



UNIVERSITÀ
DEGLI STUDI
DI PADOVA

DNS DEPARTMENT OF NEUROSCIENCE



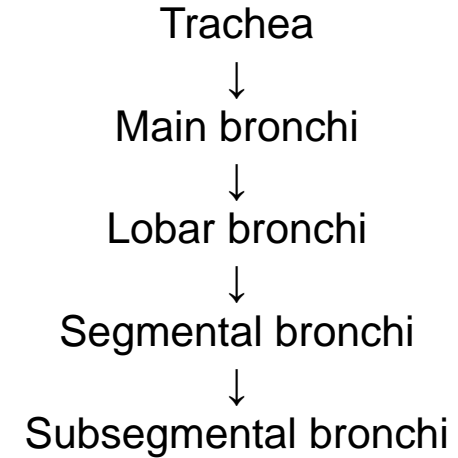
ANATOMY AND PHYSIOLOGY (C.I.)

HUMAN ANATOMY
(Mod. A)

THE RESPIRATORY SYSTEM

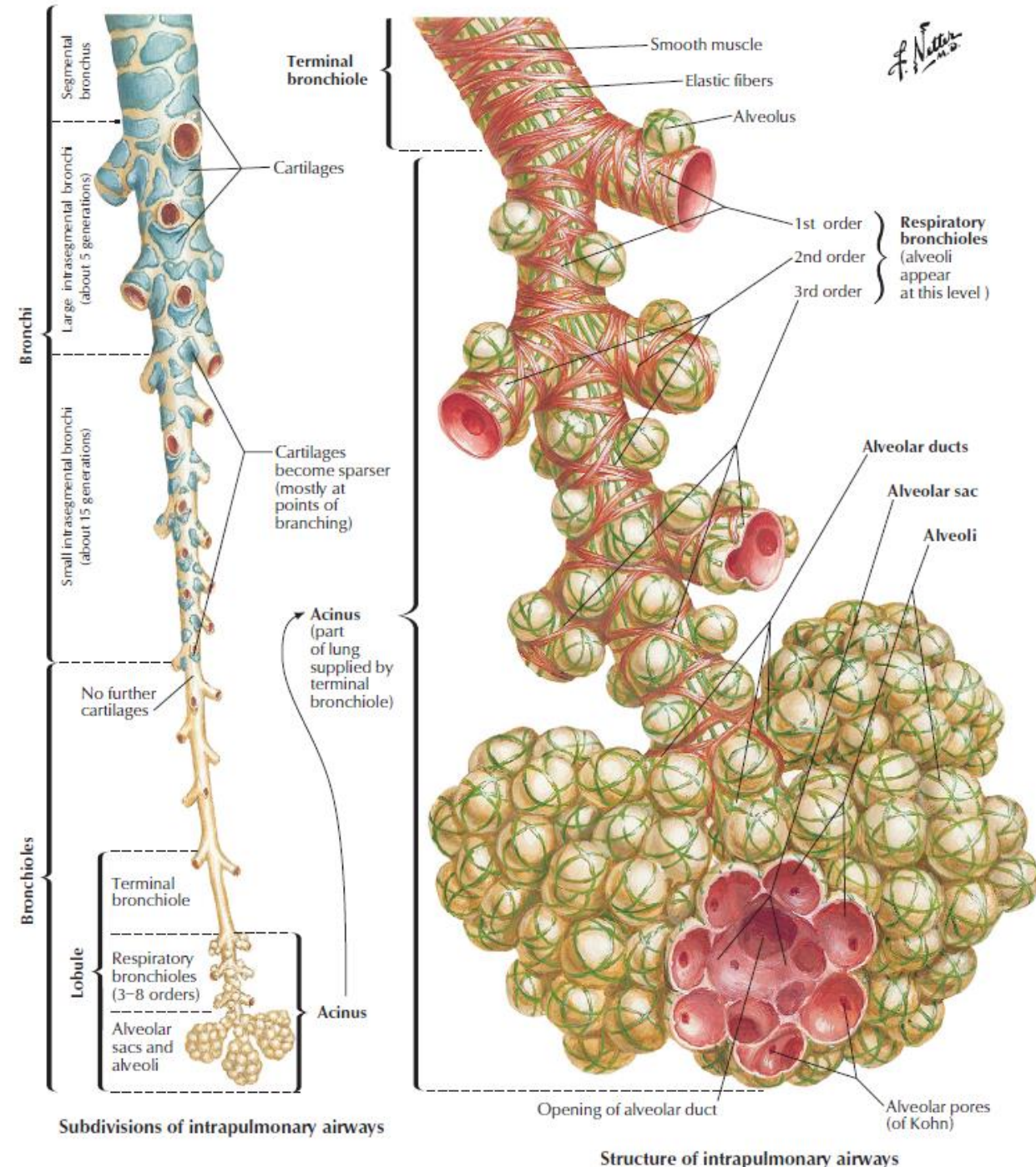
THE BRONCHIAL TREE

BRONCHIAL BRANCHES/DIVISIONS



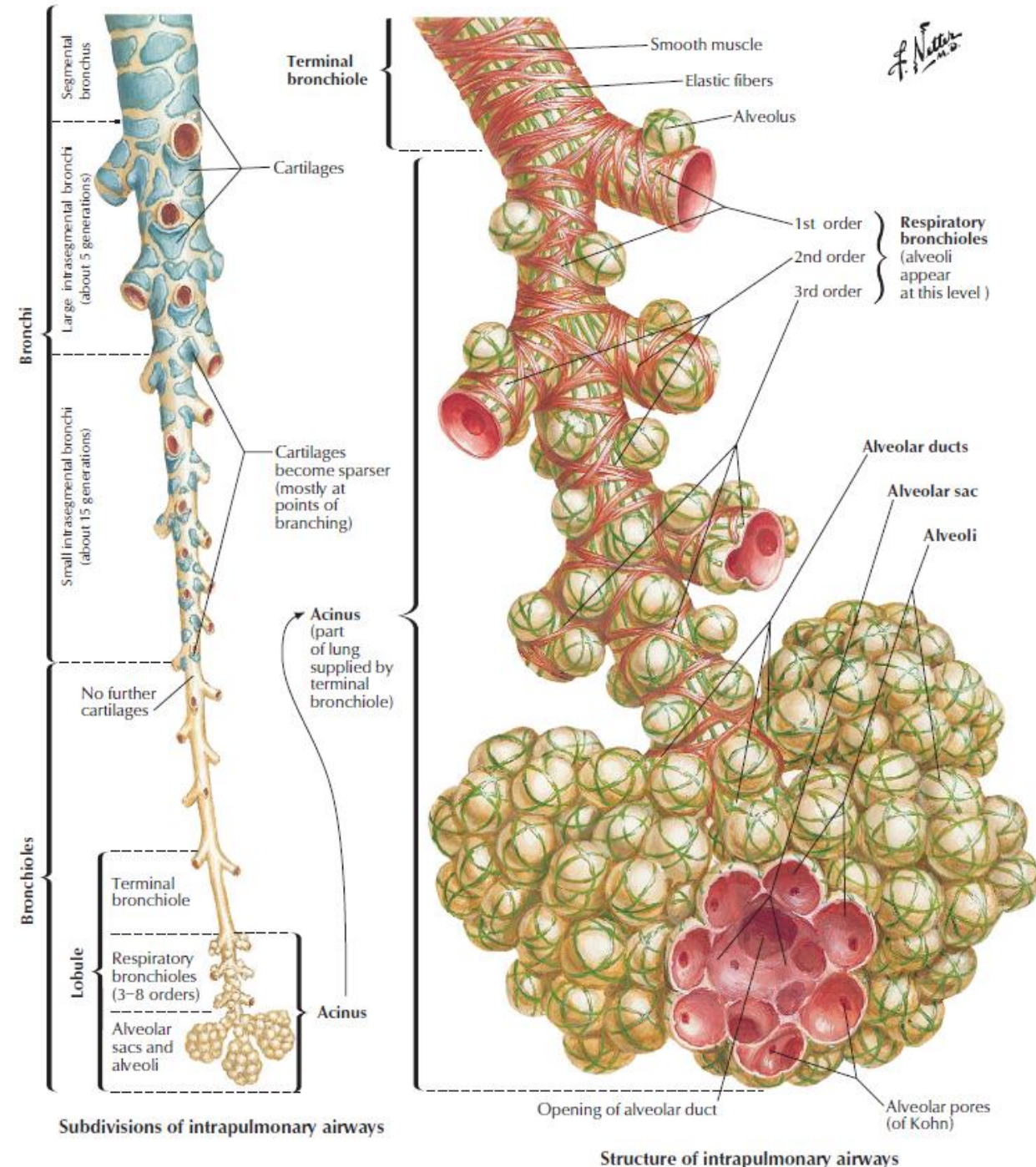
The main bronchi and the lobar bronchi maintain an organization of C-SHAPED (posteriorly incomplete) RINGS of HYALINE CARTILAGE

Starting from the **segmental bronchi**, and even more from the **subsegmental bronchi**, a fragmentation of the cartilaginous component occurs → the cartilage layer shows a more irregular organization, no longer as rings, but as **CARTILAGINE PLATES**



Subdivisions of intrapulmonary airways

Structure of intrapulmonary airways



The cartilaginous plates of the segmental and sub-segmental bronchi progressively decrease as the division into smaller bronchial branches goes on

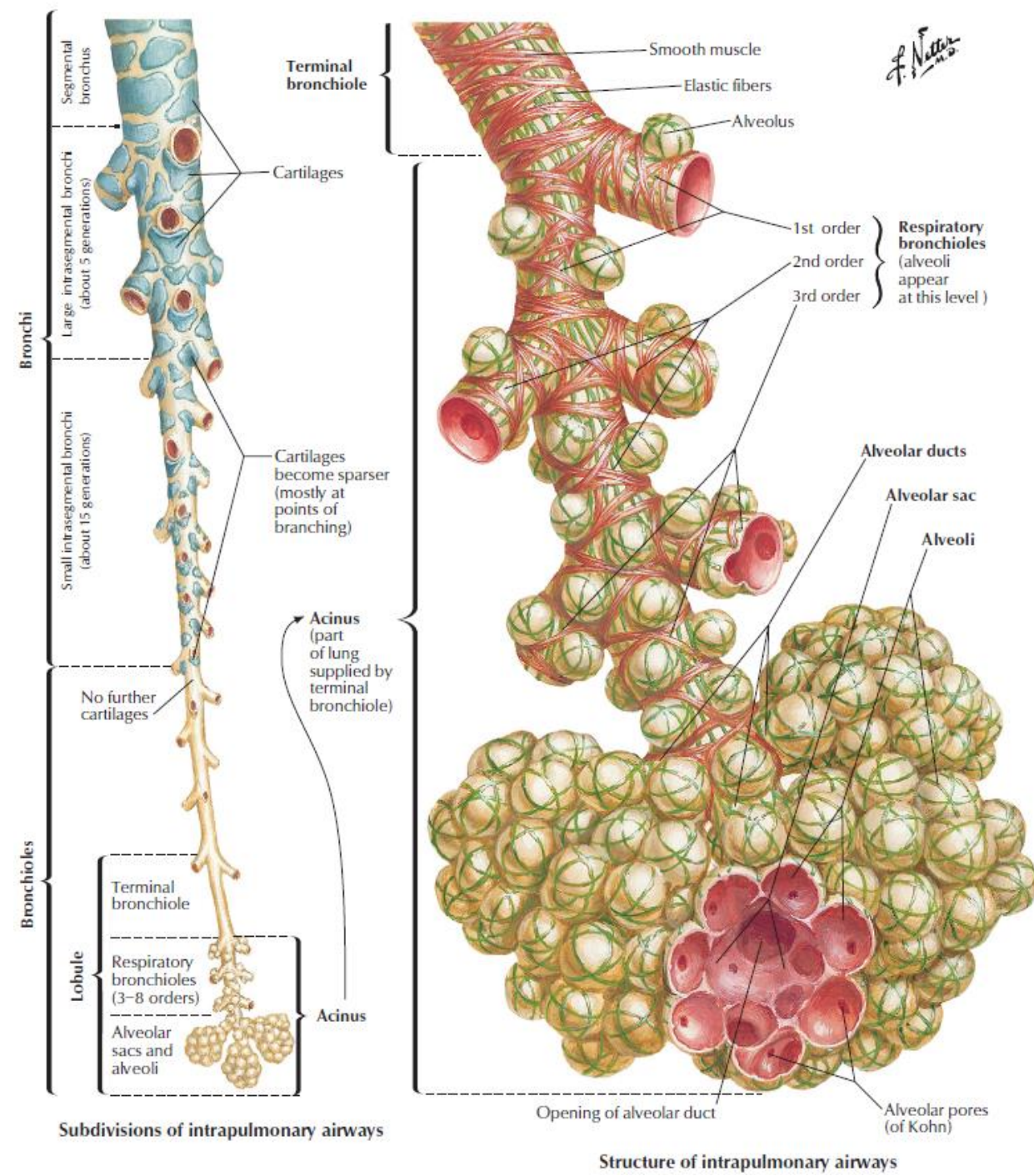
Each subsequent bronchial branch is smaller than the previous one. Furthermore, proportionately, THE CARTILAGE COMPONENT ALSO REDUCES

↓
As the diameter of the bronchial branches decreases, the percentage of the wall occupied by cartilage is reduced

Example:

- the segmental bronchus has an important cartilaginous component and is mainly made up of cartilage
- at the level of the smaller branches of the subsegmental bronchi, where multiple *generations* or *orders of division* are present, the percentage of the wall occupied by cartilage reduces as the diameter of the branches decreases

THE BRONCHIAL TREE



Once a certain degree of bronchial subdivision has been reached, the cartilaginous component actually disappears and there is no longer cartilage within the bronchial wall

This is an important step from a structural point of view, which defines the origin of the so-called

PULMONARY BRONCHIOLES

they are bronchial branches without cartilage in their wall with diameter of 1 mm or less

When the diameter of the bronchial branches reaches 1 mm, they no longer have a cartilaginous component in the wall and they are called bronchioles

The bronchioles divide further, giving rise to several BRONCHIOLAR GENERATIONS

THE BRONCHIAL TREE

The bronchioles furtherly divide, giving rise to MORE BRONCHIOLAR GENERATIONS

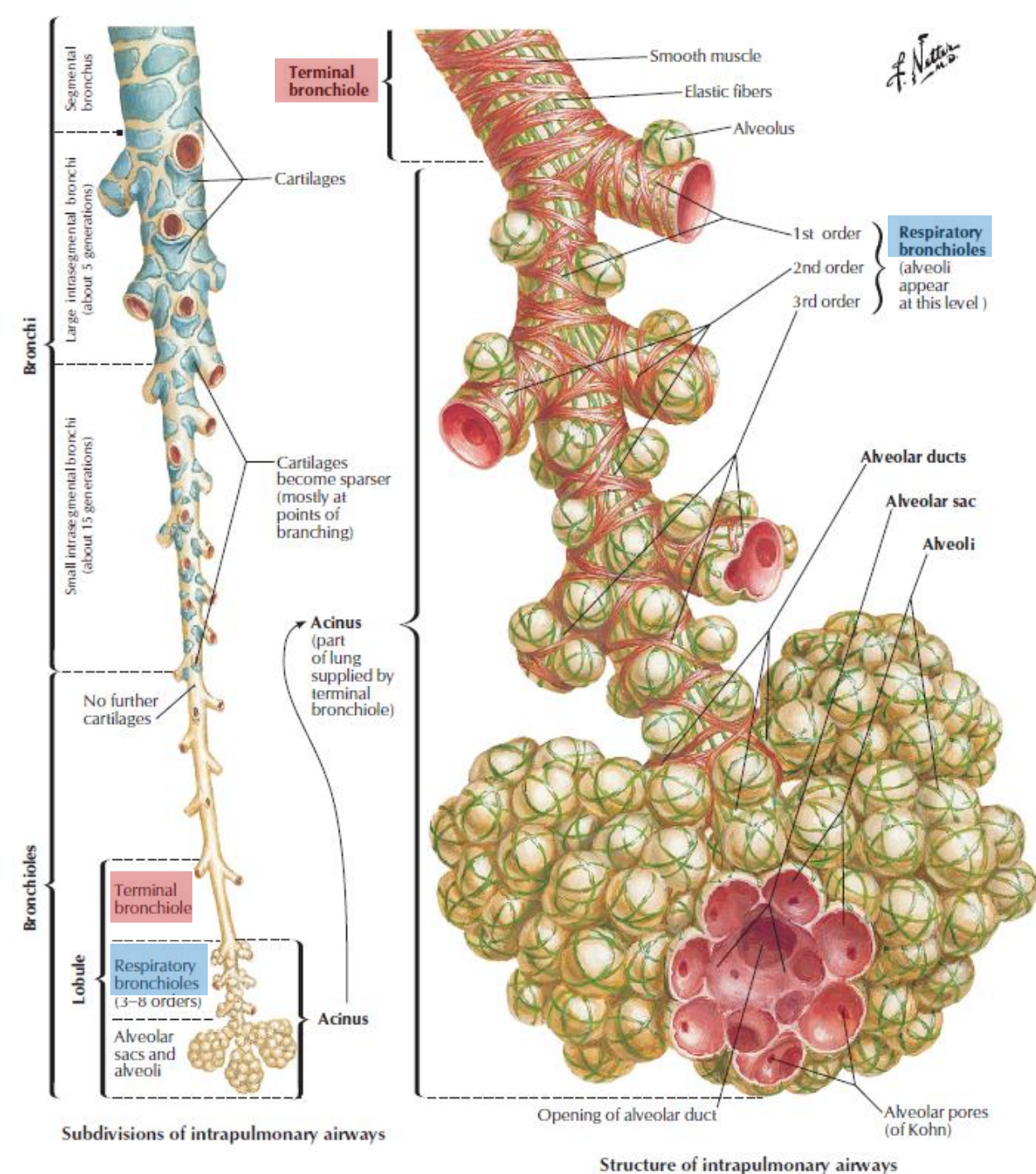
Proceeding with the bronchiolar subdivisions, we arrive at the so-called **TERMINAL BRONCHIOLE**

↓
it is the last bronchiolar branch without alveoli within its wall

The terminal bronchiole furtherly divides into smaller bronchioles, which acquire a peculiar characteristic: the PRESENCE OF **ALVEOLI** WITHIN THE WALL

The bronchioles that have **ALVEOLI** at the level of their wall are called **RESPIRATORY BRONCHIOLES**

RESPIRATION (i.e., gas exchange between the air and the blood that flows in the capillaries that supply the wall of the alveoli) begins at the level of the respiratory bronchioles



Subdivisions of intrapulmonary airways

Structure of intrapulmonary airways

ALVEOLI

They are hemispherical evaginations of the wall of the respiratory bronchioles

The gas exchanges (oxygen/carbon dioxide) take place at the level of the wall of the alveoli

The respiratory bronchioles divide again to give rise to several orders of division with a progressive increase also in the number of pulmonary alveoli

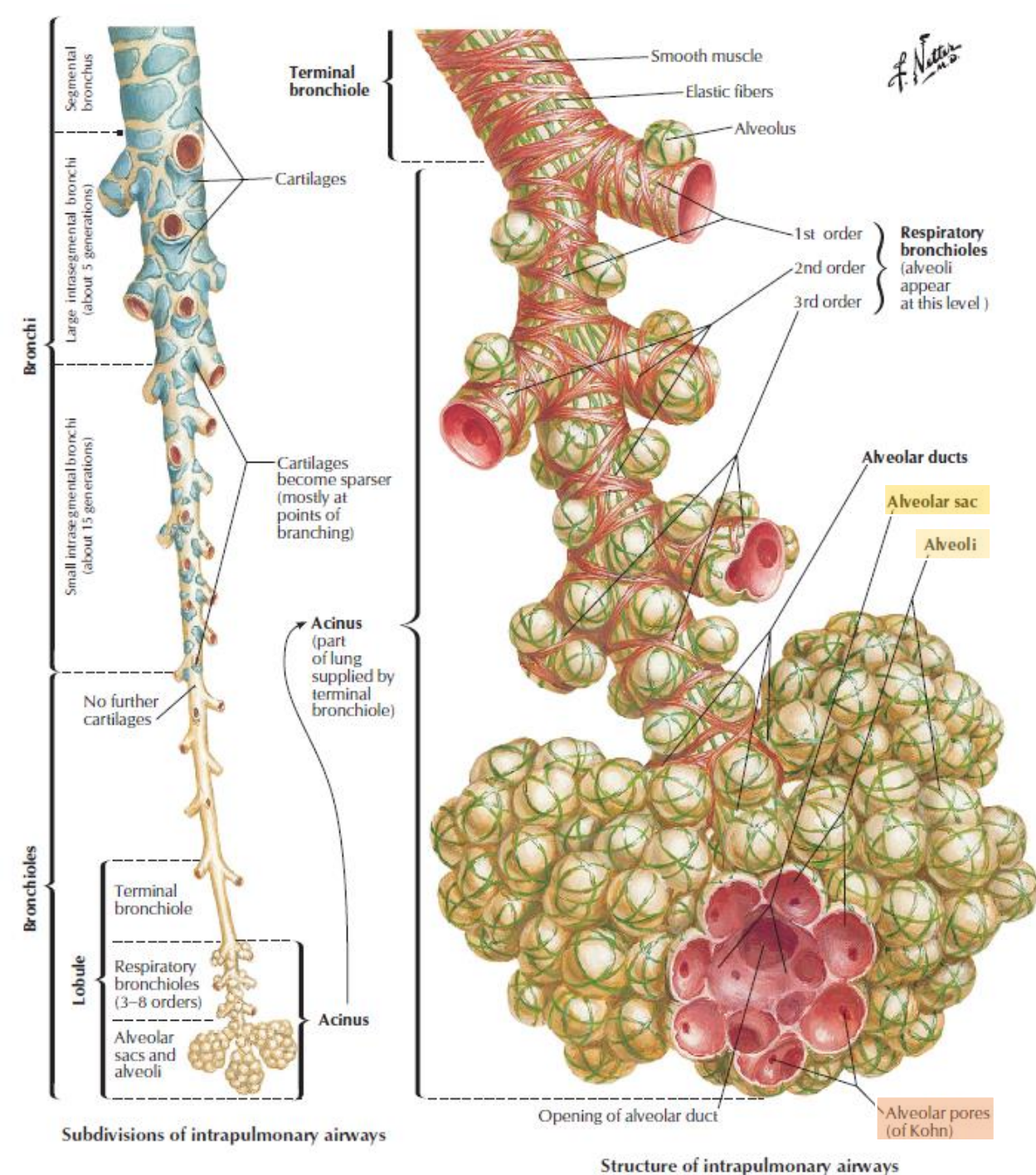
The terminal bronchial division is represented by the

ALVEOLAR SAC

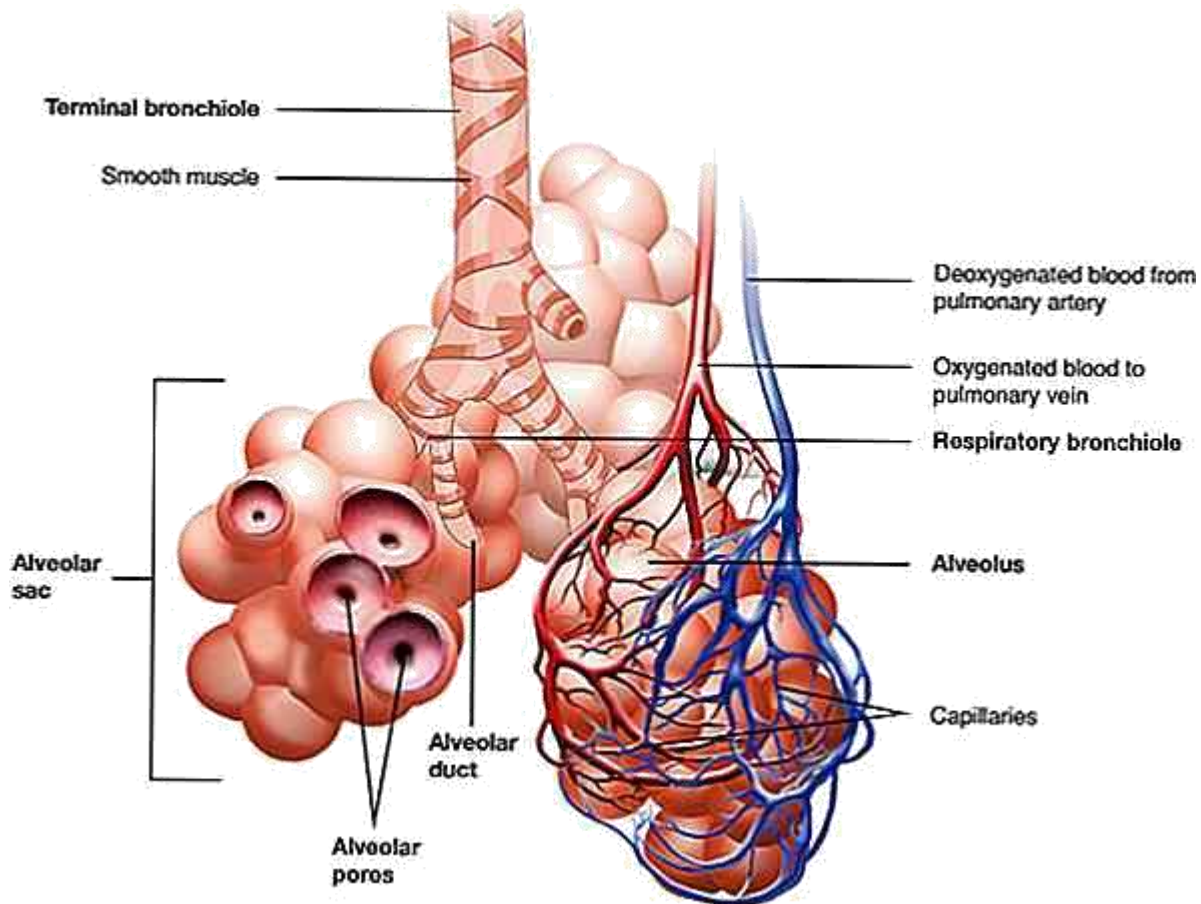


they are made up of large clusters of alveoli connected to each other

In the alveolar sacs, *the free wall of the bronchioles is no longer visible*; the alveoli are connected to each other via the so-called **KOHN PORES** = small communications between alveoli



ALVEOLI

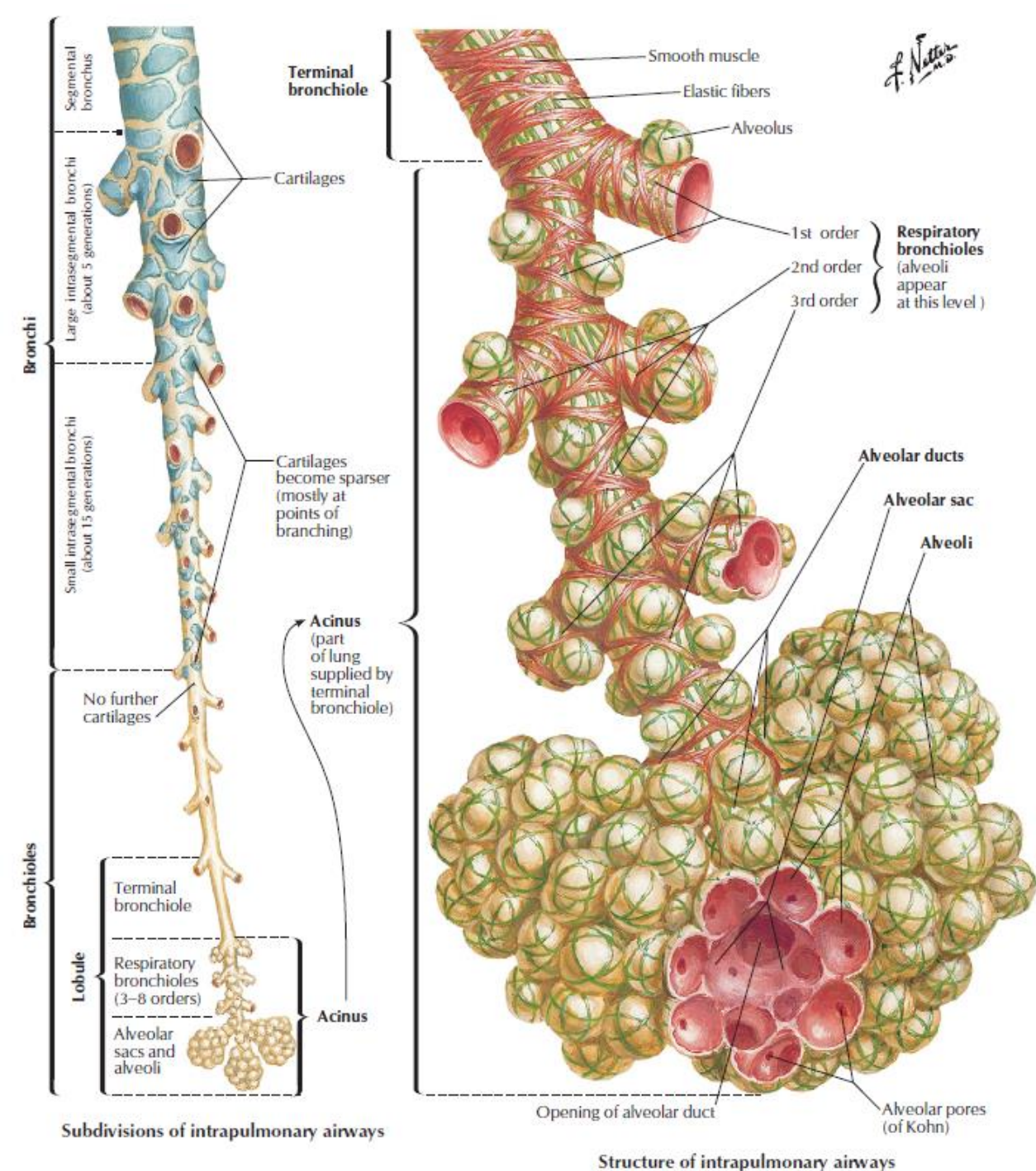


The **gas exchange** between the air contained in the airways that reaches the bronchioles and the blood that flows in the lung capillaries occur **ONLY at the level of the wall of the alveoli**, not at the level of the bronchiolar wall



- In the *terminal bronchioles*, where no alveoli are present, no gas exchange takes place
- these exchanges occur at the level of the respiratory bronchioles, and in particular **at the level of the alveoli of the respiratory bronchioles**, NOT at the level of the bronchiolar wall interposed between the alveoli

ALVEOLI MAKE UP THE FUNCTIONAL TISSUE OF THE LUNGS KNOWN AS THE LUNG PARENCHYMA



- During bronchial branching, the **MONOPODIC DIVISION** occurs up to the generation of the terminal bronchioles
- then the terminal bronchioles give rise to the **respiratory bronchioles** according to a **DICHOTOMIC DIVISION**

The anatomical structure that originates from a terminal bronchiole is called:

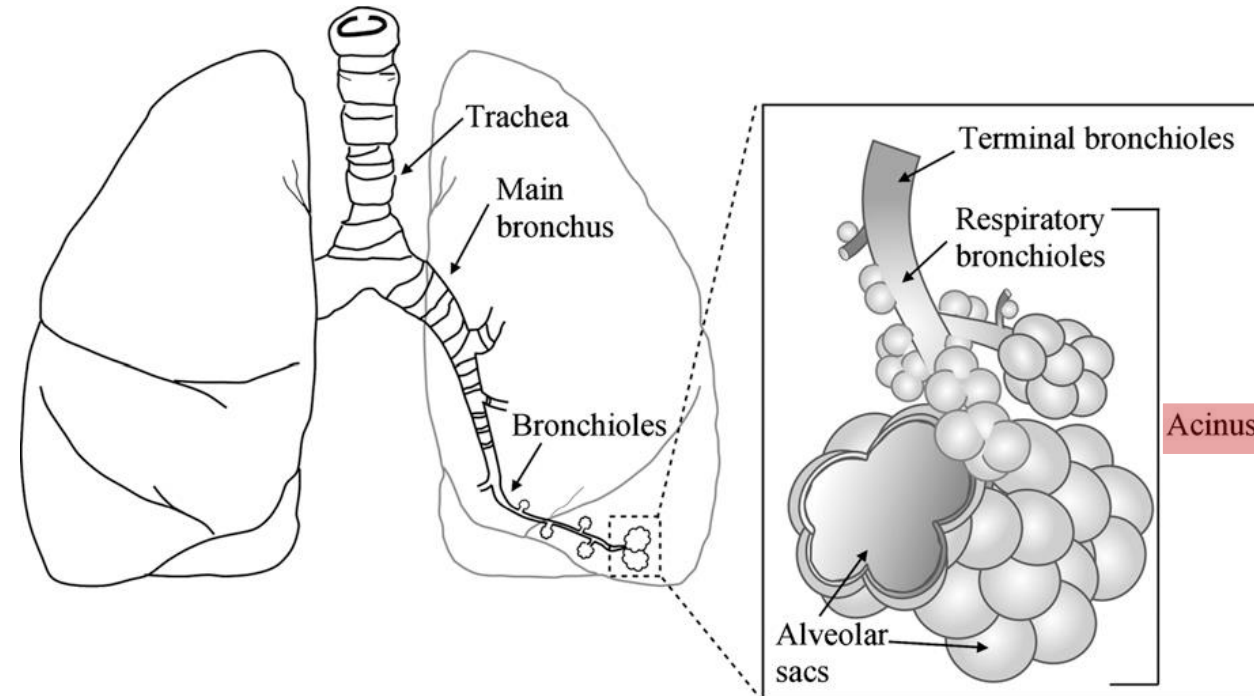
PULMONARY ACINUS



It includes the respiratory bronchioles, alveolar sacs and alveoli.
It is the anatomical unit of the lung supplied by a specific respiratory bronchiole

In the same way:

- a pulmonary lobe is the portion of the lung supplied/ventilated by a specific lobar bronchus
- a pulmonary segment is the portion of the lung supplied/ventilated by a specific segmental bronchus



MICROSCOPIC ANATOMY OF THE AIRWAYS

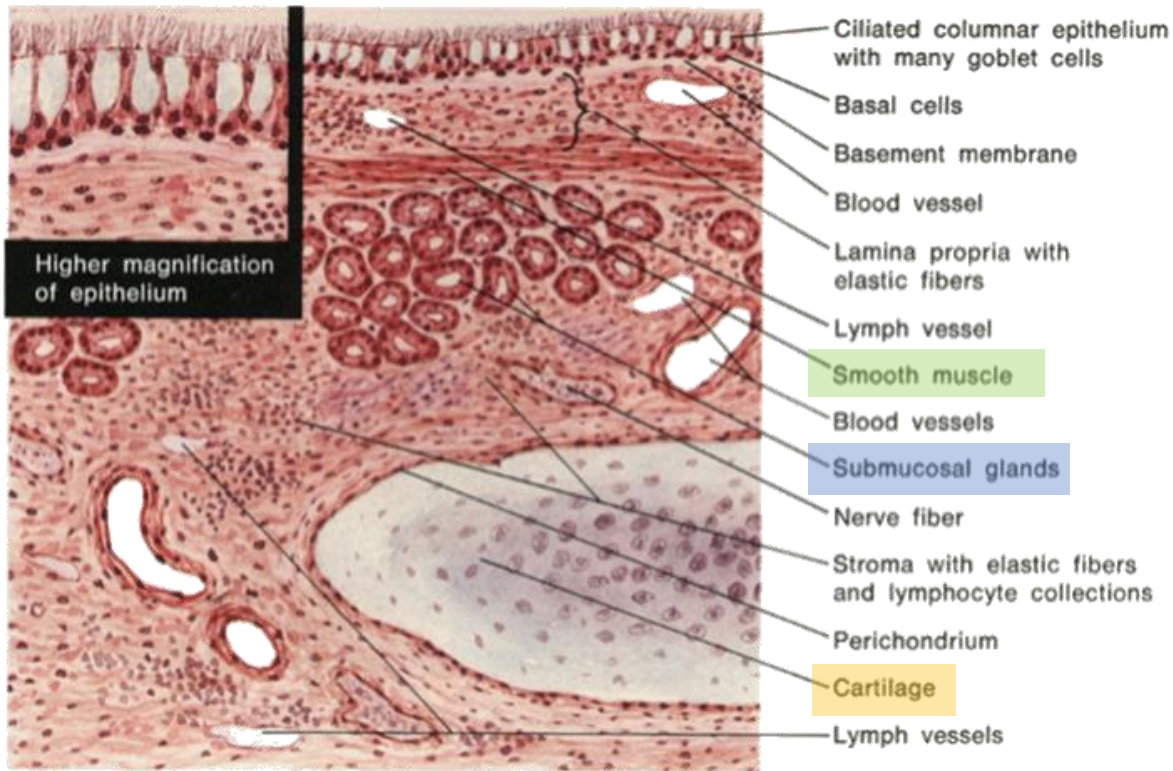
TRACHEA

The trachea structure is given by a cartilaginous component consisting on incomplete cartilaginous rings

Posteriorly the muscular component is present (trachealis muscle); internally, lining the tracheal lumen, there are a submucosa and a mucosa

In the **submucosa** there are **tracheal glands** producing serous-mucosal secretions;

*Between the mucosa and the submucosa a **smooth muscle component** is found.*



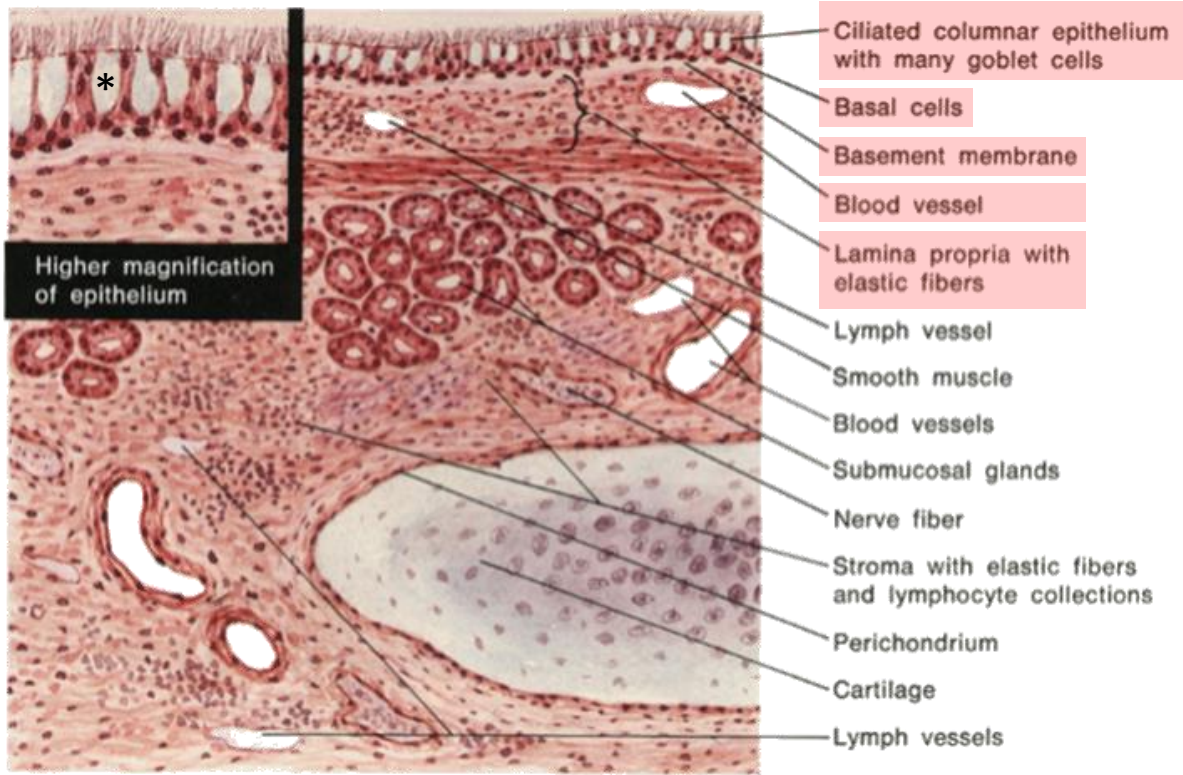
Microscopic anatomy of a trachea portion

TRACHEA

The mucosa is lined with a **RESPIRATORY EPITHELIUM**:

- **COLUMNAR, PSEUDOSTRATIFIED EPITHELIUM**
because cell nuclei are arranged in multiple layers, even if all the cells lie on the basement membrane → it seems stratified but it is not!

- **EPITHELIUM WITH CILIA and GOBLET CELLS**, which have a goblet shape, and produce mucus *



Microscopic anatomy of a trachea portion

BRONCHI

In a medium-sized bronchus (e.g., *segmental or subsegmental bronchus*):

- the cartilaginous component is greatly reduced; **cartilaginous plates** are present rather than c-shaped rings

Internally to the cartilaginous plates it is possible to identify:

- a **SUBMUCOSA** in which **bronchial glands** are present, which are seromucous glands (*they are mainly serous glands, but they can present a mucosal component*)

Internally to the submucosa there is:

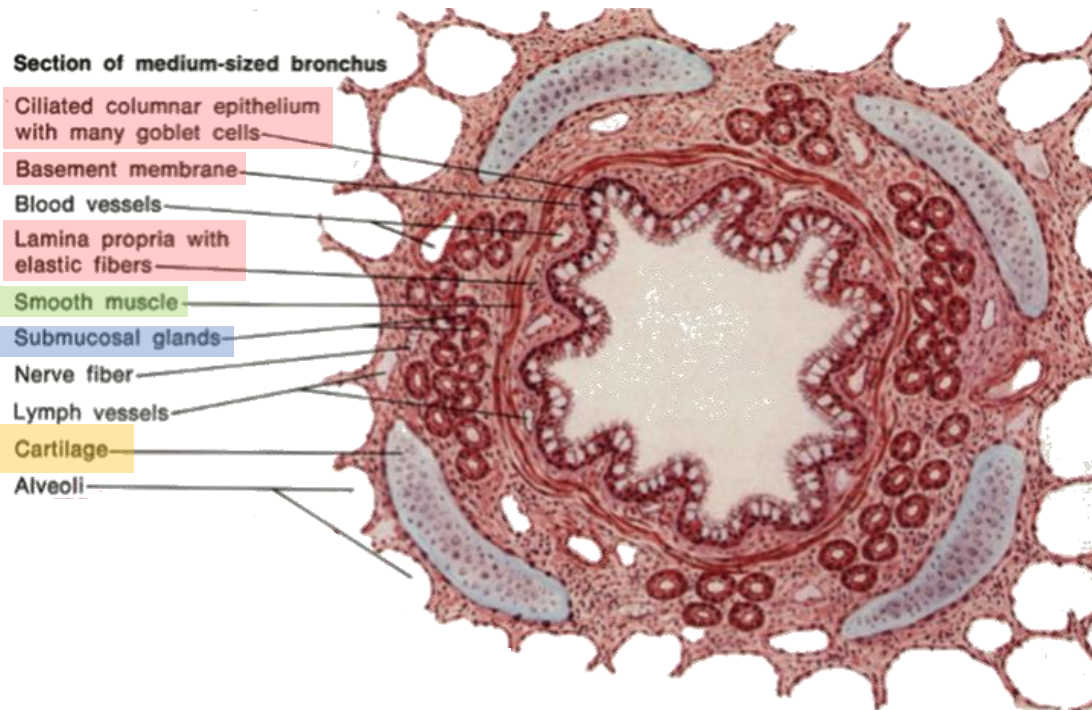
- a **THIN SMOOTH MUSCLE LAYER**

Internally to the muscle layer:

- the **MUCOSA layer**, consisting of a **lamina propria** and a **LINING EPITHELIUM** which has similar characteristics to that of the trachea

↓

Columnar pseudostratified epithelium with cilia and goblet cells



Section of medium-sized bronchus

Ciliated columnar epithelium with many goblet cells

Basement membrane

Blood vessels

Lamina propria with elastic fibers

Smooth muscle

Submucosal glands

Nerve fiber

Lymph vessels

Cartilage

Alveoli

Cross-section of a medium-sized bronchus (segmental or subsegmental bronchus)

F. Netter M.D.
© CIBA

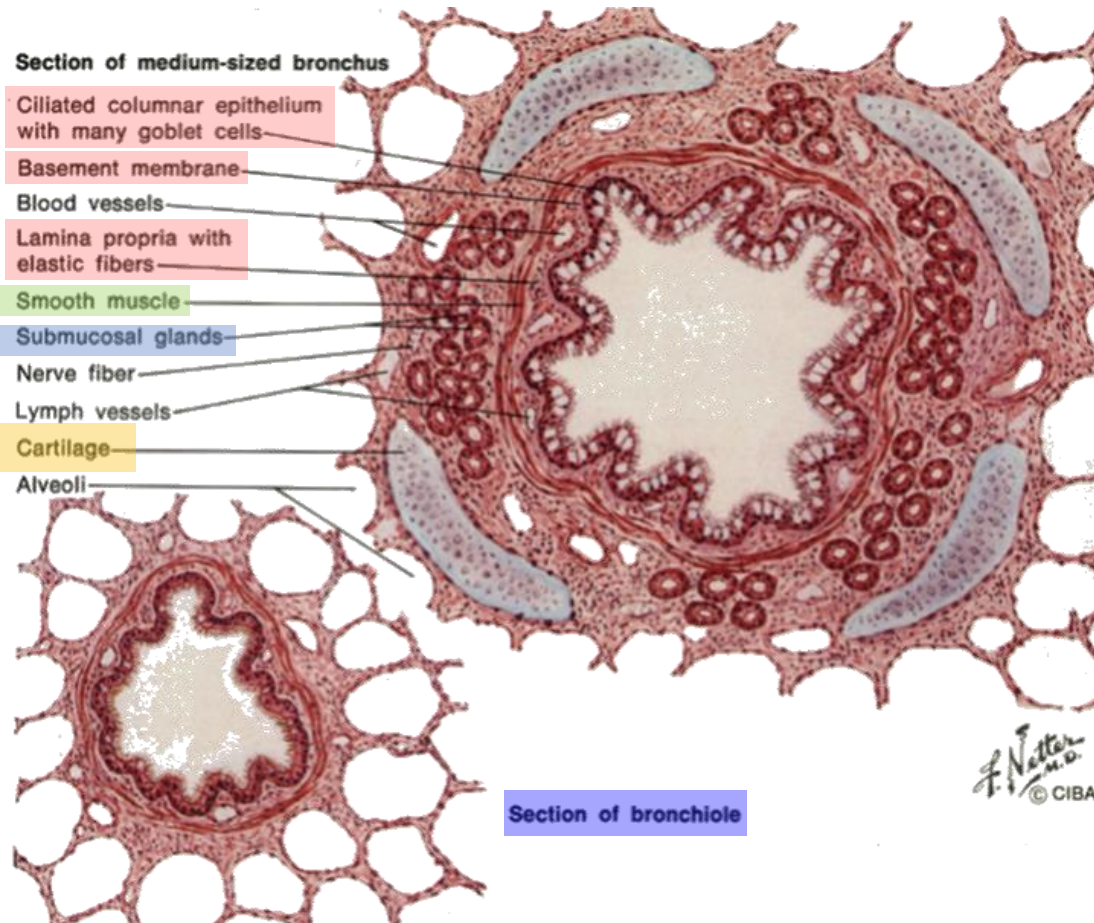
BRONCHIOLES

As the diameter of the bronchial branches is reduced, the following modifications occur:

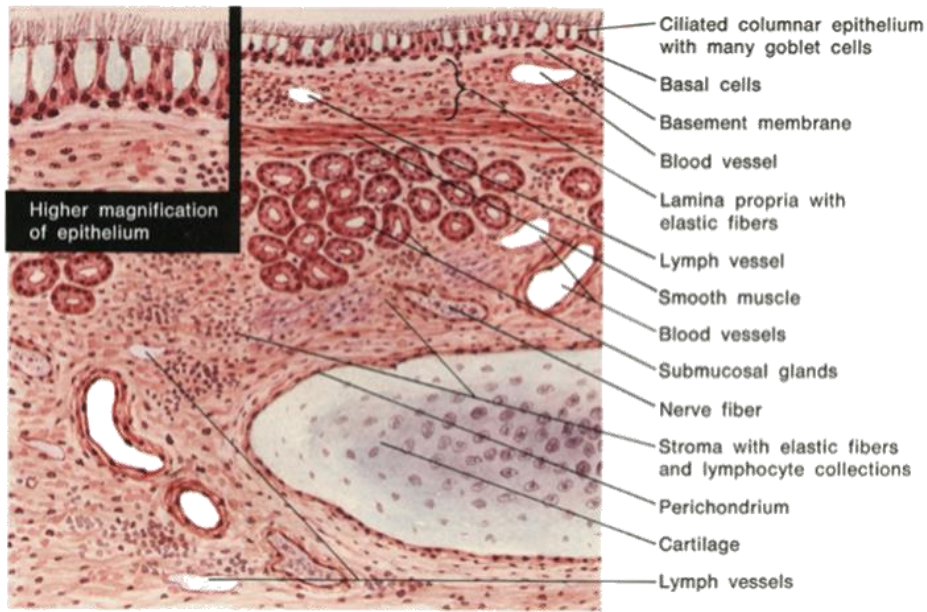
1. a progressive **reduction of the wall cartilage** and also of the **gland component of the submucosa**
2. a **simplification of the lining epithelium**, where the goblet cells become less numerous, until they are no more present; the columnar pseudostratified epithelium become a **simple columnar epithelium**, up to a **simple cuboidal epithelium** in the last bronchial divisions

Based on that, within the **bronchioles**:

- the cartilaginous component is no longer present
- the smooth muscle component is maintained
- the submucosal glands are no longer present (there is no submucosal layer)
- Internally to the thin muscular layer, the mucosa layer can be recognized, made up of a lamina propria and a lining epithelium which has almost completely lost the goblet cells → it is a simple columnar epithelium



Cross-section of a segmental bronchus and a bronchiole

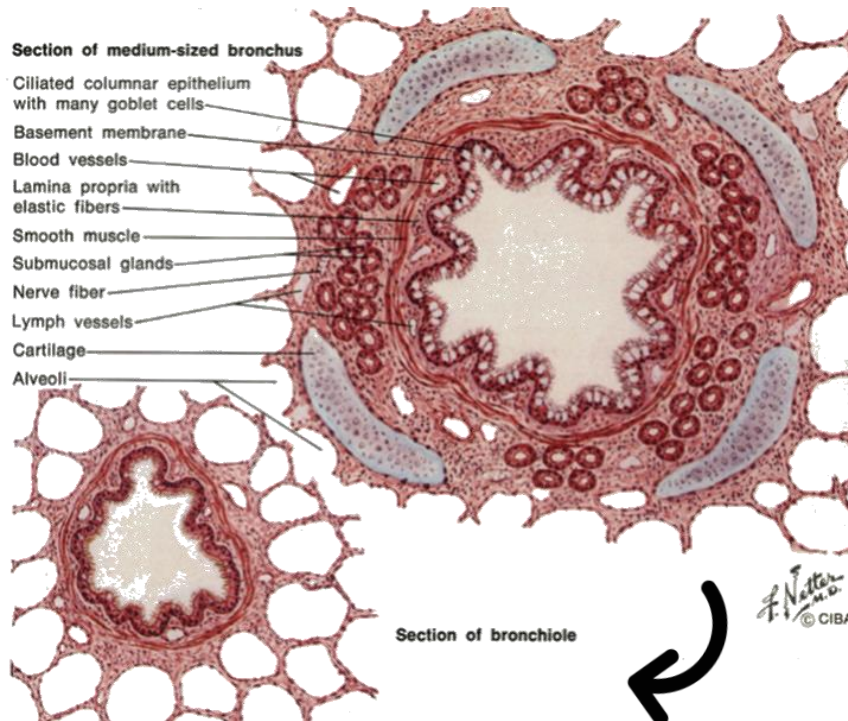


What is the functional meaning of the progressive reduction of the gland component and goblet cells, i.e. the structures that allow the production of mucus?



As the bronchial and bronchiolar branches become smaller, there is a higher risk that excessive mucus production close the lumen of the bronchial/bronchiolar branches

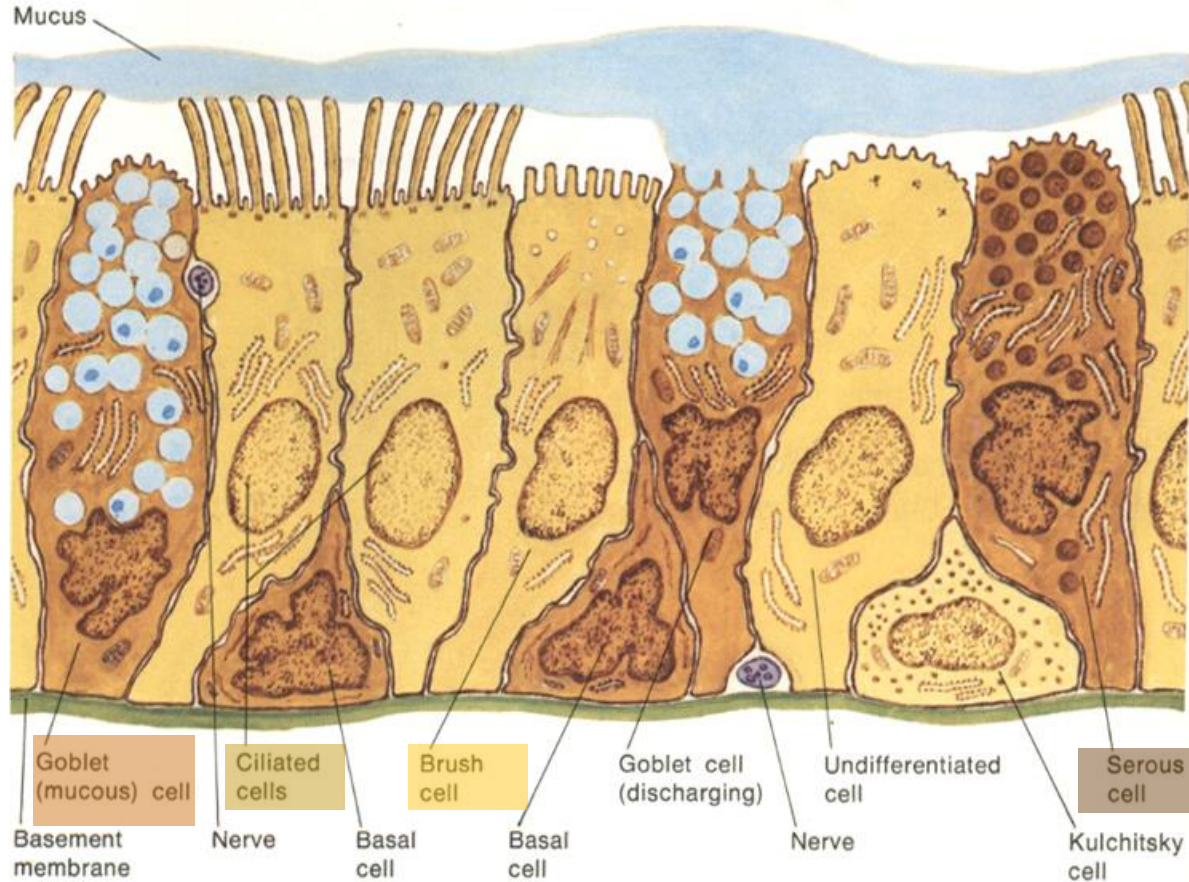
The closure of a bronchiole by a mucus plug would compromise breathing because it would prevent the air from reaching the last bronchiolar branches



In smokers, there is an increased production of mucus within the airways - On one hand, it serves to clean bronchi and bronchioles from polluting particles; on the other hand, it has deleterious consequences, altering the normal physiology of the respiratory mucosa

THE RESPIRATORY EPITHELIUM

Ultrastructure of Tracheal, Bronchial, and Bronchiolar Epithelium



Trachea and large bronchi. Ciliated and goblet cells predominant, with some serous cells and occasional brush cells, undifferentiated (intermediate) cells, and Clara cells. Numerous basal cells and occasional Kulchitsky cells present

The image represents in detail the epithelium lining the TRACHEA and BRONCHI, which is a **COLUMNAR PSEUDOSTRATIFIED, CILIATED EPITHELIUM WITH GOBLET CELLS**

We can identify:

GOBLET CELLS

Responsible for mucus production

CILIATED CELLS

they have the function of moving upwards the mucus produced by the goblet cells and glands

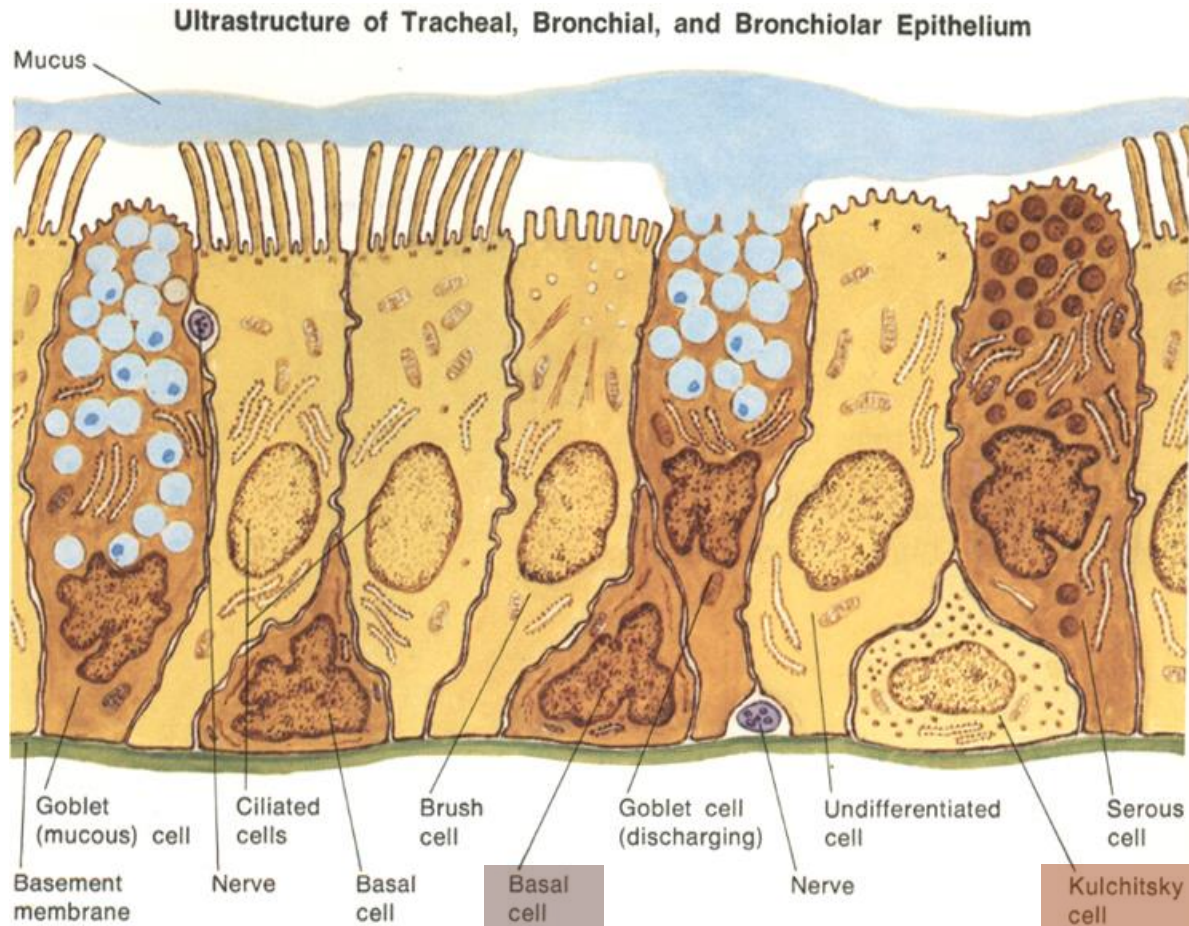
SEROUS CELLS

Responsible for the production of protein-rich secretions

BRUSH CELLS

they are cells with microvilli, thin structures that have the function of increasing the surface of the apical cell membrane to promote the exchange of electrolytes between the cell and the mucus → **this assures for correct hydration of the mucus**

THE RESPIRATORY EPITHELIUM



Trachea and large bronchi. Ciliated and goblet cells predominant, with some serous cells and occasional brush cells, undifferentiated (intermediate) cells, and Clara cells. Numerous basal cells and occasional Kulchitsky cells present

The image represents in detail the epithelium lining the TRACHEA and BRONCHI, which is a **COLUMNAR PSEUDOSTRATIFIED, CILIATED EPITHELIUM WITH GOBLET CELLS**

We can identify:

STEM CELLS (*Basal cells*)

located in a basal position, they undergo replication and differentiation into tissue-specific cell types of the epithelium

KULCHITSKY CELLS

they produce hormones which are then released into the bloodstream

THE RESPIRATORY EPITHELIUM

With the generation of BRONCHIOLES a SIMPLIFICATION of the lining epithelium occurs, which becomes a

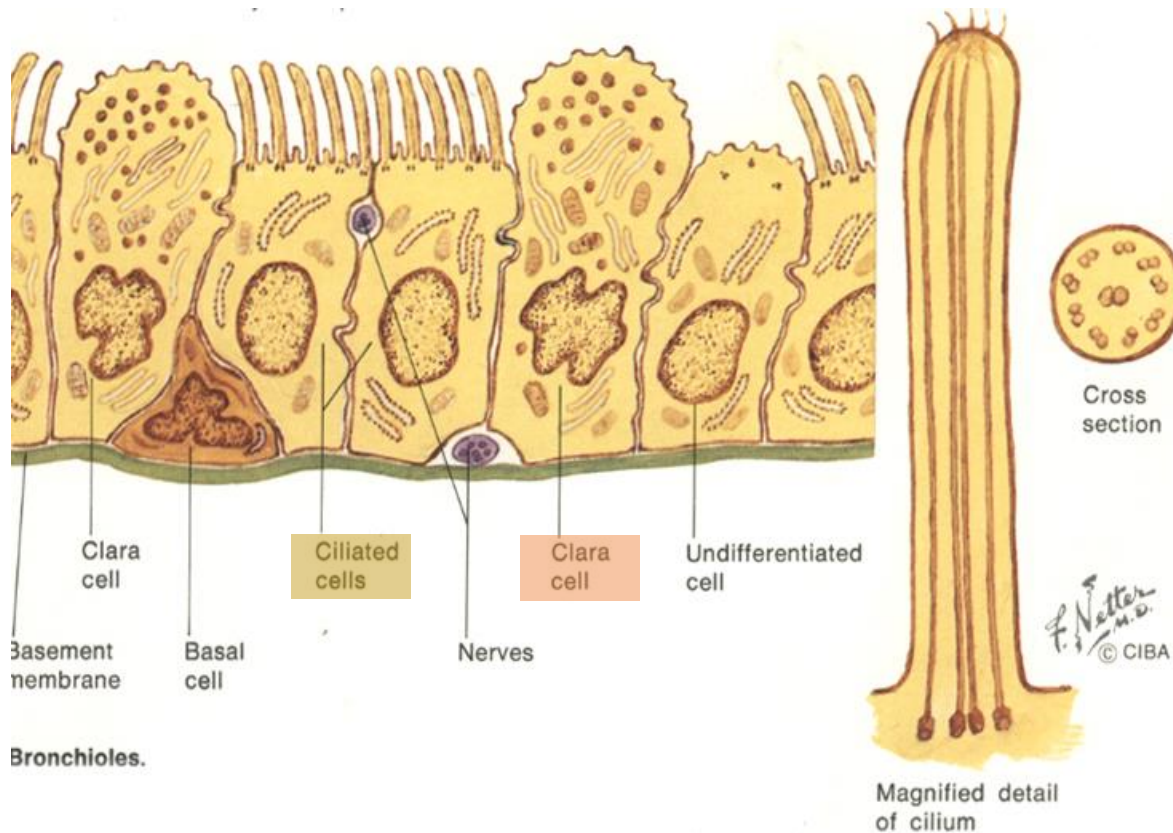
SIMPLE COLUMNAR EPITHELIUM

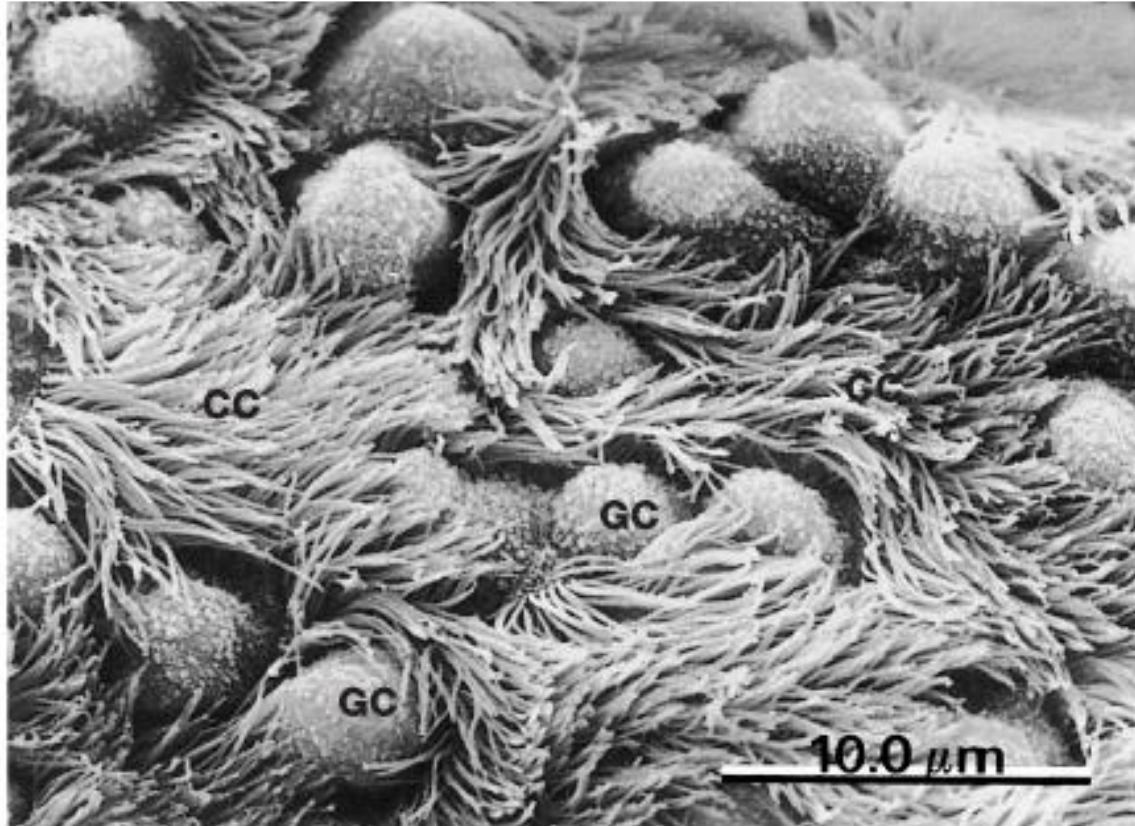
And subsequently a

SIMPLE CUBOIDAL EPITHELIUM

into the smallest bronchioles

- no goblet cells are present
- the **ciliated cells** remain, but they are reduced
- **cells with microvilli** are present to modulate the hydroelectrolytic characteristics of the mucus
- **Clara cells** appear, which produce a surfactant factor similar to that produced into the alveoli by type II pneumocytes



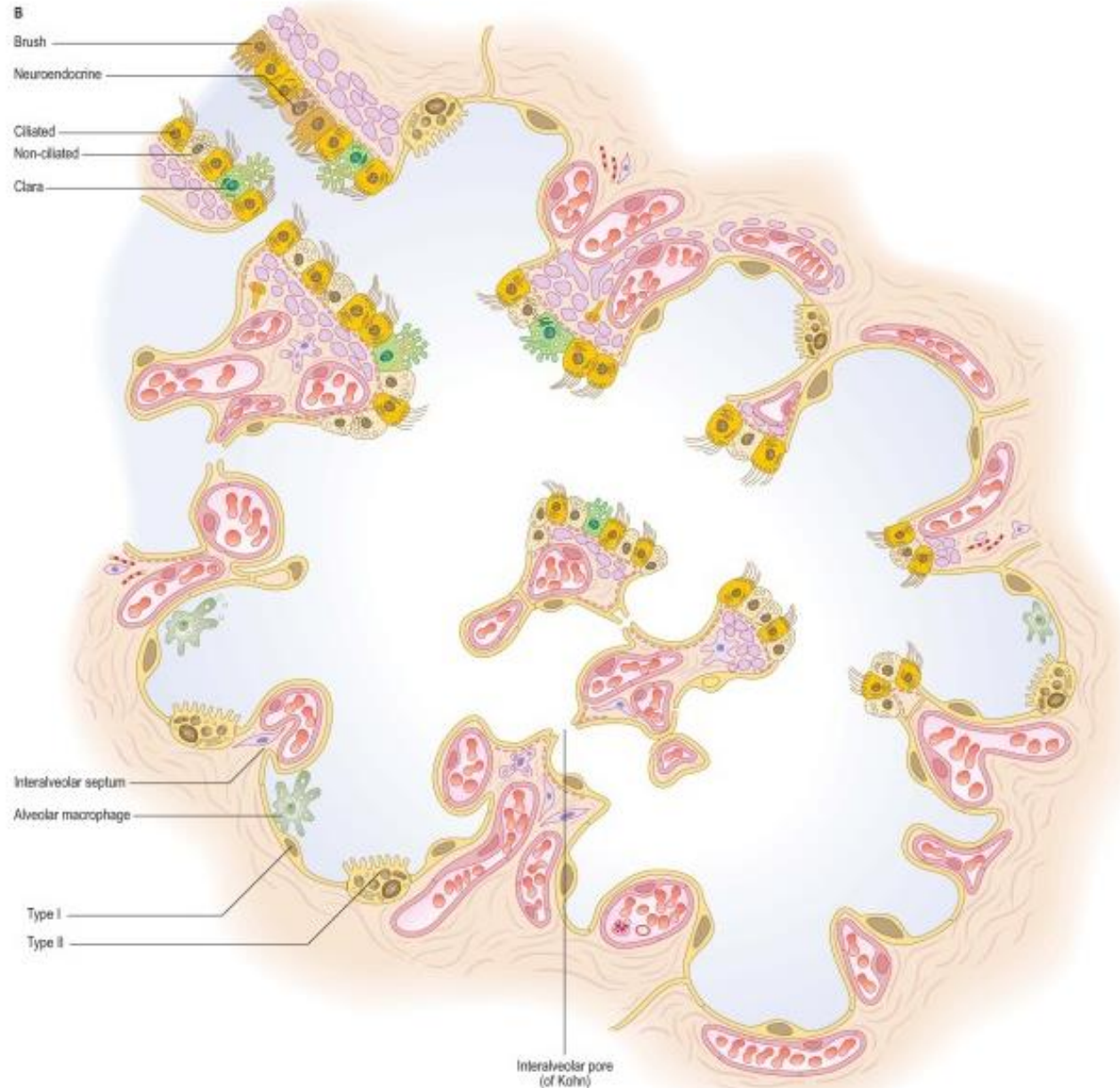


THE RESPIRATORY EPITHELIUM

This scanning electron microscopy image allows us to appreciate the three-dimensional structure of the respiratory epithelium

↓
the **mobile cilia** of the **ciliated epithelium** can be recognised

THE ALVEOLI



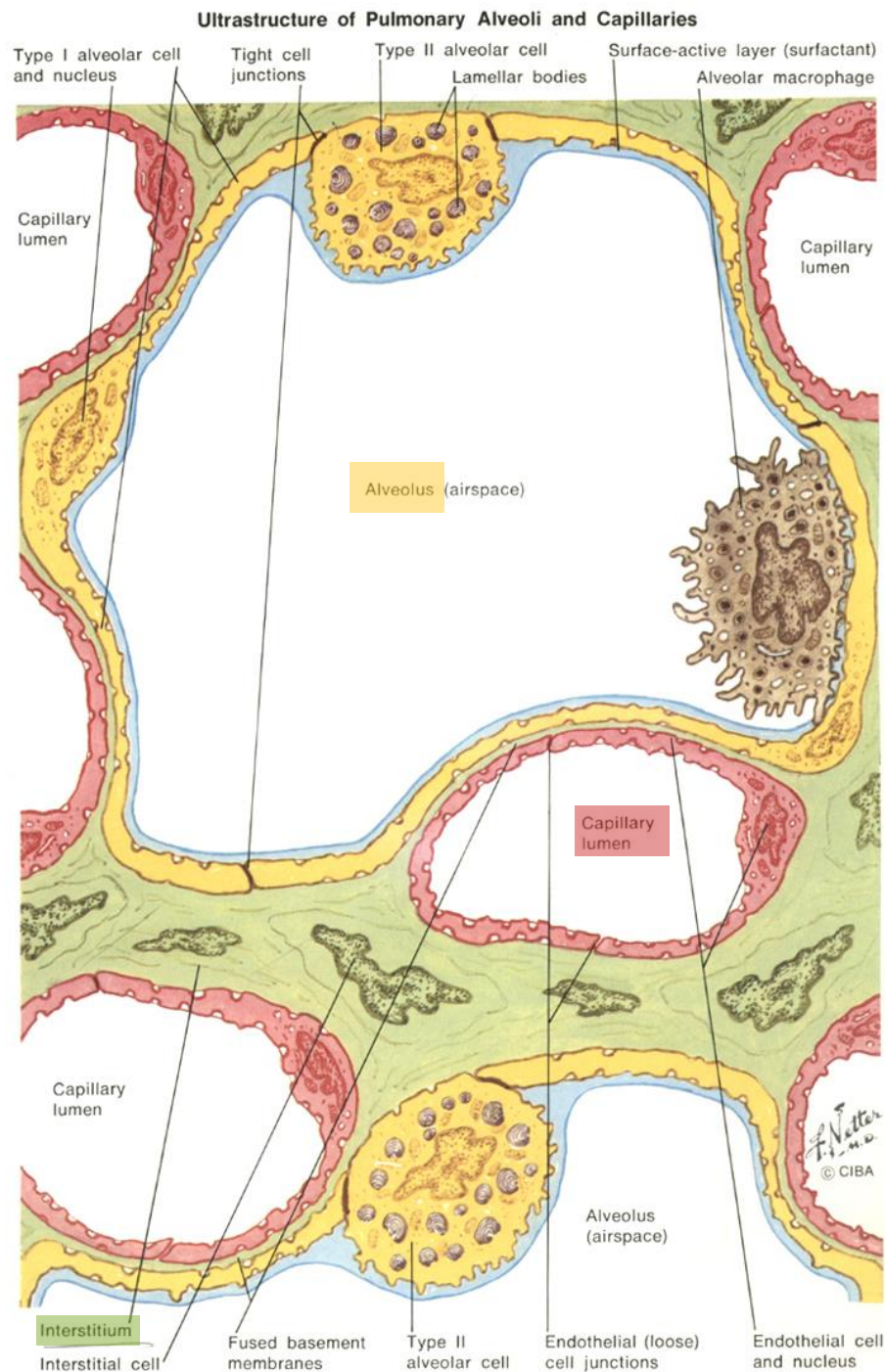
PULMONARY ALVEOLI

The image schematically represents a RESPIRATORY BRONCHIOLE where, starting from the central axis of the bronchiole, which is characterized by a simple cuboidal epithelium, there is the formation of the

ALVEOLI

↓
they are the last structure of the bronchial tree, where **respiratory exchanges** take place

↓
they are spherical-like structures that open at the level of the **respiratory bronchioles wall** and then of the **alveolar sacs wall**

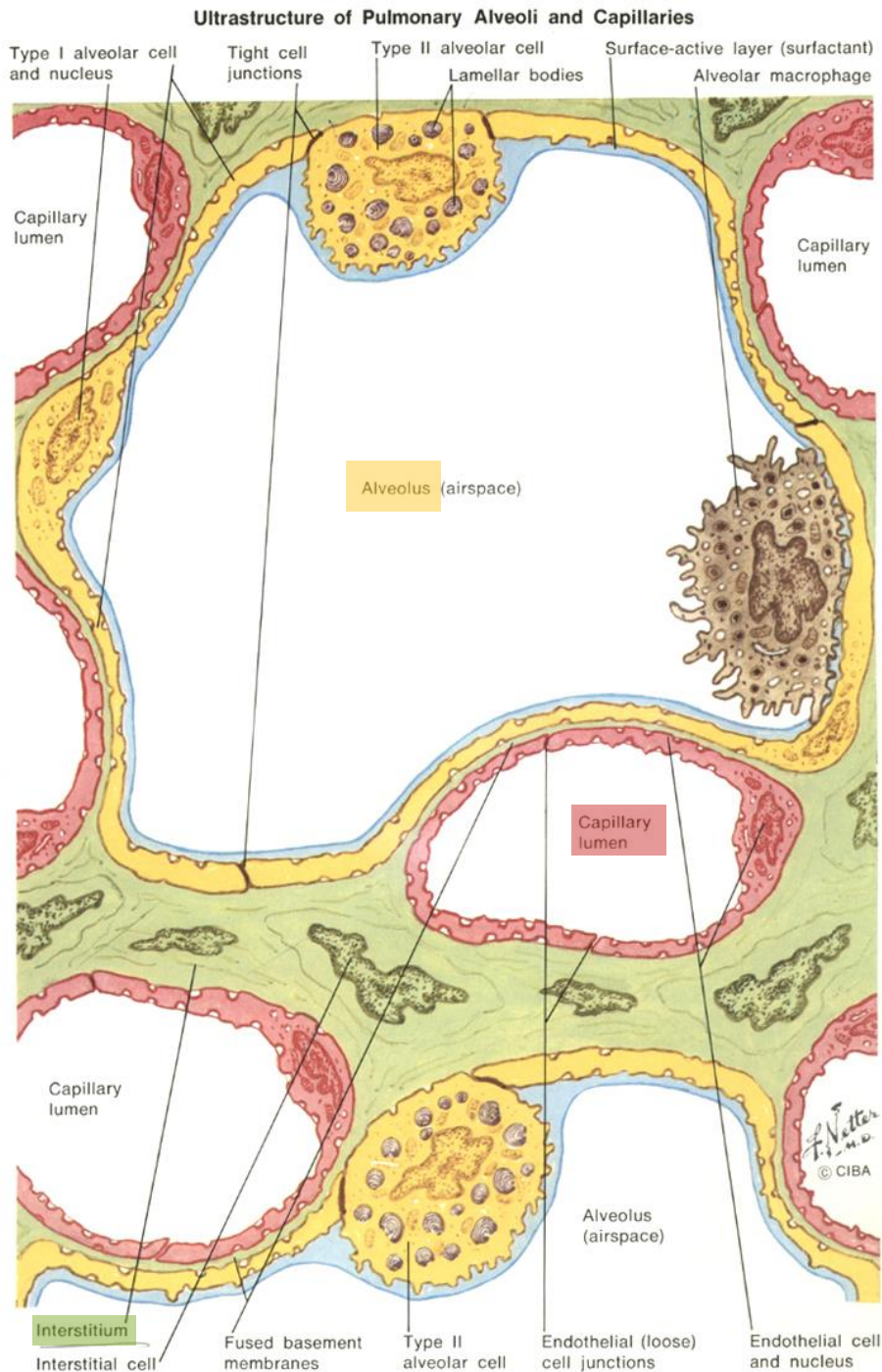


The image represents a **pulmonary alveolus**, highlighting its wall characteristics, as well as the relationship that the wall of the pulmonary alveolus establishes with the **pulmonary capillaries**

Alveoli and capillaries are located within a very thin connective tissue layer = The pulmonary connective tissue, also called **PULMONARY INTERSTITIUM**, is made up of fibroblasts and extracellular matrix.



In the lungs, the connective extracellular matrix is particularly rich in **ELASTIC FIBERS**, as these organ need particular elasticity



The wall of the pulmonary alveoli is made up of a
SIMPLE SQUAMOUS EPITHELIUM

↓
a single layer of cells lying on a thin basement membrane
(= the thin collagen layer on which the epithelium lies)

Immediately external to the basement membrane:

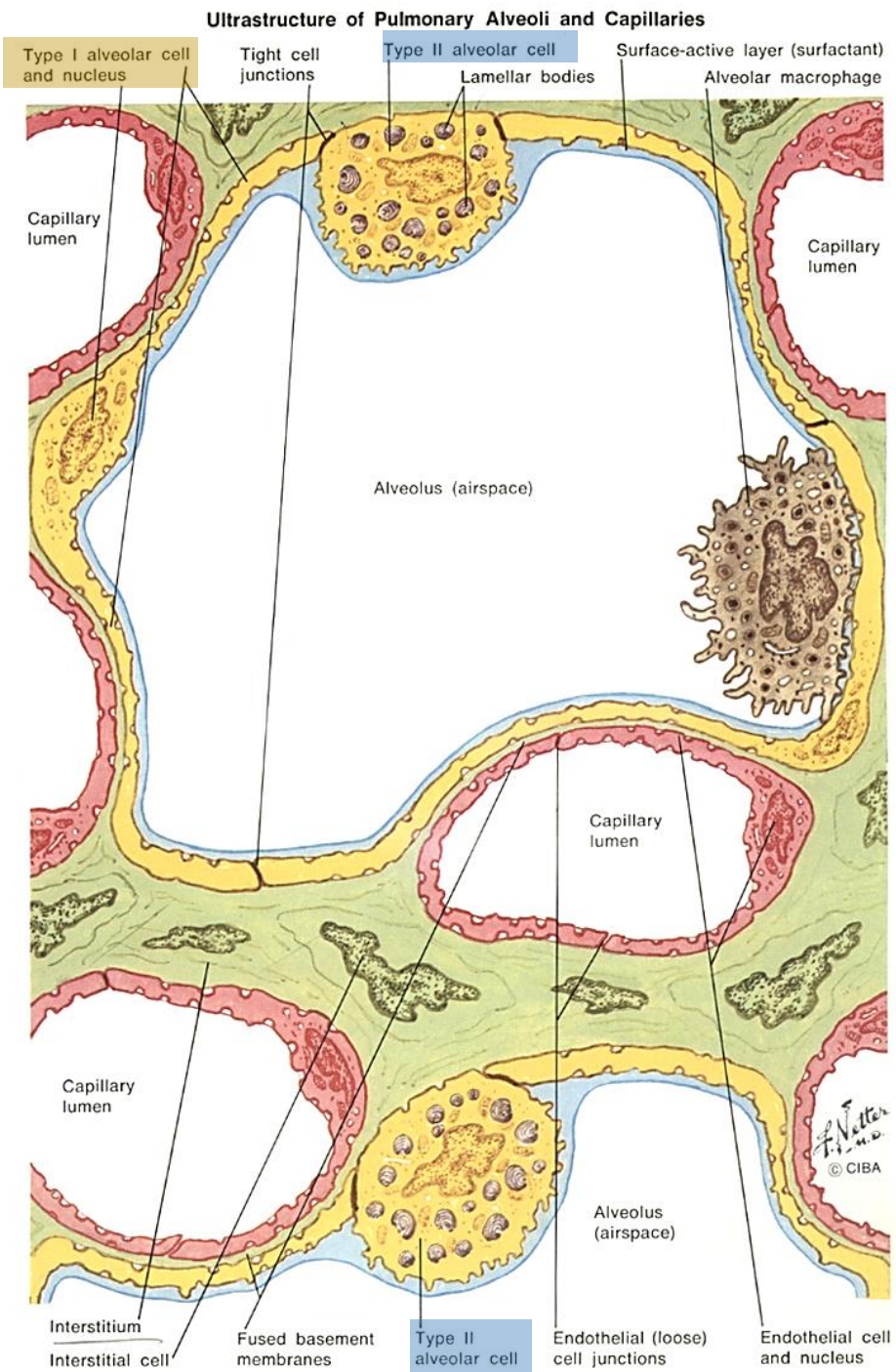
- in some regions the connective component (interstitium) is present
- in other regions, immediately outside the alveolar epithelium, the **ENDOTHELIUM** of the pulmonary capillaries is present

In some regions, the **2 basement membranes** of the alveolar epithelium and the capillary endothelium are in direct contact, being so close together that they become a **SINGLE** structure, so we will have:

Alveolar epithelium – a single, common basement membrane – **capillary endothelium**

These are the regions where:

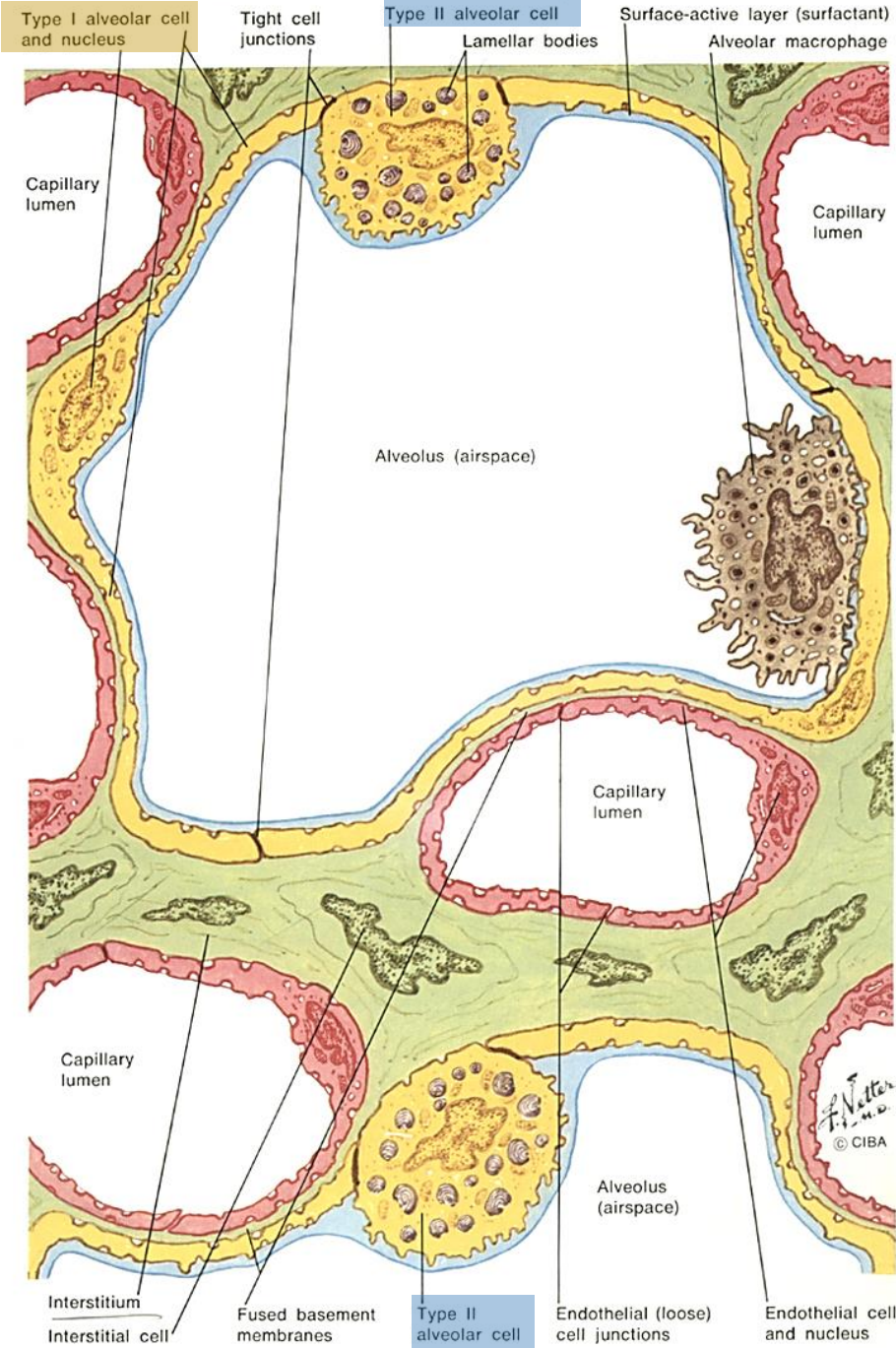
- the oxygen from the air contained in the alveolus enters the blood flowing in the capillary
- the carbon dioxide from the blood passes into the air



The SIMPLE SQUAMOUS EPITHELIUM of pulmonary alveoli mainly consists of 2 cell types:

1. **TYPE I PNEUMOCYTES**
2. **TYPE II PNEUMOCYTES**

Ultrastructure of Pulmonary Alveoli and Capillaries



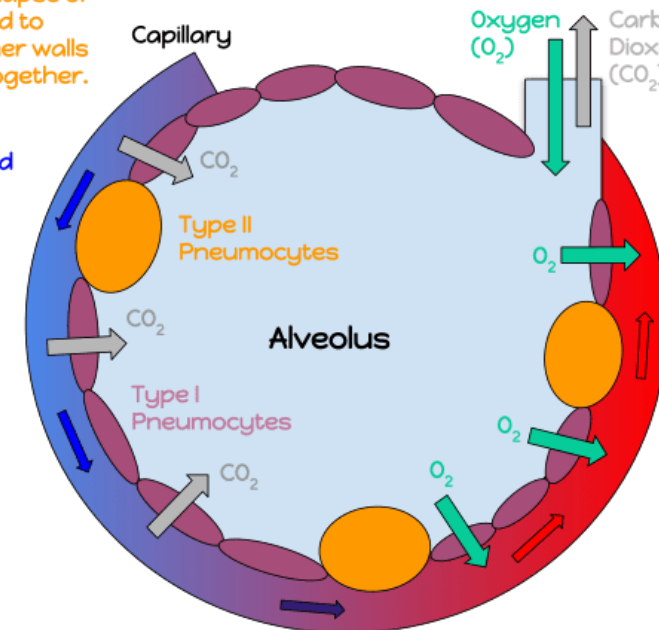
The SIMPLE SQUAMOUS EPITHELIUM of pulmonary alveoli mainly consists of 2 cell types:

- 1. TYPE I PNEUMOCYTES:** they are very thin and very large cells which occupy the majority of the surface of the alveolar epithelium. They are very simple, flat cells, with a single cellular portion, the NUCLEUS, which slightly protrudes towards the lumen of the alveolus.

↓
Thanks to their structure, these cells assure for the MINIMUM POSSIBLE OBSTACLE to the diffusion of oxygen and carbon dioxide

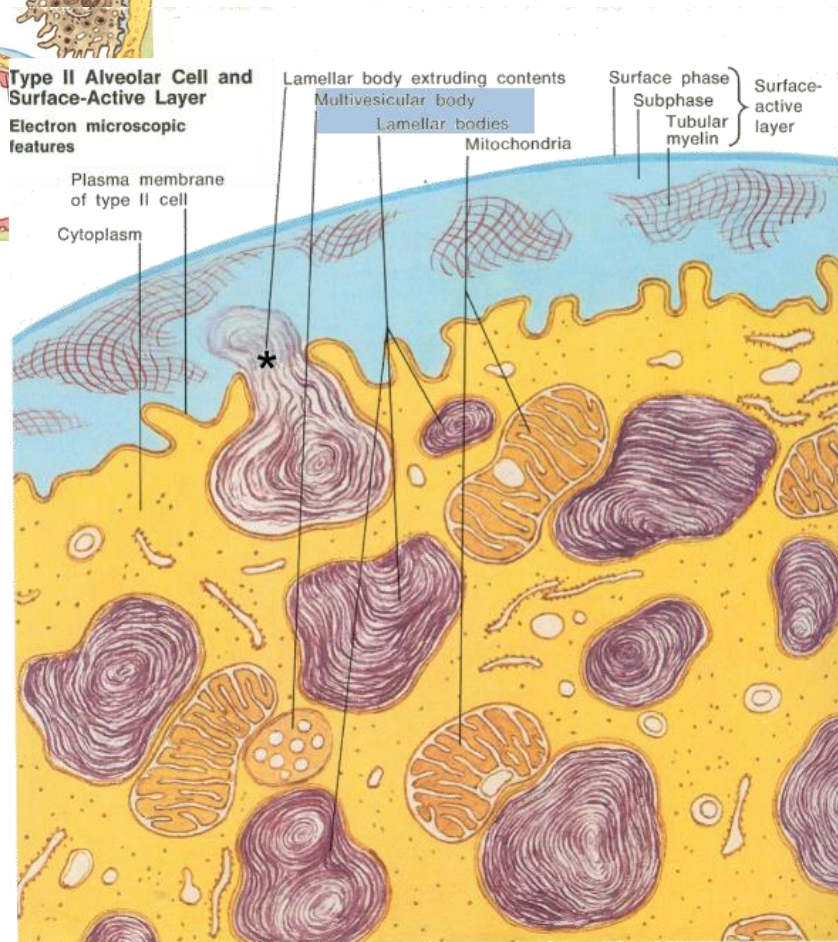
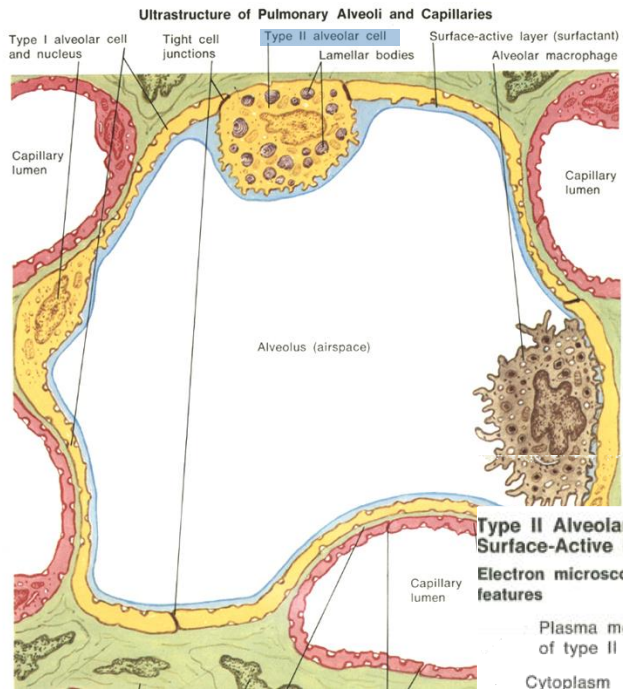
Type II pneumocytes secrete surfactant to prevent the collapse of the alveolus and to prevent the inner walls from sticking together.

Deoxygenated blood coming from heart



Oxygenated blood going to heart

Type I Pneumocytes are thin, flat cells which allow gas exchange between the alveolus and capillaries.



The SIMPME SQUAMOUS EPITHELIUM of pulmonary alveoli mainly consists of 2 cell types:

2. **TYPE II PNEUMOCYTES**: they are a minority cell type into the alveolar epithelium. They are cells of smaller dimensions, but with greater thickness (they protrude into the alveolar lumen).

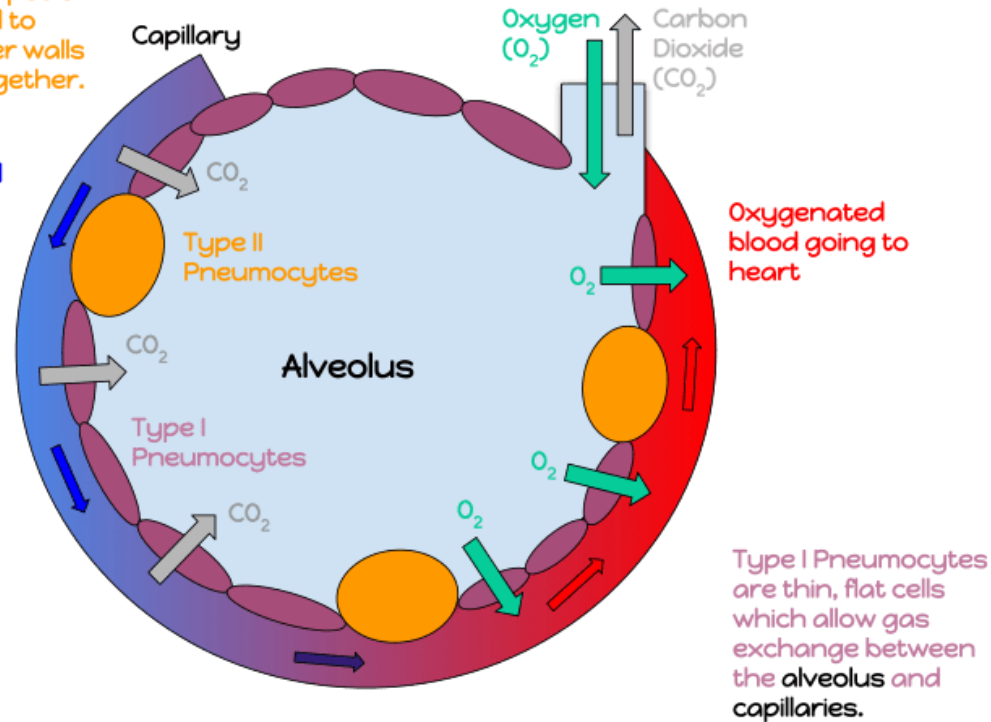
These cells contain organelles called **MULTIVESCICULAR BODIES** and **MULTILAMELLAR BODIES**

↓
they serve for the storage of the so-called **PULMONARY SURFACTANT**, which is produced and stored at the level of these organelles and then released at the surface of the alveolar epithelium

* *point where the surfactant is released outside, forming a liquid layer that wets the alveolar epithelium*

Type II pneumocytes secrete surfactant to prevent the collapse of the alveolus and to prevent the inner walls from sticking together.

Deoxygenated blood coming from heart



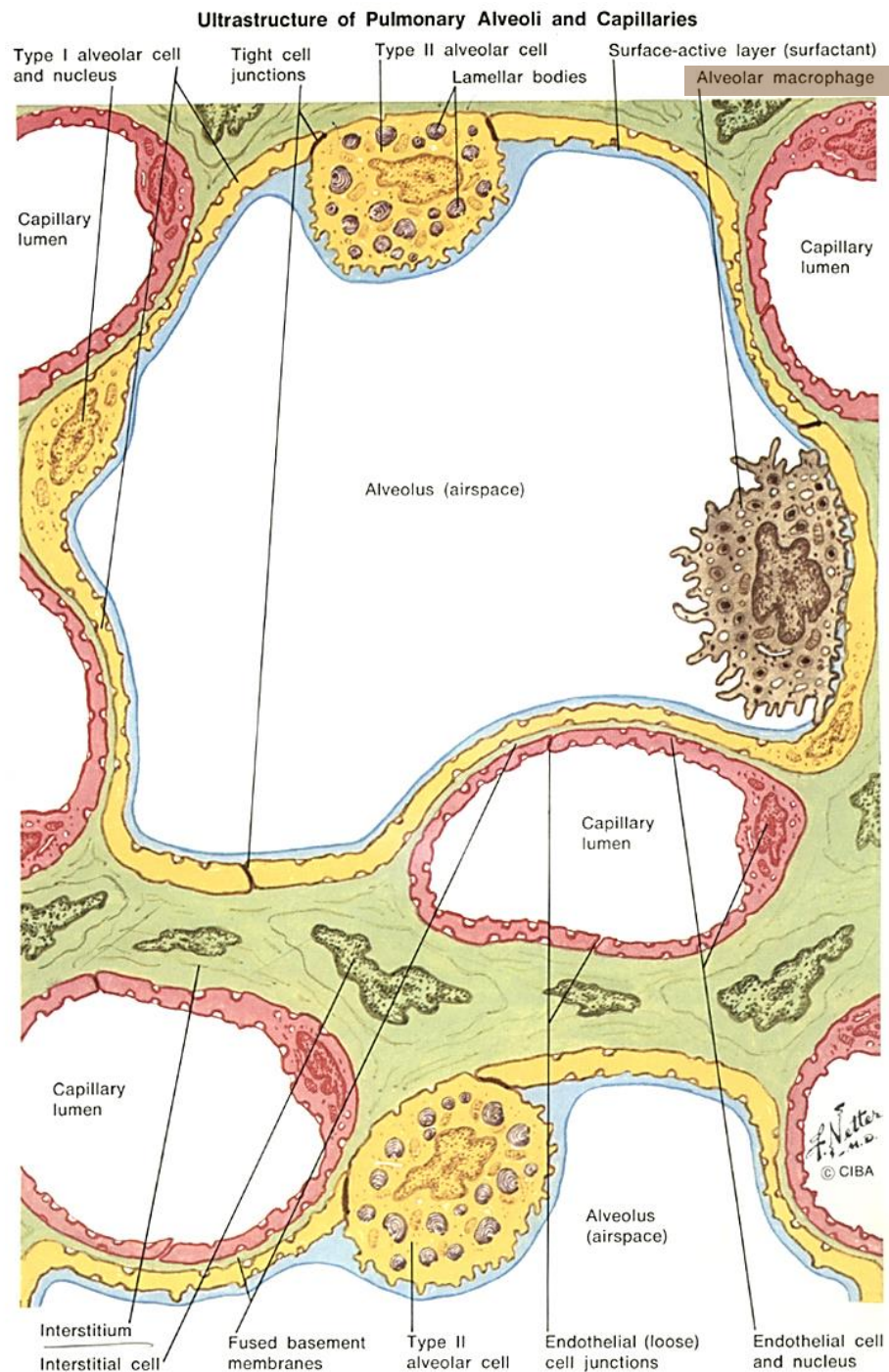
PULMONARY SURFACTANT: mixture of phospholipids and lipids (90%) and proteins (10%) which is distributed in a liquid film which internally wets the alveolar epithelium, with a **SURFACTIVE function** = it reduces the surface tension at the interface between the air contained in the alveoli and the liquid that wets the alveolar epithelium itself

Surface tension is the force that is created at the interface between a liquid and a gas

In the alveolus: it is the force that is created at the interface between the liquid that wets the alveolar epithelium and the air contained in the alveolus itself

Since the alveolus is a **very small hollow structure, wet and full of air**, this surface tension would tend to make the alveolus collapse, causing it to close.

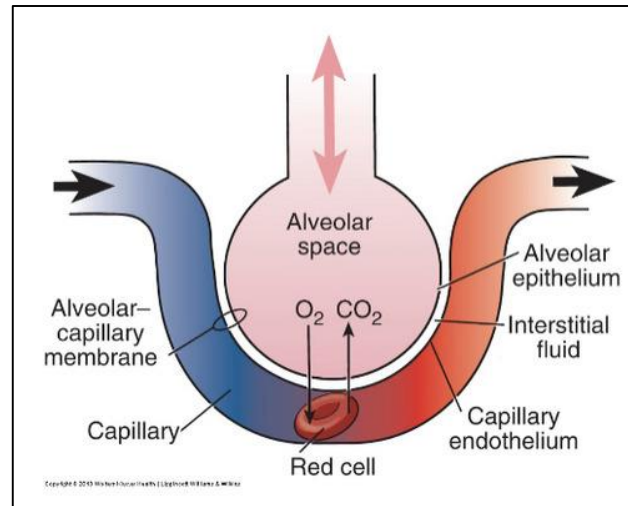
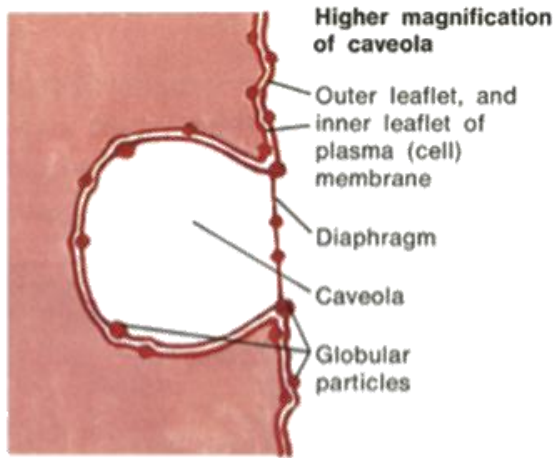
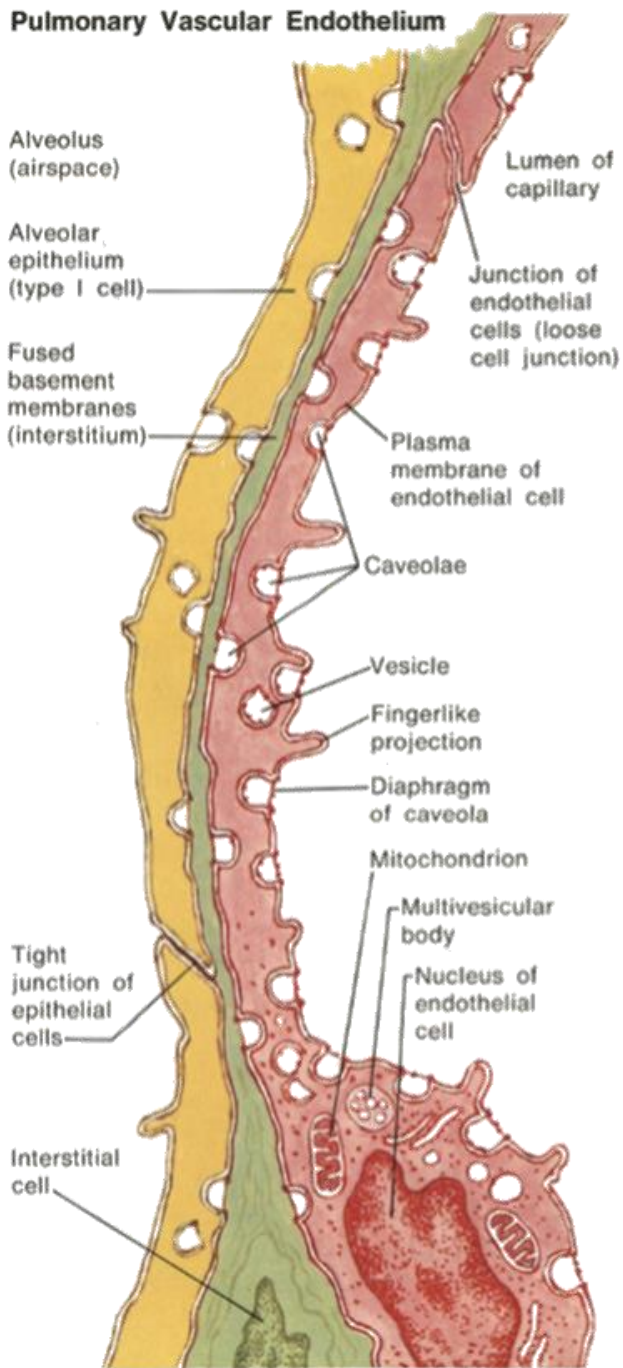
The mixture of phospholipids and proteins that constitutes the pulmonary surfactant is essential for **REMOVING THIS SURFACE TENSION AND KEEPING THE ALVEOLUS PATENT**



Another type of cells into the pulmonary alveoli are the
MACROPHAGES

↓
physiologically present in the lung tissue, they are cells with a **phagocytic action** which in the lungs have the function of eliminating foreign material bringing it into the connective component (e.g., pigment particles that arrive in the lungs with pollution/cigarette smoke)

Macrophages are responsible for the deposition of polluting pigments at the level of the connective lung tissue by cell phagocytosis of these particles at the level of the alveolar epithelium and then cell migration into the context of the connective interstitium



In the regions where the ALVEOLAR EPITHELIUM is in closest contact with the CAPILLARY ENDOTHELIUM, the thinnest structure is created for the exchanges of oxygen/carbon dioxide between the air contained in the alveoli and the blood contained in the capillaries

This structure is called

↓
ALVEOLAR-CAPILLARY MEMBRANE
 (hemo-respiratory barrier)
 consisting of:

- TYPE I PNEUMOCYTE (ALVEOLAR EPITHELIUM)**
- COMMON BASEMENT MEMBRANE**
- CAPILLARY ENDOTHELIUM**

The endothelium is also a very thin simple squamous epithelium which guarantees the least possible resistance to the passage of gas