are innervated by the autonomic nervous system.
- The autonomic nerve fibers that innervate the heart also send branches to the respiratory structures.
- Pulmonary plexus
  - Sympathetic innervation mainly causes bronchodilation
  - Parasympathetic innervation mainly causes bronchoconstriction
- The involuntary, rhythmic activities that deliver and remove respiratory gases are regulated in the brainstem.
Contact

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