**RESPIRATORY SYSTEM**

* When we talk about respiratory system we concern homeostasis of oxygen, CO2 and hydrogen.
* At the end what we care about is to be sure that oxygen available to the cells and CO2 have been removed.

 - CO2 and hydrogen are the same thing ,cuz CO2 converted to hydrogen when it binds to water [**CO2** + H2O HCO3- + **H+** ]

* The oxygen comes to the cells from arterial sources,, the blood eject from the left ventricle through the pulmonary arteries to the lungs, and it come from the lung to the left ventricle through pulmonary veins.

 -when the level of oxygen in the arteries is normal and available to the cells it will be delivered to cells through capillaries (this is our goal).

 - the end target of the respiratory system is to guarantee normal ABGs **"arterial blood gases"** ,in term of normal oxygen ,CO2 and hydrogen.

* **Hypoxia**: is the decrease of oxygen utilization by the cells.

**●what is the potential causes of hypoxia?** why we might develop hypoxia?

 1- **When there is no oxygen in the outside air**. (unavailability of oxygen)

**e.g.** Is the high altitude,

* At sea level atmospheric pressure is Patm= 760 mmHg, 21% of this is oxygen, so PO2 (oxygen partial pressure in the air)= (21/100) \*760 = 160 mmHg
* PN2=(79/100)\*760 = 600 mmHg
* PCO2 = 0% ( you can put it 0.3%)
* So the composition of room ear at sea level is 2 gases O2 + N2 .
* If you ascend to high altitude , the more you ascend the less the atmospheric pressure.
* For each 5.5 km we ascend >> the atmospheric pressure decrease to the half.
* At sea level the Patm = 760 >>at 5.5 Km the Patm = 380>> at 11 km the Patm = 190 mmHg (mount Everest approximately 10 km higher than the sea level,, and the Patm is about 220 mmHg >> 21% of it is oxygen only ,which is about 40 mmHg ).

2-now we will look at O2 delivery through the following scenario: oxygen enters through the airways; nose, mouth, pharynx, larynx, trachea and bronchial tree. ,they goes to alveoli “balloon” ,from the alveoli ,it crosses to the blood (blood is coming from the right heart and going back to the left heart adding oxygen) >>so the second level might be due to problem on the airways, they are **not opened**/ **narrowed**/ **stenosed**, this is called **increase airway resistance** (resistance is inversely proportional to the forth over the radius (R∝(1/r4))>> so the less the diameter ,the more the resistance)

Increase in the airway resistance is manifested in a big family called COPDs: chronic obstructive pulmonary diseases, an **e.g.** Of COPDs “member of the family” is :

1-Emphysema انتفاخ الرئه

2- Chronic bronchitis التهاب القصبات المزمن

 ± bronchial asthma الربو القصبي "±: means that bronchial asthma may exist or not".

>> so the first cause is **unavailability** of O2 , and the second O2 is available but theres **difficulties in** delivering the oxygen to the **airways** ,cuz these airways are partially closed.

3- alveoli “balloon” , noninflatable ( you can't add fresh air) ,noncomplitable balloon,, here airways is patent but the balloon are stiff .

* We have between 300-600 million alveoli
* If the alveoli have huge tendency to collapse, they are not born to expand “non expandabl /noninflatable /noncomplitable /stiff" , there are some sort of restriction in inflating the balloon >> so we call it **restrictive pattern or restrictive family**.

>> so there is many ways in dividing lung diseases into families,, I can divide them into obstructive (problem in the airways) and restrictive(problem in the balloon itself "alveoli/tissue of the lung") family.

* An e.g. On the restrictive family is ,RDS: respiratory distress syndrome, where we don’t have enough surfactant, and thus the collapsing forces are huge because of the increased surface tension , so the lung tend to collapse and it takes too much effort to expand
* Another ex. Is pulmonary fibrosis “تليف الرئة” ,,here you cant inflate the lung, you have restriction in inflating the lung.

We are moving with the molecular oxygen to know the causes of the hypoxia ,,from outside, airway, alveoli,, now the oxygen is going to cross the wall of the alveoli to enter to the blood in capillary.

\*\*the airways is composed of trachea then it divide to 2 main bronchus (mother or primary) >>secondary >> then tertiary bronchus

>>and keeps dividing 23 times “23 divisions, 23 generations,23 branches”,, the number 23rd is a balloon like called alveolus ,,we call this airway **bronchial tree**

* Small airways called bronchioles
* Large airways called bronchi ,,those are surrounded by cartilage, cartilage is bony like structure ,,so its not collapsible “not broncho collapsible” ,,so airway resistance is unlikely to be due to bronchi ,cuz these are uncollapsible (supported by cartilage).
* Small airways,,from 11,12 and beyond there is no more cartilage, and thus they are broncho collapsible , they may close and not allow the air to reach alveoli ,and the capillaries are only surrounding the alveoli >>so no oxygen reaches the blood.

\*\*in the alveolus we have ,,

* **type 1 cells**, which are thin >>and through them we have the exchange of gases (O2 to the blood , CO2 to alveoli)
* **type 2 cells** are columnar “not involved in gas exchange” >>they produce the surfactant.
* garbage man “**macrophages**” , they clean whatever reaches the alveoli
* the diameter of the alveolus is about 300 micrometer ,increases during inflation and decreases during deflation (between 200-300 micrometer)

4-here is the discussion of the forth cause of the hypoxia ,,**crossing the membrane** "JUST in SOME CASES it will have a PROBLEM; pneumonia ,fibrosis or pulmonary edema".

\*\*now oxygen is going to cross from the alveolus to the blood ,it will cross many membranes ,barriers:

1-epithelial cells of the alveoli>> 2-basement membrane >> 3- the interstitium >> 4- the basement membrane of the endothelium >> 5- the endothelial cells itself [these 5 layers are called the respiratory membrane ].

* the thickness of these 5 layers is only 0.2 micrometer ,very thin, and therefore oxygen can cross any membrane as if the membrane is not exist,, so normally, most of the cases of hypoxia is unlikely to be due to diffusion limitation (oxygen is not diffusion limited).

 \*\*how much time we have for the blood to move from 1 to 2 ??and to exchange the gases?

**2**

**1**

- its equal to the duration of the cardiac cycle , at rest it equal 0.8 sec

- when blood enters at point 1 (time=0) oxygen was low in the blood and when we exit from point 2 (time= 0.8) ,the oxygen is high.

- we will expresses the oxygen in blood by PO2 , cuz it “PO2” will determine the diffusion of oxygen from one area to another.

- PO2 in alveoli is 100, and PO2 in capillary is 40 ,,so oxygen diffuses from the high pressure "alveolus" to the low pressure "capillary",

- PO2 in the capillaries become 100 before crossing the first one third of the capillary ,,before spending 0.3 ,,so 0.25 sec is enough for full exchange

>>so we complete the rest of the journey “the rest of the time” with no more exchange [the rest two thirds of the capillary pathway is with no exchange].

-as a result of that,, even if the cardiac cycle is shortened due to increase heart rate ,,if the heart rate becomes 150 instead of 75 beats per min>>then the cardiac cycle will be 0.4 instead of 0.8 ,,0.4 sec is still enough for full exchange (the blood will not leave the capillary unless its fully oxygenated).

>> so normally we don’t expect diffusion to be the limiting factor(O2 is NOT diffusion limited), but everything has a limit ,,if we have infiltration of fibrous tissue, white blood cells , inflammatory cells like pneumonia ,fibrosis ,whatever , or pulmonary edema.

-Edema will cause filling of interstitial with water firstly (interstitial edema),, and then filling of alveoli(alveolar edema) ,,filling of the interstitial with water will increase the thickness of the **respiratory membrane** from (0.2 to 1 or 2 micrometer)>> in this case we expect that blood will enter and exit without being fully oxygenated ,cuz oxygen now needs longer time to diffuse.

 \*\* in this case ,,the airways Is patent and the alveoli here have alittle pressure on it caused by water ,,but the diffusion problems is another point.

>>> so number 4 of the cause of hypoxia is the membrane ,,crossing the membrane usually is not a problem ,,but in some cases like pneumonia,fibrosis,,

5- **blood problem**

\*\*now oxygen is in the blood ,,

Recall that : blood is composed of :

* 55% of the blood is plasma (92% of it is water)
* 45% is cells (mainly RBCs> RBCs contain Hb >which binds to O2 “oxihemoglobin”)

-the oxygen is carried in the blood in 2 forms:

 - 1.5% of the oxygen is **dissolved** in plasma “free”,, very little .

 - 98.5% of the oxygen is with hemoglobin.

-if you have bleeding,, so you loses blood and therefore oxygen,, then it will lead to hypoxia.

-If there was no bleeding > same blood volume (7%) but decrease in RBC ,,hematocrite or Hb decrease (e.g. instead of 15gm/dl it's 7.5gm/dl) > hypoxia .

-Thus we conclude that anemia = hypoxia .

-Let's assume that we have Hb A (Normal Hb) , 15gm/dl in males (13gm/dl in females ) , blood volume is 7% (6% in females ) "everything is ok , but any decrement of these previously mentioned numbers > > hemoglobinopathies )"اعتلالات الهيموغلوبين)

6-**heart problems**:Let's talk about the heart , heart failure is going to cause hypoxia because heart is going to eject the blood . Also , if one of the arteries is obstructed it will cause hypoxia ( localized hypoxia) as in femoral artery obstruction .

7- **mitochondrial level.**

-And at the level of tissues if the mitochondrial respiratory chain is not working ,even if the oxygen is available , it will cause hypoxia. Remember (mitochandria will utilize the O2 as electron acceptor). ( e.g. septicemia : toxins made by these gram( –ve) bacteria they poison the mitochondria and make them unable to utilize oxygen even though oxygen is available, .("اختناق خلوية"

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-Another e.g. **cyanide** that poison the respiratory chain (here everything is okay ,but when we reach the cell there is a problem)

8-**muscle /diaphragm problems.**

-Diaphragm must contract to pull the lungs down and inflate the lung, as we know , diaphragm is a skeletal muscle (skeletal = takes motor neuron in order to contract "lacks automaticity unlike cardiac muscle , needs impulse from higher center; medulla oblongata ") , the nerve that goes to the diaphragm is the phrenis nerve , the cell body of it is in the Spinal Cord cervically between C3-C5 , so injuries there are so dangerous .

Myasthenia gravis مرض في العضلات

9- **nerve problems.**

-In the medulla we have the respiratory centers , cells responsible for repetitive stimuli (pacemakers) , these cells send impulses for the phrenic neurons every 5 seconds , so in 1 minute the respiratory rate is "60/5=12" ,( they send impulses for 2 seconds and stop beating for 3seconds , so the cycle is 5 seconds) , therefore inspiration is for 2 seconds and expiration for 3 seconds .

-Poliovirus loves motor neurons if it ascends up , it may affect the diaphragm causing death .

-Drug overdose / anesthesia, both may affect **the respiratory centers**, they may suppress cells in respiratory centers.

Polio: pathological condition in the nerves.

tumor , trauma, infection ,compression

>>All these they may affect the respiratory centers in the medulla.

\*\*in the medulla we have cardiac centers ,vascular centers, respiratory center. these are the vital signs ( blood pressure , heart rate "HR" , and above in the hypothalamus for temperature).

Special thanks to my friend **batool hiari** ☺

