RESPIRATORY SYSTEM

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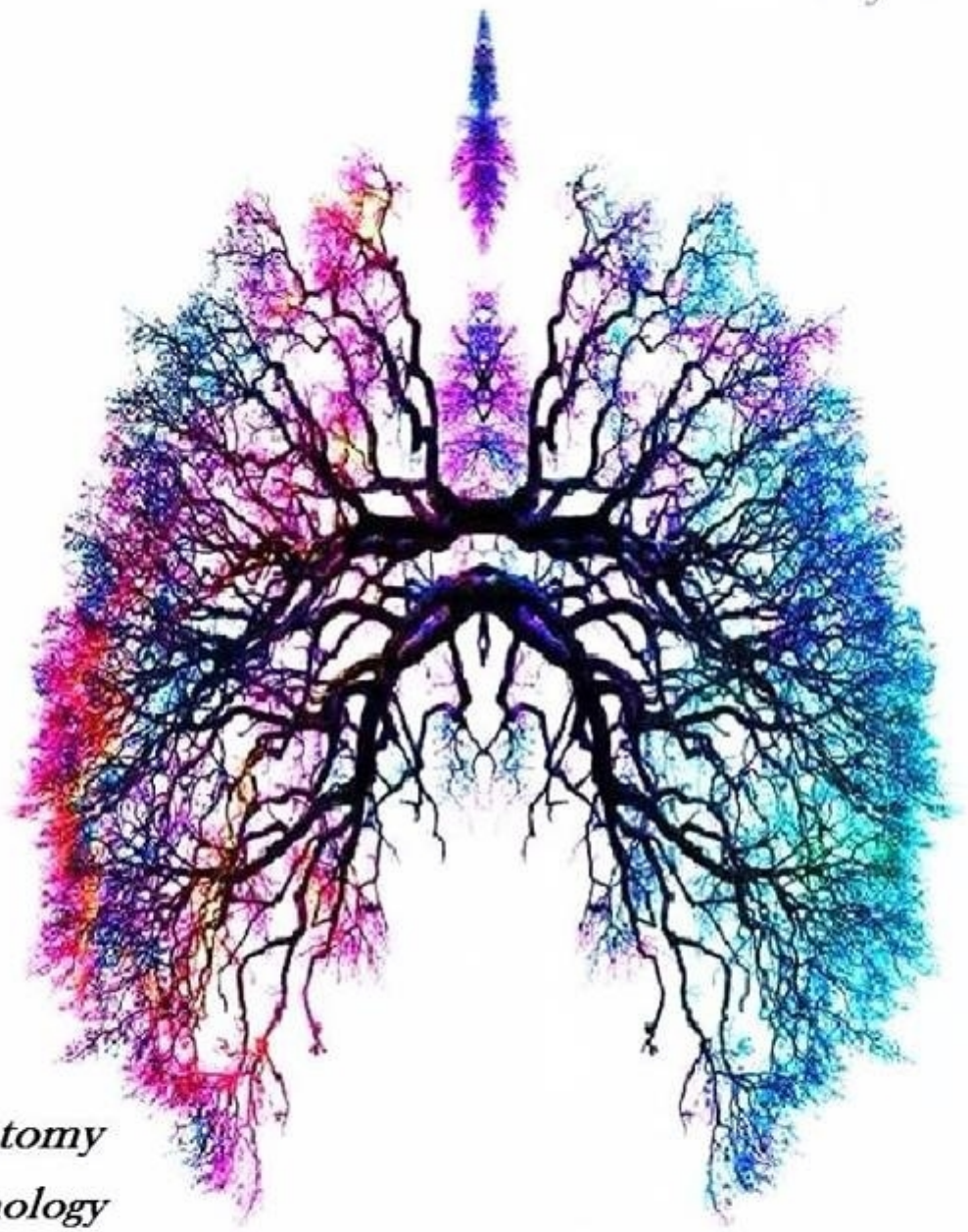

- ○ Anatomy
- ○ Pathology
- ● Physiology
- ○ Pharmacology
- ○ Microbiology
- ○ PBL

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Lecture # 8
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Gas Exchange and Transport

The doctor asked me not to record the lecture, and I respond to his willing. Here are notes I tried to write during the lecture, contain all what the doctor wanted the absent and attending students to know.

CO2 Transport

- CO2 is transported to cells by 3 different means;
  1- Dissolved in plasma;
  = PCO2 * Solubility = 40 * 0.06 = 2.4 ml/dl

➔ More CO2 solubility than O2 leads to More dissolved amount.

2- Bound to Hb (CarbaminoHb).

3- As HCO3-;

➔ CO2 in RBCs reacts with H2O, with the effect of Carbonic Anhydrase enzyme, to form H2CO3, which in turn is cleaved to: H+ & HCO3-. HCO3- leaves the RBC to the plasma in exchange for Cl-.

➔ More HCO3- levels found in venous blood.

➔ It's another advantage to the Hb to be found inside the RBCs, that the CA enzyme is found there.

	Arterial blood	Venous blood	V-A (difference)	%
HCO3-	43.2 ml	45.6 ml	2.6 ml	60%
Hb-CO2	2.4 ml	3.6 ml	1.2 ml	30%
Dissolved CO2	2.4 ml	2.8 ml	0.4 ml	10%
Total	48 ml	52 ml	4 ml	100%

➔ For each 100 ml of blood, the venous blood contains 4 ml CO2 more than the arterial blood.

➔ Each 100 ml of blood gives 5 ml O2 to tissues, and receives 4 ml CO2 from tissues.

➔ Extraction Ratio = 4/5 = 200/250 = 80%
Recall that we extract 5 ml O2 out of 20 carried in 1 dl blood, thus as a total, we extract 250 ml O2 from the 5L blood and produce 200 ml CO2 (4ml*50dl).

- While blood circulates, the O2 levels should decrease, and the CO2 levels should increase. However, at early stages, you will find the O2 levels is decreasing as expected, but you won't find the CO2 levels increased. Why?

➔ The CO2-Hb dissociation curve goes linearly in the physiologic concentrations of CO2; meaning that: PCO2 will increase as you increase the CO2 content.
Unlike O2 that goes sigmoidally, so the increase in PO2 at certain levels (60-100 mmHg) will not lead to a significant increase in the content.

- CO2 is associated with H+.

➔ If CO2 increases, H+ will increase above normal, and you will have an Acidosis; Acidosis suppresses CNS enzymes → coma & death.

➔ If CO2 decreases, H+ decreases, you will have an Alkalosis; Alkalosis stimulates motor neurons and causes your muscles to be repetitively contracted → convulsions, spasm of diaphragm → death.

- Different enzymes have their optimal pH values to work in; acidosis/alkalosis will affect their function.
- CO2 was used as narcotic for surgical purposes, but it's not used anymore for its bad effects on high doses.

- When you hold your breath → alveolar CO2 increases > 40 ml & O2 decreases < 100 ml.
The CO2 will increase only up to 50 ml (limited increase), why?

➔ The increase in CO2 will be associated with an increase in H+ too. These increasings will stimulate the respiratory center to overcome the phrenic neuron cortical inhibitory effect → Breathing is reestablished!

HOWEVER; the decrease in O2 levels to 90 mmHg won't stimulate the respiratory center in your brain. The respiratory center is much more sensitive to the changes in CO2 due to the fact that CO2 has much more bad effects on your cells, and it's again accompanied with H+ levels changes.

➔ In lung diseases, the O2 is affected before CO2;
Testing the ABGs: you will notice at early stages that PO2 decreases with normal PCO2. Later on, you'll notice the increase in PCO2.

- Imagine you are having the right lung normal or HYPOventilates, and the left lung HYPERventilates (decreases CO2); the problem here is solved by:
1- The right lung HYPOventilation will correct the situation and will increase the CO2; *Thanks to the Linear curve!*
2- The respiratory center will sense the problem and act to neutralize the levels of CO2; *Thanks to the Self compensation!*
3- The respiratory membrane is much more permeable to CO2 than O2.

Diffusion-limited & Perfusion-limited exchange;

- <u>Perfusion-limited exchange:</u>
In the capillary; the difference between Alveolar O2 and arterial O2 (A-a gradient) = 0; the equilibrium is achieved early in the capillary. So it's not the diffusion that limits the O2 exchange, it is the perfusion that does. So, perfuse more to get more O2!

➔ If you eject 20 L of blood to the lungs/min, the lungs will be able to oxygenate these amounts of blood.

- <u>Diffusion-limited exchange:</u>
Occurs when the tissue of the lung is damaged or fibrosed. Here the transport of O2 will become diffusion-limited; it's a problem in the tissue itself that limits the exchange, and the capillary is leaving with a blood having less O2. (A-a gradient > 0)
- Some gases, physiologically, are exchanged in a perfusion-limited pattern, others are diffusion-limited.

O2 consumption

- At rest, the cells consume 250 ml O2 each minute.
- During exercising, the cellular O2 consumption will increase, How?

➔ By increasing the blood flow and/or the extraction ratio.

➔ The O2 consumption is genetically determined; it differes from person to person. And can only increase by 10% during exercising.

➔ There are 3 factors appear to limit the maximum O2 consumption (VO2max), and are discussed below;
1- Lung capacity
2- CVS and Hb levels
3- Mitochondrial work and numbers at cellular levels

ASK: which factor is the limiting factor for VO2max?

➔ If a person is cycling (using his legs), he will reach the VO2max. If he started to move his upper limbs (more mitochondria), the VO2max won't be increased. → Exclude factor 3 out of limitations.

➔ If you surgically remove one lobe of your lung, you can still reach the VO2max during exercising. → Exclude Factor 1.

➔ Actually, It is factor 2 (the CVS & Hb) that limits the VO2max. HOW?

- First, let's define the "Contractility" of the heart;
  It is the behavior of the cardiac muscle at fixed preload (EDV, fixed sarcomere length) and fixed afterload.
- When you apply a +ve inotropic agent, it will affect the Ca++ levels and its binding to troponin C → Increasing contractility & VO2max!

CO Poisoning

- Hb affinity to CO is 250 times more than that to O2.

➔ If you have a mixture of gases, with PO2 = 250 mmHg, and PCO= 1 mmHg →

50% of Hb will be bound to CO, and 50% of it will be bound to O2!

➔ Applying this ratio on normal ABGs, when PO2=100 mmHg, if you have only 0.4 mmHg of CO → 50% of Hb will be bound to CO, and 50% of it will be bound to O2!

➔ This causes the dissociation curve to shift to the left and downwards. This also tells that 2 chains out of 4 of the Hb molecules are saturated with O2 (50% saturation).
➔ You have: normal PO2, decreased sat% of O2, decreased [O2].

➔ A pulse-oxymeter is used to tell you about the sat% of O2 in patients blood. But the problem is that this oxymeter cannot differentiate between O2 and CO.

In cases of CO poisoning, the oxymeter will give you a result of 100% saturation with O2, however this is not true, and the patient may be dying of CO poisoning.

➔ Treat with high-pressure O2 therapy, and some CO2. The CO2 will induce hyperventilation to wash out the CO.

Hyperventilation is described as
"the ventilation that decreases CO2 levels."
➔ You are trying to make the alveolar PCO2 (40) similar to the PCO2 in outside air (zero), and the alveolar PO2 to equal 150 mmHg!

- The alveolar CO2 increases by increased production of CO2, and decreases by increased ventilation.
- During exercising: if ventilation increases 2 times, and the PCO2 remains as it is→ this is increased ventilation not hyperventilation.
- Remember that: Alveolar ventilation = Tidal volume – ADS volume.

THE END