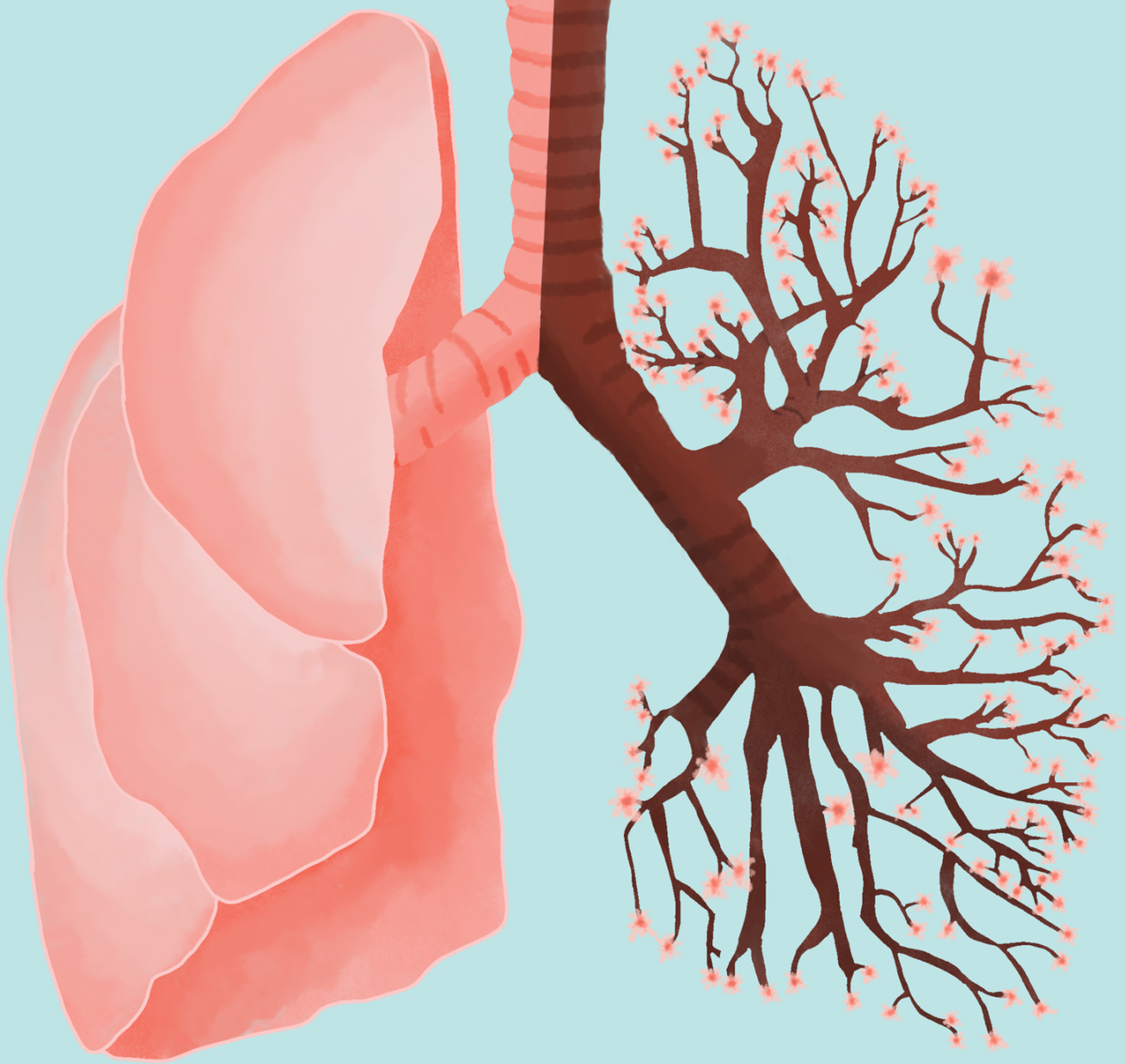
RESPIRATORY SYSTEM PHYSIOLOGY



Title: Sheet 1 – Basics of the Respiratory System

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First off, the respiratory system has some non-respiratory functions. For instance, it plays a crucial role in 1. homeostasis of (O_2, CO_2 and H+), thus a role in acid-base balance, 2. blood and lymph flow as inspiration increases the venous return and 3. BP regulation by converting angiotensin I to angiotensin II, and the list goes on. Refer to slide no. 3 to have a brief look at these functions. (The doctor said you are not required to memorize them as they are not covered in the course)

Concept: The respiratory system and the cardiovascular system are highly interconnected—that is; lung disease probably will develop heart failure and vice versa. If a person, for example, has left HF they will also develop pulmonary edema, and if they have lung disease (thus decreased O_2 supplied by it) that will result in cor pulmonale.* (cor pulmonale*= right heart dilatation ± HF due to lung disease)

Concept: Hypoxia

Hypoxia is decreased O_2 utilization by the cells.

What causes hypoxia?

1. Mostly, it is due to **pulmonary disease** such as: increased airway resistance, non-inflatable lung tissue, and thick respiratory membrane which creates problems in diffusion (developing pneumonia).

2. **Extra-pulmonary disease** like left heart failure and anaemia (both result in inadequate transport of O_2), localized ischemia and decreased muscle activity like in diaphragmatic paralysis.

3. The lungs can be intact but other factors cause the hypoxia such as: **living at high altitudes** (low O_2 pressure), **cyanide poisoning** (cancels the work of mitochondria thus no cellular respiration) and **septicemia** (O_2 is present but the cells cannot utilize it due to toxins from bacteria).

4. **Suppression of** the phrenic neurons that innervate the diaphragm or **suppression of** the respiratory centers in the brain that stimulate the phrenic nerve in the first place. Thus, the patient develops apnea (cessation of breathing) and dies.

Concept: Respiration

Respiration is the series of exchanges that lead to the uptake of O_2 by the blood (external with respect to cells) then inside the cells (internally) and the release of CO_2 to the lungs.

Respiration has 3 determinants and 4 steps:

3 determinants		
Lungs Must be adequately ventilated and capable of adequate gas exchange.	***Blood*** Must pick up, carry and deliver O_2 and CO_2 in amounts that are appropriate to the body's needs. It depends on the presence of adequate amounts of the correct type of hemoglobin, the cardiac output, and local perfusion.	***Tissue*** Individual cells must be capable of taking up and utilizing O_2 properly.
Hypoxia can therefore result from a fault at any point along this lungs-blood-tissue chain		
4 steps		
(Step 1) Ventilation: Includes inspiration and expiration • ***Ventilation is determined by:*** The activity of the **control system** (respiratory centre in the medulla), the adequacy of the **feedback control systems** (neural and hormonal) and the efficiency of the **effector system** (muscles of respiration) ***(Step 2) External Respiration:*** Includes exchange between the lungs, alveoli, and blood (pulmonary capillaries) at the level of the respiratory membrane ***(Step 3) Transport of gases in blood:*** Depends on hemoglobin (HbO_2) ***(Step 4) Internal Respiration:*** Includes exchange between blood and cells		

Concept: Cellular Respiration

Cellular respiration is the use of oxygen and ATP at the mitochondrial level.

Concept: Gas Exchange

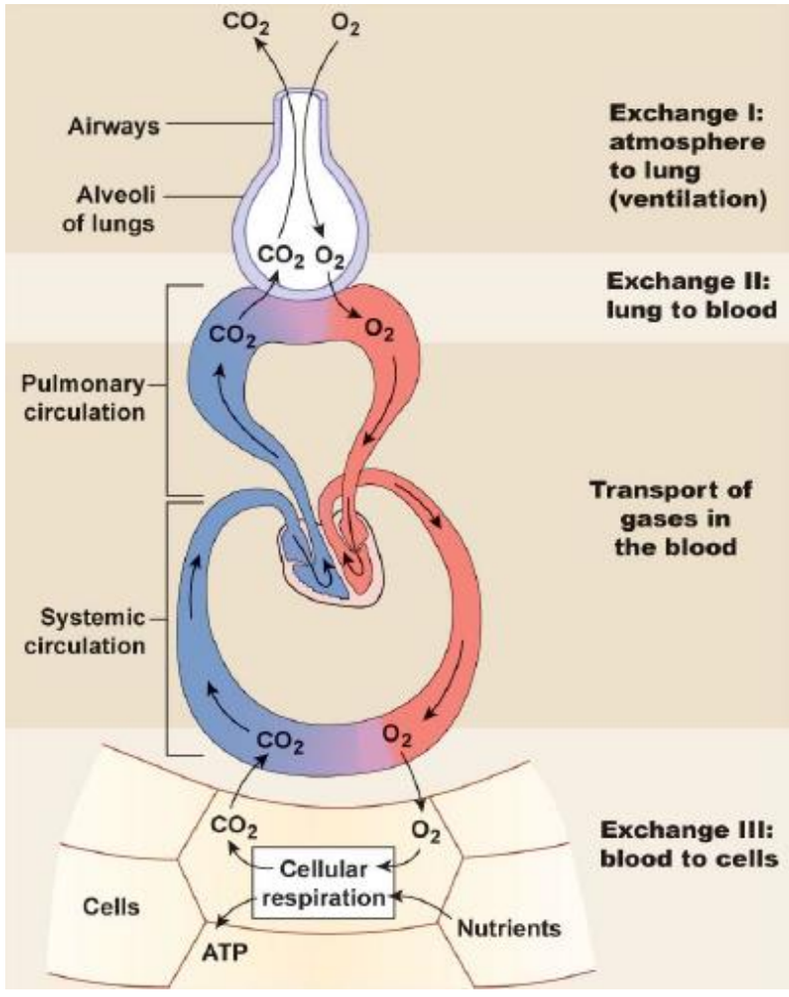
Gas exchange depends on:

- The patency of the airways.
- The "diffusability" of individual gases.
- The thickness of the exchange membrane.
- The pressure gradient across the alveolar-capillary membrane.

✓ **NOTE:** Directionality of gas exchange depends on the pressure gradient (lungs-blood-tissue chain): Atmosphere → Blood → Tissues

Notice this schematic view of the respiration process:

- O_2 in. CO_2 out.
- RV → Pulmonary Artery (blue)
  Note: **High pulmonary vascular resistance** causes the RV to dilate (cor pulmonale).



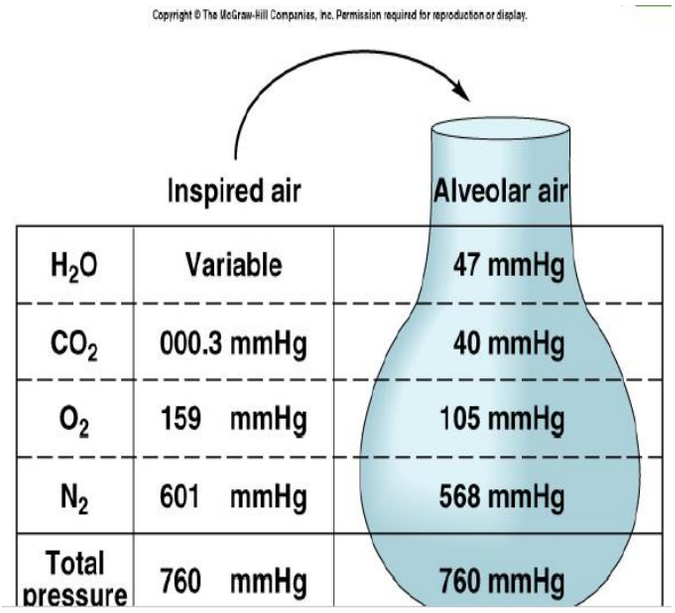
- Pulmonary Veins (red) → LV
  Note: **LV failure** causes congestion of the pulmonary veins → capillaries→ arteries. This congestion increases the pressure at the pulmonary arteries thus increases the diffusion towards the lungs → **interstitial or alveolar PULMONARY EDEMA.**

- O_2 travels from the aorta→ systemic arteries → systemic capillaries → interstitium → cell
  Note: There is a pressure gradient (higher pressure to lower pressure) between these compartments thus the sequence of O_2 diffusion and CO_2. In the case of CO_2 exchange, cells have the highest pressure, interstitium has a lower pressure and capillaries have even lower pressure and so on.

    - **Arterial Blood Gases (ABGs): Values that indicate the state of the lung, whether it is working or not.**

Numbers to memorize: Arterial Blood Gases (normal values)
PaO_2 = 100 mmHg maximum (pressure of arterial O_2)
$PaCO_2$ = 40 mmHg maximum
A sample of blood was taken from the radial artery. It was noticed that PaO_2 = 100 mmHg and $PaCO_2$ = 40 mmHg, what does that tell you?
It tells you that the lungs are properly functioning.

Note: the doctor stated a difference between PaO_2 (ARTERIAL) and PAO_2 (ALVEOLAR)



Notice the figure

—Inspired air = atmospheric = 760 mmHg

21% is O_2 pressure = 160 mmHg

78% is N_2 pressure = 600 mmHg

PCO_2 is ALMOST ZERO

H_2O (water vapour) pressure is variable

—Alveolar air = lung airways

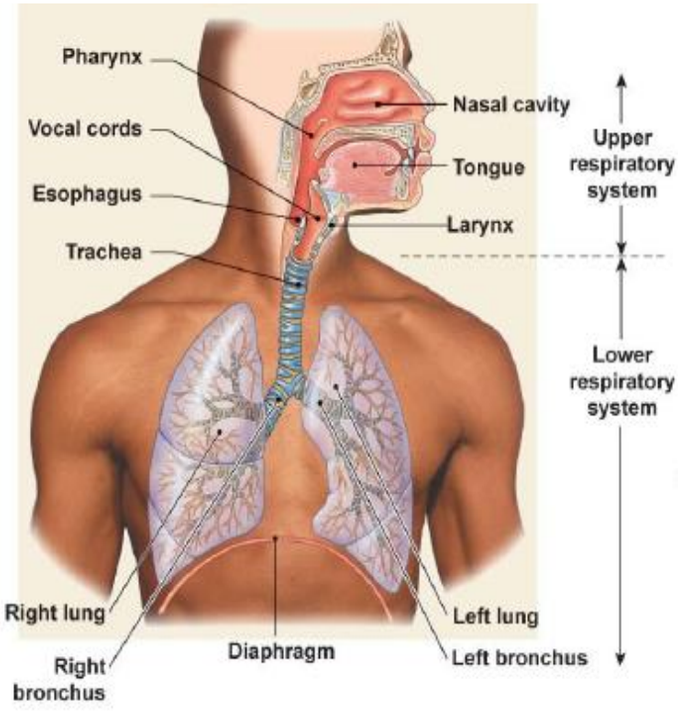
PO_2 = 100 mmHg (is being distributed to the tissues)

PCO_2 = 40 mmHg (is being brought to the lung by the tissues)

PH_2O = 47 mmHg

To understand the functional anatomy of the respiratory system, it is of good benefit to have the system subdivided into 2 zones:

- **Conducting Zone (Airways) (Anatomical Dead Space)**: Only conduction of gas occurs with no exchange because of their thick membranes.
  ADS volume= 2 mL/kg of body weight.
- **Respiratory Zone:** Exchange of gas occurs.
  Note: The trachea bifurcates into 2 primary bronchi which branch into secondary divisions/generations/ branches which branch into tertiary divisions and so on (23 divisions overall).
  Divisions (0-16) → **Dead space (conducting zone)**
  Divisions (17-23) (23 mainly) → **Respiratory zone**



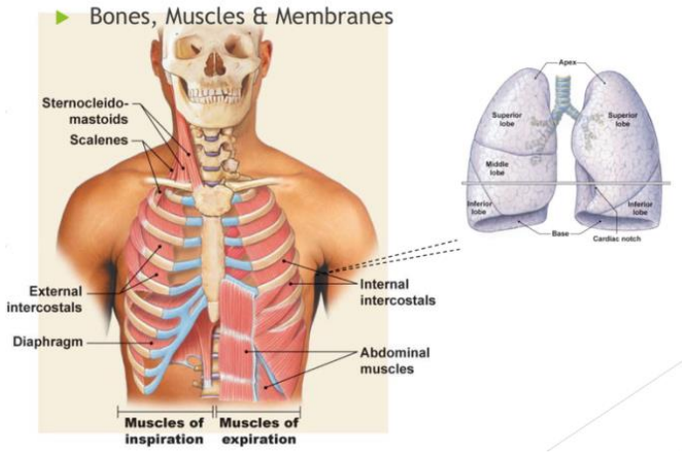
So, the respiratory tract is divided into upper & lower respiratory tracts.

Upper respiratory tract: Nasal cavity → the entrance of the larynx

Lower respiratory tract: Larynx → alveoli (trachea→lung)

■ Other structures involved in ventilation:

- Skeletal muscles (for inhalation and exhalation)
- Pleural membranes (for diffusion)
- Neural pathways (for control)



Notice the figure

The most important muscle involved in respiration is the diaphragm. We also have the external intercostal muscles that control the movement of the ribs thus affecting the diameter of the thoracic cavity during respiration. Also, we have the accessory muscles such as neck muscles (sternocleidomastoid muscles for example) that are not usually used, but are used in case of a problem in respiration.

❖ Inspiration is active and expiration is passive.

This means that inspiration requires muscle contraction (ATP) so it is an active process. On the other hand, expiration does NOT require ATP; it is due to the relaxation of the muscles (relaxation is passive). **However,** sometimes expiration can be ACTIVE (in cases of forced expiration or sports). That is why we have some expiratory muscles such as the internal intercostal muscles and to a certain extent the abdominal muscles.

▪ Anatomy and Functionality, a great combination:

Anatomy: The lungs are covered by the **pleural membrane** which consists of 2 layers: **parietal or outer pleura** that lines the inside of the thoracic cavity and **inner or visceral pleura** that covers the lungs. Between these two is the **pleural space or cavity**.

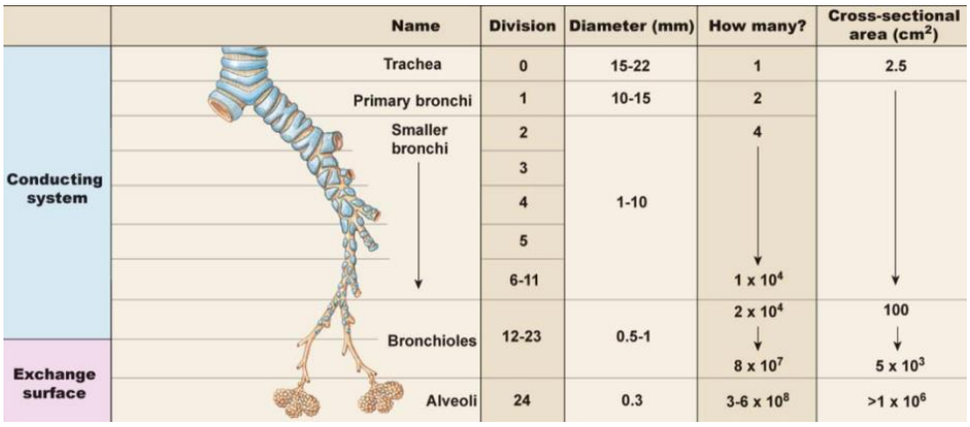
Functionality: 1. The pressure in the **pleural cavity** is **sub-atmospheric** (less than that of the atmosphere i.e. <760 mmHg which is our reference point so we can denote it as 0 mmHg as well). This difference between the intra-alveolar pressure (same as the intrapleural pressure) and the atmospheric pressure creates a **pressure-gradient** that allows the air to flow into the lungs.

2. The **pleural cavity** has (30 ml) of **serous fluid** that creates an attraction (cohesion) between the two sheets of membrane so that the pressure surrounding the lung is **negative** so the lung stays inflated. This tells us that any disruption of the integrity of the pleural membrane will result in a rapid equalization of pressure and loss of ventilation function → pneumothorax and collapsed lung.

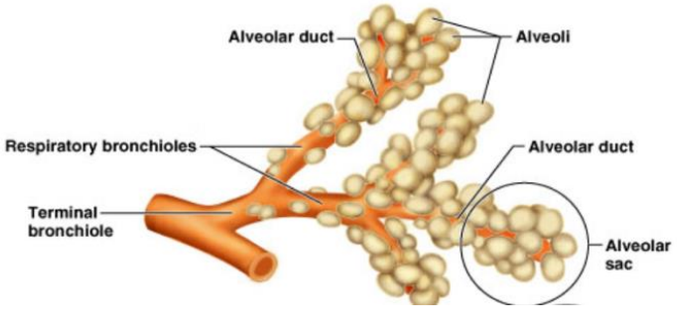
Result: Pressure gradient depends on these anatomical structures: the attachments of the muscles to the ribs, the attachments of the diaphragm to the base of the lungs and pleural membranes, the cohesion between the parietal and visceral membranes, and expansion and recoil of the lungs and alveoli with the movement of the overlying structures.

Now to sum up the functional anatomy of the respiratory system, look at the figure.

Note: the numbers in the figure are not accurate because of differences between books. However, stick to the numbers mentioned by the doctor.



As we said, the respiratory tree begins with the mother trachea (division 0) that ends up with 23 divisions overall. The respiratory tree is similar to the vascular component. (The aorta branches into large arteries which branch into smaller arteries and so on)



Divisions 0-16: Trachea, primary + secondary + tertiary bronchi (bronchioles) (diameter < 1mm) (division 16 = terminal bronchiole) → conducting zone or anatomical dead space which contains 2 mL/kg volume of inspired air.

Divisions 17-23:

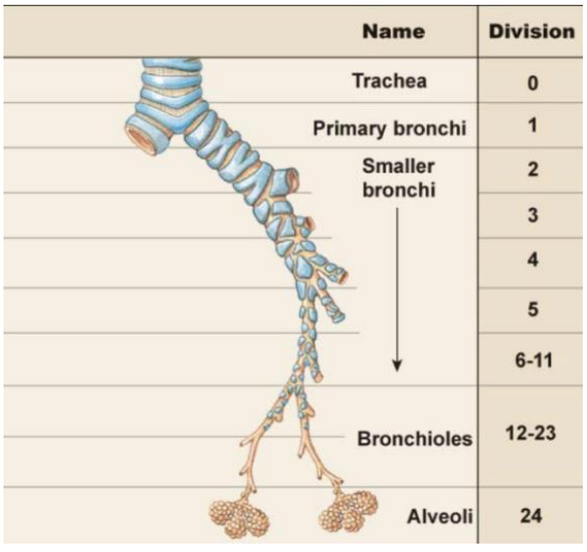
Terminal bronchioles <u>with</u> few alveolar pouches and alveolar ducts (division 17 = respiratory bronchiole) (sometimes, divisions 17-19 are called the transitional zone and divisions 20-23 are called alveolar ducts and are 0.5 mm in diameter) → respiratory or exchange zone with **division 23** being the most important because it has millions of alveoli → very large surface area. We all agree that **flow = area * velocity.** With the flow of air being constant, the **higher** the cross-sectional area (like in the case of the sum of the alveoli) the **lower** the velocity and that is desirable for gas exchange.

(Alveoli (smaller airways) → very large cross-sectional area → lower velocity → optimum gas exchange)

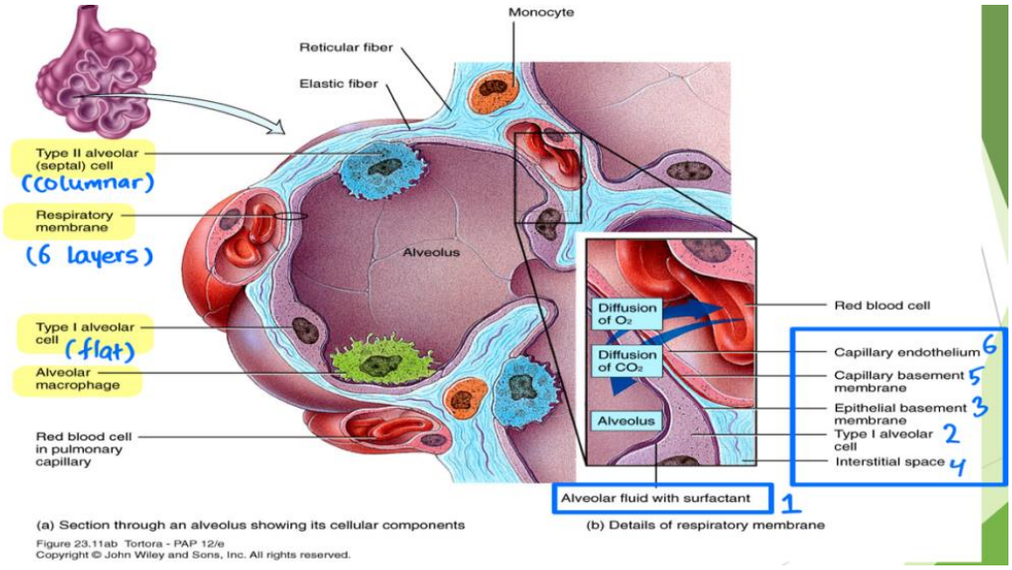
(Trachea (larger airway) → small cross-sectional area → high velocity → no gas exchange)

<u>Cartilage and its protection</u>: notice the figure

Notice how the **first 10 divisions** have cartilage. Cartilage provides support to these and makes them **non-collapsible,** thus decreasing the resistance to air flow, whereas **divisions 12-16** (bronchioles) lack cartilage. This renders them **susceptible to collapse** which increases airway resistance.



Lastly, we are going to talk about the components of an alveolus. Notice the adjacent figure.



- ✓ The alveolus has 3 types of cells:
  1. **Type I cells:** Flat cells for gas exchange.
  2. **Type II cells (septal cells):** Columnar cells that secrete a surfactant substance. (we will talk about this in another lecture)
  3. **Alveolar macrophages (garbage man of the alveoli):** They serve to phagocytose small inhaled substances that are not entrapped by the anatomic dead space.

- ✓ The alveolus has the **Respiratory membrane** (thickness < 0.5 µm) between the alveolar wall and the pulmonary capillary wall. This membrane is made of 6 layers (inside → outside) as follows:
  Surfactant layer → alveolar epithelial cells (type I cells) → epithelial basement membrane → interstitial compartment → capillary basement membrane → capillary endothelium.
  Interstitial edema or **pneumonia** or **asbestosis** can <u>thicken the respiratory membrane</u> which leads to problems in diffusion. Blood enters and leaves but with <u>no complete exchange of gases</u>. ABGs indicate low PaO_2.

- O_2 crosses from the alveoli to the capillaries easily (highly diffusible). CO_2 crosses from the capillaries to the alveoli even more easily (20x more diffusible). Therefore, it makes sense why O_2 is affected **first** in lung disease. In <u>type I respiratory failure</u>, ABGs will indicate a drop in PaO_2 while $PaCO_2$ is still normal. While in <u>type II (advanced) respiratory failure</u>, ABGs will show a drop in PaO_2 and an elevated $PaCO_2$ (too much destruction of the lung).

Aspire to shine… Good luck