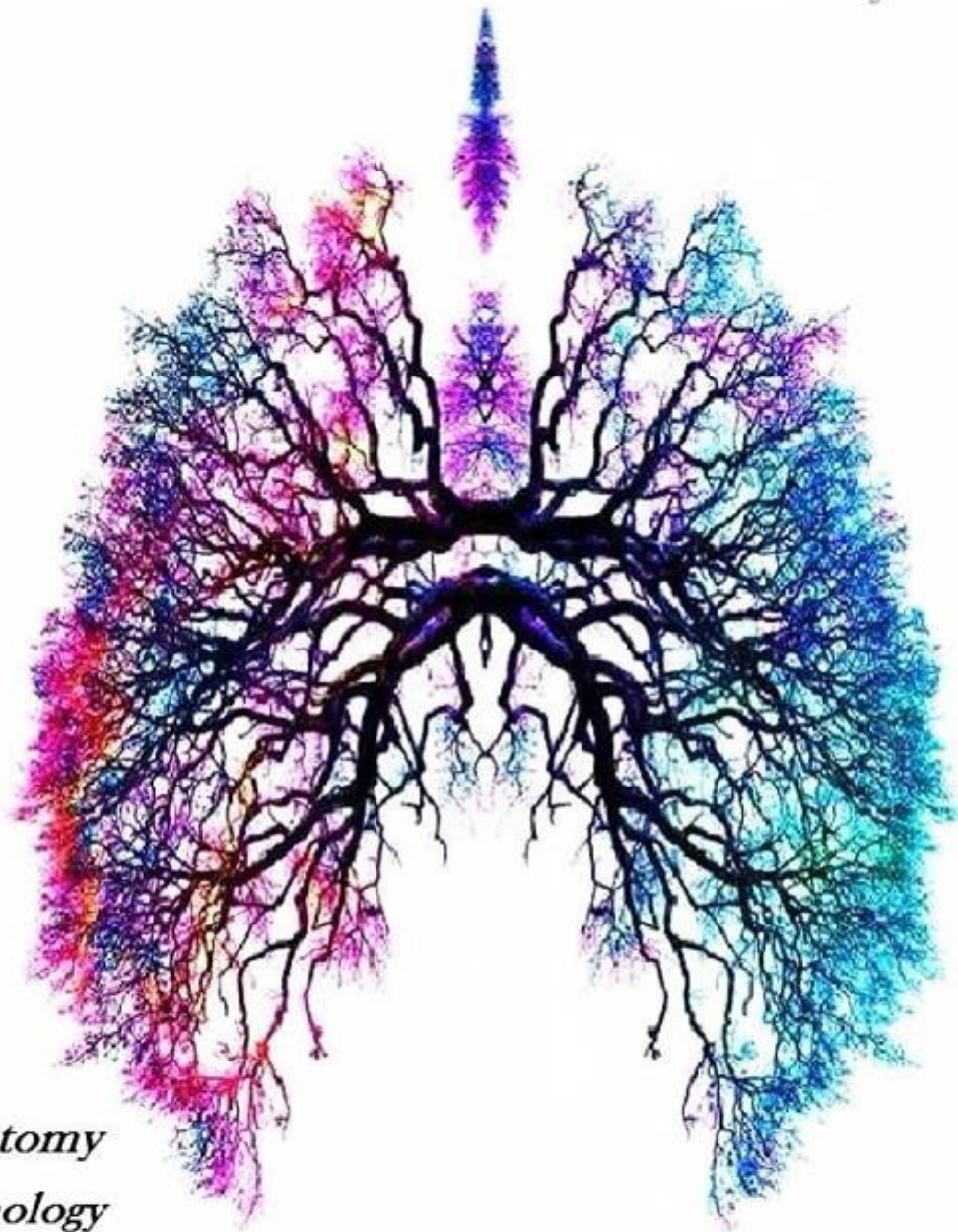# RESPIRATORY SYSTEM

Cover by: Aseil Khatib

O Anatomy

O Pathology

● Physiology

O Pharmacology

O Microbiology

O PBL

Dr Name: Yanal Shafagoj

Lecture # 1

Done By: Anas Zughayer

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The Respiratory System

The respiratory system and the cardiovascular system are highly connected to each other. For example, left heart failure results in pulmonary edema so the lungs cannot function anymore. Also, lung disease results in the so called *Cor Pulmonale* (which is the enlargement and failure of the right ventricle of the heart as a response to increased vascular resistance or high blood pressure in the lungs). So the heart is highly connected to the lungs.

The right side of the heart ejects blood to the lungs to pick up oxygen and to give up carbon dioxide. The blood then returns back to the left side of the heart to be ejected through the arterial system to reach the capillaries. In the capillaries, the blood is exchanged with the interstitium. Then, the interstitium exchanges with the intracellular compartment. So we have many compartments that we should discuss.

The end result of the respiratory system is to maintain homeostasis for oxygen, carbon dioxide and hydrogen (Acid-base balance).

-*Oxygen:*

If the cells are unable –for some reason- to utilize the proper amount of oxygen this is called **Hypoxia**. So hypoxia, briefly, is the decreased oxygen utilization by the cells. Normally, the cells utilize oxygen in the mitochondria because oxygen accepts electrons and generate ATP there. So the main role of oxygen is to make ATP. The respiratory system, by itself, utilizes less than 5% of the total ATP produced leaving more than 95% of the ATP to the rest of the body which makes it a very efficient machine.

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Now **Hypoxia:**

What might be the potential causes of hypoxia? This will be the subject of the upcoming ten lectures; in each lecture one cause will be discussed. But before, some important anatomy will be discussed.

The respiratory system is composed of upper airways above the larynx and lower airways. So we have the nose, the mouth, the pharynx, the larynx and the trachea.

The trachea divides into left and right primary/mother bronchi. The primary divides into secondary bronchus, the secondary divides into tertiary and so on up to 23 branches/divisions/generations. Trachea being generation #0 and main bronchi (left&right) being generation #1. The area of generations from 0 to 16 is called the conducting zone where there is no gas exchange and number 16 being the terminal bronchiole. From 17 to 23, this is called the respiratory zone where there is gas exchange mainly by the last one, which is a bulb-like alveolus. The diameter of the alveolus ranges from 100 to 300 micrometers surrounded by a huge network of capillaries. So number 23 is the alveolus and number 17 is the respiratory bronchiole. There are between 300 to 600 million of alveoli in both lungs.

Again, the respiratory system is composed of two zones; the conducting zone and the respiratory zone.

-Potential causes of Hypoxia:

1) The unavailability of oxygen in the outside air:

At sea level, the atmospheric pressure equals 760 mmHg. At 5.5 km altitude, this atmospheric pressure will be halved to 380 mmHg. At 11 km, => 190 mmHg, so for every 5.5 km there will be decrease by 50%. At the top of Mount Everest, which is less than 10 km altitude, the atmospheric pressure is 226 mmHg.

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Dry Air (no water vapor) is composed of 79% nitrogen and 21% oxygen, the total pressure of this mixture at sea level averages 760 mmHg (P atm).

The partial pressure of a gas (P gas) is calculated by this equation:

P gas= Fraction of gas * P atm.

Each gas contributes for total pressure in direct proportion to its fraction, therefore, 79% of the 760 mmHg is caused by N2 so pN2= 600mmHg and 21% by O2 so pO2 = 160 mmHg.

For example, at high altitudes such as the top of Mount Everest where the P atm is 226 mmHg, the pO2 = 21% * 226, resulting in around 45 mmHg which is a low amount of oxygen in the outside air. The fraction of gas remains the same regardless the level.

2) Airway resistance:

Resistance is inversely proportional to the <u>fourth</u> power of radius, $R \propto 1/r^4$. A slight decrease in radius results in high increase in resistance, 10% decrease in radius results in probably 50% increase in resistance, so small bronchoconstriction can elicit a big problem.

Inspiration (flow of air into the lung) is caused by the driving force which is atmospheric pressure (outside) minus alveolar pressure (inside) divided by the resistance that the air is going to face through airway ducts. F = ΔP (P atm – P alv)/R.

If the resistance is increased ten times, the ΔP must increase ten times in order to maintain the same flow which is very hard to be achieved so this results in problem. Example of increasing airway resistance is chronic obstructive pulmonary diseases (COPD) such as emphysema and chronic bronchitis either with or without asthma.

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3) Problem in the lung itself:

Imagine the lung as an elastic balloon, this elastic balloon has tendency to recoil back to its resting state/volume, so there are always collapsing forces on the lung. If these forces become higher than normal or the compliance of the lung decreased there will be problem in inflating this balloon. Compliance is the change of volume per unit change of pressure ($\Delta V/\Delta P$). If we have large change in volume by small change in the pressure then we have high compliance, but if the change in volume is small, here we have low compliance (the lung is stiff). This can be caused by **RDS** (respiratory distress syndrome) whether it is **IRDS** (infant) or **ARDS** (acute). *Too much compliance is bad and very low compliance is also bad.

4) Increased thickness of the respiratory membrane:

This membrane (respiratory membrane) is 0.2-0.6μm thick and is composed of 5 layers:

1- Alveolar epithelium.

2- Alveolar basement membrane.

3- Interstitium.

4- Capillary basement membrane.

5- Capillary endothelium.

Structures in the Respiratory Membrane
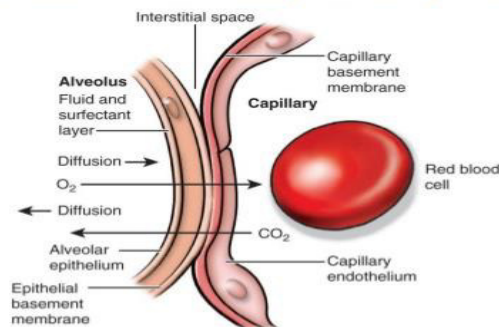
Note: Alveolus has 2 types of cells, alveolar type(1); it is thin, so gas exchange happens here, and alveolar type(2); it is thick relatively, so it does not function in gas exchange but it has another function which is the secretion of surfactant. There might be also macrophages in the alveolus to remove any foreign particles reaching the alveolus.

-Oxygen can cross any biological membrane as if the membrane doesn't exist. So oxygen diffuses through lipid bilayer freely without the need of channels.

-CO_2 is going to cross from the blood to the alveoli, its ability to diffuse through lipid bilayer is 20 times higher than O_2 which makes it has clinical importance.

-Blood comes from the right ventricle as partially deoxgenated with 75% saturation of oxygen, passes through pulmonary capaillaries and then returns back to the left atrium as fully oxygenated (100% saturation). If there is some destruction (early destruction) in the respiratory membrane, the percentage of O_2 reaching the left atrium will be low, leaving the CO_2 percentage as it is (since CO_2 is 20 times easier to diffuse). But if the destruction is too much, both O_2 and CO_2 will be affected. When both are abnormal, then it is an advanced severe case.

-O_2 availability to the tissues normally is not diffusion-limited. Diffusion is inversely proportional to the thickness. If the membrane gets inflamed or fibrotic or in cases of pulmonary edema, pneumonia or TB; its thickness will increase making it harder for O_2 to cross (now it becomes diffusion-limited) =>hypoxia.

5) Blood abnormalities:

Anemia, hypovolemia(quantity) and hemoglobinopathies(quality).

So blood oxygen-carrying capacity will decrease.

6) Heart failure:

Heart won't be able to supply proper amount of oxygen to the tissues.

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7) Occlusion in the arterial system

8) Decreased O2 utilization by cells:

Caused by cyanide or septic shock(septicemia) which poison the mitochondria and their respiratory chain so no oxygen utilization.

9) Problem in the diaphragm:

Inspiration needs contraction of the diaphragm. The diaphragm is a skeletal muscle that lacks automaticity (unable to create its own action potential) so it needs motor neurons that come from the spinal cord (through the phrenic nerve) which are controlled by higher neurons in the respiratory centers in the brain. When these centers are inhibited by drugs like morphine, valium and narcotics or drug overdose, diaphragm won't be stimulated, no inspiration and death as a result of respiratory failure.

Polio virus, which affects motor neurons, might ascend and affect the phrenic neurons which are located between C3-C5 and inhibit the contraction of the respiratory skeletal muscle.

This was an overview of some of the potential causes of hypoxia, now we will go back to the first cause to discuss it deeply.

-Outside air:-

We've already mentioned that P atm is 760 mmHg, 21% O2 (160 mmHg) and 79% N2 (600 mmHg). Now we are going to inhale fresh air to the conductive zone. It is also called anatomic dead space because there is no gas exchange across its wall but actually it is not dead and performs different functions. This space is lined by respiratory epithelia which have cilia that moves towards the larynx to expell foreign particles trapped by mucous secreted by goblet cells. This space also warms the air making its temperature 37 and the most important function is to humidify the inspired air, adding water vapor to it.

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P H_2O, at 37°C and when the air is fully saturated with water vapor (100% humidified), is 47 mmHg. The total pressure reamins 760 mmHg regardless what gases are present.

The new coming gas (H_2O) is going to replace other gases according to their percentages :

760 – 47 = 713 mmHg, we now have 21% O_2 of this 713 = 150 mmHg PO_2.So PO_2 outside (first compartment) was 160. It is 150 in the anatomic dead space (second compartment) . PCO_2 is still 0 (in first and second compartments).

Venous blood is going to become arterial blood by passing through capillaries. O_2 diffues from the alveoli to the blood so PO_2 alveolar will decrease to become 100 mmHg (third compartment). Now new gas in the alveoli, which is CO_2 with PCO_2 of 40 mmHg (alveolar). PH_2O is always 47 mmHg as long as the body temperature is 37. PN_2 in the third compartment (alveolar) is 760 – (100+40+47) = 573 mmHg. Usually, arterial blood is the mirror image of alveolar air.

The blood that comes from the venous system is mixed mainly from the pulmonary trunk. PO_2 venous is 40 mmHg. PO_2 alveoli is 100 mmHg. As the blood moves from veins towards arteries through capillaries, PO_2 is increasing until it reaches 100 mmHg at the arterial side. RBCs are going to stay in the capillaries for 0.8 seconds (cardiac cycle duration). They will take only 0.3 seconds for complete exchange of gases leaving two thirds of the time with no exchange, so we utlize only one third of the gases in our lungs and keep the rest (two thirds) as a reserve (too much reserve) . PCO_2 venous is 45 mmHg, will be exchanged with alveolar air for about 0.25 seconds (less time than O_2 ecxhange which takes 0.3 seconds because CO_2 is 20 times higher in diffusion than O_2). PCO_2 arterial will become 40 mmHg.

PO_2 interstitium is 40 mmHg. Oxygen diffuses from the capillary (100 mmHg) to the interstitium until it becomes 40 in the capillary (equilibrium between the capillary and the interstitium).

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PO2 intracellular should be less than 40 so that oxygen can diffuse inside the cell.

PCO2 interstitium is 45 mmHg. CO2 diffuses out from the interstitium to the capillary (40 mmHg) until it becomes 45 in the capillary (equilibrium between the capillary and the interstitium). So PCO2 intracellular should be more than 45 mmHg so that CO2 diffuses to the interstitium and then into the capillary.

So the blood leaves with PO2 of 40 mmHg and PCO2 of 45mmHg (venous).

-**ABGs**: Arterial Blood Gases

PO2 : 100 mmHg, PCO2 : 40 mmHg

If the ABGs are normal, then the lungs are doing their job.

If a patient suffers from hypoxia, and the ABGs are normal, then its not related to the lungs (bleeding, heart failure,...).

-**CPR** (Cardiopulmonary resuscitation):

You give your expiratory air to inflate the patient's lungs. Does this expiratory air contain enough oxygen?

Tidal volume: is the volume inspired or expired with each breath and equals to 500 mL. This 500 mL is divided into 350 mL that goes to the alveoli (fresh air) and 150 mL that stays in the anatomic dead space. So the volume of the anatomic dead space is 150 mL (2 mL/Kg). If your tidal volume is 150 mL, there is no chance to renew the alveolar air.

During expiration, firstly you're going to exhale the anatomic dead space air (150 mL) then you exhale the alveolar air (350 mL). The first 150 mL has PO2 of 150 mmHg. The second 350 mL has PO2 of 100 mmHg.

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The PO2 exhaled will be 150x150 + 350x100)/500 = 116 mmHg. So there is enough oxygen in the exhaled air.

For CO2, PCO2 alveolar is 40 mmHg, PCO2 in anatomic dead space is zero. The PCO2 exhaled will be (150x0 + 350x40)/500 = 28 mmHg.

The end.

Dedicated to Zaghloul, Saint F.Khuffash, Ab yanal, Maswadeh, Tarawneh, Arman, Sultan, Laluji & the good company.

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