RESPIRATORY SYSTEM

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It consists of two regions:

1- **Conducting portion**: The main conducting airways in the upper part of the respiratory tract have walls that are reinforced with bone or cartilage to keep them open, and their mucosal lining is adapted for cleaning and conditioning air on its way to the lungs. The incoming air passes through a succession of cavities and passageways, namely the nasal cavities, nasopharynx, larynx, trachea, and next enters several generations of progressively smaller bronchi, followed by a larger number of different orders of bronchioles.

2- **Respiratory portion**: includes: respiratory bronchioles, alveolar ducts, sacs, and alveoli.

The main functions of the conducting part are:

1. Act as a **conduit** (pathway) to transport air to and from lungs. This is achieved by the presence of cartilage, to support the walls, and prevents the collapse of its lumen. The walls are richly supplied with elastic fibers for the flexibility, while smooth muscles regulate air flow during inspiration and expiration, by their contraction.

2. Conditioning of air: through:
   - **Vibrissae**: they are specialized hair which is thick and short, present in the inner surface of the nostrils, to remove coarse dust particles.
   - **Layer of mucous and serous secretion** in the nasal fossae traps the particles and gas impurities, and moistens the air.
   - **Presence of conchae**, where the air pass through them, to increase the surface area, and turbulence of air flow.

The main function of the respiratory portion is the exchange of oxygen and carbon dioxide between inspired air and blood.

**RESPIRATORY EPITHELIUM**

Pseudostratified columnar ciliated epith., with goblet cells. It lines most of the conducting part. It consists of five types of cells:

1. **Ciliated columnar cells**: represent the most common type. Each cell has about 300 cilia on the apical surface. Beneath these cilia, there is a basal body, and small mitochondria, to supply ATP for ciliary beating.

   Ciliary movement transports a continuous layer of mucous to the pharynx. Foreign particles will be trapped in this mucous, so this will protect lungs from any particulate matter and any bacteria.
**Immotile cilia syndrome**, a disorder that causes infertility in men and chronic respiratory tract infections in both sexes, is caused by immobility of cilia and flagella induced, in some cases, by deficiency of dynein; protein normally present in the cilia. Dynein participates in the ciliary movement.

2- **Mucous goblet cells**: they are global in shape, and their apical part contains mucous droplets composed of glycoproteins.

3- **Brush cells**: they have numerous microvilli on their apical surface. They are considered as sensory receptors due to the presence of afferent nerve endings on their basal surface.

4- **Basal (short) cells**: small, rounded cells, lie on the basal lamina, but do not extend to the luminal surface of the epithelium. They are believed to be the generative cells for other cell types.

5- **Small granule cells**: small, rounded cells, with numerous granules, 100-300 nm in diameter, with dense core. They are part of the diffuse neuro endocrine system (DNES), also known as Kulchsky cells. They produce calcitonin, somatostatin, serotonin, and bombesin. These cells are demonstrated by using silver stain, which react with their granules. With the use of EM, granule cells show fine tapering cytoplasmic processes towards the lumen. The function of granule cells is still not understood well, but they may function in reflexes regulating the air-way or vascular caliber.

From the nasal cavity through the larynx, portions of the epithelium are stratified squamous. This type of epithelium is evident in regions exposed to direct airflow or physical abrasion (eg, oropharynx, epiglottis, vocal folds); it provides more protection from attrition than does typical respiratory epithelium. If airflow currents are altered or new abrasive sites develop, the affected areas can convert from typical ciliated pseudostratified columnar epithelium to stratified squamous epithelium. Similarly, in smokers, the proportion of ciliated cells to goblet cells is altered to aid in clearing the increased particulate and gaseous pollutants (eg, CO, SO₂). Although the greater numbers of goblet cells in a smoker's epithelium provide for a more rapid clearance of pollutants, the reduction in ciliated cells caused by excessive intake of CO results in decreased movement of the mucous layer and frequently leads to congestion of the smaller airway.

**Nasal cavity**

It is opened anteriorly into the nares, and posteriorly into the nasopharynx, at the choanae. Its wall is well supported by bone and cartilage.
Nasal cavity consists of two structures:

1- **Vestibule**: it is the most anterior and dilated part of the nasal cavity. The nares (nostrils) are the anterior openings and are covered by skin (stratified seq. keratinized ), which is rich in sebaceous and sweat glands, in addition to the thick short hair, or vibrissae. Inside the vestibule, the epith. will change into respiratory epith.

2- **Nasal fossae**: They are two cavernous chambers within the skull, separated by nasal septum. From each lateral wall projects three boney shelf-like projections; the chonchae, or turbinates. The middle and inferior ones are lined by respiratory epith. Superior choncha is covered by a specialized olfactory epith. It is about 10 cm² in area, and up to 100μm in thickness. It is composed of three types of cells:

   a- **Supporting cells**: they have broad cylindrical apices with narrow bases. On their free surface, are microvilli which are covered by fluid layer. Well developed junctional complexes bind these cells to the adjacent olfactory cells. The nucleus lies in the upper half of the cell. The cytoplasm contains RER, SER, and mitochondria. A yellow pigment is found in the cytoplasm similar to lipofuscin. Theses cells act as glial cells, providing both metabolic and mechanical support.

   b- **Basal cells**: small, spherical or cone shaped cells, rest on the basement membrane. Their cytoplasm contains few organelles, and they act as stem cells for other respiratory cells.

   c- **Olfactory cells**: Bipolar neurons. Their nuclei lie in a level bellow that of the supporting cells. The apices have elevated and dilated areas; the olfactory vesicle. from which arise 6-8 non motile long cilia, (although some research suggest some limited motility). The plasma membrane of cilia contains odorant-binding protein that act as receptors for smell sensation. These cilia extend radially in a plane parallel to the surface epithelium. The afferent axons of bipolar cells unite to form the olfactory nerve, which traverse the cribiform plate of ethmoid bone, then enter olfactory bulbs of olfactory cortex. Olfactory cells have a life span of one month, and they are replaced if injured, so they are the only neurons that replaced during postnatal life.

   Lamina propria of the olfactory epith.contains the glands of Bowman, a branched tubuloalveolar serous glands, which secretes a fluid around the olfactory cilia to facilitate the dissolve of odoriferous substances to stimulate olfactory cells. The lamina propria of the concha contains large venous plexuses known as the swell bodies. Every 20-30 minutes the swell bodies on one side of the nasal fossae become engorged with blood, resulting in distention of the conchal mucosa, and decrease in the flow of air. These periodic intervals of occlusion reduce the air flow, allowing the respiratory epith. to recover from dryness.

   Allergic reactions and inflammation can cause abnormal engorgement of swell bodies in both fossae, severely restricting the air flow.
PARANASAL SINUSES

They are closed cavities in the frontal, maxillary, ethmoidal, and sphenoid bones. They are lined by thin respiratory epith., with few goblet cells. Their lamina propria contains small glands. They communicate with nasal cavity through small openings. Mucous produced in the sinuses is swept into nasal cavity by ciliated cells.

Sinusitis is an inflammatory process of the sinuses that may persist for long periods of time, mainly because of obstruction of drainage orifices. Chronic sinusitis and bronchitis are components of immotile cilia syndrome, which is characterized by defective ciliary action.

NASOPHARYNX

It is the first part of the pharynx, lined by respiratory epith. At the contact with soft palate. It communicates with middle ear by Eustachian tube. Its wall is rich in diffuse and nodular lymphatic tissue.

LARYNX

An irregular tube that connects the pharynx to the trachea. The skeleton of the larynx is made of cartilage within the lamina propria. The large cartilages are hyaline, while the small ones are elastic. These cartilages support the larynx to maintain an open air way, and prevent swallowed food from entering the trachea, also they participate in sound production (phonation). Larynx also counteract obstruction or irritation by coughing.

Epiglottis: is one the small elastic cartilages that projects from the anterior wall of the larynx. It has both lingual and laryngeal surfaces. Lingual surface (anterior surface), and the apical part of epiglottis is covered by stratified seq.non keratinized epith. The lower part of the laryngeal surface (posterior surface) is covered by respiratory epith.

Bellow the epith., the lamina propria contains both mucous and serous glands.

Bellow the epiglottis, the mucosa forms two pairs of folds that projects into the lumen of the larynx. The upper pair constitutes the false vocal folds, which are covered by respiratory epith. The lower pair represents the true vocal cords, and lined by stratified seq. epith. These folds are oriented in an antero-posterior direction, and define the lateral boundaries of the opening of the larynx; rima glottis. Within these folds, there is large bundles of parallel elastic fibers composing the vocal ligament. The tention and length of vocal ligament determines the kind of sounds produced. Parallel to this ligament, are bundles of skeletal muscle fibers; the vocalis muscle.
TRACHEA

Thin walled tube, about 10cm length, and 2.5 cm diameter, extends from the larynx into the thorax where it bifurcates into two primary bronchi. The wall consists of three layers:

1- **Mucosa**: consists of respiratory epith. and lamina propria of loose connective tissue, with diffuse lymphatic tissue, some times of nodular form.

2- **Submucosa**: loose connective tissue, rich in lymphatic tissue. It is separated from lamina propria by an elastic membrane. Muco-serous glands; *tracheal glands* also present that produce mucous fluid.

3- **Cartilage layer**: There are 16-20 C- shaped hyaline cartilage to keep tracheal lumen opened.

   A fibro-elastic ligament binds the open ends of the cartilage to prevent over distention of the lumen. Deep to this ligament, a band of smooth muscle; *trachealis* muscle regulates the lumen of trachea. The more flexible area between the cartilages is supported by dense fibroelastic connective tissue continuous with the perichondrium, to facilitate the extension of trachea if the head is tilted back, or during respiration.

4- **Adventitia**: loose connective tissue rich in blood vessels and nerves.

BRONCHEAL TREE

The trachea divides into two main bronchi, each enters the lung through the hilum, where arteries, veins, and lymphatics enter and leave the lungs, where they are invested by dense connective tissue.

Each primary bronchus course downwards dividing into three bronchi in the right lung, and two in the left lung, each supply a pulmonary lobe. These *lobar bronchi* divide repeatedly into *bronchioles*, then 5-7 *terminal bronchioles*.

**BRONCHUS:**

*Primary bronchus* has the same histological structure as trachea, except that the cartilage is a complete ring. At the level of *secondary bronchus*, the cartilage become as an isolated plates.

Lamina propria is rich in elastic fibers, mucous and serous glands, lymphocytes, and lymphatic nodules. Well developed smooth muscle fibers also present.

**BRONCHIOLES:**

They are an intralobular air ways with a diameter of 1-5mm or less. They are lined by respiratory epith., with few goblet cells. No glands and no cartilage present in their wall.
**Terminal Bronchioles:**

They are lined by simple columnar or simple cuboidal cells, ciliated with *Clara cells*. Clara cells are non ciliated, and have an apical secretary granules that secrete *glycosaminoglycans*, which has a protective function against oxidative agents and inflammation, and has a detoxifying effect on noxious inhaled particulate matters. Goblet cells disappear above the level where ciliated cells disappear.

Lamina propria has smooth muscle fibers and elastic fibers arranged in a helical crisscrossing pattern.

Bronchioles also exhibit specialized regions called *neuroepithelial bodies*. These are formed by groups of 80-100 cells that contain secretory granules and receive cholinergic nerve endings. Their function is poorly understood, but they are probably *chemoreceptors* that react to changes in gas composition within the airway. They also may be involved in the reparative process of airway epithelial cell renewal after injury.

The increase in bronchiole diameter in response to stimulation of the sympathetic nervous system explains why epinephrine and other sympathomimetic drugs are frequently used to relax smooth muscle during asthma attacks. When the thickness of the bronchial walls is compared with that of the bronchial walls, it can be seen that the bronchiolar muscle layer is more developed. Increased airway resistance in asthma is believed to be due mainly to contraction of bronchiolar smooth muscle.

**Respiratory Bronchioles:**

Each terminal bronchiole gives two or three respiratory bronchioles. These are lined by simple ciliated cuboidal cells, with non ciliated Clara cells.

Lamina propria is rich in smooth muscle fibers and elastic fibers. The wall of respiratory bronchioles is interrupted by the alveolar sacs and alveolar ducts, where the epith. changes into simple seq. epith.

**Alveolar Duct:**

It is a tubular structure that is connected to the respiratory bronchioles. It is lined by simple seq. epith.

Lamina propria has smooth muscles which disappear distally, and replaced by elastic and reticular fibers.

**Alveolar Sac:**

It is a space where a group of alveoli open at each other. It is lined by simple seq. epith., and invested by elastic and reticular fibers. The elastic fibers are for the expansion and contraction, while reticular fibers prevent over distention.

**Alveoli:**

Sac like evaginations of respiratory bronchioles, alveolar ducts, and sacs. They are about 200µm in diameter, and are specialized for O₂ and CO₂ exchange between air and blood.
Each alveolus is lined by simple squamous epithelium, and is separated from adjacent alveoli by the inter-alveolar septum. Within this septum, we have the Blood-Air Barrier which separates the air in the alveolus from blood in the capillaries.

Blood-Air barrier consists of the following structures:

1- Cytoplasm of the alveolar cell wall.
2- Fused basal laminae of alveolar and capillary endothelial cells.
3- Cytoplasm of endothelial cells.

This barrier is about 0.1-1.5 µm in thickness.

There are four types of cells in the inter-alveolar septum:

1- Endothelial cells: extremely thin, where the nucleus and organelles are clustered in one side to increase the efficiency of gas exchange. It is of the continuous type, with no fenestrae. The cytoplasm contains large number of pinocytotic vesicles.

2- Type I (squamous alveolar cell): extremely thin cells, and constitute about 97% of the alveolar surface. The organelles are grouped around the nucleus, leaving large area of free cytoplasm with large number of pinocytotic vesicles, to remove contaminants. These cells act as a barrier with minimal thickness.

3- Type II (great alveolar cells) or septal cells: they form only 3% of the alveolar surface, found in between type I cells, and connected to them by desmosomes and occluding junctions. They are cuboidal in shape, and found in groups at the angles of alveolar wall. These cells are rich in mitochondria, RER, well developed Golgi apparatus, with microvilli on their apical surface. Their cytoplasm contains lamellar bodies of 1-2µm in diameter, that contain concentric or parallel lamellae limited by a membrane. These bodies contain phospholipids, glycosaminoglycans, and proteins, which are continuously synthesized and released at the apical surface. The lamellar bodies produce the pulmonary surfactant, which spread over the alveolar surface as a coating to lower their surface tension, so, less inspiratory force is needed to inflate the alveoli, and also to prevent alveolar collapse during expiration. Type II cells divide by mitosis to replace their own type and type I cells.

4- Macrophage: They are called dust cells, and seen on the surface of alveoli, also in the connective tissue around major blood vessels or in the pleura. These cells phagocytize debris that passed from alveolar lumen by pinocytotic vesicles of type I cells. Macrophages that found on the outer surface of the surfactant are carried to the pharynx and swallowed. These macrophages originate from circulating monocytes in adjacent capillaries.

In congestive heart failure, the lungs become congested with blood, and erythrocytes pass into the alveoli, where they are phagocytosed by alveolar macrophages. In such cases, these macrophages are called heart failure cells when present in the lung and sputum; they are identified by a positive histochemical reaction for iron pigment (hemosiderin).
**Alveolar pores:** These are pores of 10-15µm diameter, found at the inter-alveolar septum. They equalize the pressure between alveoli and act as collateral of air if a bronchiole is obstructed.

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**Pulmonary blood vessels**

They include two systems:

**Systemic circulation:** is the nutrient circulation for the lung. The vessels follow the bronchial tree up to the respiratory bronchioles, where they will anastamose with small branches of the pulmonary artery.

**Pulmonary circulation:** represents the functional circulation. Pulmonary arteries are thin walled, because of the low pressure(25mmHg/5mmHg). Within the lungs, these arteries branch, up to the level of alveolar ducts, where they will give off capillary network in the inter-alveolar septum. Venules collect blood from capillaries. They have thin wall of connective tissue, and they follow the bronchial tree towards the hilum.

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**Pulmonary lymphatic vessels**

**Superficial network:** present at the visceral pleura, and it drains lymph into hilum. **Deep network:** follow the bronchi and pulmonary vessels, drain into the hilar lymph nodes. Lymphatic vessels are absent in the terminal bronchioles and alveolar ducts.

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**Pleura**

Serous membrane that covers the lungs. It consists of two layers; *parietal* and *visceral*. Pleura consists of mesothelial cells that rest on fine connective tissue layer of collagen and elastic fibers. There is a cavity between parietal and visceral pleurae which is lined by mesothelial cells, called *pleural cavity*. It contains a thin film of liquid act as a lubricant for smooth sliding during respiration.

Lungs lie protected by the thoracic cage. Each lung is invaginated into its own pleural cavity, which is accordingly reduced to a narrow potential space. This cavity is lined with simple squamous serosal mesothelium, which together with a subserosal layer of dense fibroelastic connective tissue constitutes a lining layer known as the pleura. At the hilum of the lung, the site at which major blood vessels, air passages, lymphatics, and nerves enter or emerge, the parietal pleura lining the walls of the pleural cavity is continuous with the visceral pleura investing the lung.