7. THE RESPIRATORY SYSTEM

Oxygen (O_2) is an element necessary for all cells in order to complete the chemical and biological processes that convert energy into biologically useful forms (e.g. ATP). On the other hand, carbon dioxide (CO_2) is a metabolic waste product of the cells that has to be eliminated from the body. The respiratory system is responsible for these major functions: it provides the body with the precious O_2 and at the same time expels CO_2 in a constant manner. The term **respiration** has therefore double meaning: at the *macroscopic* level means "breathing" (inhaling and exhaling air) but at the *microscopic-cellular* level denotes the process of O_2 utilization and CO_2 production by the cells.

The respiratory system is responsible for this gaseous exchange for the cellular respiratory process. However it is also important for other functions as well. The **production of sound** (and voice) is obtained by means of expelling air through the larynx and especially through the vocal cords. Another important function of the respiratory system is the **self-cleaning reflexes** of coughing and sneezing; these reflexes are provoked by irritation of the respiratory tract that forces compressed air through the respiratory system. Finally, the respiratory system aids the **increase** in the **abdominal pressure** which is necessary in straining. During natural functions such as urination, defecation or parturition (delivery) the necessary increase in abdominal pressure is aided by "breath-holding". This is achieved by inhaling air and keeping it under pressure in the respiratory system. The same mechanism aids athletes during exercise and sports like weight-lifting.

The respiratory system comprises of **cavities** and **tubes** and tissue with microscopic air pockets. The cavities and tubes transport air and gases to the **air pockets** (the **alveoli**) where gas exchange between air and blood takes place. It is important to remember that gas exchange is limited to the alveoli; the tubes are just for air transportation. Thus the respiratory system can be divided in a **conducting** (the air tracts) and a **respiratory division** (the alveoli).

The function of breathing can be divided in two parts: an **inspiration (inhalation)** phase and an **expiration (exhalation)** phase. Normally, these functions occur without notice; we breathe approximately 12- 14 times every minute, 8500 to 12500 liters of air per day without paying any attention to it! Several mechanisms automatically control our breathing pattern by adjusting it according to the concentration of O_2 and CO_2 in the blood. The main ***respiratory center*** is located in the part of the brain called **cerebral trunk**.

Inspiration is an active procedure. The main muscle of quiet respiration is the **diaphragm**, a dome-shaped muscle that separates the thoracic from the abdominal cavity. Rythmic contraction of the diaphragm (which is controlled by the **vagus nerves**) increases the capacity of the thoracic cavity, creates **negative pressure** in the **lungs** and air flows in the respiratory tubes. The air is inhaled through the **nose** (or occasionally the **mouth**) and then reaches the **pharynx**, a cavity where both the nasal and oral cavities converge. From the pharynx air passes through the **larynx** and then the **trachea** and the **bronchi**, finally reaching all the way to the remote air pockets in the lungs, the **alveoli**. Remember that this is the part of the system where gas exchange occurs.
Expiration on the other hand is a passive movement: the diaphragm and the thoracic wall structures simply relax. The lungs are *elastic* structures and therefore air is expelled passively through the air tracts.

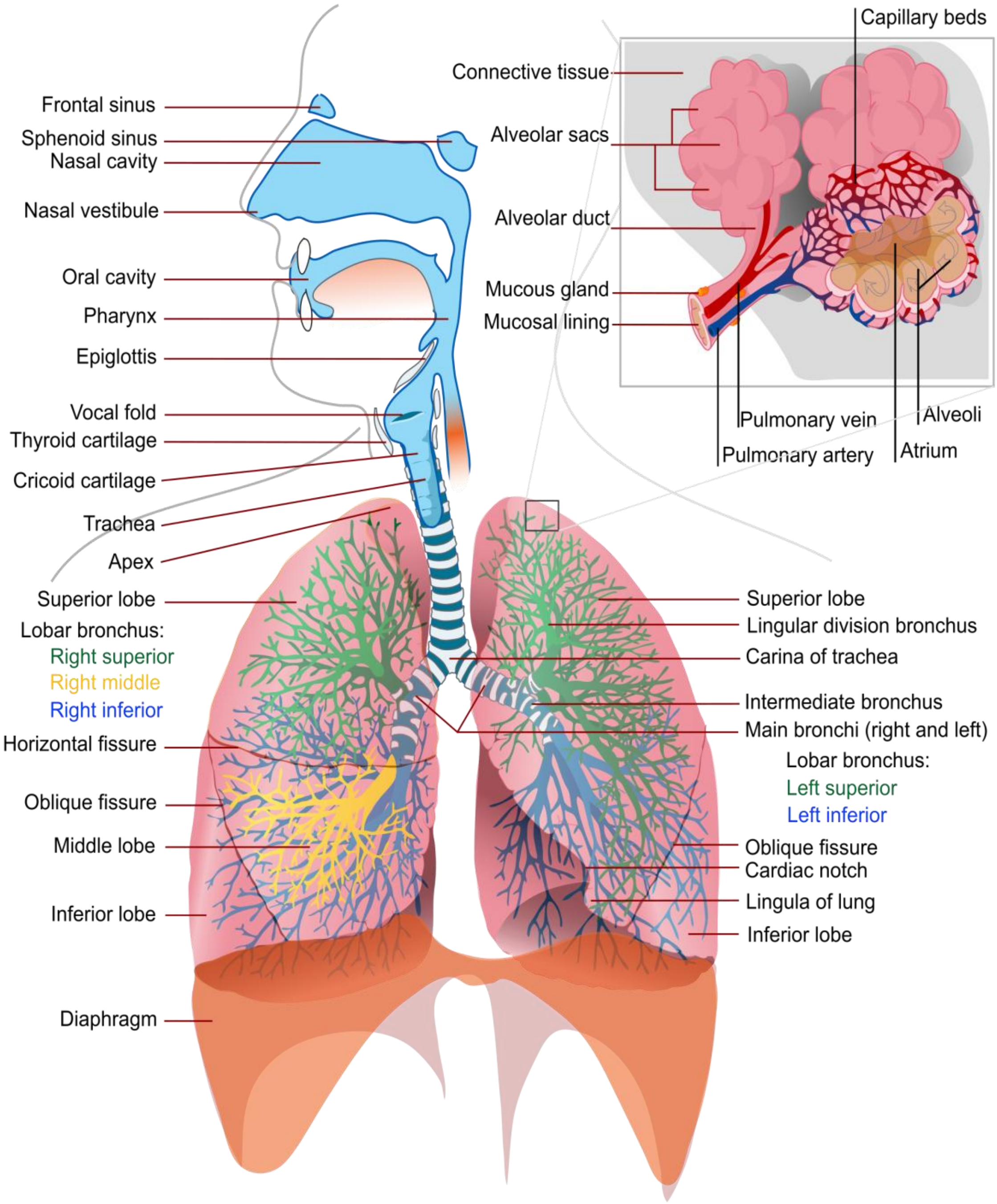

Fig. 7.1 An overview of the respiratory system.

The nasal and oral cavity.

The mouth and nose are the airway cavities directly in contact with the outside environment. In normal conditions we breathe air through our nose. The skeleton of our nose is formed mainly by the **nasal bones** and by **cartilages**. There are two openings (**anterior nostrils**) that lead to the entrance of the nasal cavity, the **vestibule**. This area bears coarse ***hairs*** which prevent air particles from entering the lower airways. The nasal cavity is divided in two symmetric parts (the **nasal fossae**) by a diaphragm, the **nasal septum**. Each fossa is covered by *ciliated columnar epithelium* that secretes mucus to entrap particles (eg dust, pollen etc). At the lateral walls of each nasal fossa three bony projections create the nasal concavities called **conchae** (***superior, middle and inferior***). Beneath each concha an opening (**meatus**) allows communication of the nasal cavity with an **air sinus**, a cavity within the facial bones.
The superior medial part of the nasal cavity is covered by a specialized type of epithelium called **olfactory epithelium** that is responsible for recognizing smells and odors (See Chapter 12).

Breathing through the nose is the right way to breathe; the mucosa has the ability to **trap particles** in the mucous and with the cilia to expel them through the nostrils. Another important function of the nasal mucosa is to **warm the air** we inhale. The conchae are covered by a highly vascular nasal epithelium; the air comes in contact with the capillaries that are very ***close to the surface*** and gets warmer through this contact. However, this also explains why **bleeding** of the nose (**epistaxis**) is so common.

The oral cavity is part of both the digestive and the respiratory system (See also Chapter 8). When we are in need of deeper breathing or when the nose is obstructed by eg. mucous, we have to breathe through our mouth. At the posterior opening of the mouth lies the **isthmus** of the **fauces**, which is created by the **palatoglossal folds**, the **tongue** and the **palate** with the **uvula**. This is the entrance to the **pharynx** (see below). At each lateral side of the palatoglossal folds lies the **tonsil**, a mass of lymph tissue that acts as a first line defense. Infection of the tonsils (tonsillitis) is common mainly in children and the gland becomes swollen, painful and covered by pus.

The pharynx.

The pharynx is a muscular tube that extends from the base of the skull to the level of the C6 vertebra. It lies behind the nasal and the oral cavity and the larynx and allows their communication. Accordingly, it can be divided in three parts: the **nasopharynx**, the **oropharynx** and the **laryngopharynx**. The natural continuity of the pharynx is the *esophagus*.

In the nasopharynx lies the opening of the **auditory tube** (or Eustachian canal), which connects the **middle ear** with the nasal cavity and hence with the outer environment. This communication is essential for the **pressure balance** between the atmospheric pressure and the pressure of the air in the middle ear. When the auditory tube is obstructed (eg by mucous) the ability to counterbalance the outer pressure is lost and this causes pain in the ear. This is common in **air flights or diving**.

The pharynx plays an important role for both the respiratory and digestive system. The muscles of the pharynx are innervated by the **autonomic system** (symphathetic pharyngeal plexus and parasympathetic fibers) and are **coordinating** the procedure of swallowing in a progressive fashion. At the same time, the uvula at the soft palate and the larynx close off in order to prevent food entering the nasal or laryngeal openings, respectively. In this way, coordination of the pharyngeal muscles allows food to enter only the esophagus.

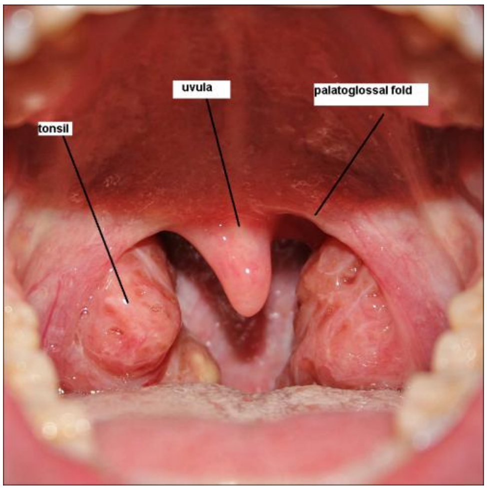

Fig. 7. The nasal and oral cavities.

Fig. 7. The pharynx

The larynx.

The tube that forms the entrance to the trachea is called the **larynx**. It is made by **cartilages**, **muscles** and **ligaments** and works as a "**sphincter**" protecting the tracheal inlet. The main function of the larynx is to prevent food or liquid to enter the trachea and bronchi. Moreover, it is the human "**voice-box**": the action of its muscles, tendons and chords is responsible for **sound production** and **phonation** (speech).

The larynx is composed from **nine hyaline cartilages** and a thin bone (**hyoid bone**), connected with membranes, muscles and ligaments, thus forming a rather triangular tube. The largest cartilage is the **thyroid cartilage**, which protrudes through the skin of the frontal surface of the neck, forming the "***Adam's apple***". At the upper entrance of the larynx lies the spoon-shaped **epiglottis**, which closes the tube like a shutter. The ***extrinsic*** laryngeal muscles elevate the larynx and close the epiglottis during swallowing. Another important function of these muscles is to keep the epiglottis closed when **increased intrathoracic pressure** is required. That is important during straining eg weight lifting, abdominal straining during defecation or vomiting etc.

Within the larynx lie two horizontal folds: the **vocal cords**. The ***intrinsic*** muscles of the larynx modulate the **length** and **tension** of the vocal chords, changing the ***frequency*** of the sound that is produced as air is forced through the narrow opening between the chords (*rima glottides*). The movement of the columns of air through the cords is producing sounds for speech and singing. The air at the lower parts of the respiratory tract (trachea, bronchi and lungs) acts as the cabinet of a loudspeaker, increasing the ***sound resonance***.

> The thyroid cartilage is more prominent in **males** than in females (that is why it is called the "Adam's apple". This is due to the effect of the male hormones (**androgens**) on the development of the larynx during **puberty**. The accelerated **growth** of the cartilages makes the male larynx larger and this accounts for the deeper voice of the males.

The trachea and bronchi.

The trachea and bronchi are constructed of **cartilage rings** that are connected with membranes. This construction allows for flexibility but also holds the tubes constantly patent. The lumen is covered by **striated columnar epithelium** that produces mucous and aids the self-cleaning of the airway tracts by trapping airborne particles like dust or smoke. When the epithelial lining of the trachea and bronchi is irritated, a strong **coughing reflex** is elicited, forcing air violently through the airways. This reflex has a protective and cleansing role for the **tracheobronchal tree** and the alveoli.

The trachea divides behind the sternum to form the **<u>two</u> major (primary) bronchi**: left and right. Note that the <u>right</u> bronchus is larger and more vertical than the left. That explains why inhaled foreign objects tend to pass to the right main bronchus and obstruct it.

After the bifurcation of the trachea, each main bronchus enters the **lung** at the **hilum**, the inner surface where the bronchi and vessels pass to the lung. From there the bronchial tree is divided into continuously smaller bronchi that bring air to several ***segments*** of the lung. The final, smallest branches of the bronchial tree are called **bronchioles**. From that point the bronchioles open at the ***alveolar ducts and the alveoli***, which **<u>do not</u>** possess cartilage in their wall structure. Remember that gas exchange does not occur in the bronchial tree but only at the thin –walled alveoli.

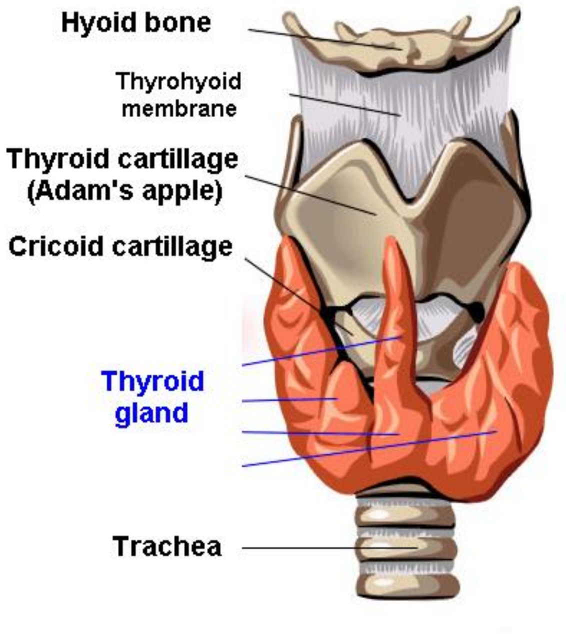

Fig. 7 The larynx

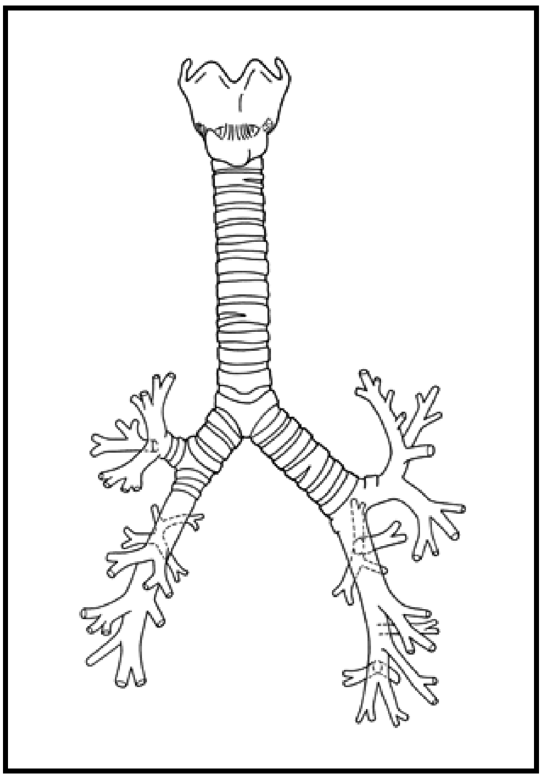

Fig 7 The tracheobronchal tree.

The lungs and the thoracic cavity.

The **lungs** are two paired organs within the thoracic cavity. These organs look like big **sponges**, with ***highly vascularised air cavities*** where the exchange of gases takes place (the alveoli). The two lungs are not exactly equal: the ***right lung is larger*** and is divided into 3 lobes. The left lung has only 2 lobes and is smaller because it features a concave area, the **cardiac notch**, where the heart is lying. The two lungs are separated by the **mediastinum**, the area which the heart, the big vessels and nerves, the trachea and the esophagus occupy in the thoracic cavity.

Each lung has four surfaces. The **apex** is the top of the lung, lying at the lower neck area behind the clavicles. The **costal surface** is the area of the lung that is in contact with the ribs. The **diaphragmatic surface** is referred to the inferior base of the lung which is in contact with the diaphragm. Finally, the **mediastinal surface** is slightly concave and features a slit called **hilum** (the “entrance” site for bronchi, vessels and nerves).

The lungs are coated by a thin serosal membrane called the **pleura**. In this way each lung is wrapped in its own serosal, pleural sac. The pleura has two leaflets: one that covers the surface of the lung tightly as a glove (the **visceral pleura**) and another that lines the inside of the thoracic wall and the upper surface of the diaphragm (the **parietal pleura**). Between these two layers a small cavity is created (the **pleural cavity**), filled with a **serous liquid** that prevents friction between the layers. The pleural cavity holds **negative pressure** (approximately -2.5mmHg below atmospheric pressure) and aids inspiration, by forcing the lung to follow the movements of the thoracic wall. In this way, the negative pressure in the pleural cavity increases by the thoracic movements (eg the lowering of the diaphragm) causing air to inflate the lungs.

Inflammation of the pleurae is called **pleuritis** and is usually secondary to an infectious disease of the respiratory system. The **parietal pleura** (but not the visceral pleura) has rich supply in **pain fibres** by somatic intercostals nerves and thus inflammation may cause severe pain during respiration (**pleurisy**). Additionally, excessive **liquid or pus** may accumulate in the pleural cavity.

The function of the lungs as part of the respiratory system is closely related to the **cardiovascular system**. The goal of respiration is to expel CO_2 and deliver O_2 to all tissues. The vascular supply of the lungs is of outmost importance. The vessels that carry blood from the heart to the lungs are called **pulmonary arteries** and the vessels that bring the blood from the lungs to the heart are called **pulmonary veins**. This circuit (heart-lungs-heart) is called **small circulation**.

Note that in case of the small circulation the **pulmonary arteries** carry **non oxygenated blood**, while the **pulmonary veins** bring **oxygenated blood** to the heart. This is the ***exception*** to the rule that arterial blood is bright red, well oxygenated!! Remember that arteries and veins should be named after their **structure** differences, irrespectively of what type of liquid they carry! Thus arteries will always be strong, elastic vessels, able to sustain the pressure crated by the heart pulse.

In a similar manner with the bronchial tree, the pulmonary arteries **branch** into the pulmonary parenchyma following the segments of the lobes. In that way, each pulmonary segment has its own bronchi, arteries and veins. The pulmonary arteries continuously divide into smaller branches (just like bronchi and bronchioles) until they become fine, **alveolar arterioles** (capillaries). In a reverse way, fine veins (**venules**) keep forming larger venous branches until they form the **two major pulmonary veins**.

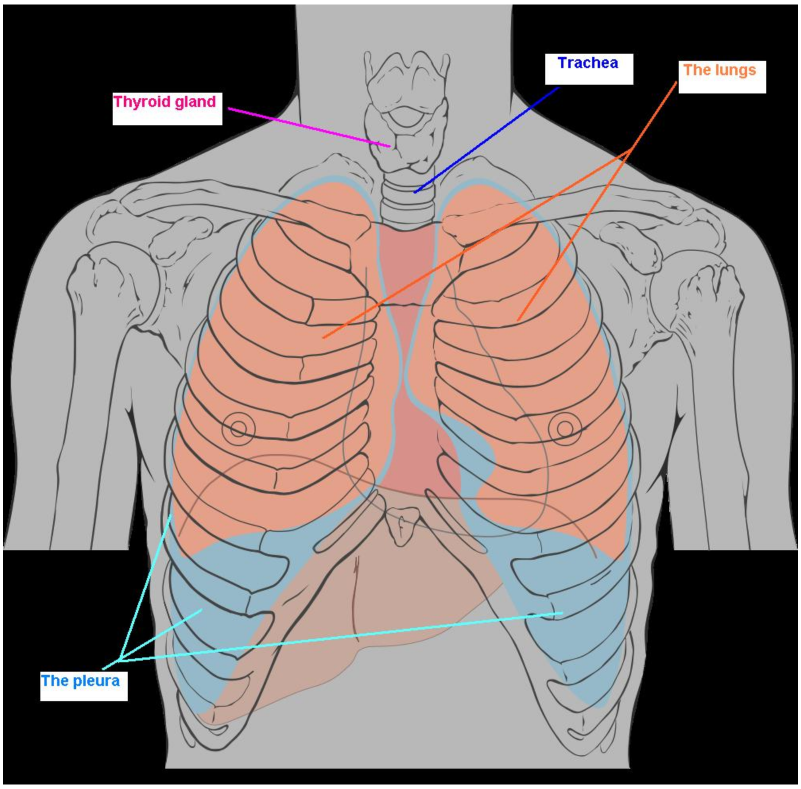

Fig. 7 Position of the lungs in the thoracic cavity.

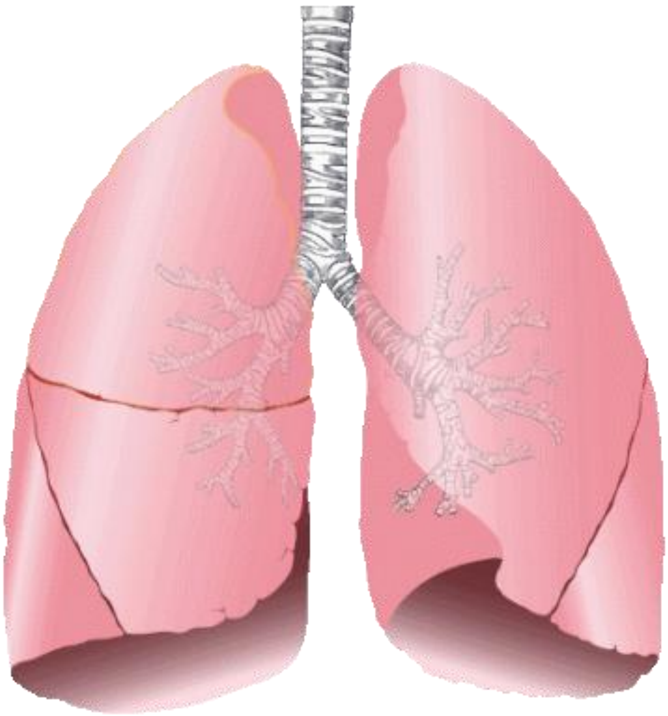

Fig. 7 The trachea, the bronchi and lungs.

The alveoli.

The terminal **bronchioles** branch into many alveolar ducts that lead to bunches of air-filled alveoli, the **alveolar sacs**. These sacs consist of several **alveoli** that open into a single chamber. The alveolar ***ducts*** are lined with ***simple cuboidal epithelium***, whereas the alveoli are lined with **simple, single layer squamous epithelium**. Specific cells of this cuboidal epithelium (**pneumocytes type II**) produce a liquid substance made of lipoproteins and phospholipids. This substance is called **surfactant** and keeps the alveolar surface **moist** and also **expanded** during both inspiration and expiration. The branches of the pulmonary arteries and veins follow the divisions of the bronchial and alveolar tree, finally dispersing capillaries around the alveolar wall. In this way, the alveolar wall creates a **barrier** between blood and air.

The ***layers*** of the barrier are forming the membrane through which the gas exchange will take place. There are ***four layers***, two from each system (alveolus - vessel):

- The alveolar epithelium.
- The basal lamina of the alveolar epithelium.
- The basal lamina of the capillary endothelium.
- The endothelium of the blood capillary.

In general, the passage of a gas through a membrane depends on the **permeability** of the membrane and the **partial pressure** of the gas on each side. In the case of the blood-air barrier, the permeability of both the alveolar wall and the capillary endothelium is high enough not to limit the diffusion of gases. Therefore, the main factor that determines gas exchange in the lungs is the partial pressure of each gas (O_2, CO_2 or any other gas) in blood or air.

> Note that the capillaries around the alveolar wall are extremely thin, with a mean lumen diameter of 5-6 μm. In this way, only one re blood cell can move through it. This is very important for gas exchange. Imagine the blood red cells as vehicles that line up one after the other and are passing through a narrow toll station, where they slow down their flow sufficiently for gas exchange to occur. The special protein of the red blood cells (hemoglobin) contains iron, which has high affinity for O_2 and a lesser affinity for CO_2

PARTIAL PRESSURE OF RESPIRATORY GASES (in kPa)

GAS	ATMOSPHERIC	ALVEOLAR	VENOUS BLOOD	ARTERIAL BLOOD
O_2	21.2	13.5	5.3	13.3
CO_2	0.04	5.2	6.1	5.3
N_2	80.0	76.4	76.4	76.4

> Imagine that the surface of the respiratory membrane if expanded would be 40 times the surface of the human body. Anything that may affect the quality of the respiratory membrane may influence the procedure of gas exchange. Chronic inflammation, smoking or environmental factors may lead to destruction of the permeability of the membrane, thus affecting the exchange of gases.

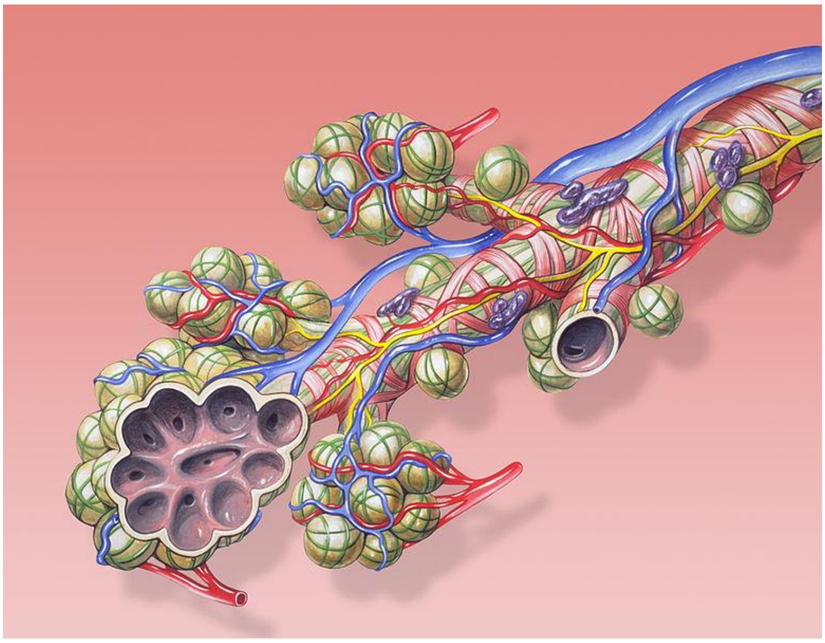

Fig. 7 The bronchial and alveolar anatomy. *(by Patrick Lynch)*

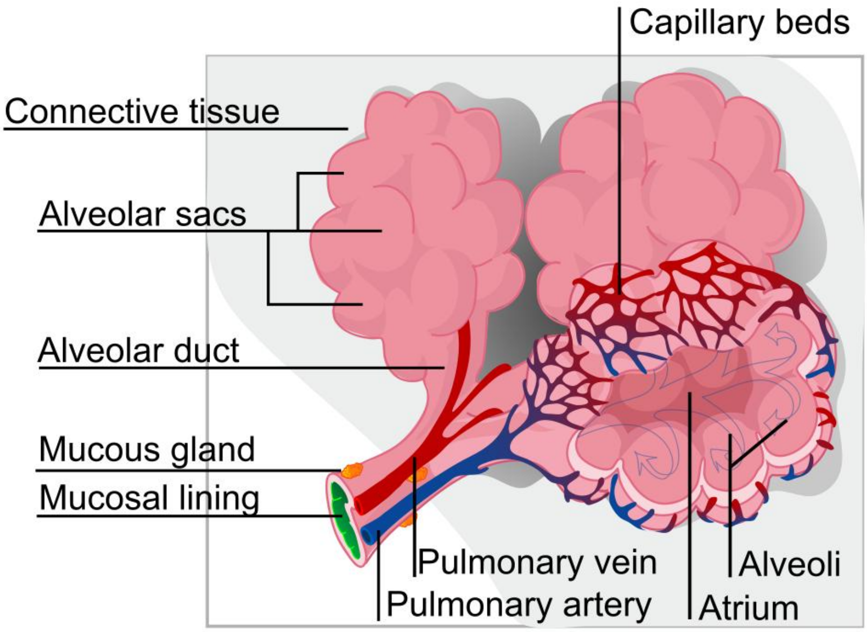

Fig. 7. The gaseous exchange system at the alveolar level.