RESPIRATORY SYSTEM

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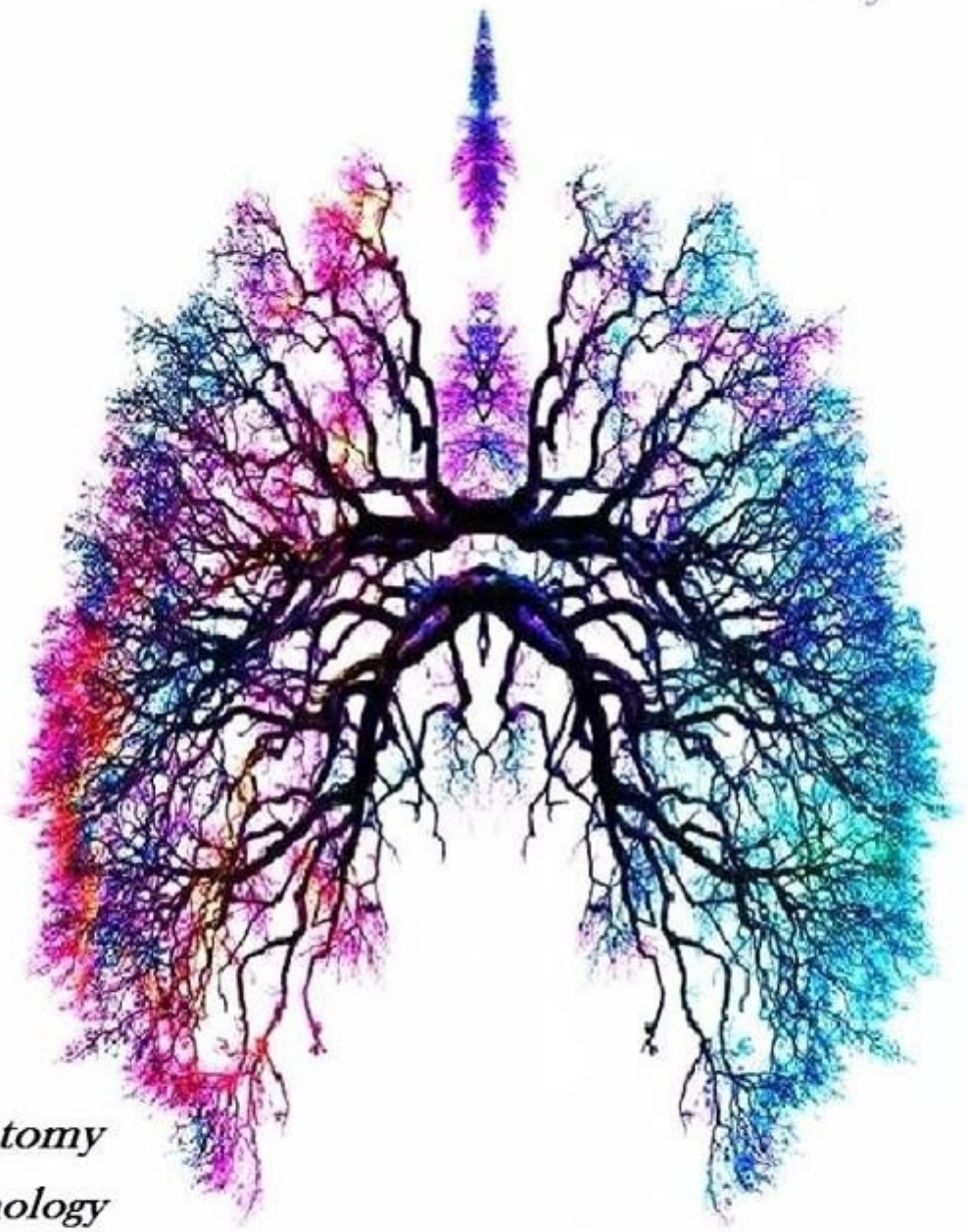

- ○ Anatomy
- ○ Pathology
- ● Physiology
- ○ Pharmacology
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- ○ PBL

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Lecture # 6
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Ventilation-Perfusion Ratios

Diffusion capacity (D_L) of the respiratory membrane

The ability of the respiratory membrane to exchange a gas (oxygen as an example) between the alveoli and the pulmonary blood can be expressed in quantitative terms by its diffusing capacity.

How is the Diffusion Capacity (D_L (L stands for lung)) measured?

Starting off with Ohm's law: the flow is equal to the driving force over the resistance.

$$Flow = \frac{Driving\ Force}{Resistance}$$

Taking oxygen as an example, let's have a look at each element of the previous equation:

- **Flow** (volume per unit time)**:** the flow of oxygen is the amount (volume) of oxygen that passes through the respiratory membrane per unit time (minute). This is actually equal to oxygen consumption (**Vo2**) which is equal to 250ml/min at rest. **Vo2** can be easily calculated by making a person breathe in a closed bag with a known amount of oxygen for several minutes and see how much oxygen is left. So we replace flow with Vo2.

- **Driving Force:** the pressure gradient of oxygen (ΔP) between alveoli and the capillary ($P_{Ao2} - P_{CapO2}$)

- **Resistance:** the opposite of resistance is conductance, or, in other words, permeability. Permeability is the same as diffusion capacity. So:

$$Resistance = \frac{1}{Diffusion\ Capacity}$$

Combine both equations and you'll get:

$$Diffusion\ Capacity = \frac{Vo2}{\Delta P}$$

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We learned earlier how Vo2 can be calculated. As for ΔP, its exact net value is hard to calculate due to the fact that gas exchange occurs only in a small part of the capillary, while the rest of the capillary is under equilibrium (ΔP = 0).

This leaves us with the diffusion capacity which is **defined as the volume of a gas (oxygen as an example) that diffuses through the membrane each minute for a pressure difference of 1mmHg.** (The definition was obviously obtained from the third equation).

Another equation for D_L is:

$$Diffusion\ Capacity = \left(\frac{Area}{Thickness}\right) \times Diffusion\ Coefficent$$

This equation (Fick's Law) shows the factors that affect the diffusion capacity:

1. Area of the respiratory membrane. Directly proportional to D_L.
2. Thickness of the respiratory membrane. Inversely proportional to D_L.
3. **Diffusion coefficient (D):** every gas has a unique D since D depends on the **solubility** of the gas as well as its **molecular weight**.

Notes:

- The area and thickness are difficult to measure.
- Differences in molecular weight between different gases are extremely small and are therefore negligible.

Now, assuming the D for oxygen is 1, the D for **CO_2** will be 20 (since the solubility of CO_2 is 20 times more than oxygen), and the D for **CO** will be 0.8.

Note: those values are not true values. They are relative to oxygen when we assumed its D was 1.

Why did we mention Carbon Monoxide (CO)?

Due to its high affinity towards hemoglobin, CO binds quickly and completely to hemoglobin leaving no CO in the blood which makes the partial pressure of CO in the blood equal to zero which means ΔP will equal to the P_{CO} in the alveoli. This is useful because now we are able to measure D_L for CO. How?

By using the single breath method, a subject is allowed to breathe a gas mixture containing a low, known, concentration of CO. The amount diffused ($\mathbf{V}_{CO}$) will be calculated as well as ΔP (since it is equal to the partial pressure of CO in the alveoli which can be calculated). Using the third equation, D_L for CO is calculated.

Now, using the D_L for CO (which is around 17) and the relative values of diffusion coefficient D mentioned previously, we can calculate the D_L for oxygen by dividing 17 over 0.8 giving us around 21. Then we multiply that by 20 to get the D_L for CO_2.

How did the previously applied math work?

We mentioned that: $DL = \left(\frac{Area}{thickness}\right) \times D$

Now, as we said, DLCO (DL for CO) is experimentally calculated and is around 17.

So: $17 = \left(\frac{Area}{Thickness}\right) \times D(for\ CO)$

But, we mentioned that D for oxygen is 1 and for CO it is 0.8.

So: $D(for\ CO) = 0.8 \times D(for\ oxygen)$

By substitution: $17 = (\frac{Area}{Thickness}) \times 0.8 \times D(for\ oxygen)$

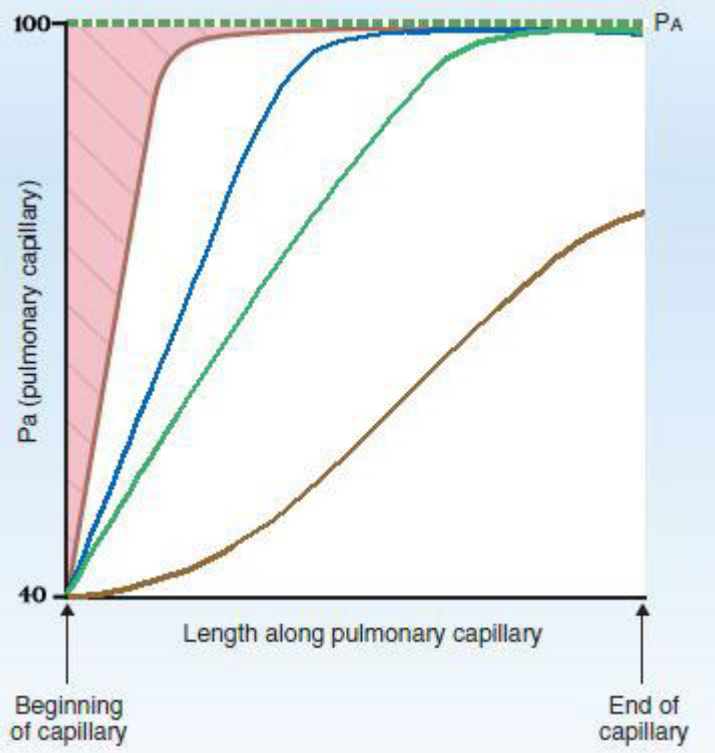
Then: $21.25 = \left(\frac{Area}{Thickness}\right) \times D(for\ oxygen)$

Finally $21.25 = DL\ for\ oxygen$

Note how the area and thickness of the respiratory membrane, that, as we said, were difficult to calculate, were not used in the calculation since they are the same for the individual. Any change in the area or thickness affects the diffusion capacity as in certain pathologies. For example; in **emphysema**, the area is decreased leading to a **decrease** in D_L. Moreover, the thickness can increase in cases of **fibrosis** and that also leads to a **decrease** in D_L. And that reveals the purpose of measuring D_L which is to determine if the patient has an abnormality in his respiratory membrane even before the appearance of symptoms.

The graph in the next page shows how the pressure gradient across the respiratory membrane differs along the length of the capillary. Each line represents a case.

We mentioned before that in normal conditions, gas exchange occurs only at a small part of the capillary (about one third) and at the rest of the capillary no exchange occurs because the partial pressure of oxygen in the alveoli, at the remaining two thirds, is now equal to that in the capillary. This is represented by the first (purple) line. The part of no gas exchange (the two thirds) acts as a "reserve" to be used when needed in an attempt to compensate for the increased demand for oxygen which might be caused by exercise.



Now, if the thickness of the membrane increases due to fibrosis for example, the diffusion distance for gases increases and D_L decreases. This increased diffusion distance slows the rate of diffusion, leading to increased usage of "the reserve" and the line in the graph gradually becomes like the one next to it (the blue). And with further increase in thickness, the line becomes like the third one (the green), until the reserve is completely used up (fourth brown line) and that prevents equilibrium by maintaining the partial pressure gradient of oxygen along the entire length of the capillary.

Note: symptoms (such as hypoxia) appear when the reserve is fully used up. They are worsened by increased physical exercise due to increased heart rate which leads to a decrease in the time the RBCs stay in the capillary WHICH then leads to decreased diffusion and, as a result, decreased oxygen consumption.

Note: thickening of the membrane can be also caused by phosphate dust inhalation as in those who work in phosphate mines.

To conclude, we measure the D_L for a person in order to investigate the status of his respiratory membrane. Decreased levels of D_L indicate abnormalities in the respiratory membrane even if there were no symptoms. Having no symptoms YET tells you that the reserve is not completely consumed yet.

V_{O2max} (maximum oxygen consumption)

Oxygen consumption at rest is about 250ml/min. With increasing physical activity and exercise, oxygen consumption starts to increase up to a certain point which is V_{O2max}. Any increase in the intensity of the exercise beyond this point will not increase your oxygen consumption leaving you extremely tired. V_{O2max} differs from one person to another. It is genetically determined, and training can only increase V_{O2max} up to a limit; that is why not everyone can become a marathon runner.

What determines/limits your V_{O2max}?

Many factors determine your V_{O2max}; cardiac output, pulmonary diffusion capacity, oxygen carrying capacity, and other peripheral limitations like muscle diffusion capacity, mitochondrial enzymes, and capillary density are all examples of V_{O2max} determinants. The body works as a system.

Testing D_L for an individual gives an idea about the status of you respiratory membrane and how well can you trust your V_{O2max}.

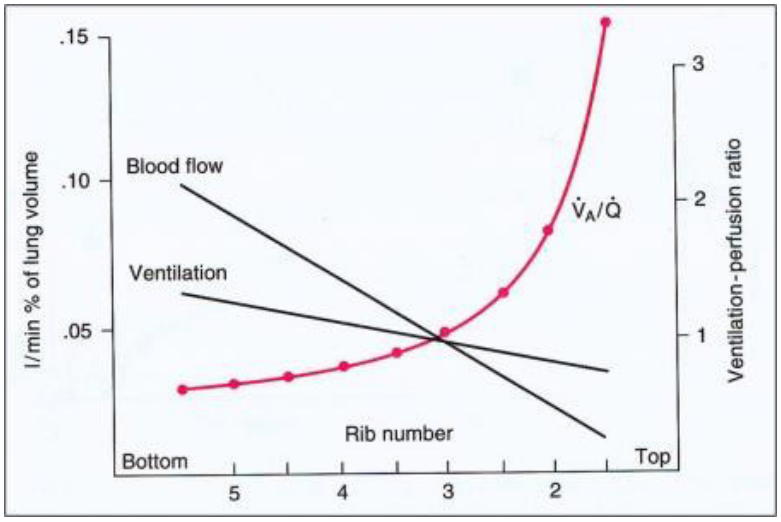
Partial pressure of oxygen

We mentioned in the previous lectures that P_{O_2} arterial is 100mmHg equal to that in the alveoli. But in reality (when we test ABGs), P_{O_2} arterial is actually less than that (around 95mmHg). Why?

- Mixing of arterial and venous blood. How?
  - Bronchial circulation: 50% of the veins drain into the left heart through the pulmonary veins.
  - Small cardiac veins (Thebesian) drain into the left ventricle.
  - 2-5% of the cardiac output from the right heart never gets the chance to reach the alveoli. They bypass the alveoli through a right to left shunt (anastomosis).

- Ventilation-perfusion inequality (V/Q ratio regional differences).

In the lung, as we go from the apex down to the base, ventilation increases. Perfusion also increases but in a more apparent fashion due to gravity. This is shown in this figure. In the apex, ventilation is higher than perfusion so the ratio will be higher than 1 (it is around 3-3.5). In the base, perfusion is higher so the ratio will be less than 1 (it is around 0.6).



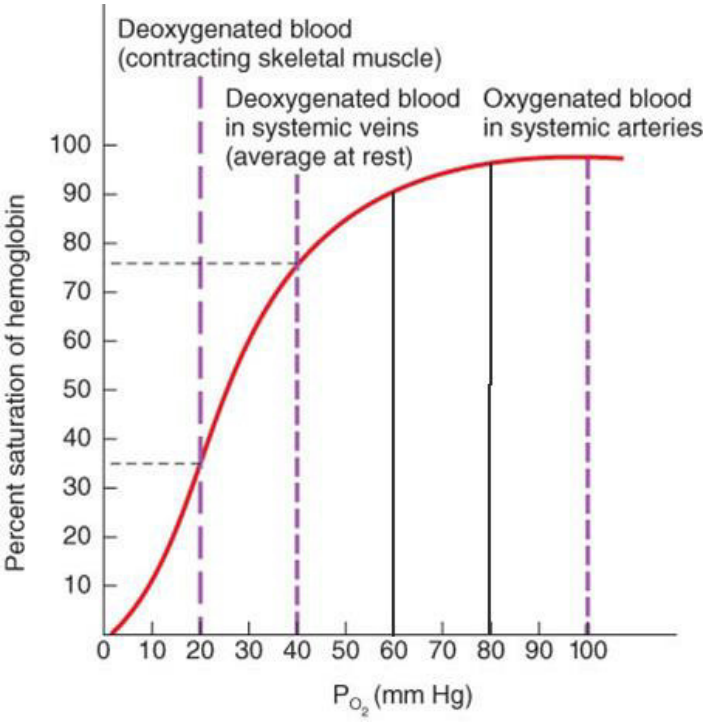
What do these facts cause? A difference in the composition of alveolar air between apex and base:

- ✓ The partial pressure of oxygen in an alveoli residing in the apex will be higher than 100mmHg (around 130mmHg).
- ✓ The partial pressure of oxygen in an alveoli residing in the base will be less than 100mmHg (around 90mmHg).

Note: TB bacilli, which are aerobic bacteria, like to build their nests in the apices of the lungs where there is more oxygen.

Now, let's go back to this question: How do the differences in V/Q ratio make the partial pressure of oxygen in the blood less than 100mmHg (around 95mmHg)?

The key factor here is **hemoglobin**. Its oxygen-dissociation curve is sigmoidal and not linear; which means that a partial pressure of oxygen higher than 100mmHg will not make the hemoglobin carry any more oxygen than it already has (it is already saturated). And this means that a hyperventilated lung cannot compensate for the hypoventilated lung in the case of oxygen in blood. In other words, the blood coming from the base which has a P_{O_2} around 90mmHg will not be corrected into becomming100mmHg upon mixing with the blood coming from the apex EVEN IF the P_{O_2} there was 130mmHg. So, an increase or decrease in P_{O_2} does not correspond to the same change in oxygen content.



To conclude, the overall partial pressure of oxygen in the blood (arterial) coming out of the heart will be around 90-95mmHg and not exactly 100mmHg.

Now, study the previous figure. Notice how a decrease in P_{O_2} from 100mmHg to 60mmHg corresponds only to a 10% decrease in saturation of hemoglobin. Keep in mind that at 100% saturation the concentration of oxygen in the blood is 20ml/dl. And at 90% saturation, the concentration is 18ml/dl. That is why we can tolerate high altitudes up to the level where P_{O_2} becomes 60mmHg. Beyond that, any decrease in P_{O_2} will correspond to a higher decrease in saturation. And that is why the respiratory control centers in the medulla oblongata are not stimulated unless the P_{O_2} becomes less than **60mmHg** in which case the signals will start firing to reach the respiratory muscles to increase inspiration.

Note: In the peripheral tissues, 25% of oxygen (around 5ml/dl) is taken up from the blood at rest, leaving the venous blood with 75% of oxygen. So it is safe to say that blood is not completely deoxygenated (only partially).

All the factors mentioned in page 5 affect oxygen but they do not affect CO_2, so the P_{CO_2} in the blood stays 40mmHg as it is. Why?

Because the CO_2-dissociation curve at the physiological levels of P_{CO_2} is almost linear and not sigmoidal. Which means CO_2 can, unlike oxygen, correct itself. Meaning, any decrease or increase in P_{CO_2} corresponds to the same change in the content of CO_2 (this is not true in the case of oxygen as was explained earlier). And, as we know, CO_2 change means a change in hydrogen; resulting in either acidosis or alkalosis and both are, of course, bad. That is why any slight change in CO_2 content will be immediately sensed by the respiratory control centers in the medulla oblongata in order to correct the change back to the normal 40mmHg, which means that these centers are under the control of CO_2 rather than oxygen.