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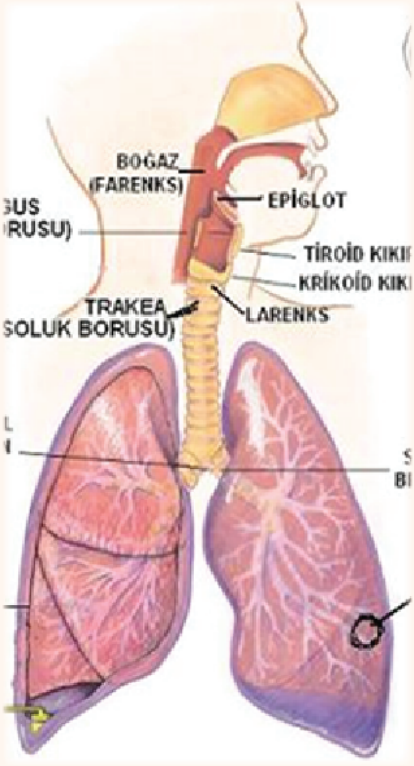

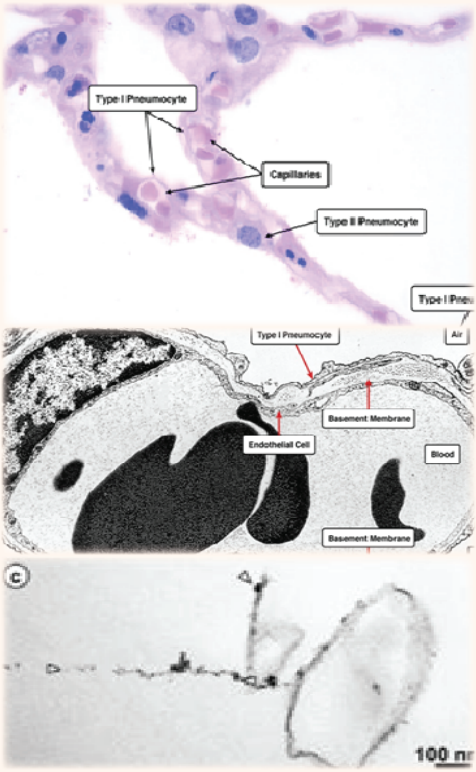

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PREFACE

The respiratory system begins with the nostrils through which the air is taken, continues with the duct structures called the respiratory tract, and ends with the structures where gas exchange takes place. In addition, the airways of the respiratory system consist of a conductive respiratory part and a respiratory part. The conductive part of the respiratory system consists of the airways leading to the respiratory part, where gas exchange takes place in the lungs. The conducting segments are located both inside and outside the lungs. Organs that make up the system: Nasal cavity, nasopharynx, larynx, air pipe and lungs. Diseases seen in the respiratory system are compatible with the structure and function of the system. The respiratory tract is constantly open to harmful factors. These harmful factors are taken both with the inhaled air and through the blood. These are microorganisms such as bacteria, fungi, viruses, as well as toxic substances or particles. Especially the presence of many animals together and breathing the same air increases these negative effects. Thus, the respiratory system has a great

function in the living organism for the continuation of both physiological and metabolic activities. Thus, understanding the morphology, physiology and all the features of the respiratory system makes a great contribution to science.

CONTENTS

INTRODUCTION

The respiratory system begins with the nostrils through which the air is taken, continues with the duct structures called the respiratory tract, and ends with the structures where gas exchange takes place. In addition, the respiratory system consists of a pair of lungs and a series of airways that carry air to the lungs. Within the lung, the airways branch into smaller and smaller tubes until the alveoli, the smallest air space, are reached. There are three main functions performed by the respiratory system: air conduction, air filtration and gas exchange (respiration). Respiration takes place in the alveoli. In addition, air passing through the larynx is used to produce sound, and air passing over the olfactory mucosa in the nasal cavities (nasal cavities) carries stimuli for the sense of smell. In addition, the respiratory system plays a role in endocrine functions (hormone production and secretion) to a lesser extent, and also contributes to the regulation of immune responses to inhaled antigens. Since the wall structures of the respiratory system are strengthened by cartilages, connective tissue threads and muscles, they have the

opportunity to remain open all the time. When animals came ashore from a water-based environment, they had to develop a system to use oxygen from the air and expel waste gases such as carbon dioxide. In mammals, the respiratory system is generally divided into the upper respiratory tract and the lower respiratory tract. The upper airway encompasses the nose or nostrils, nasal cavity, mouth, and throat (pharynx) and ends in the voice box (larynx). The lower respiratory tract consists of the trachea and lungs; they are further divided into terminal and respiratory tracts and peripheral alveoli where gas exchange occurs (Fig. 1a). Lungs are found in most land animals, including amphibians, birds, reptiles, and mammals. Although lung structure differs between species, gas exchange with the cardiovascular system remains its main function. Coordinating the development and homeostasis of an organ as complex as the lungs requires critical cell-specific changes and cell-cell interactions. To achieve this complexity, the mammalian lung undergoes a progressive developmental process beginning with the specification of endoderm progenitors in the foregut, followed by postnatal maturation of the gas

exchange interface. These processes are also characterized by specific cellular and tissue developmental events such as proximal-distal modeling of endoderm and mesenchyme to determine large and small airways, branching morphogenesis of airways. Thus, it has been observed that it widens the airway and provides the formation of postnatal alveogenesis by dividing the peripheral alveoli into a larger surface area to ensure optimal gas exchange. In order for animals to maintain their function and function throughout life, it has been observed that the respiratory system exhibits a regenerative response, repopulating the tissue with different types of cells and protecting it against insults and injuries [1].

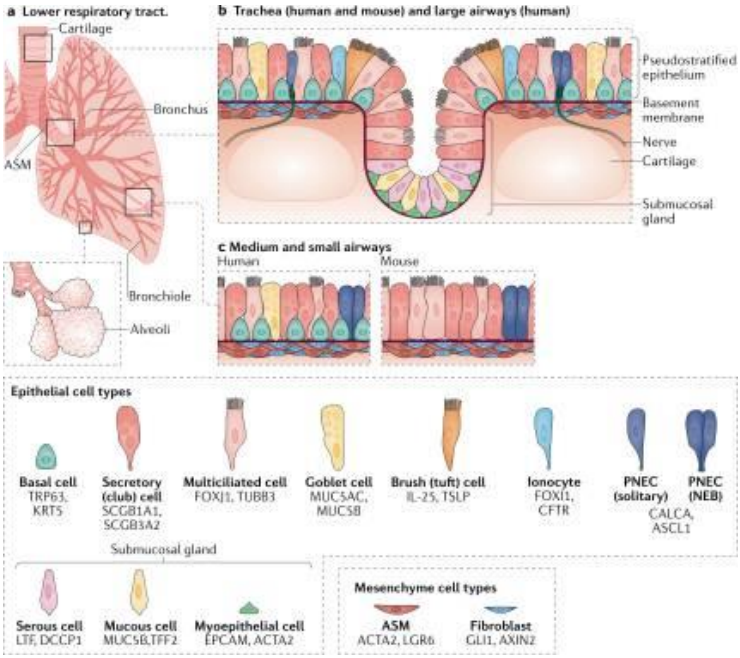


Figure:1 |The cellular composition of the airways [1].

a | In the proximal region of the lower airway, the branched large and small trachea, located at the end of the alveoli, proceed distally to form airways. The tubes in this airway located in the lower respiratory tract are surrounded by smooth muscles. b , c| The respiratory epithelium in mice and humans consists of many different cell types: These are goblet cells, these cells secrete mucus to trap particles in the inhaled air, and the attached cells expel the mucus

along with the particles; Another cell type is club cells, which are defined as secretory cells that produce various factors and detoxify harmful substances, since these cells have protective properties and have immunomodulatory functions; When we look at basal cells, they are the progenitor cells of the airway epithelium; pulmonary neuroendocrine cells (PNECs; singly and in clusters known as neuroendocrine bodies (NEBs)) are involved in regulating immune responses as well as influencing smooth muscle tone. There are also rare epithelial cell types, including brush (tuft) cells involved in the regulation of allergen-induced type 2 immune responses, and recently identified ionocytes. These cells are the most important source of cystic fibrosis transmembrane conductance regulator (CFTR) activity and have been shown to regulate mucus productionAirway smooth muscle (ASM), fibroblasts (stromal cells such as sonic hedgehog sensitive (sonic hedgehog) Gli1 positive) and WNT sensitive (Axin2 positive), ligands that modulate airway epithelial cell turnover and restrict airway tube diameter, and extracellular provides a matrix. When we examine the tracheal region, it has been revealed in studies

that there are large airways in the human respiratory tract and tracheal cartilage rings and submucosal glands in mice. It also contains mucous cells, serous cells and myoepithelial cells, and goblet cells in the trachea region, which together with goblet cells are responsible for luminal mucus production. The small airways found in the mouse do not contain basal or goblet cells, unlike the human airways [1].

Cellular computing

Solunum sistemi, hava yolları ve kan damarları dahil olmak üzere çok sayıda dallı doku sisteminden meydana gelmiştir. Although the branching patterns of these tissues differ between species, the overall tissue organization is remarkably similar. The entire mammalian respiratory system is lined with epithelial cells. Larger airways, including the respiratory tract, were found to be lined with rings of cartilage, both with bands of smooth muscle to provide support and tone to airway flow. When we look at the branched structure of the airways, the last part is the pulmonary vasculature, which can diffuse the gas by

intersecting with the cells in the alveoli and form the interface.

Major epithelial cell types

In both humans and mice, the trachea and proximal airways are composed of a pseudo-epithelium containing multiple cell lineages, including multiciliated cells, secretory cells, goblet cells, and basal stem/progenitor cells (BSCs). The goblet and secretory cells in the respiratory tract are responsible for producing mucus, and it has been demonstrated in studies that they constitute a critical first line of defense to capture particles and microorganisms in the inhaled air. BSCs act as resident stem cells for the trachea and proximal airways of the human respiratory system and as resident stem cells for the trachea and main stem bronchi of the mouse respiratory system and can repopulate the false epithelium during homeostasis and after injury. It has been seen in studies that it originates from heterogeneous mesenchymal cells, including the trachea and airways, cartilage, smooth muscle and interstitial fibroblasts around the trachea [2]. It has been shown that the mammalian lung differs from

the proximal airways in terms of alveolar structure and development. The two main epithelial roots within the alveoli are known as alveolar type 1 (AT1) and AT2 epithelial cells. AT1 cells are flattened and seromucous. It constitutes more than 95% of the gas exchange surface of the lung and the underlying endothelial capillary plexus (Fig. 2a) is able to diffuse thin gas and forms the interface. The structure of AT2 cells is cubic, and it has been suggested that they reduce surface tension by producing surface pulmonary surfactant to prevent alveolar collapse during respiration. Moreover, when AT2 cells exhibit a final burst of proliferation, AT2 cells can act as progenitors for AT1 cells in the adult lung, and to a lesser extent during early postnatal lung maturation, AT2 cells exhibit a final burst of proliferation. The underlying endothelial capillary plexus develops through intussusceptive angiogenesis in the alveolar region [3]. In order to perform this process, with the spread of a thin endothelial cell extension, the holes or pores found here are formed to provide connections to other endothelial cells, and it has been suggested in the studies that they form a large network-like structureIn addition to the

functions of epithelial and endothelial cells, the lung alveoli appear to contain several mesenchymal cell lines with different properties that support alveolar homeostasis and repair after injury [4].

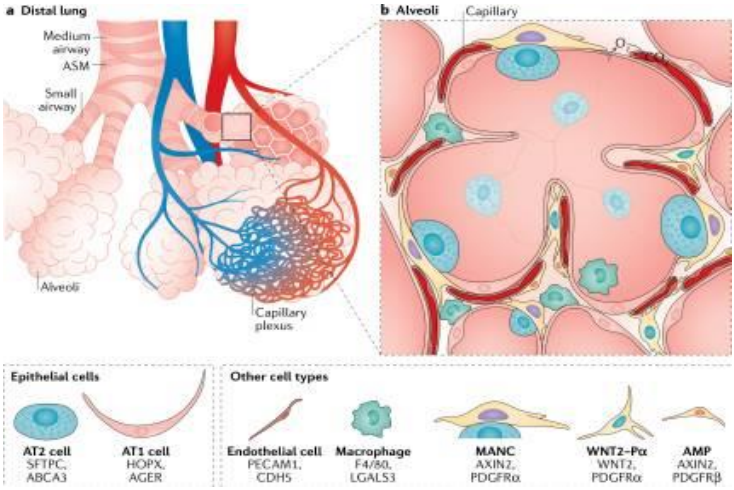
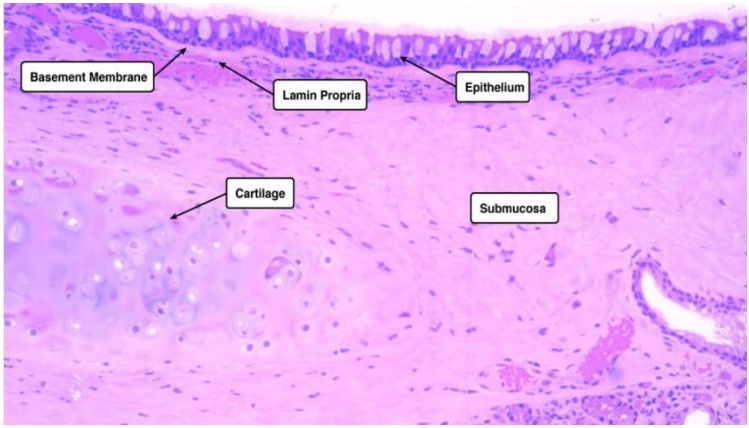


Figure 2. Cellular composition of alveoli [1].

a | When we examine the structure of the small airways, it has been shown in many studies that the air taken in these ways causes oxygen-carbon dioxide gas exchange, which takes place in the capillary plexus, and this change ends in the alveolar sacs. b | The alveolar niche is divided into two, and it has been suggested that these are alveolar type 1

(AT1) and alveolar type 2 (AT2) cells. When we examine the alveolar AT1 cells, it is seen that they have a thin and long structure and cover the gas exchange surface area since they are closely related to the capillary plexus. When we look at alveolar type AT2 cells, studies have shown that they protect the surface tension of the alveoli by producing pulmonary surfactant by preventing collapse when breathing.

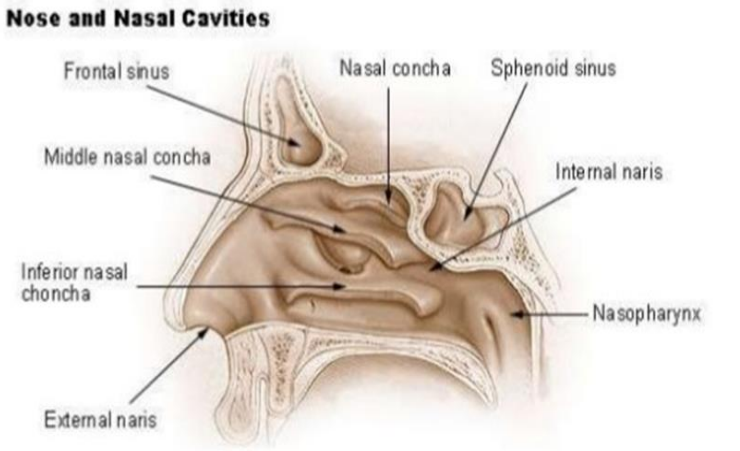
When we consider the structure of the respiratory system, many studies have shown that the epicardium, which forms the outer structure of the heart and covers its surface, shows a similar structure and is surrounded by a layer of mesothelium. The mesothelium forms specific and specific groups of mesenchymal cells during development, and also has many promoting properties and plays a major role in regulating and modeling the airways, proliferation and differentiation of mesenchymal cells, thereby making it possible for many cells including fibroblast growth factors (FGFs) and WNTs. It has been shown to be a rich source of paracrine growth factor [5].



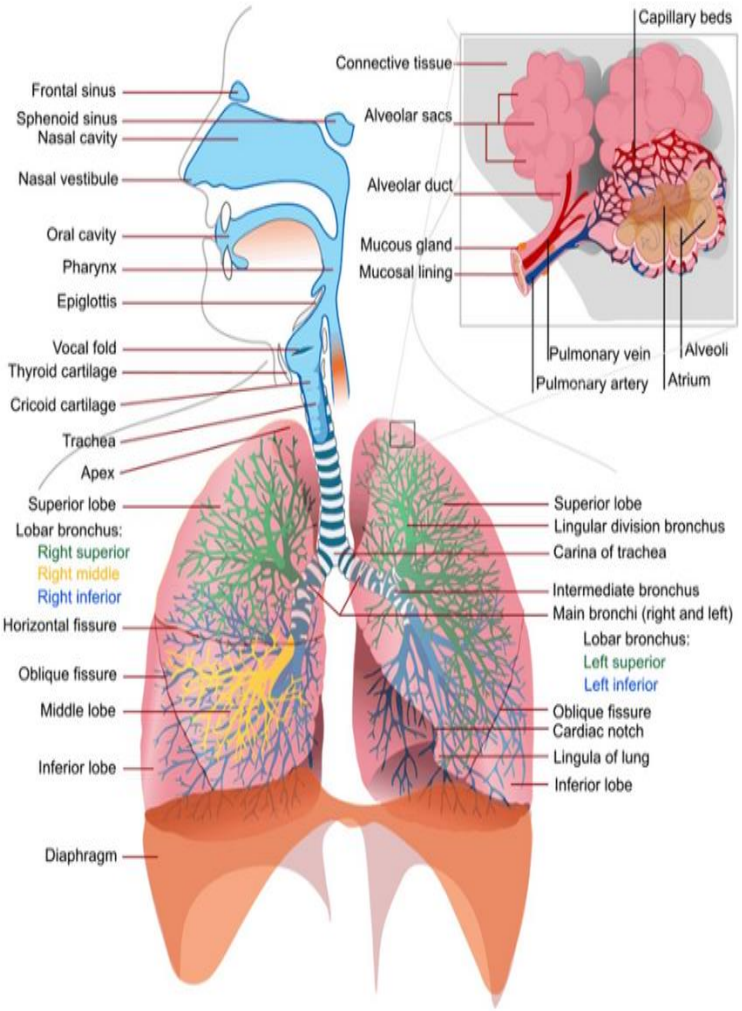
Mucous membrane of the respiratory system outside the nostrils

The region has been shown to be covered by glandular respiratory mucosa. In addition to these, when we look at the nasal cavity, there is a mucous membrane with a special structure and it is of great importance for odor. When we look at the epithelium of the respiratory system, it has been shown that it has an endodermal epithelium. It has been shown that this structure, which we have called the respiratory diverticulum, that is, the lung bud, from the beginning in the embryonic period, transforms into the thoracic mesenchyme.

In addition, the airways in the respiratory system are formed in the respiratory part and provide the conductive feature. When we look at the conductive part in the respiratory system, it consists of the airways that reach the respiratory part where gas exchange or exchange occurs in the lung. In addition, studies have shown that the lungs, which we call conductive segments, are both inside and outside. When we look at the organs that make up the respiratory system, these are; It appears to be the nasal cavity, nasopharynx, larynx, air tube, and lungs.



Respiratory System



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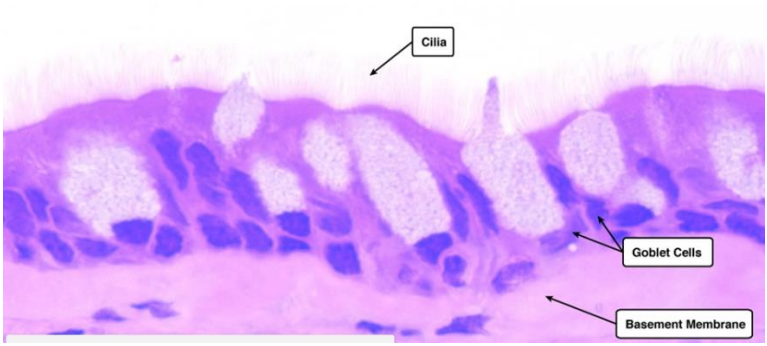


Sections outside the lungs include:

- The nasal cavities are two large air-filled cavities at the top of the respiratory system (which also contributes to the oral cavity below the nasal cavities during a vigorous breath).

- This structure, which we call the nasopharynx, has a very soft structure at the back of the nasal cavity and is located above the level of the palate, and connects with the oropharynx, which is located in the lower part of the oral cavity and is located at the back of the oral cavity.

- When we look at the structure and characteristics of the larynx, it can be named as a hollow tube-like

organ that is responsible for the formation of sound and also exhibits a cartilage structure and contains a skeleton.

- When we look at the structure of the trachea, it is called an air tube with a flexible structure starting from the larynx and extending to the thorax. It acts as a passage for air and divides into two main bronchi in the mediastinum.

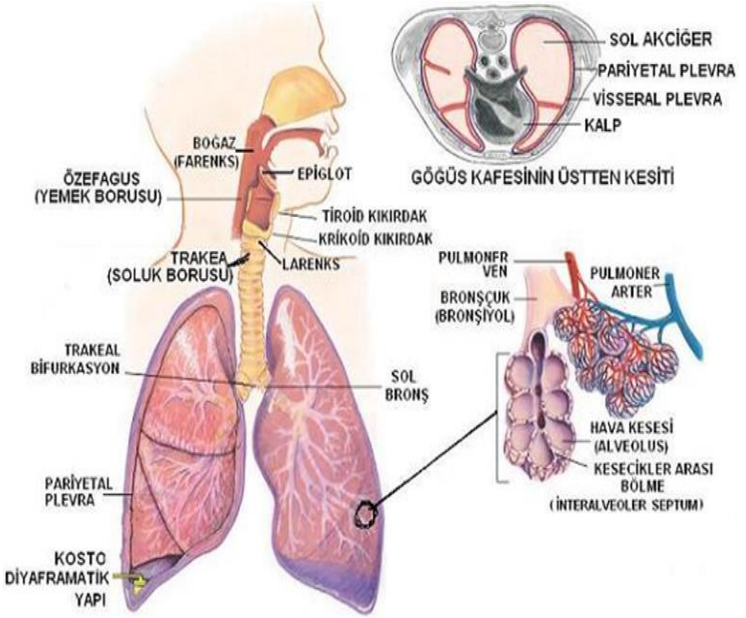
- Two main (primary) bronchi enter the right or left lung.

The main bronchus spreads widely within the lungs and eventually forms the distributing bronchioles. The bronchioles represent the last part of the conducting segment. The internal bronchi and bronchioles together form the bronchial tree. Gas exchange takes place in the respiratory part of the respiratory system (respiratory part). It includes the following sequential structures:

- The most important task of respiratory bronchioles is to provide air conduction, and they are responsible for gas exchange.

- When we look at the alveolar ducts, there are openings leading to the alveoli and these openings combine to form a long airway.
- They are hollow structures consisting of clusters of alveoli surrounded by alveolar sacs.
- When I look at the alveoli, it is the main area where gas exchange takes place.

In addition, studies have shown that blood vessels enter the lungs together with the bronchi. Thus, arteries follow the bronchus to enter the lungs and branch off into smaller vessels. The most important task of the capillaries is to be in close contact with the alveoli. This close relationship in the alveolar, air spaces, and pulmonary capillaries provides a structural basis for gas exchange in the lung parenchyma.



The alveoli are known as the place where gas exchange takes place. By creating a suitable surface area to ensure gas exchange, it provides an increase thanks to the alveoli in the lung. In addition, the lungs, which are an important part of the respiratory system, form the terminal air spaces and form an important area where gas exchange occurs between the air and blood. In addition, each alveoli is surrounded by a network of capillaries and its task is to carry the blood to the near air space within the alveoli.

Studies have shown that there are approximately 150-250 million alveoli in each adult lung.

- The ducts (ductus alveolaris) in the alveolar have a long airway and appear to have almost no walls. Alveoli are also found in the peripheral nervous system. In the interalveolar septum structure, smooth muscle rings exhibit a tuber-like structure.

- The sacs in the alveolar are also called saccus alveolaris, and studies have shown that they consist of spaces surrounded by alveolar clusters. In addition, the alveoli open into these sacs.

However, studies have shown that alveolar sacs can be found along the elongated canal as well as at the tip. Alveoli are surrounded by a thin connective tissue and contain capillaries. In addition, the tissue between the air spaces in the adjacent alveolar is called the alveolar septum or septal wall.

When we look at the structure of the alveolar epithelium, it has been observed that it consists of type I and type II alveolar cells, and very little of it consists of brushy cells.

The alveolar surface forms a sensitive biological interface that is constantly exposed to surface destabilizing forces and inhaled particles, pathogens and toxins. The epithelium of the alveoli consists of several specialized cells and contains their products. When we look at the most important task of these products, some of them play a defensive role and some play a protective role.

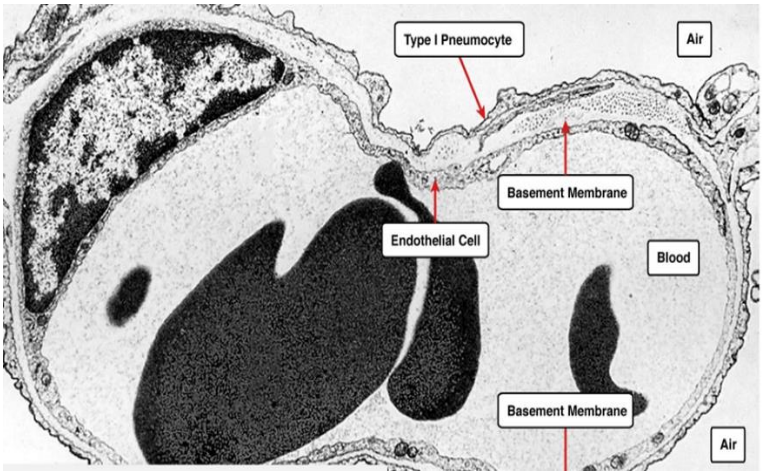
- When we look at the alveolar cells called type I, they are called type I pneumocytes.

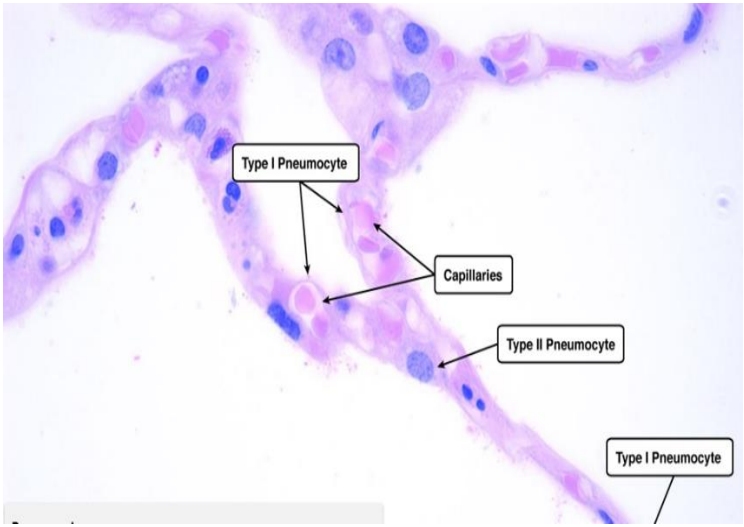
- When we examine type II alveolar cells, they are also known as secretory cells, and they are called septal cells in type II pneumocytosis. It is distributed among type I cells with cuboidal cell structure, but tends to aggregate at septal junctions.

- Cells with a brush-like structure are located in the alveolar wall and their number is quite low. They act as receptors in order to increase the air quality, which has a very important place in the lungs.

In addition, when we look at the very important tasks of the surfactant, it plays an active role in the removal and

elimination of foreign materials and also in reducing the alveolar surface tension. It also appears to reduce the surface tension at the air-epithelial interface, called the surfactant layer produced by type II alveolar cells. It has a specific phospholipid structure called dipalmitoilfos fatidylcholine, which is known as the most important agent to ensure stability in the air space, and is responsible for reducing the surface tension.





Studies have shown that gas exchange in the lung is generally provided through the air-blood barrier located in the septal wall of the alveoli. The epithelium covering the surface of the alveolar appears to be covered with a thin and continuous layer of liquid lining. In addition, studies have shown that the most important task of pulmonary surfactant is very effective at the air-liquid interface. Thanks to the biophysical activities of the surfactant, it keeps the alveoli open, dry and clean. In addition to these, there is also a glycocalyx structure in the epithelium of the alveoli. We will evaluate this glycocalyx structure in the

epithelium using electron microscopy. The application of colloidal thorium dioxide, known as a staining agent, reveals the differences of epithelial cells in type I and type II alveolar and shows that the glycocalyx establishes a close contact with the sub-products of the intraalveolar surface as an active substance, such as tubular myelin. It has been suggested in studies that these morphological findings, together with the components in the active substance system on the surface, and the glycocalic components in the alveolar epithelium, provide alveolar homeostasis and maintain the functional integrity of the air-blood barrier, which is realized thanks to the alveolar micromechanics, and specific interactions are found to provide this protection. The thickness in the layer of alveoli appears to provide a defense against pathogens [6]. The most important function provided by the main structure of the lungs is gas exchange and accordingly adapted itself to optimal conditions. It has been observed that air and blood are distributed over hundreds of millions of alveoli with a very short distance. The wall separating the neighboring alveoli from each other consists of three main compartments that form the air-blood barrier; The

alveolar epithelium is known as the capillary endothelium and the interstitium in between [7].

Interspersed, characteristic secretory organelles are single cubic AEII cells that are easily recognized by layered bodies that store surfactant. Epithelial regeneration and repair of both cell types are provided by AEII cells [8]. Shortly after the first demonstration by electron microscopy (EM) of a continuous alveolar epithelium in the mammalian lung, it became apparent that this epithelium was not bare [9]. It is covered by a fluid alveolar lining layer consisting of two phases: a surface film and an aqueous hypophase. Subsequent cryo-EM studies confirmed the existence of a thin and continuous layer of alveolar lining [10]. Surfactant, a secretory product of AEII cells, is a central component of this layer, that is, it performs its functions at the air-liquid interface of the lung alveoli.

Surfactant has a very complex structure and exhibits both a biochemical and ultrastructural structure. Studies show that it consists of approximately 90% lipid and 10% protein. It is seen that it is synthesized by the AEII cells,

which are named as active substance components on the entire surface, and it is recycled to a significant extent by storage secretion. Before the surfactant is secreted in the cell, it is ensured that it is combined in layered bodies. It has been suggested that the newly secreted surfactant, as the lamella body material, transforms the surface film into tubular myelin, which is a potential precursor. In addition, it has been shown to form surfactant reservoirs with a multi-layer structure. When we look at the structure of the surfactant, which does not show active properties, it has been shown that it is usually in the form of single lamellar vesicles consisting of small structures [11].

Alveolar Epithelial Glycocalyx

When we look at the Greek name of the glycocalyx, it is stated that it is a sweet crust" [12]. When we look at the structure of the cells with the glycocalyx, the sugar that shows a common feature in the cells facing the lumen is quite high and covers the cell from the outside. The glycocalyx is attached to the apical cell membrane and has two important molecular structures. These are proteoglycans with long unbranched glycosaminoglycan

side chains and glycoproteins with short branched carbohydrate side chains [13].

Glikokaliksin Elektron Mikroskobu ile Görselleştirilmesi

To understand the alveolar epithelial glycocalyx more deeply, it is necessary to visualize it. The detailed architecture of the alveolar epithelium can only be resolved by EM. Moreover, the high resolution offered by EM is also required to visualize the glycocalyx in the context of fine structural cells and tissues. However, it should be noted that no fixation method for EM provides a "true in vivo" representation of lung structure. Although conventional chemical fixation for EM (based on glutaraldehyde and osmium tetroxide) results in generally good preservation of cell and tissue infrastructure, the selective nature of chemical interactions (not very well understood) during fixation, processing and dehydration may result. works. Therefore, careful interpretation of the morphological features and differences observed in biological EM samples and the relevant preparation steps need to be known. This point is well appreciated in EM

studies of lung surfactant, but is important at least for studies on the glycocalyx [14]. Based on the known information, the preferred method for in vivo preservation of the glycocalyx with EM is to avoid chemical fixatives and to perform cryo-EM of vitreous sections (CEMOVIS). The cooling conditions required to avoid cryofixation artifacts in EM (especially ice crystal formation) are achieved by freezing very small tissue samples (thickness only up to 200 μm, i.e. roughly the diameter of a single alveoli in a human lung). very high pressure (approximately 2000 bar), CEMOVIS can be used in selected single experiments to visualize surfactant-containing layered bodies within AEII cells [15]. Cryo-methods have also occasionally been used to visualize the glycocalyx, eg the combination of slam freezing and freezing substitution of bovine aorta and rat fat pad endothelial cells in vitro [16]. However, high-pressure freezing leads to forced collapse of the alveoli and hence destruction of the delicate alveolar lining layer, in which both the alveolar epithelial glycocalyx and the intraalveolar surfactant film are located. Moreover, this approach is not suitable for quantitative microscopic

analyzes of whole lungs by stereology because it precludes adequate sampling where the entire (fixed) organ must be present. Currently, this can only be achieved by chemical fixation of the whole lung under carefully controlled conditions by airway instillation or preferably by vascular perfusion; both in space (homogeneity) and time (repeatability). Therefore, at least in the near future, chemical fixation approaches will continue to be the routine method(s) of choice for studying the alveolar epithelial glycocalyx in large-scale experimental studies.

Regarding EM visualization of the glycocalyx, routine chemical fixation protocols often yield poor results. Therefore, it is necessary to add coloring agents that bind to the components of the glycocalyx. Generally, these high atomic number agents scatter beam electrons, providing an "electron-dense" dark contrast [17]. These cytochemical methods work well as structural tools. However, a molecular interpretation is problematic due to the severely limited specificity of the staining agents. Moreover, it has been reviewed based on studies on the endothelial glycocalyx, and all these methods are likely to

underestimate the true height of the glycocalyx to some extent.

Stains used for the glycocalyx include ruthenium red, colloidal iron, phosphotungstic acid, lanthanum nitrate, alcian blue and lectins such as concanavalin A, wheat germ agglutinin and peanut agglutinin. Many of these methods have also been applied to the alveolar surface, for example colloidal iron, ruthenium red, phosphotungstic acid and concanavalin A . In some, a different staining pattern was highlighted between AEI and AEII cells [18]. The lectin binding patterns for AEI and AEII cells were then used as surface markers for these cell types. However, the results have not always been consistent. These early studies are nicely reviewed by Martins and Bairos [19]. A particularly interesting staining method for EM visualization of the glycocalyx is based on cationic aqueous thorium dioxide colloids (cThO 2), which has been shown to provide better tissue penetration and more intense staining compared to other staining agents. The size of CThO 2 particles ranges from 1 to 1.7 nm. This approach has been successfully applied to study the

glomerular endothelial glycocalyx in the kidney [20]. We transferred this method to the lung to investigate the fine structure of the alveolar epithelial glycocalyx and its possible relationships with surfactant. Fixed samples with a side length of 1 to 2 mm from mouse and human lungs were immersed in 100 mM sodium acetate buffer (NaAc) at pH 3.0 for 5 min, 0.5% cThO 2 in NaAc for 5 min, and again in NaAc for 5 min. , this is followed by more post-fixation and embedding compared to our routine lung EM protocol. During immersion in NaAc and cThO 2, the samples were gently massaged with a wooden skewer to allow the solutions to diffuse into the alveoli. Low pH increases the specificity of negatively charged glycocalyx components.

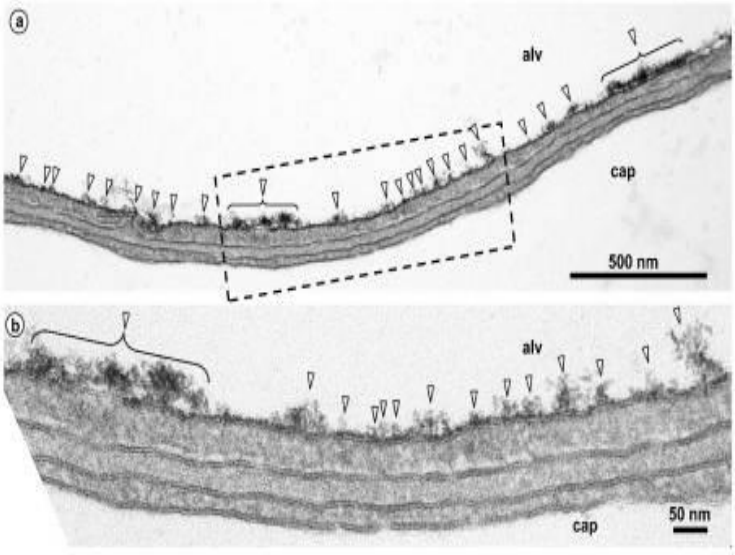


Figure 3. Mouse lung. Glycocalyx staining is shown at lower (a) and higher (b) magnification. The alveolar lumen (alv) and capillary lumen (cap) are separated by the air-blood barrier, which consists of a continuous alveolar epithelium, an interstitium, and a continuous capillary endothelium. A thin section of the air-blood barrier is shown here. The epithelium consists of thin extensions of alveolar epithelial type I cells. The interstitium is reduced to a common basal lamina shared by the epithelium and endothelium. The endothelium is of the unfenestrated type. The alveolar epithelial surface is clearly stained after

treatment with colloidal thorium dioxide (arrowheads). The boxed area in (a) is shown at higher magnification in (b) [6].

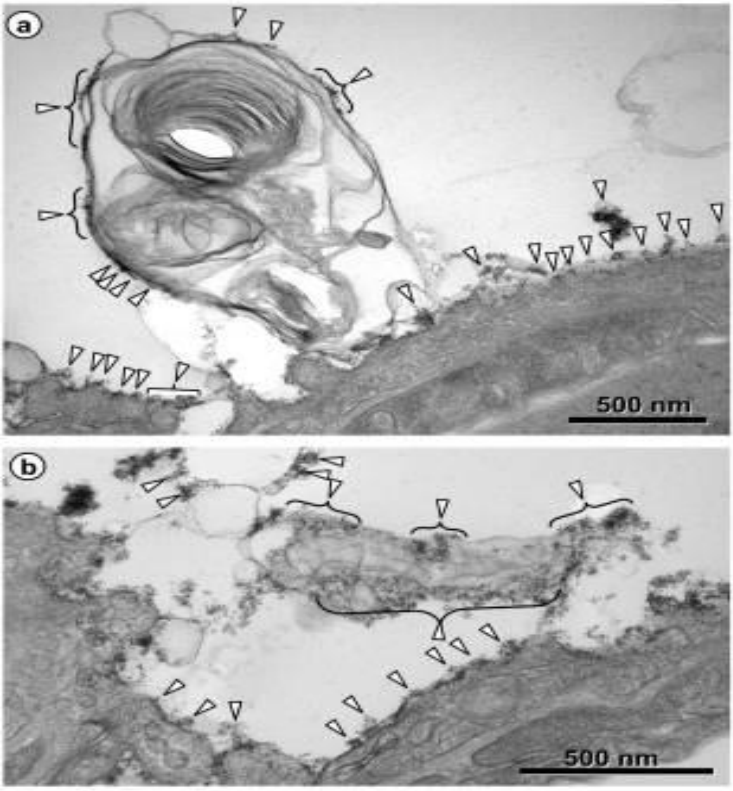


Figure 4. Mouse lung. Glycocalyx staining on intraalveolar surfactant. Intraalveolar surfactant can be seen as lamellar body content (a) secreted above the

alveolar epithelium and tubular myelin (b) with a cage-like structure. Both, like the surface of the alveolar epithelium (arrowheads), are stained with thorium dioxide, especially outside.[6].

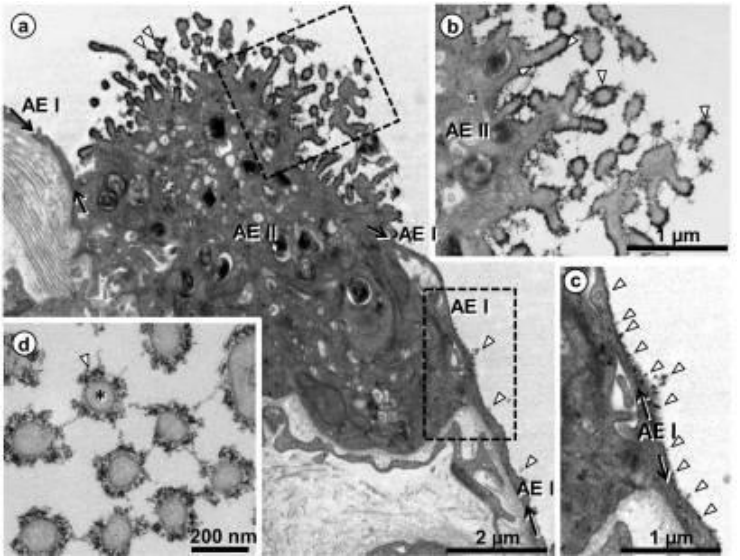


Figure 5. Human lung. Visualization of the glycocalyx on the surface of alveolar epithelial type I (AEI) and type II (AEII) cells. (a) Overview showing an AEII cell and neighboring thin AEI cell extensions, the latter's progeny highlighted by arrows. Black lines and dots (arrowheads in (a)) on the cell surfaces depict the glycocalyx labeled

with colloidal thorium dioxide. Boxed areas are shown at higher magnification in (b , c). Note the heavily stained microvilli (arrowheads in (b)) and staining in the apical cell membrane of the AEI cell (arrowheads in (c). (d) Profiles of microvilli (one of which is marked with an asterisk) cross-section of an AEII cell. The arrowhead in the glycocalyx (d) surrounds the microvilli and also appears as threads between them [6].

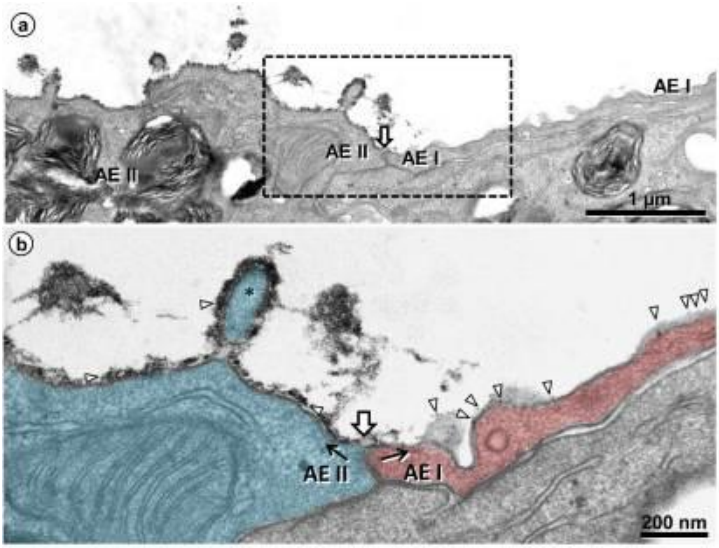


Figure 6. Human lung. Comparison of the glycocalyx of an alveolar epithelial type I (AEI) and type II (AEII) cell. (a) Alveolar surface shown sequentially from an AEII cell

(left) to an AEI cell (right) along cell contact (block arrow). The boxed area is shown in (b) at higher magnification. (b) AEII (left, colored blue) and AEI (right, colored red) density of different glycocalyx in the cell (along black arrows). Thorium dioxide deposition (marked by arrowheads) is dense in the AEII cell, forming an almost continuous layer that can also be seen on a microvilli (asterisk), while in the AEI cell it appears quite punctual [6].

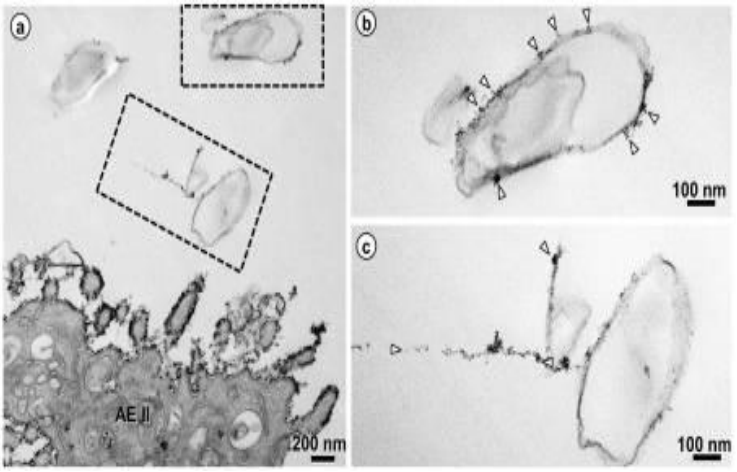


Figure 7. Human lung. Glycocalyx staining on intraalveolar surfactant. (a) Intraalveolar surfactant (boxed areas) in the airspace of an alveolar near an alveolar

epithelial type II (AEII) cell decorated with thorium dioxide. Boxed areas are shown at higher magnification in (b , c). The stain on the intraalveolar surfactant (arrowheads) is less intense than the stain on an AEII cell, comparable to the punctate stain on an AEI cell [6].

Respiratory system development

The development of the respiratory tract has a very complex structure and includes the adaptive morphogenesis of the epithelium and the development of the mesenchyme (Figure 3a, b).b. Studies show that the development of the lower respiratory tract is determined in the embryonic period, but the most important stages of alveolar maturation occur after birth.

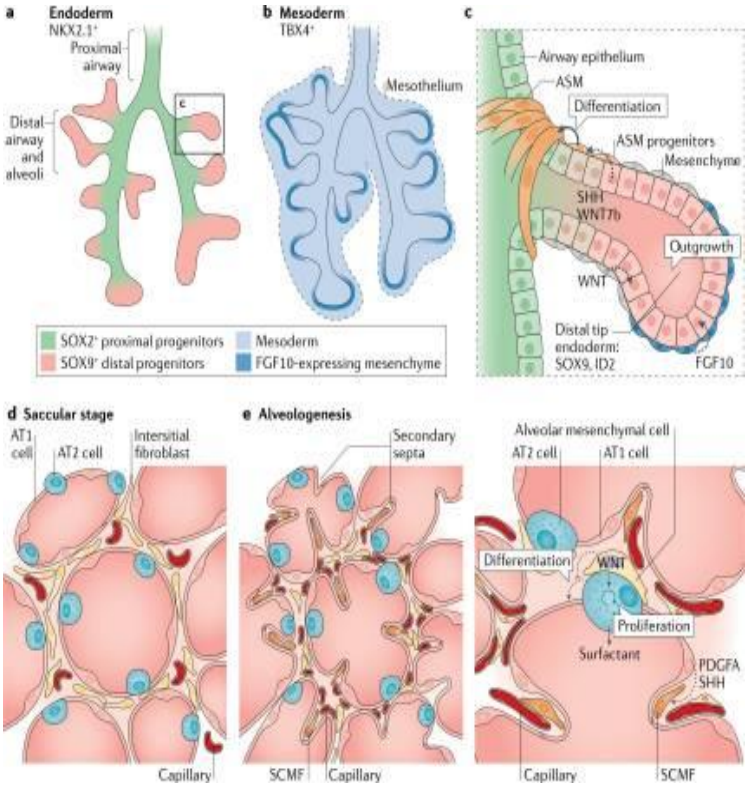


Figure 7. How the airway is formed and how the interactions between endoderm and mesoderm are provided [1].

Homeostasis and regeneration

When we make a comparison with the tissues that are exposed to the external environment and act as barriers

such as the GIS and skin, it is seen that the airway and alveolar regions of the lung are relatively immobile, but they perform an important task in homeostasis and provide a low cell turnover and proliferation. In addition to these, various stem cells that can renew themselves and differentiate into many cells during tissue damage enable the activation of various stem cells. There are many technical developments that can reveal these different stem cell formations.

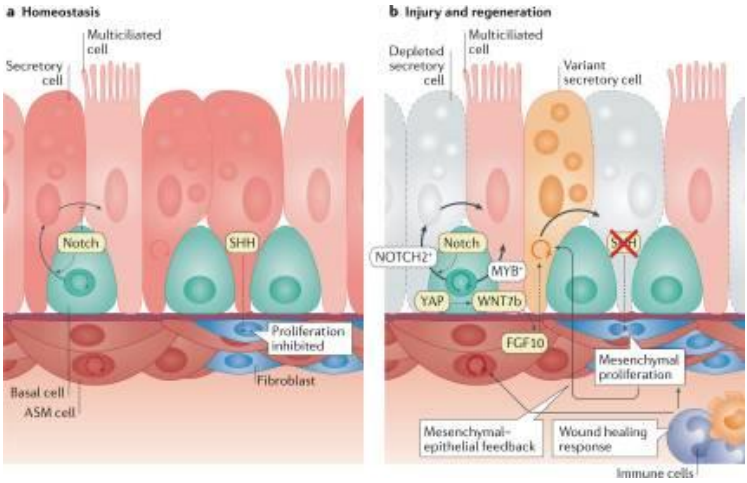


Figure 9. The formation of the stem cell cycle in the airway in homeostasis and the formation of the response to the injury [1].

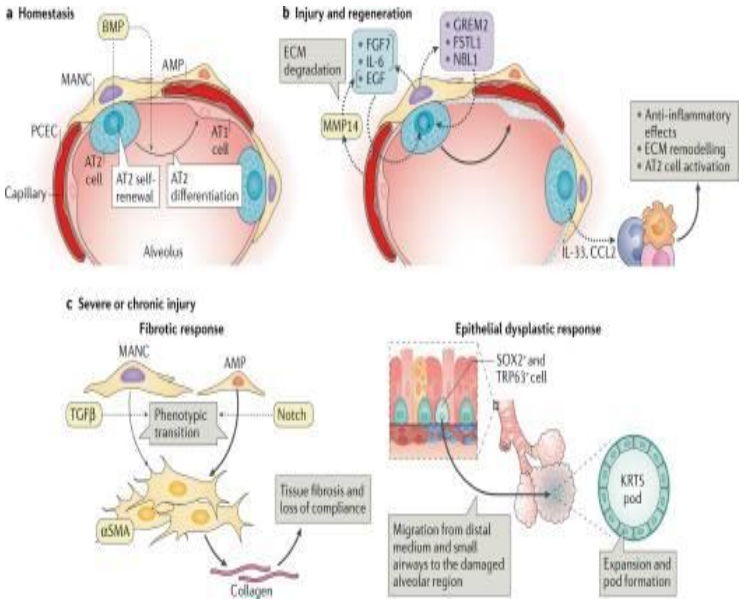


Figure 10. Formation of the response of the stem cell and niche in the alveoli to tissue damage [1].

Studies have shown that it is the most affected regenerative tissue during tissue damage in the lung, and it is very significantly affected by the next inflammatory responses that will occur. Molecular patterns (DAMPs and PAMPs) in which necrotic cell death and viral spread type 2 that we have observed after acute injury are associated with damage and pathogens that stimulate resident immune immunity and cell types that will remove foreign

substances, such as alveolar macrophages since they are innate lymphoid cells.) is released. It contains a large number of immune-providing cells in response to this inflammatory response as a result of injury caused by bleomycin or as a result of injury caused by influenza infection, and studies show that it restores homeostasis by removing microbial by-products from the environment.

Lung Anatomy

Respiration, in which oxygen from the environment is delivered to the cells, and carbon dioxide is

It is a process in which it is thrown out through the road. Breathing takes place in three stages:

- Pulmonary ventilation: It is the exchange of air between the atmosphere and the alveoli in the lung. It occurs with inspiration and expiration.
- External exchange of gases: It is the passage of oxygen from the alveoli to the blood and carbon dioxide from the blood to the alveoli in the lungs.

- Internal exchange of gases: It is the passage of oxygen from the blood to the cells, and of carbon dioxide from the cells to the blood.

The term respiration is also used for processes at the cellular level.
(1,2). In cellular respiration, oxygen is taken into the cell and energy is obtained from food used in. Carbon dioxide is a waste product of cellular respiration. As can be understood from these stages; Gas exchange close to the respiratory and circulatory systems. It requires being in a relationship. respiratory organs; nose (nasus), pharynx, larynx, trachea, bronchus and bronchioles and lungs (pulmones). Trachea, bronchi and lung anatomy of the thorax is discussed in a way to include the structure [21].

Thorax

Thorax Bones

Costae (Ribs) Ribs

(costae) thoracic vertebrae together with the sternum and costal cartilages make up the skeleton of the thorax.

Humans normally have 12 pairs of ribs. Each rib consists of a curved flat bone. All costa have the following features in common [22]: The vertebral end of the rib is called the caput costae. The articular surface (facies articularis capitis costae), which articulates with the fovea costalis in the vertebra, is divided into upper and lower two parts by a comb in the middle. The ridge that divides the joint into two is called the crista capitis costae. The narrow part connecting the head to the object is called collum costae. The sharp upper edge of Collum costae is called crista colli costae. On the outer surface of the posterior part of the costa, after the sleeve, a bulge named tuberculum costae can be seen. The tubercle is more prominent on the upper ribs. The small articular surface called facies articularis tuberculi costae, located in the inner part of the tubercle, articulates with the articular surface at the anterior end of the vertebral transverse process. The part where the bone bends forward at various degrees after the tubercle is called angulus costae. The corpus costae that comes after this has two outer and inner sides and two upper and lower edges. Along the lower edge, a more pronounced slight groove is visible on the inside. This groove, through which

the intercostal vessels and nerves pass, is called the sulcus costae. Since the costa body also shows a slight bend around its long axis, if it is placed on a flat surface, both ends cannot touch the ground at the same time. The anterior end of the rib, which articulates with the costal cartilage, is called extremitas sternalis.

Cartilago Costales (Costal Cartilages)

The costal cartilages are rods of hyaline cartilage that provide the connection between the sternal end of the rib and the sternum in the 1-10 ribs. The 1–7 costal cartilages articulate with the incisura costalis on the sides of the sternum [22].

Sternum

It is a flat bone composed of 3 parts from top to bottom. Its upper part, called the manubrium sterni, is combined with the middle part, called the corpus sterni, by a synchondrosis joint (synchondrosis sternalis). This joint makes a very large angle between the two parts. This angle, called the angulus sterni or Ludovici angle, can be felt with palpation. T4 is at the lower level of the vertebra

and shows the 2nd costal cartilage. The notch that makes the upper border of the manubrium is called incisura jugularis. In its upper-lateral parts, there are notches called incisura clavicularis, which articulate with the clavicle. Slightly below them and right on the sides are incisura costalis I for the I. costal cartilage. In the corners where the manubrium meets the corpus, incisura costalis II. takes place. Corpus sterni slightly dilated downwards. Next to them, from top to bottom, III., IV., V., VI. and an incisura costalis for the VII costal cartilages. Processus xiphoideus is the third part attached to the lower end of the body. It is attached to the object by a synchondrosis joint. It remains in the form of cartilage for a long time. The xifosternal joint ossifies only around 40 years of age. Its lower end is located at the level of the T10 or T11 vertebra.

Thorax Joints

Art. Costovertebrales: The hoods of the 1st and 2nd ribs make synovial joints with the thoracic vertebrae. 1st, 10th, 11th and 12th ribs with a single vertebra, between 2nd and 9th ribs

The ribs articulate with two adjacent vertebrae. There are internal ligaments (intraarticular ligaments) inside these joints (4–10). In addition, the capsules are externally attached to the ligamenta capitum costarum. It is supported by ligaments called radiate. Art. Costotransversaria: The tubercles of the upper ten ribs, excluding the 11th and 12th ribs, combine with the articular surfaces at the tip and anterior surface of the vertebral transverse processes and form these joints of the synovial type. The costotransverse joints are supported externally by strong external ligaments. These ligaments fill the space between the costal neck and the upper transverse process. Another importance of these ligaments is that they form the lateral border of the foramen costotransversarium, from which the spinal nerve roots emerge. The costovertebral and costotransverse joints move together. Art. Costochondralis: It is the joint between the costal cartilage and the rib. The first rib is directly fused to the external angle of the manubrium by a cartilaginous bridge (synchondrosis sternocostalis). This joint is the only synchondrosis joint that continues in adult life. 2–7 costal cartilages join the sternum with synovial joints. Increase

these joints. They are called chondrosternales. They are attached to the sternum by internal ligaments (ligamenta intraarticulare). Joint capsules ligate externally. It is supported by external ligaments called the sternocostal radiatum. These ligaments contain abundant elastic fibers. The fibers of the ligaments cross the anterior and posterior surfaces of the sternum on the inside and mix with the periosteum, and on the outside with the membranes of the cartilages. These fibers are joined by m.pectoralis major and m.transversus thoracis beams, and they eventually form a fibrous membrane called the membrane sterni, by enclosing the sternum like a bag. The second rib inserts into the notch between the manubrium and the corpus and articulates with both. Since the first rib is hidden by the clavicle, the counting of the ribs starts from the second rib.[23]. Art. Manubriosternalis: There is a synchondrosis type joint between the manubrium and the corpus sterni. A fibrous tissue is inserted between the cartilages covering the ends of the bones. This joint may ossify in advanced ages. The manubriosternal joint participates in breathing with its elastic movements. Likewise, the corpus sterni and

the xiphoid process are increased. fuses with xiphosternale.

Trachea, Bronchi and Lungs

The trachea is a 10-12 cm long tube that continues down the lower part of the larynx. The first tracheal cartilage is attached to the upper rim of the cricoid cartilage via the cricotracheale. From here, the cavity of the cavitas infraglottica continues directly with the lumen of the trachea. The walls of the trachea are made of rings of hyaline cartilage so that its lumen is never closed. The trachea lies between the C6 vertebra and the lower level of the T4 vertebra. Here it is divided into two bronchus principalis. The part where it divides into two (bifurcatio trachea) is determined anteriorly by the angulus sterni (Ludovici angle) and posteriorly by the linea interspinalis [24]. The trachea is flexible and can easily change its size. In deep inspiration, it can go down to the level of the T6 vertebra. The cross-section of the trachea is not perfectly cylindrical. It is flat on the back. The neighborhoods of the cervical and thoracic parts of the trachea are different. Neck part (pars cervicalis) anteriorly; It is adjacent to

arcus venosus juguli, isthmus thyroidea, fascia pretrachealis, v.thyroidea inferior, thymus remnants and a.thyroidea ima if present. The anterior neighborhood of the trachea neck piece is clinically extremely important because of trachetomy surgery. on the sides; It is adjacent to the glandula thyroidea lobes, n.laryngeus recurrens, a.carotis communis and a.thyroidea inferior. The thoracic part (pars thoracica) is located in the upper mediastinum. Ahead; manubrium sterni is adjacent to thymus, v.thyroidea inferior, v.brachiocephalica sinistra, truncus brachiocephalicus, arcus aortae, and a.carotis communis dextra. Right; right lung, with v.azygos, v.brachiocephalica dextra, v.cava superior and n.vagus, left; arcus aortae, a.carotis communis sinistra, a. It is adjacent to subclavia sinistra and n.laryngealis recurrens. The esophagus is attached posteriorly along the trachea. The trachea descends in an upright-comfortable position, not fully vertically, but slightly backwards. In the supine position, the lower end is further back and the upper end is more forward. The trachea is made of half rings of hyaline cartilage. In between are fibrous tissue and smooth muscle fibers. The mucous membrane lines the lumen.

The number of cartilages is between 12-16. If the trachea and bronchi are examined with a bronchoscope, a bulge called the carina is seen in the middle of the point where the trachea divides into the two main bronchi. Carina is normally midline. If the tracheobronchial lymph nodes swell for any reason (eg, lymphatic metastasis of bronchogenic cancer), the carina appears broad and fixed. Carina's mucous membrane is one of the most sensitive points of the respiratory system. Anything touching it will cause a violent cough reflex. Carina is the last line of reflex defense.

Bronchi (Bronchii)

The trachea is divided into two at the bifurcatio trachea (Y) at the lower level of the T4 vertebra. These airways, which enter the right and left lungs and are the continuation of the trachea, are called bronchus principales. Bronchus principalis sinistra is 5 cm long. It enters the left lung from the radix pulmonis at the level of the T6 vertebra. It passes under the left bronchus arcus aortae. It crosses the esophagus anteriorly. A. pulmonalis sinistra passes through the upper and anterior part of the

left bronchus. According to its position to the artery, the left main bronchus is called the hypoarterial bronchus [25]. In the hilus of the lung, it is divided into two as bronchus lobaris superior and bronchus lobaris inferior. Both lobar bronchi are in the hypoarterial position. Bronchus principalis dextra 2.5 cm long, shorter than the left and in a more vertical position. It enters the right lung at the level of the T5 vertebra. A. pulmonalis dextra is first below and then in front of the bronchus. According to its position to the artery, the right main bronchus is called the epiarterial bronchus. V. azygos crosses this bronchus posteriorly. The right main bronchus divides into three bronchus lobaris, superior, medius, and inferior in the hilus of the lung. Bronchus lobaris are divided into branches called bronchus segmentalis in the lung and disperse in certain positions. The lung section ventilated by a bronchus segmentalis forms a complete anatomical and functional lung unit. This lung unit, in which a segmental bronchus is distributed, is called segmentum bronchopulmonale. These segments are named according to their anatomical position in the lung. Each bronchopulmonary segment is surrounded by connective

tissue, which is an extension of the visceral pleura. Infections rarely move from one segment to another, but malignant tumor and tuberculosis can pass from one segment to another. These segments have gained importance in new thoracic surgery: a) Diseased segments can be removed by surgery, b) Radiopaque material can be injected into them for diagnosis, c) Natural drainage can be provided from the sick segment by adjusting the posture in a certain way. The apical segments of the lower and upper lobes are the regions where lung abscesses are most common [26]. As the tracheobronchial tree branches and approaches the alveoli, the structure of its wall changes. Although the walls of the trachea, main bronchi, and lobar bronchi are kept open by cartilaginous rings, the cartilaginous rings in the wall of segmental bronchi become less frequent islets of cartilage. As the bronchus branches and thins, the cartilage islets become sparse and the cartilage begins to be replaced by active smooth muscle tissue. The bronchi are divided into smaller bronchi branching up to 15 rows. At the distal end of these small bronchi, the cartilage completely disappears, leaving only smooth muscle tissue in the wall. From this point on,

the airway is called the bronchiolus. They go up to the proximal part of the alveolar region and branch into the bronchiolus terminalis (1–7). The part from the trachea to the terminal bronchioles is called the conducting airways, and the part more distally is called the respiratory airways. There is no gas exchange in the bronchi, bronchioles, and terminal bronchioles, these are called anatomical dead spaces. The volume of air in the anatomical dead space is 150 ml. Due to the anatomical dead space, gas exchange takes place in only 350 ml of 500 ml of air taken into the lungs with each respiration (2). Gas exchange areas are respiratory bronchiole, ductuli alveolares and alveolar vesicles. The lung unit ventilated by a single terminal bronchiole is called the acinus (primary lobule). Secondary lobule consists of 5-6 acini connected to a terminal bronchiole [27]. Within the acinus, the terminal bronchiole divides into 3–8 bronchioli respiratorii. These, in turn, open into alveolar sacs with canals called ductuli alveolares.

Vessels and Lymphatics of Trachea and Lungs

The upper part of the trachea receives its blood from the a.thyroidea inferior. The lower part and the tracheobronchial tree, which are the most important, are nourished by the a.bronchialis. They anastomose with the inferior branches of a.thyroidea. Veins v. thyroidea inferior and vv. pours into the bronchiales. Blood enters the lung both to nourish its tissues (vasa privatae) and for the general interest of the body (vasa publicae). A. pulmonalis; brings venous blood to the lungs. It distributes parallel to the segmental bronchi and supplies the lung segmentally. Oxygen-carbon dioxide exchange takes place between their capillaries and alveolar air. Aa.bronchiales; the tracheobronchial tree, the tissue of the lung itself, nourishes the pleura and the walls of the pulmonary vessels. There is one bronchial artery on the right and two on the left. It arises mostly from the intercostal artery on the right. Those on the left arise from the aorta descendens. W. pulmonales; carries oxygenated blood from the lungs to the left atrium of the heart. Venules originating from the pulmonary capillaries merge

into interlobular septums to form larger veins. A vein is formed within each bronchopulmonary segment. This vein is in front of the bronchus. Finally, two vv. pulmonales emerge from the lungs on the right and on the left. Pulmonary veins are intersegmental in character. Vv. bronchiales; It starts from the larger branches of the bronchi. The right bronchial vein drains into v.azygos, and the left bronchial vein into v.hemiazygos accessorius. In Pulmonary Thrombo Embolism (PTE), for example; After fractures of the lower extremities, embolism from the leg veins partially or completely occludes the pulmonary artery. As a result, although a part of the lung gets air, it does not function because the pulmonary artery blood cannot come. A large embolism may occlude the entire truncus pulmonalis or a major branch. A medium-sized embolism may occlude a bronchopulmonary segment artery, leading to infarction. The lymphatic pathways of the lung drain from two superficial and deep plexuses. From the superficial plexus, the subpleural lymph flows deep into the bronchial and surrounding bronchial channels. Lymph passes through the small pulmonary nodes in the lung and heads towards the hilum pulmonis.

After passing the nodi lymphatici bronchopulmonale (hilar nodes) around the bronchi, it reaches the tracheobronchial nodes. There are no lymph channels in the wall of the alveoli [26]. Lymph from the entire right lung drains to the right tracheobronchial nodes, and lymph from the entire left lung to the left tracheobronchial nodes. However, some lymph from the lower lobe of the left lung is poured into the right tracheobronchial nodes. Therefore, cancer cells in the right tracheobronchial lymph nodes can metastasize to the left lower lobe of the lung by lymphogenic pathway. Lymph from both lungs mixes with the venous circulation with the right and left bronchomediastinal trunks. Innervation of the Lungs Sensory fibers of the lung and visceral pleura go in the n.vagus. There is no pain sensation. These fibers play a role in important reflex activities such as reflex control of breathing, cough reflex, and regulation of blood pressure. Parasympathetics n. They come from the vagus. They synapse in the plexus pulmonalis at the level of the tracheobronchial tree. Parasympathetics are vasodilator, bronchoconstrictor, and secretomotor. The preganglionic fibers of the sympathetic nerves arise from the T1-T5

segments. They synapse in the lower cervical and thoracic sympathetic chain ganglia. It settles in the lung via the plexus cardiacus and plexus pulmonalis. From here, the fibers are distributed along the vessels to the lung tissue. The sympathetics act as vasoconstrictors, bronchodilators, and secretoinhibitors [26].

Lungs

They are the main respiratory organs. There are two lungs separated from each other by the mediastinum. The lung is bright pink in color and has a spongy structure. It can swim in water. It is easily torn. The pink color in childhood turns to gray in old age. Black islets and lines are formed on its surface due to carbon granules. This dark color is more specific in males. Its posterior margin is darker than its anterior margin. Right lung 625 gr., left lung 565 gr. income. Lung 3700 cc. can breathe. However, 500 cc in calm breathing. takes air. In deep respiration, the total epithelial surface is about 70 m2 [7]. The lungs are completely surrounded by the visceral pleura, except for a small part called the hilum pulmonis, and each is located within a pleural cavity. A lung fills its own pleural cavity

with little. It is free in this space and can move. Lungs are cone-shaped. Apex, basis contain three sides and two faces. Apex Pulmonis: Due to the anterior curvature of the Apertura thoracis superior, it rises 3-4 cm above the first costal cartilage, towards the root of the neck. The pleura cervicalis covers this part like a tent. The neighborhood of the apex is through the pleura [28]. front face; a. posterior surface with subclavia; ganglion cervicalis inferior (G.stellare), with ventral ramus of T1 nerve and a.intercostalis superior, its outer surface; m. with scalenius medius, inside right; truncus brachiocephalicus, right v. brachiocephalica, left with trachea; a. subclavia sinistra is adjacent to the left v.brachiocephalica. On lung auscultation, the apex should also be listened to with a stethoscope above the inside 1/3 of the clavicle. Penetrating injuries of the cupula pleura may also damage the apex of the lung. Basis Pulmonis: The lower surfaces of the lungs sit above the diaphragm. In accordance with the convexity of the diaphragm towards the thoracic cavity, the lung bases are also concave. This concavity is greater on the right due to the presence of the underlying liver [28]. The lower edges of the lung surrounding the

basis are inserted sharply into the recessus costodiaphragmaticus. Facies Costalis (Costal Face): It has a convexity that matches the inner surface of the walls of the thoracic cavity. On this face, the costa left traces called impressiones costales. Facies Medialis (Inner Face): It consists of two parts, vertebral posteriorly and mediastinal anteriorly. Its vertebral part fits on the lateral aspects of the vertebral column. In the middle of the mediastinal face, there are wide pits, called the impressio cardiaca, into which the heart is located. This pit is deeper on the left. In the upper posterior part of this concavity, there are triangular pits called hilum pulmonis. Here, the radix pulmonis, which consists of formations entering and exiting the lung, is located. The pleural leaves surrounding the radix pulmonis hang below the hilum pulmonis and along the posterior border of the impressio cardiaca. These extensions of the mediastinal pleura, which, after wrapping the upper, anterior and posterior surfaces of the radix pulmonis, hang transversely to the diaphragm between the two lungs, are called ligamentum pulmonale. Apart from these formations, there are some pits and scars on the mediastinal surface. But these are different in the

two lungs. In the right lung, the sulcus v. cava superior rises vertically from the anterior part of the hilum pulmonis to the anterior of the apex. This groove is named sulcus v.brachiocephalica in front of the apex. Behind this groove is the area trachealis. Behind it, the sulcus oesophagus continues up to the hill. Deep, sulcus v.azygos crosses the top of the hilum pulmonis in the form of an arc. Extending along the posterior margins of the hilum pulmonis and pulmonary ligament, the broad sulcus oesophagus cuts below the lower margin. In front of the pulmonary ligament and below the impressio cardiaca, the lower border is cut by the inferior sulcus v. cava . In the left lung, the front of the apex is crossed with sulcus v. brachiocephalica and sulcus a. subclavia. Along the posterior margin of the hilum pulmonis, the deep sulcus aortae descendens ascends. This sulcus radix pulmonis curves forward and continues in the form of an arc. This arch is called sulcus arcus aortae. Sometimes near the lower edge, anterior to the sulcus aortae descendens, the esophagus touches the left lung and makes a groove.

Pleura

It is a serous membrane that surrounds each lung individually. The part that covers the thoracic wall, the mediastinum and the upper surface of the diaphragm is called the pleura parietalis, and the part that covers the outer surface of the lungs is called the pleura visceralis. The visceral pleura also enters into the lung fissures. During breathing, the facing sides of the parietal and visceral pleura rub slightly. The space between the two is called cavitas pleuralis. There is a very thin layer of slippery liquid here. In the radix, the parietal and visceral pleura are a continuation of each other. The parietal pleura is named according to its location and its four parts continue with each other. a. Costal Pleura (Pars Costalis); It surrounds the sternum, ribs and the inner surface of the muscles. Beneath the costal pleura is loose connective tissue called the fascia endothoracica. This corresponds to the fascia transversalis in the abdomen.

a. Costal Pleura (Pars Costalis); It surrounds the sternum, ribs and the inner surface of the muscles. Beneath the costal pleura is loose connective tissue called the fascia endothoracica. This corresponds to the fascia transversalis

in the abdomen. CHAPTER 1 | Lung Anatomy 21 A b. Mediastinal Pleura (Pars Mediastinalis); Anteriorly, the costal pleura curves sharply into the mediastinum and continues with the mediastinal pleura. This curling edge is called the anterior edge of the pleura. In this folded corner, the space between the pleura leaves is called recessus costomediastinalis. The mediastinal pleura forms the outer borders of the mediastinum and covers the mediastinal surfaces of the lungs. It folds over the radix pulmonis and jumps from the periphery of the hilum pulmonis to the surface of the lungs and becomes the visceral pleura. The mediastinal pleura leaves, which cover the upper, anterior and posterior surfaces of the radix pulmonis, lie in a double layer between the esophagus and the lungs and hang down. This part is called the ligamentum pulmonale. The mediastinal pleura makes two folds posteriorly, posterior to the esophagus. Their cavity is called recessus retroesophagei. NS. Cervical Pleura (Cupula Pleurae); It is the continuation of the costal pleura above the apex of the lung. This part is strengthened by the dome-shaped membrane suprapleuralis made by the fascia endothoendothoracica. A muscle called m.scalenius

minimus is attached to the top of it. The top of the dome rises to the level of the C7 vertebral spine. A 2.5 cm high curved line drawn from the sternoclavicular joint to the 1/3 of the clavicle gives the reflexion of this pleura. The cervical pleura is also called the cupula pleura [29]. Because this pleura rises in the form of a dome from the edges of the apertura thoracis superior. Since the cupula pleura is adjacent to the truncus symphatheticus, ganglion cervicalis inferior (ganglion stellare) and T1 nerve posteriorly, paralysis of the intrinsic muscles of the hand and Horner's Syndrome can be seen in lung diseases in this region. Cupula pleura, above the clavicle, 2.5 cm longitudinally. Open pneumothorax occurs in penetrating injuries in this region .

D. Diaphragmatic Pleura (Pars Diaphragmatica); The costal pleura jumps to the upper surface of the diaphragm along the costodiaphragmatic reflexion line and is called the diaphragmatic pleura. The diaphragmatic pleura is attached to the diaphragm only in the centrum tendineum region through the fascia phrenicopleuralis, which consists of the fascia endothoracica. Around the diaphragm, at the

transitional edges where the diaphragmatic pleura jumps to the thoracic wall and becomes the costal pleura, the pleural cavity forms sharp circle-shaped cul-de-sacs. This dead end is called recessus costodiaphragmaticus. Visceral Pleura: It is formed by the mediastinal parietal pleura jumping from the borders of the hilum pulmonis to the surfaces of the lungs and completely enveloping them. The visceral pleura also penetrates into the fissures and extends to the hilum pulmonis and completely separates the lung lobes from each other. Thinner extensions of the visceral pleura penetrate into the lung tissue, forming thin connective tissue walls between the bronchopulmonary segments . When inhaled, the lungs are inserted into the recesses, filling them. Recessus alone cannot completely fill the costodiaphragmaticus. Here remains an interval called the complementary interval. The exudate that occurs during pleural inflammation is first collected here. If exudate builds up, it can push the lungs up. The relationship between the 12th rib and the lower border of the pleura is important. The lower border of the pleura crosses the 12th rib at the outer edge of the m.erector spina. But sometimes if the 12th rib remains rudimentary,

the 11th rib can be mistaken for the 12th rib. The pleural space can be entered if a stab is made at this level. Lung lower margins: a. Mid-clavicular line, 6th rib, b. Mid-axillary line, 8th rib, c. Mid-scapular line, 10th rib, d. 3 cm from the posterior median line. away, it descends to the level of the T10 vertebral spina. In these lines, the lower edge of the pleura is roughly two ribs below the lower edge of the lung. Veins of the Pleura: Parietal pleura, a. intercostalis, a. The branches emerging from thoracica interna and a.phrenica superior nourish it. Its veins drain into veins of the same name. Visceral pleura a. bronchialis feeds branches. Its veins drain into the pulmonary veins. Since the intrapulmonary lymphatic system and the pleural lymph system are separate, pleural abscesses cannot pass into the lungs. Nerves of the Pleura: N. intercostalis, n.thoracoabdominales, n. subcostalis and n.phrenicus branches carry the sense of the parietal pleura. Touch and heat stimulations cause pain in the parietal pleura. The nerves of the visceral pleura come from the plexus pulmonalis. There is no pain sensation in the visceral pleura. The parietal pleura (especially in the costal part) is hypersensitive to pain. Irritation of the costal and

peripheral diaphragmatic areas causes local or acute pain. This pain can be felt in the thoracic wall, abdominal wall, lower neck and shoulder.

REFERENCES

1. Zepp JA, Morrisey EE. Cellular crosstalk in the development and regeneration of the respiratory system. Nat Rev Mol Cell Biol. 2019 Sep;20(9):551-566.
2. Lee JH, Tammela T, Hofree M, et al. Anatomically and Functionally Distinct Lung Mesenchymal Populations Marked by Lgr5 and Lgr6. Cell. 2017 Sep 7;170(6):1149-1163.e12.
3. Caduff JH, Fischer LC, Burri PH. Scanning electron microscope study of the developing microvasculature in the postnatal rat lung. Anat Rec. 1986 Oct;216(2):154-64.
4. Chung MI, Bujnis M, Barkauskas CE, et al. Niche-mediated BMP/SMAD signaling regulates lung alveolar stem cell proliferation and differentiation. Development. 2018 May 11;145(9).
5. von Gise A, Stevens SM, Honor LB, et al. Contribution of Fetal, but Not Adult, Pulmonary Mesothelium to Mesenchymal Lineages in Lung Homeostasis and

Fibrosis. Am J Respir Cell Mol Biol. 2016 Feb;54(2):222-30.

6. Ochs M, Hegermann J, Lopez-Rodriguez E, et al. On Top of the Alveolar Epithelium: Surfactant and the Glycocalyx. Int J Mol Sci. 2020 Apr 27;21(9).
7. Schneider JP, Wrede C, Hegermann J, et al. On the Topological Complexity of Human Alveolar Epithelial Type 1 Cells. Am J Respir Crit Care Med. 2019 May 1;199(9):1153-1156.
8. Hsia CC, Hyde DM, Weibel ER. Lung Structure and the Intrinsic Challenges of Gas Exchange. Compr Physiol. 2016 Mar 15;6(2):827-95.
9. Low FN. The pulmonary alveolar epithelium of laboratory mammals and man. Anat Rec. 1953 Oct;117(2):241-63.
10. Bastacky J, Lee CY, Goerke J, et al. Alveolar lining layer is thin and continuous: low-temperature scanning electron microscopy of rat lung. J Appl Physiol (1985). 1995 Nov;79(5):1615-28.
11. Fishman AP. Pulmonary diseases and disorders. Pulmonary diseases and disorders1980. p. 1835-1835.

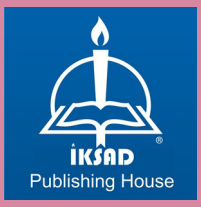
12. Bennett HS. Morphological aspects of extracellular polysaccharides. Journal of histochemistry & cytochemistry. 1963;11(1):14-23.
13. LaRivière WB, Schmidt EP. The Pulmonary Endothelial Glycocalyx in ARDS: A Critical Role for Heparan Sulfate. Curr Top Membr. 2018;82:33-52.
14. Ochs M. The closer we look the more we see? Quantitative microscopic analysis of the pulmonary surfactant system. Cell Physiol Biochem. 2010;25(1):27-40.
15. Vanhecke D, Herrmann G, Graber W, et al. Lamellar body ultrastructure revisited: high-pressure freezing and cryo-electron microscopy of vitreous sections. Histochem Cell Biol. 2010 Oct;134(4):319-26.
16. Ebong EE, Macaluso FP, Spray DC, et al. Imaging the endothelial glycocalyx in vitro by rapid freezing/freeze substitution transmission electron microscopy. Arterioscler Thromb Vasc Biol. 2011 Aug;31(8):1908-15.
17. Hayat MA. Stains and cytochemical methods. Springer Science & Business Media; 1993.

18. Roth J. Ultrahistochemical demonstration of saccharide components of complex carbohydrates at the alveolar cell surface and at the mesothelial cell surface of the pleura visceralis of mice by means of concanavalin A. Exp Pathol (Jena). 1973;8(3):157-67.
19. Martins Mde F, Bairos VA. Glycocalyx of lung epithelial cells. Int Rev Cytol. 2002;216:131-73.
20. Hegermann J, Lünsdorf H, Ochs M, et al. Visualization of the glomerular endothelial glycocalyx by electron microscopy using cationic colloidal thorium dioxide. Histochem Cell Biol. 2016 Jan;145(1):41-51.
21. Chandra A, Conry S. In-flight Medical Emergencies. West J Emerg Med. 2013 Sep;14(5):499-504.
22. Coker RK, Shiner RJ, Partridge MR. Is air travel safe for those with lung disease? Eur Respir J. 2007 Dec;30(6):1057-63.
23. Dillard TA, Rosenberg AP, Berg BW. Hypoxemia during altitude exposure. A meta-analysis of chronic

obstructive pulmonary disease. Chest. 1993 Feb;103(2):422-5.

24. Verjee MA, Crone R, Ostrovskiy G. Medical issues in flight and updating the emergency medical kit. Open access emergency medicine: OAEM. 2018;10:47.
25. Cummin AR, Nicholson AN. Aviation medicine and the airline passenger. Arnold; 2002.
26. Edvardsen A, Akerø A, Christensen CC, et al. Air travel and chronic obstructive pulmonary disease: a new algorithm for pre-flight evaluation. Thorax. 2012 Nov;67(11):964-9.
27. Lien D, Turner M. Recommendations for patients with chronic respiratory disease considering air travel: a statement from the Canadian Thoracic Society. Can Respir J. 1998 Mar-Apr;5(2):95-100.
28. Josephs LK, Coker RK, Thomas M. Managing patients with stable respiratory disease planning air travel: a primary care summary of the British Thoracic Society recommendations. Prim Care Respir J. 2013 Jun;22(2):234-8.

29. Kelly PT, Swanney MP, Stanton JD, et al. Supplemental oxygen effect on hypoxemia at moderate altitude in patients with COPD. Aviat Space Environ Med. 2009 Sep;80(9):815-9.



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