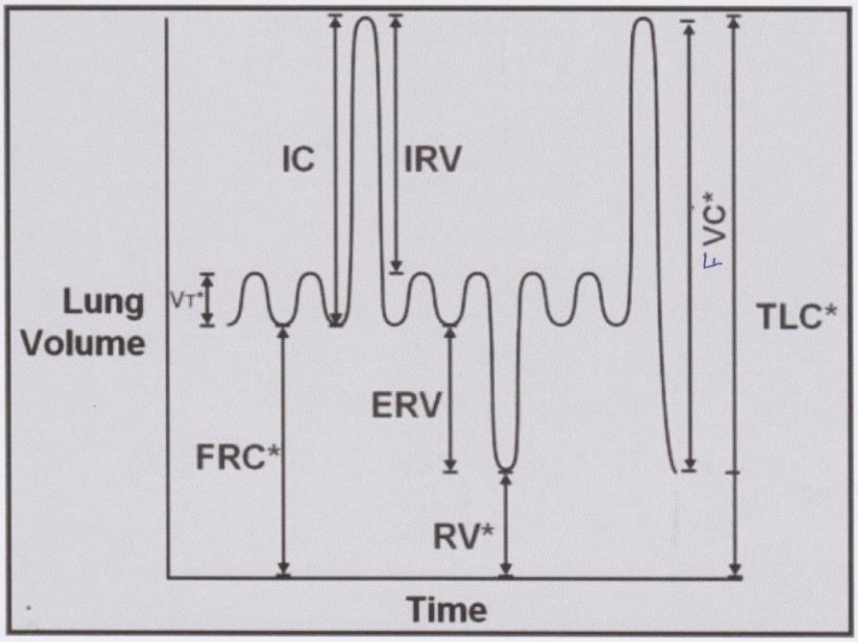
Video #1
Lung volumes
29th.12.2016



1) ***Tidal Volume (*VT*):** The normal inspiratory and expiratory volume.
*Normal inspiratory/expiratory volume→ 500 mL.

2) ***Forced Vital Capacity (*FVC*):** The maximum volume of air that can be expired from the lung.

3) ***Residual Volume (*RV*):** The volume that is left in the lung after maximum expiration.

4) ***Functional Residual Capacity (*FRC*):** The volume that remains in the lung after a normal expiration.

5) ***Inspiratory Capacity (*IC*):** The maximum volume inhaled after a normal expiration i.e. the maximum inspired volume in a normal person.

TLC = FVC + RV TLC = FRC + IC

TLC ⇒ Total Lung Capacity

Video #2
Ventilation
29th.12.2016

*The lung is divided into two functional zones

1) **Conducting zone:** consists of the air ways; bronchus, bronchioles, trachea and all the way out to nostrils, and gas exchange doesn't occur at this zone

2) **Respiratory zone:** Where alveoli are found, and where gaseous exchange takes place

*The air that is trapped in the conducting zone is known as **physiological dead space**, and it measures 150mL in a normal person, or 1mL/pound.

*A patient was administered with respiratory rate of 15/min (regular), after few minutes the rate increased to 40/min (rapid and shallow).

→ If he is breathing is shallow he's is mostly exchanging air from the conducting zone; not deep enough to reach the respiratory zone**.** In other words, he decreased/depressed his **alveolar ventilation** because of the rapid movement of air, because of that, he couldn't get rid of the CO_2 coming from the blood.

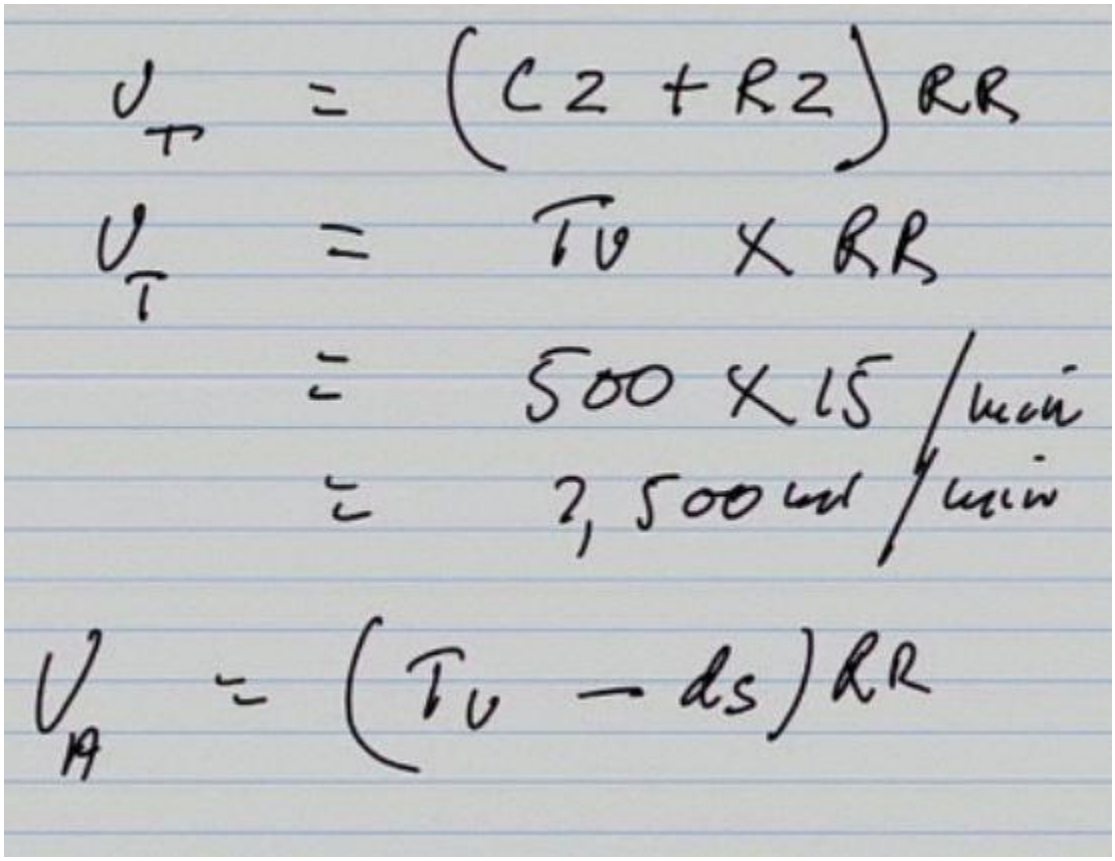
*In order to get rid of the CO_2 in the alveoli, alveolar ventilation and respiratory zone involvement are essential.

*This patient will accumulate CO_2 and will become <u>acidotic</u>.

*Alveolar ventilation and hyper respiration aren't the same.

*Hyperventilation and hyper respiration aren't the same.

Video #2
Ventilation
29th.12.2016



*__Total ventilation (V_T):__ Amount of air moved in and out of the lungs per minute.

*For a healthy individual this equals to 7,500 mL/minute.*Part and not all of this air (7.5k) reach the alveolus.

*__Alveolar ventilation (V_A)__, for a healthy individual this equals to 5,250 mL/minute.

*Therefore there is 2,250 mL of air lost/trapped in the system, specifically at the dead space, we should be cautious about the dead space.

*The physiological dead space can affect the alveolar ventilation, if the volume of the air trapped in the dead space increases, the alveolar ventilation will decrease.

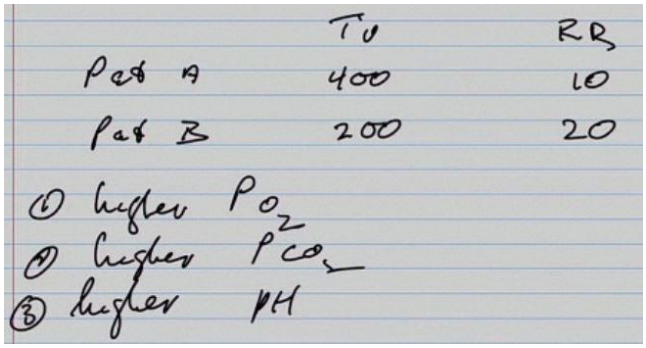
Video #2
Ventilation
29th.12.2016

*We already have 150 mL of air trapped in the dead space, and that's physiological, however, there are certain diseases that increase this volume→**pathological dead space.**

***Emphysema,** bulbous alveoli trapping air inside, this trapped air in the alveoli is not involved in gas exchange and becomes part of the dead space.

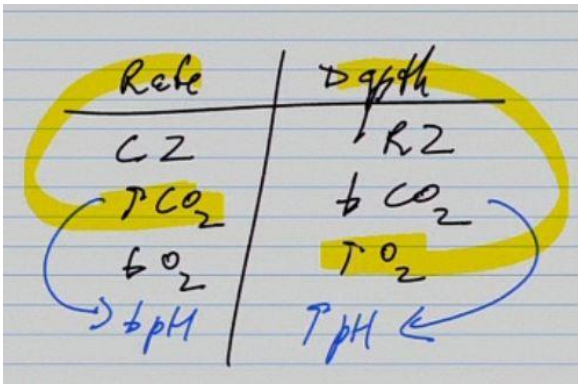
*If we increase the volume of air trapped in the dead space, this will decrease alveolar ventilation which means we are not blowing out carbon dioxide out resulting in an increase in alveolar carbon dioxide $PaCO_2$, this explains why emphysema patients have ***hypercapnia*** and acidosis.

*<u>**Comparing tidal volume and rate:**</u>



*Note that the T_V is the depth and the RR is rate.

*To distinguish and make a clinical picture to answer the above question you need to understand the comparison between T_V and rate.

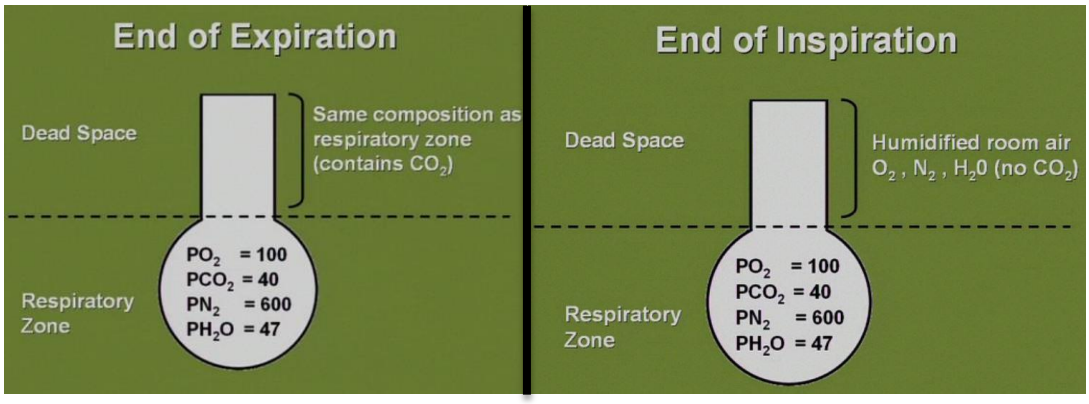


*The higher the rate, the more conducting zone involvement (The faster the shallower), higher CO_2, less CO_2 and lower P_H.
*More depth, more respiratory zone involvement, the more you get rid of CO_2, more O_2 and higher P_H.

*Rate→ Carbon Dioxide (CO_2).

*Depth→ Oxygen (O_2).

*Answer the question above.



*__Question__: Which of the following gases is least likely to be found in the conducting zone at the end of <u>*inspiration*</u> in a person breathing normal atmospheric air?

a) O_2

b) **CO_2.**

c) N_2

d) H_2O

*During <u>*expiration*</u> the source of carbon dioxide in the conducting zone is the blood/alveolus, and we find oxygen because we don't dissolve all of the oxygen in the inspired air.

*We don't expect carbon dioxide in a person breathing normal atmospheric air; the idea is to differentiate between room air at which carbon dioxide is present as a pollutant by human activity and atmospheric air at which carbon dioxide isn't expected to be found.

Video #3
Lung mechanics
29th.12.2016

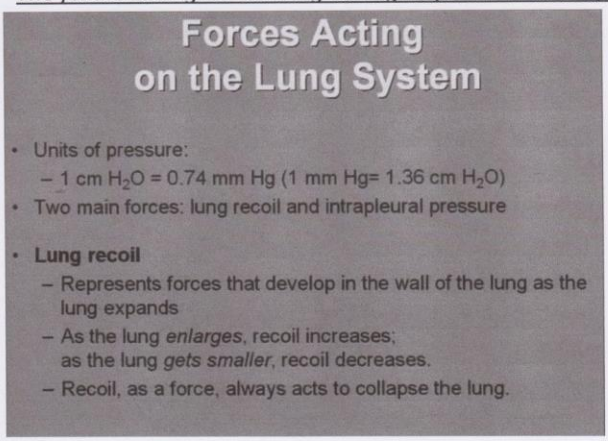
*Respiration involves inspiration and expiration.

*Inspiration is a very active process and it involves contraction of muscles mainly the diaphragm in addition to the intercostal muscles (accessory).

*Expiration is a passive process under resting conditions.

*During respiratory system examination you should pay attention to these two points mentioned above.

*<u>*The forces acting on the lung during inspiration and expiration:*</u>



Units of pressure:
cmH_2O
1 cm H_2O = 0.73 mmHg
(1mm Hg = 1.36 cm H_2O)

1) **Lung recoil**
2) **Intrapleural pressure**

*When you inflate a balloon the tension in the walls increases, and we you release the balloon it collapses and the air inside the balloon goes out because as you expand the balloon the tension in the walls increases and this is what we call ***Recoil Force***.

Video #3
Lung mechanics
29th.12.2016

Forces Acting on the Lung System

- **Intrapleural pressure**
  - The pressure in the thin film of fluid between the lung and the chest wall
  - Subatmospheric pressures (-) act as a force to *expand* the lung, and positive pressures (+) act as a force to *collapse* the lung.
  - In normal restful breathing, intrapleural pressure is always subatmospheric or negative, and thus acts as a force to expand the lung.

Forces Acting on the Lung System

- **Important points**
  - Intrapleural pressure > lung recoil → **lungs expand**
  - Intrapleural pressure < lung recoil → **lungs collapse**
  - Intrapleural pressure = lung recoil → **lung size constant**

*Here we mean by higher than, is more negative i.e. when we say the higher the intrapleural pressure we mean the more negative it becomes.

*When the intrapleural pressure is equal to the recoil force, the lung is said to be in a stable state.

Video #4
Lung mechanics 2
29th.12.2016

*In a normal lung before inspiration (after expiration), the intrapleural pressure is -5 cm H_2O, the recoil force is +5 cm H_2O, and at this time the **alveolar pressure** equals to zero cm H_2O.

*the alveolar pressure is zero because the alveolus is connected to the outside (zero cm H_2O) via bronchioles, bronchus, trachea and nostrils, and equilibrium will be established between these.

*At this stage (before inspiration) we say that the lung in a stable state not expanded nor collapsed and the lung volume at this very stage is the **functional residual capacity (*fRC*).**

***Boyle's law:** Pressure is inversely proportional to the volume if we keep constant pressure.

****During inspiration:***

Diaphragm contraction pulls the lung downwards and increases Intrathoracic volume, therefore decreases intrathoracic pressure.

→ The intrapleural pressure decreases to values less than -5 cm H_2O (-8), the intrapleural pressure is more negative and expands the lung.

→The recoil forces increases because the volume of the lung is increased and reaches values above +5 cm H_2O (+8).

→The two forces are now equal at the end of inspiration, and the lung reaches dynamic equilibrium; the forces are equal and opposite and there is no more expansion and no more collapse.

→The alveoli are pulled and expanded with the lung, and their volume increases and according to Boyel's law their pressure drops to negative values (-1 cm H_2O).

→**The atmospheric pressure (P_{atm})** is zero, and the alveolar pressure is -1, so pressure gradient is established and air rushes inside the alveoli.

*At the end of inspiration, alveolar pressure goes back to zero, and air flow stops.

***Question:** When do you expect the greatest air flow into the alveoli?

→At the middle of inspiration, the time at which we have the greatest pressure gradient.

***Any pathology that occurs in the respiratory system that interferes with the ability of the lung to develop a negative alveolar pressure (P_A) is termed a <u>Restrictive disease</u>**.

*Examples on restrictive diseases:

1) Pulmonary fibrosis.
2) Asbestosis.
3) Silicosis
4) Sarcoidosis.

→ Anything related to –osis, to osis is to restrict, all of the diseases of the respiratory system that end with –osis are restrictive.

***Question:** In a patient with pulmonary fibrosis, which of the following statements is most appropriate?

→ Loss in the ability to develop negative alveolar pressure.

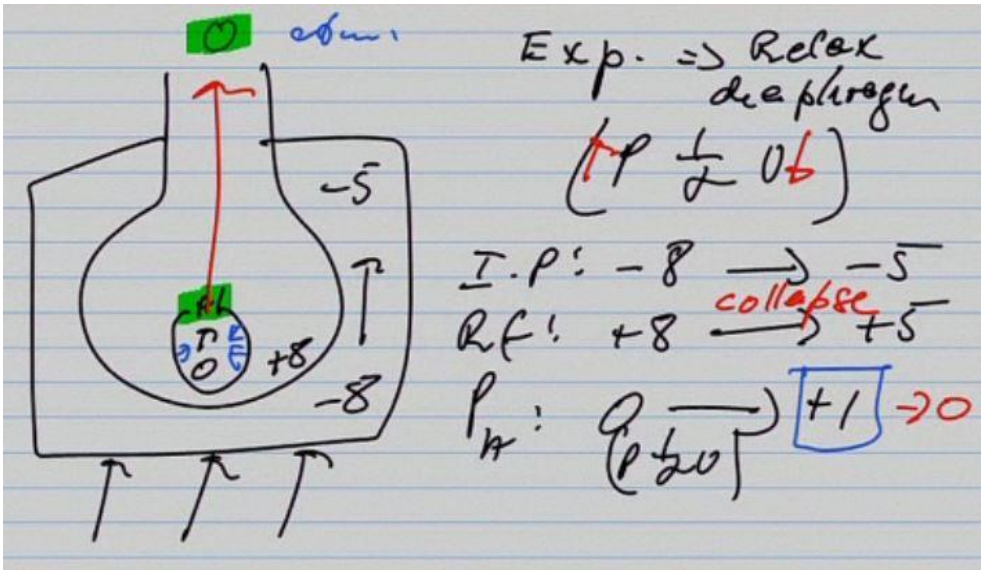
***Question:** At the end of deep inspiration, what would you expect the the alveolar pressure to be?

a) +1
b) +2
c) -1
d) -2
e) **zero**

Video #4
Lung mechanics 2
29th.12.2016

*<u>During expiration</u>

*the opposite will take place.



*Sniffing/ sucking air will make the air flow to your conducting zone, as the alveolar air is increased due to pressure gradient not due to sniffing, same applies if you force the air out, you are emptying the conducting zone not the respiratory zone (alveoli).

***Any pathology that occurs in the respiratory system that interferes with the ability of the lung to develop positive alveolar pressure (P_A) is termed an Obstructive disease.**

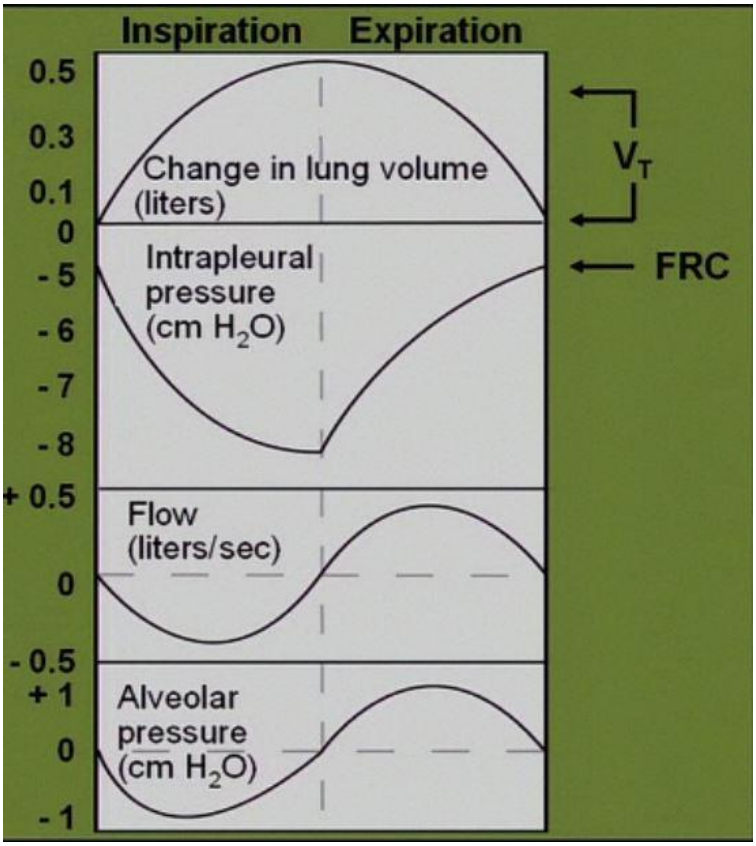
*E.g. on obstructive pulmonary diseases:

1) Emphysema
2) Asthma
3) Chronic bronchitis

→ these are called COPD's or obstructive diseases.

*In ***emphysema*** there's loss elasticity of the alveoli, they become bulbous and lose the ability to recoil, and therefore loss of ability to develop positive alveolar pressure so air can't leave the emphysematous alveoli, when we examine the chest we hear hyper resonance sound, and patients are at risk of developing barrel chest, as the alveoli and the lung are pushing against the chest wall.

*In ***chronic bronchitis***, because of the occlusion of the airways that is trapping air in the alveoli forcing the alveoli to be expanded and with time loss of the ability to develop positive alveolar pressure.



*Notice the mid-point of inspiration at which we achieve maximum pressure gradient and consequently maximum air flow, same applies to expiration.

Video #5
The impact of inspiration/expiration on blood pressure and heart rate.
29th.12.2016

*During respiratory inspiration, the intrapleural pressure decreases, the pressure acting on the right atrium decreases so right atrial pressure decreases which will drain more blood from the vena cavae.

*During inspiration, when we take a deep breath we pull the diaphragm, increasing the thoracic volume and decreasing thoracic pressure, this will create tremendous pressure gradient between the vessels in the thorax and the dependent veins in the periphery which leads to massive venous return.

*As venous return increases, cardiac output from the right ventricle to the pulmonary circulation increases, this serves in utilizing the inspired oxygen.

*This also leads to temporary **pooling of blood** in the lung during inspiration that means that flow to the left side of the heart (left atrium) is momentarily decreased and decreased flow to the left ventricle which means less cardiac output is momentarily decreased during inspiration, and as a result temporary decrease in blood pressure.

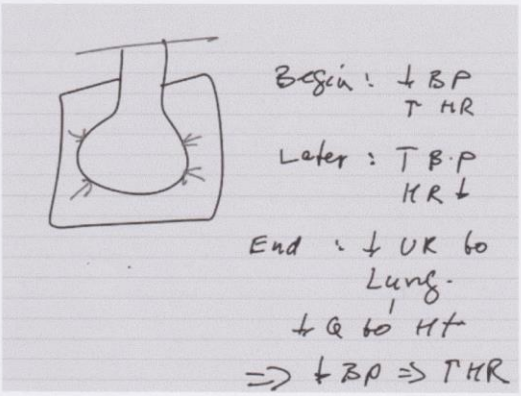
*That's why during taking blood pressure for a patient, he should be calm and not taking in deep inspiration, it could give you 10 mmHg difference.

*Immediate **baroreflex** will occur, that leads to transient increase in heart rate, which is called ***paradoxical fall in blood pressure during inspiration***.

*The increased intrathoracic pressure during expiration will push blood towards the left side and the opposite will occur.

Video #5
The impact of inspiration/expiration on blood pressure and heart rate.
29th.12.2016

*Valsalva maneuver: taking deep breath, closing nostrils and mouth and squeezing the abdominal muscles and all the muscles that will collapse the lung (diaphragm and intercostals)



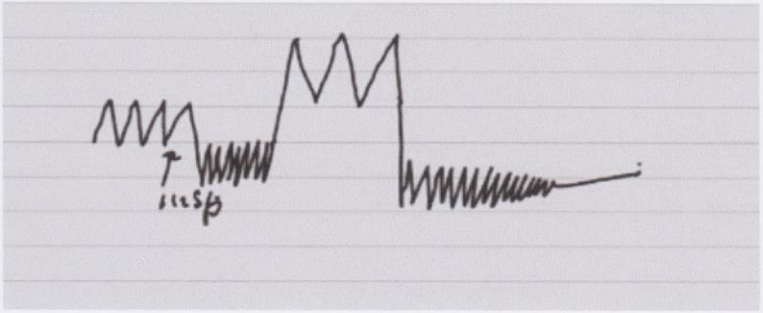
*Beginning of Valsalva is basically inspiration, so what happens in that phase is what happens in inspiration mentioned above.

*Later in Valsalva as you are squeezing and keeping the air inside, blood pressure increases because you are forcing blood to the heart and heart rate will decrease as a reflex.

*As you continue in the maneuver (end of Valsalva) i.e. prolonged increase in thoracic pressure this will lead to decreased venous return due to loss of pressure gradient between right atrium, vena cava and peripheral veins this means decreased flow to the heart.

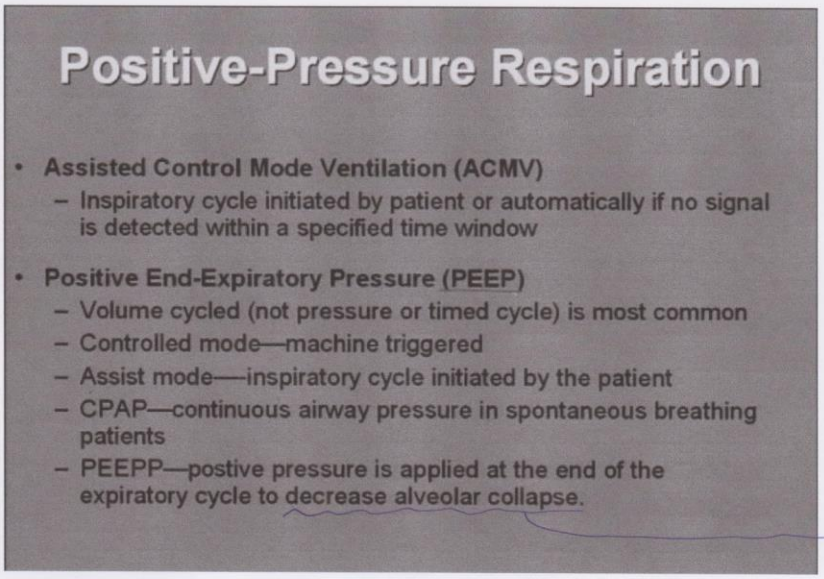
*Decreased flow to the heart will lead to decrease in blood pressure and an increase in heart rate.

Video #5
The impact of inspiration/expiration on blood pressure and heart rate.
29th.12.2016



*This represents the eventual changes in blood pressure and heart rate in a patient doing Valsalva maneuver.

Video #6
Positive-Pressure Respiration .
29th.12.2016



Ask about this

*Positive-Pressure Respiration is often called the PEEP which is the ventilator being used.

*The idea here is that if a patient has ***atelectasis*** or ***respiratory failure*** secondary to emphysema he/she will be unable to empty their lungs, in other words unable to create positive alveolar pressure, air will accumulate in the bulbous alveoli.

*To help this patient empty his alveoli, if we can create a positive alveolar pressure for him/her which is basically what is the ventilator will try to do by enhancing the patient's ability to create positive alveolar pressure, and their comes the name ***Positive End-Expiratory Pressure Ventilating*** to substitute the positive pressure for him/her.

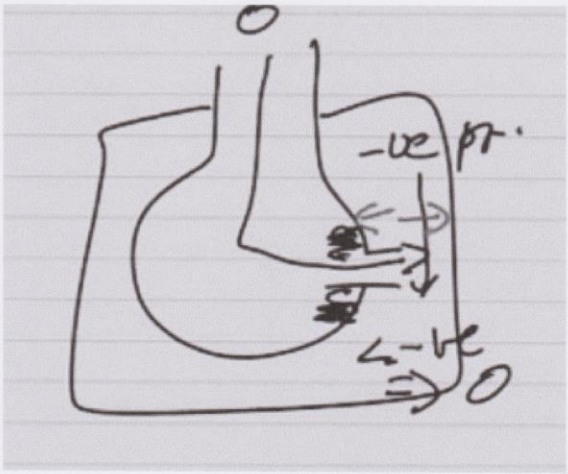
Video #7
Pneumothorax.
29th.12.2016

*What would you expect to happen in a simple pneumothorax, the etiology of pneumothorax usually is rupture of the pulmonary blebs; this result in an opening/passage between atmospheric pressure and pleural cavity, air can flow to the pleural cavity until the intrapleural pressure equalizes the atmospheric pressure (zero).

*The lungs lose their ability to expand due to loss of negative pressure in the pleural cavity, and that can force the lungs to collapse as it pushes the lung away to other side.

*This increased intrapleural pressure can also push against the chest wall.

*so, simple pneumothorax the principle here we are losing the negative intrapleural pressure, therefore losing the ability of the lungs to expand and the net result is lung collapse.



Video #8
Lung Compliance.
30th.11.2016

*__compliance:__ is the change of volume divided by the change in pressure, in other words is the change of volume per pressure.

*Compliance is proportional to ΔV.

*ΔV is inversely proportional to elasticity, as elasticity increases the change in volume decreases, as the tendency to come back to the original volume is increased (elasticity).

*__elasticity__ is the ability to recoil when stretched.

*We can conclude that elasticity is inversely proportional to compliance.

*One year old kid → young lung → perfectly elastic → **less compliance**.
*Sixty years old man → old lung → loss of elasticity → **more compliance**.

*Elasticity is recoil, and therefore compliance is inversely proportional to recoil.

*The forces responsible for recoil are:
1) ***Surface tension.***
2) ***La Place Law.***
3) ***Elastin fibers*** (role of α1-antitrypsin and its relation to emphysema).

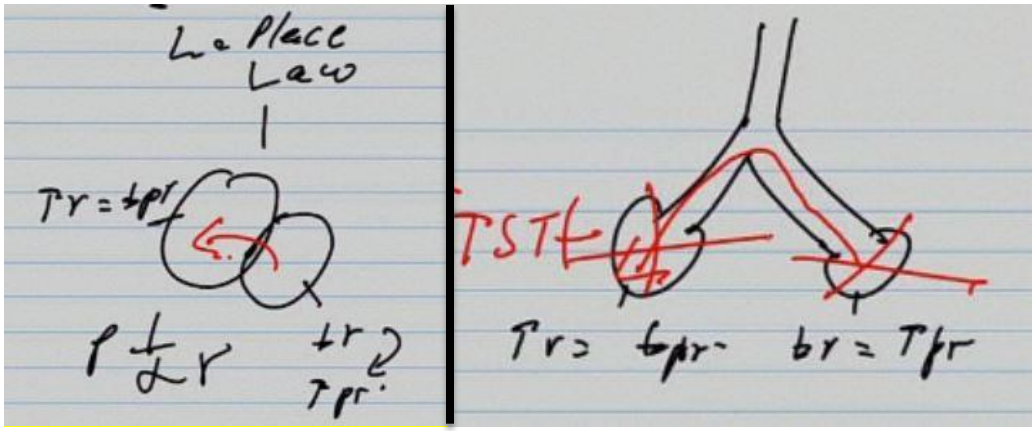
*Surface tension occurs whenever we have liquid/air interface, whenever water and air meet at a surface, surface tension can be found, and this force serves to collapse.

*The alveoli lining is moisture, and air is found inside these air sacs, which means that there's water/air interface.

*The alveoli are micro structures and this force can cause alveolar collapse, but in fact they are not.

Video #8
Lung Compliance.
30th.11.2016

*__*la place law*__ stats that the pressure is inversely proportional to the radius, double bubble mystery in the video.



*The alveoli vary in size; the alveoli with smaller radius have higher pressure compared to that in the alveoli with bigger radius, and according to La Place air will move from the small one to the bigger down pressure gradient resulting in eventual collapse in the small alveoli, also according to La Place the small one should collapse.

*This leads to increased surface tension in the large alveoli, surface tension is a collapsing force and this means that the larger alveoli should also collapse.

*These two points explain why the natural state of the lung is to be collapsed, and because of La Place and surface tension the fetal lung stays collapsed during development.

*Two weeks before birth, __*type II pneumocytes*__ start to synthesize what's called __*surfactants*__; these prevent the collapse of the lung by the increased surface tension and according to La Place.

Video #8
Lung Compliance.
30th.11.2016

*Surfactants roles:

1) Decreases surface tension force by interceding between the liquid/air interface, therefore they increase compliance, decreasing the collapsing ability of the lung.
2) Opposes La Place effect on alveoli, especially the small ones, stabilizes the small alveoli.
3) Decreases **capillary filtration force**.

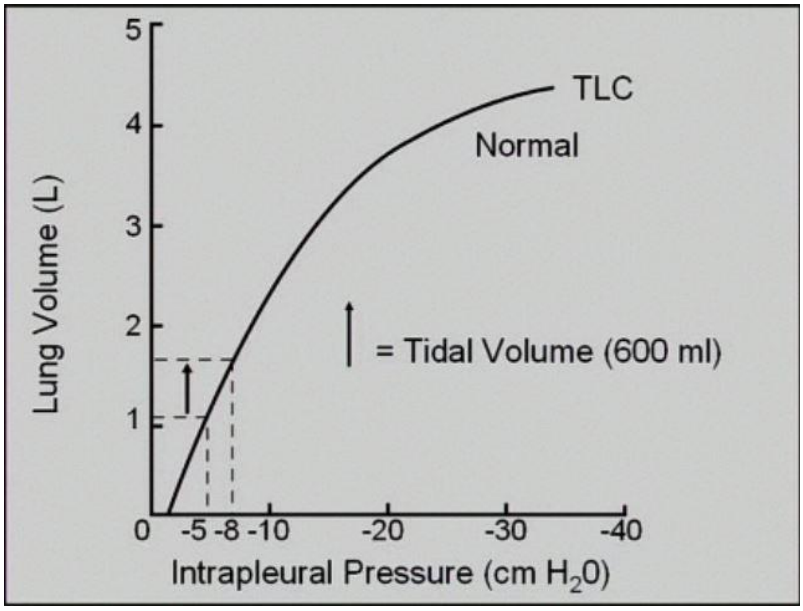
*If a child is born with deficient surfactants, he/she will eventually develop ***Respiratory Distress Syndrome (RDS)***.

*we diagnose RDS by assessing Lecithin/Sphingomyelin ratio; if the ratio is less than two it means RDS.

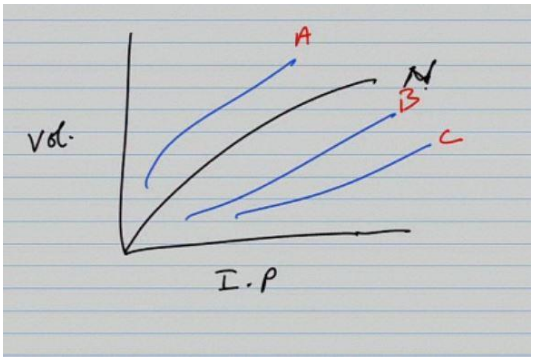
*Symptoms of RDS:

1) Inspiratory difficulty.
2) Increased surface tension force, which means decreased compliance.
3) ***Atelectasis***, the child is at risk of alveolar collapse.
4) Pulmonary edema, due to increased capillary filtration force.

Video #8
Lung Compliance.
30th.11.2016



*Compliance equals the slope of this curve.
→Rise/Run, ΔY/ΔX



*If **N** represents the normal compliance.
*Which graph represents ***normal aging***? → **A**
*Which graph represents ***emphysematous lung***? → **A**
*Which graph represents ***RDS***? → **B**
*Which graph represents a person with ***atelectasis***? → **C**
*Note that atelectasis is the end stage of RDS.

Video #9
Airway Resistance.
30th.11.2016

*The impact of radius on ***air flow resistance.***

*Recall ***Poiseuille's law, flow (Q)*** is inversely proportional to ***resistance (R),*** and resistance is inversely proportional to fourth power of ***radius (r^4).***

*The radius of the airway is under the influence of autonomic nervous system control.

*Parasympathetic stimulation -Muscarinic receptor stimulation- leads to bronchoconstriction i.e. increases radius.
*Sympathetic stimulation –β2 receptor stimulation- leads to bronchodilation i.e. increases radius, that's why in the treatment of a disease with constricted bronchi we use beta-2 agonists or muscarinic receptor blocker such as ***ipratropium.***

*During inspiration, we will have more negative intrapleural pressure from -5 to -8 mmH_2O, which will lead to expansion of the airways i.e. less radius and that will decrease the resistance to air flow which facilitates the air flow through the airways.
***The more negative intrapleural pressure, the lower the resistance.**

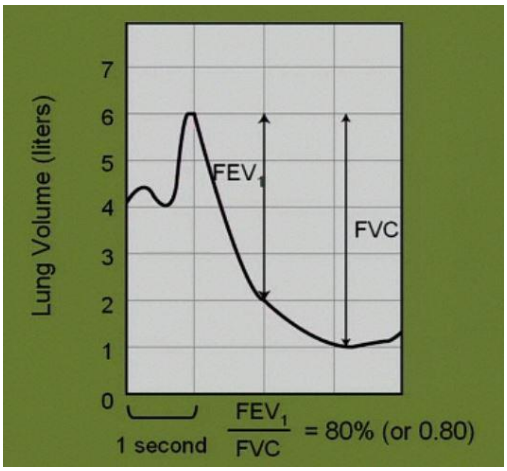
****The dynamic compression of the airways,*** which is a reflex that is present in the airways.
→ When ***expire***, ***forcefully*** and for a ***short time*** (short burst of expiration).
→ This empties the conducting zone which isn't involved in gas exchange.
→ This elicits a reflex that decreases the radius of the airways.
→ Creating what is called ***dynamic compression of the airways***.
→ The air flow becomes independent of the effort, and totally dependent on the radius, in other words it takes away the control of flow of air out of the lung by the effort to blow, but rather its determined by the radius of the airways (flow decreases) and therefore they are able to delay the emptying of the lung to the outside.

Video #9
Airway Resistance.
30th.11.2016

*The radius takes over the rate at which air leaves the lung

Video #10
Pulmonary function test.
30th.11.2016

__Pulmonary function test__ is a screening test, it can't diagnose specific conditions, but it can tell you whether it is obstructive or restrictive lung disease but won't distinguish between diseases within the two.



*This graph represents the readout sheet in a pulmonary function test.

*__Tidal volume (T_V)__ is 500mL.
*__Inspiratory capacity (IC)__ is approximately 2L, the maximum inspired air.
*__Functional residual capacity (FRC) is__ 4L, the volume of air that remains after a normal expiration.
*__Total lung capacity (TLC)__ is 6L.

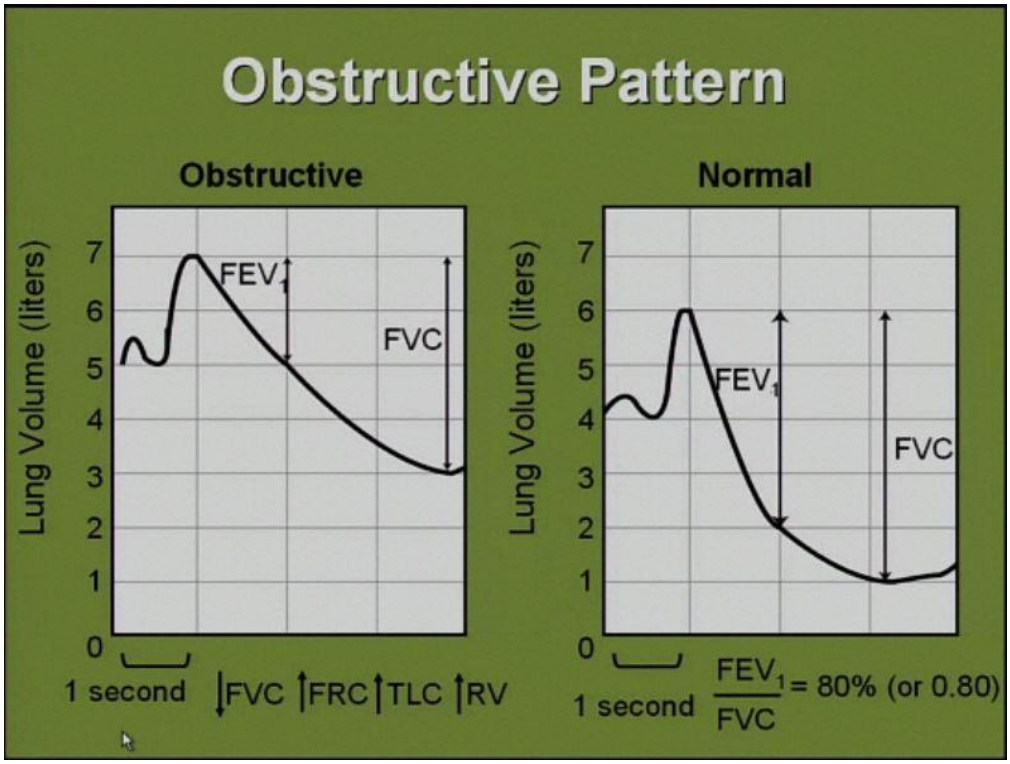
*The physician asks the patient to take and a deep breath (IC), and then to expire maximally, the volume that is expired in first second of expiration is called __First Expiratory Volume (FEV_1).__
→ Normal value for a healthy individual is 4L.

*__Forced vital capacity (FVC)__ is 5L, the maximum air that can be expired.
*__Residual volume (RV)__ is 1L, and it's what remains after fVC.
*__FEV_1/fVC ratio__ equals ⅘ which is 80%.

Video #10
Pulmonary function test.
30th.11.2016

Patterns of pulmonary function test with obstructive and restrictive lung diseases.

A) Obstructive pattern:



*Total lung volume (TLC) **increases**, reaches 7L.

*Inspiratory capacity (IC) remains the same, **not affected** stays 2L.

*Functional residual capacity (FRC) **increases**, reaches 5L.

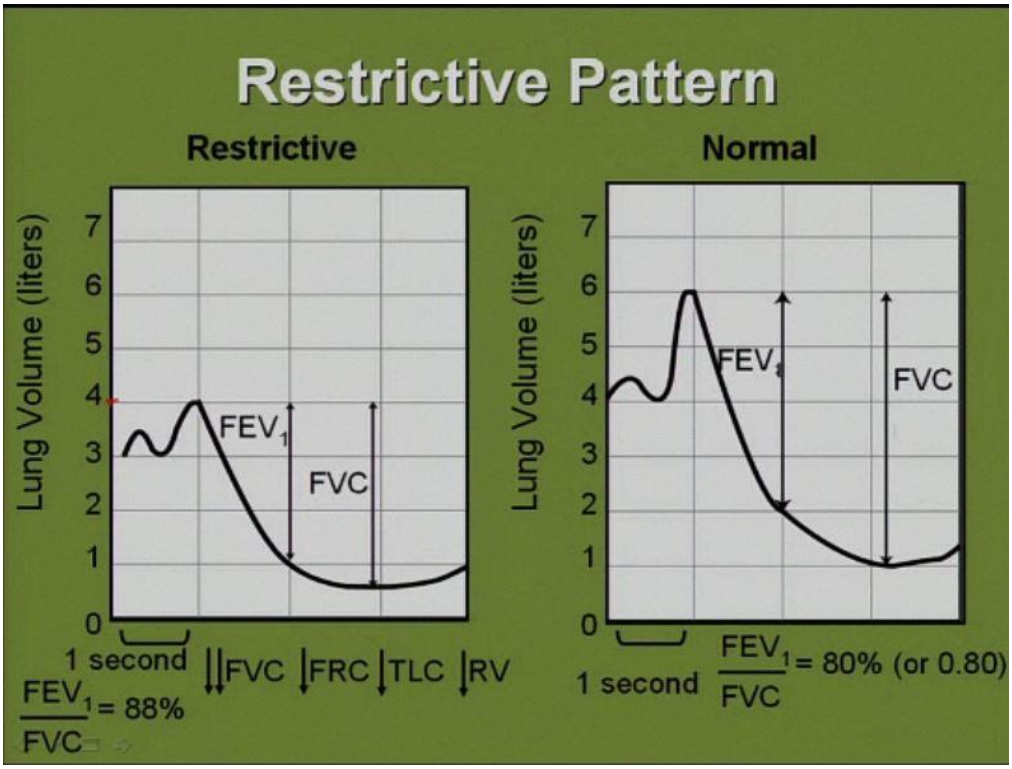
*First expiratory volume (FEV_1) **decreases**, reaches 2L.

*Forced vital capacity (FVC) **decreases**, reaches 4L.

*Residual volume (RV) **increases**, reaches more than 1L.

*FEV_1/FVC ratio **decreases**, reaches 50%.

B) Restrictive pattern:



*TLC: **Decreases**.

*IC: **Decreases**.

*FRC: **Decreases**.

*FEV_1: **Decreases**.

*FVC: **Decreases**.

*RV: **Decreases**.

*FEV_1/FVC ratio: **Increases**, can reach 90%

Video #10
Pulmonary function test.
30th.11.2016

*Summary:

Obstructive vs. Restrictive Pattern

Variable	Obstructive Pattern e.g., Emphysema	Restrictive Pattern e.g., Fibrosis
Total lung capacity	↑	↓↓
FEV_1	↓↓	↓
Forced vital capacity	↓	↓↓
FEV_1 / FVC	↓	↑ or normal
Peak flow	↓	↓
Functional residual capacity	↑	↓
Residual volume	↑	↓

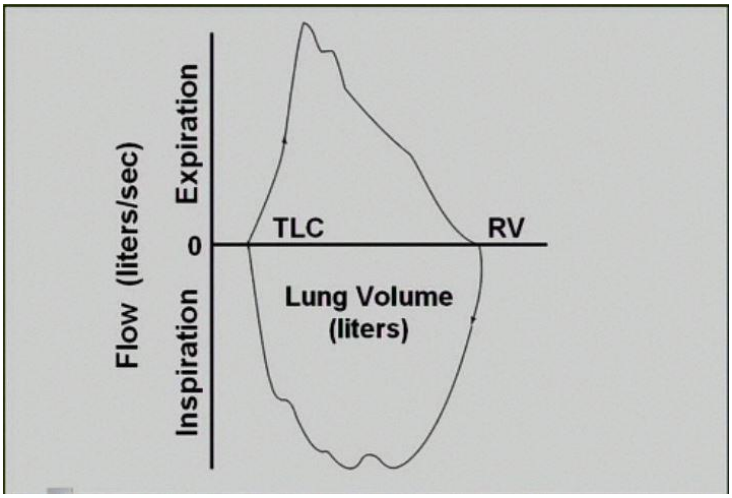
*<u>*Explanation:*</u>

*Pay attention to the fact that FEV_1 and FVC decreases in both conditions however, this decrease is not the same within each disease (note the arrows in the table that represent that relative decrease.

→ I.e. in obstructive disease FEV_1 decreases more than FVC.

→ And in restrictive disease FVC decreases more than FEV_1.

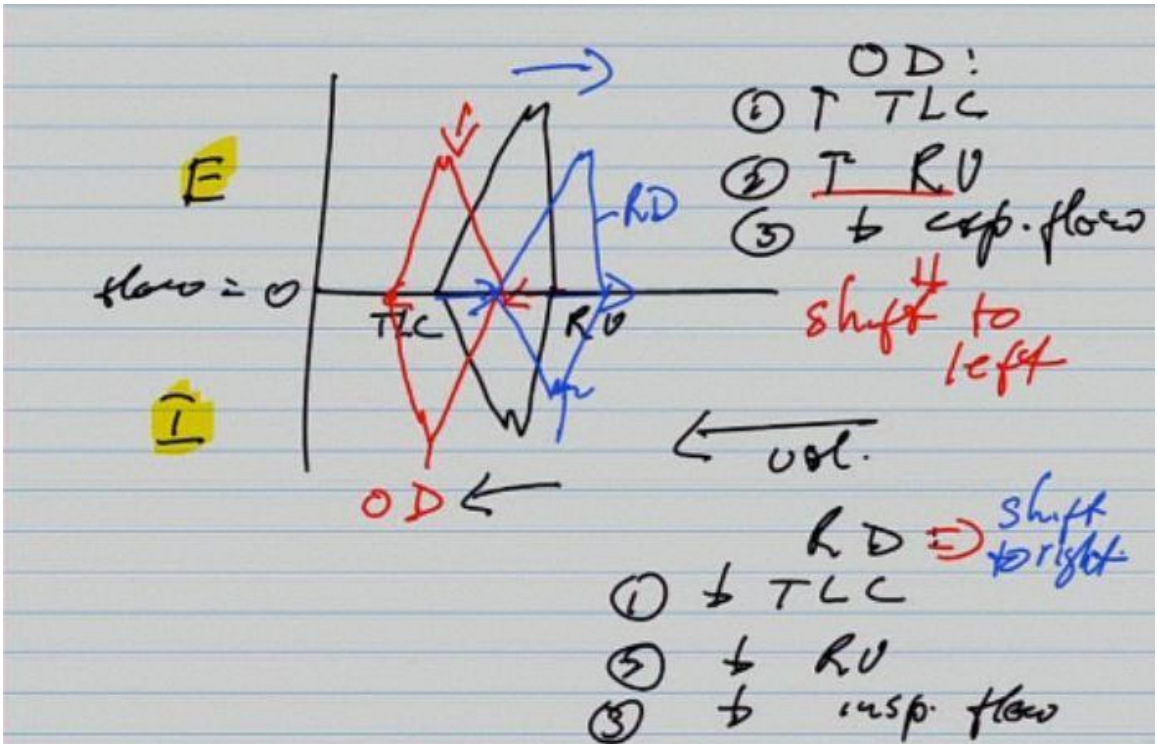
*This brings us to the ***Pulmonary Flow Loop***.



Video #10
Pulmonary function test.
30th.11.2016

*Expiration starts at TLC and end with RV, while inspiration starts with RV and ends with TLC.

*Pay attention that the volume (χ-axis) **increases to the left.**

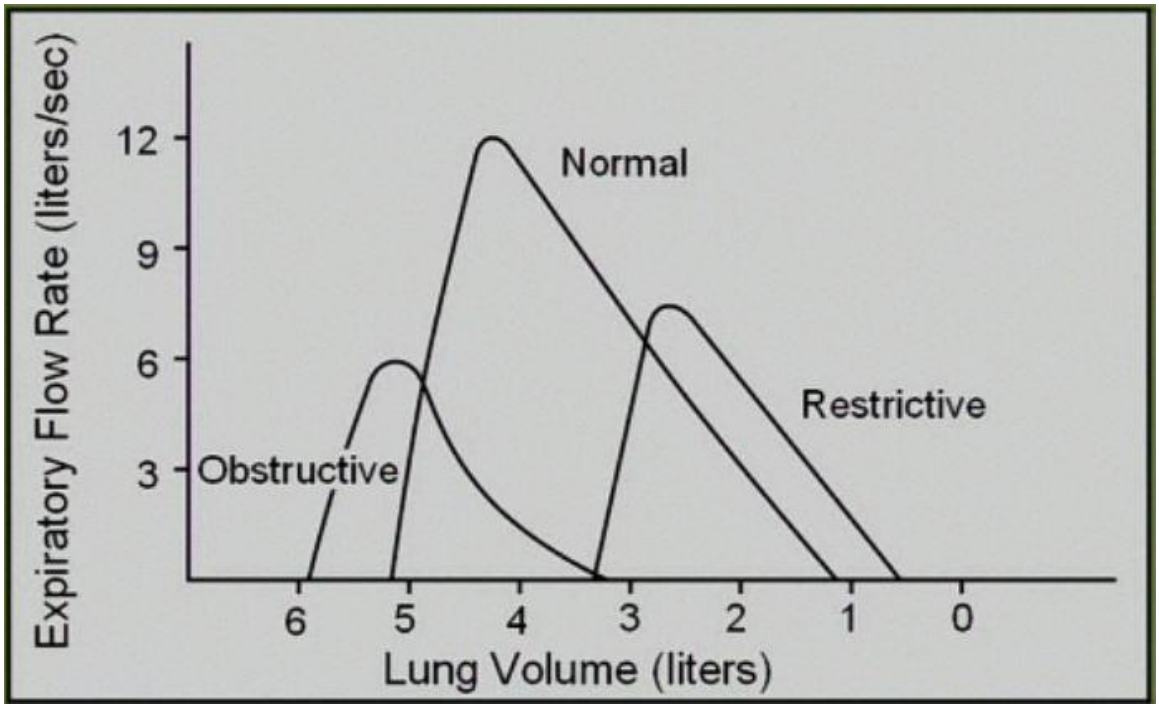


*Note the decrease in expiratory flow in obstructive lung disease and the decrease in the inspiratory flow in restrictive lung disease.

*Obstructive lung disease→ Left shift.
*<u>R</u>estrictive lung disease→ <u>R</u>ight shift.

Video #10
Pulmonary function test.
30th.11.2016

*Graph that only shows the expiratory portion.



Video #11
Alveoli-blood gas exchange.
30th.11.2016

*Factors that determine/rule gas exchange between the capillary and the alveolus.

*__Partial pressure of gas P_{gas}__ is the multiplication of the concentration of that gas in air times the atmospheric pressure

*$P_{Gas} = F_{Gas} \times P_{atm}$

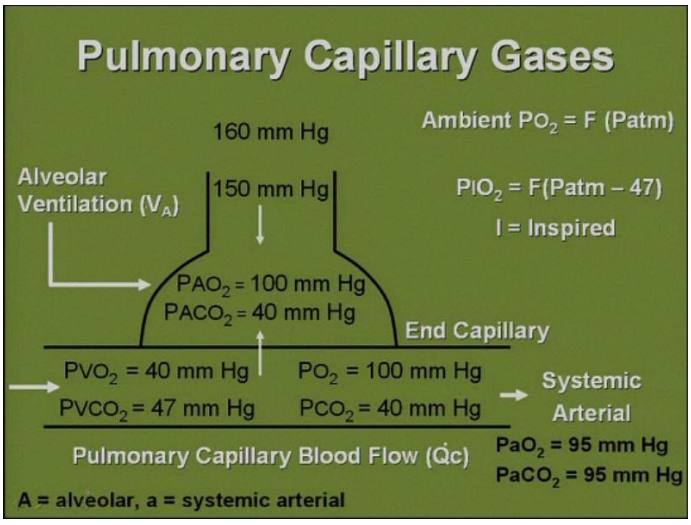
*P_{O2} = 160 mmHg (in the ambient air).

*For partial pressure of a gas in the inspired air, the air in the conducting zone that is sometimes referred as PI_{Gas}.

→$P_{O2} = F_{Gas} \times (P_{atm} - P_{H2O})$

*note that the partial pressure of H_2O is constant.

*P_{O2} = 150 mmHg (in the inspired air and we mean the air in the conducting zone).



*Gasses will diffuse down pressure gradient until they reach equilibrium.

*Therefore $P_{A\,O2}$ will be equal to $P_{a\,O2}$ that is 100 mmHg.

*And the $P_{A\,CO2}$ will be equal to $P_{a\,CO2}$ that is 40 mmHg.

Video #11
Alveoli-blood gas exchange.
30th.11.2016

*Diffusion equation:

$$\rightarrow \boldsymbol{Diffusion} = \frac{\boldsymbol{Surface\ area\ (SA)} \times \boldsymbol{Pressure\ difference\ (\Delta P)} \times \boldsymbol{Solubility}}{\boldsymbol{Membrane\ thickness\ (T)} \times \sqrt{\boldsymbol{Molecular\ weight\ (mW)}}}$$

*ΔP_{CO2} = 7 mmHg
*ΔP_{O2} = 60 mmHg

Solubility: CO > CO_2 > O_2.
*The solubility of carbon monoxide is the highest ***at the same pressure.***

*Therefore, in the diffusion across the alveolar wall is higher for carbon dioxide than oxygen even though oxygen has higher pressure gradient.

Video #12
Factors affecting alveolar P_{CO2}.
30th.11.2016

*Remember that alveolar oxygen equals the arterial oxygen and that the alveolar carbon dioxide equals the arterial carbon dioxide.

*Whatever factor affecting the alveolar carbon dioxide ($P_{A\ CO2}$) will affect arterial carbon dioxide ($P_{a\ CO2}$), this is in the absence of pathologies because one is sort of proportional to the other.

$$\rightarrow \boldsymbol{alveolar\ CO_2\ partial\ pressure}\left(P_{A\ CO_{2=}}\right) = \frac{\boldsymbol{Metabolism}}{\boldsymbol{Alveolar\ Ventilation}\ (\boldsymbol{V_A})}$$

$$\rightarrow \boldsymbol{P_{A\ CO2}} \ \frac{\mathbf{1}}{\propto}\ \boldsymbol{V_A}$$

*Hyperventilation → $P_{A\ CO2}$ **Decreases**
*Hypoventilation → $P_{A\ CO2}$ **Increases**

*Distinguish between alveolar ventilation and respiration, Hyperventilation involves respiratory zone blowing out carbon dioxide (deep breathing), while hypoventilation is shallow breathing and involves respiratory zone less so retaining carbon dioxide.

Video #13
Factors affecting alveolar O_2.
30th.11.2016

*Whatever factor affecting $P_{A\,O2}$ will affect $P_{a\,O2}$, assuming that there's no pathology, because they are proportional to each other.

*__*The gas equation*__ gives us all the factors that determine the partial pressure of oxygen in the alveolus

→$$\boldsymbol{Alveolar\ oxygen\ partial\ pressure\ (P_{A\,O2}) = (P_{atm} - 47)F_{O2} - \frac{P_{A\,CO2}}{R}}$$

*This equation gives us the partial pressure of oxygen in the alveolus that is in the respiratory zone and not in the inspired air in the conducting zone.
*47 represent the ***partial pressure of water vapor (P_{H2O})*** which is constant.
* ***F_{O2}*** represents the fraction of oxygen in the air and it equals .21
*__*Gas constant (R)*__ equals 0.8.
*P_{Co2} Here is the alveolar carbon dioxide partial pressure and its 40mmHg.

*$P_{A\,O2}$ = 100 mmHg

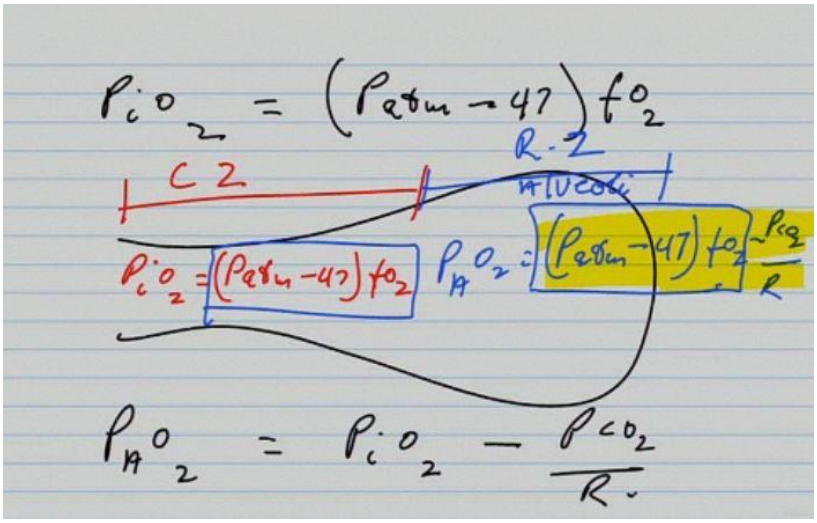
*Factors that affect alveolar oxygen are:
1) Atmospheric pressure (P_{atm})
2) Oxygen fraction (F_{O2})
---These two are the most important
3) $P_{A\,CO2}$, but variation in this parameter is low so it won't affect that much.

*If atmospheric pressure decreases as in high altitudes, partial pressure of oxygen in alveolus will decrease.

*A decrease in oxygen fraction, partial pressure of oxygen in the alveolus will decrease.

*These two factors will affect partial pressure of oxygen in the alveoli and arterial partial pressure of oxygen in the same way.

Video #13
Factors affecting alveolar O_2.
30th.11.2016



$$P_{A\,O2} = P_{i\,O2} - \frac{P_{CO2}}{R}$$

Video #14
Diffusion capacity of the lung.
30th.11.2016

*If the substance equilibrates between the capillary and the interstitium, it is said to be in a ***perfusion-limited*** situation.

*if it doesn't it is said to be in a ***diffusion-limited*** situation, and here we are referring to the alveoli not the capillary.

*In terms of solubility: $CO > CO_2 >> O_2$.
*In terms of affinity to hemoglobin: $CO > O_2 >> CO_2$.

***Question:** Which of the following gases is best indicator to measure the diffusion capacity of the lung at sea level?

(a) Oxygen
(b) Carbon dioxide
(c) Nitrogen
(d) Carbon monoxide
(e) Helium

→ CO is the most soluble gas.

****Diffusion capacity of the lung:*** Ability of the lung to allow gases to diffuse across its wall.

*Carbon monoxide CO has an extremely high affinity for the lung for the hemoglobin.

****When it is present in the blood, essentially all is combined with Hb, and the amount dissolved in plasma is zero i.e. diffusion-limited situation.***

*The uptake of carbon monoxide depends only on the structural features of the lung which is the diffusion capacity.

*Carbon monoxide is a unique gas in that it's always in a diffusion-limited situation.

*Carbon monoxide poisoning, because of the greater solubility of CO, it will out-diffuse other gases and will dissolve in the blood, however, due to its huge affinity towards Hb it will immediately bind Hb competing with O_2 for hemoglobin and this is reflected at its partial pressure (P_{CO}) which goes to zero.

→All of the CO will upload to hemoglobin, P_{CO}= zero.

Video #15
Transport of gases.
30th.11.2016

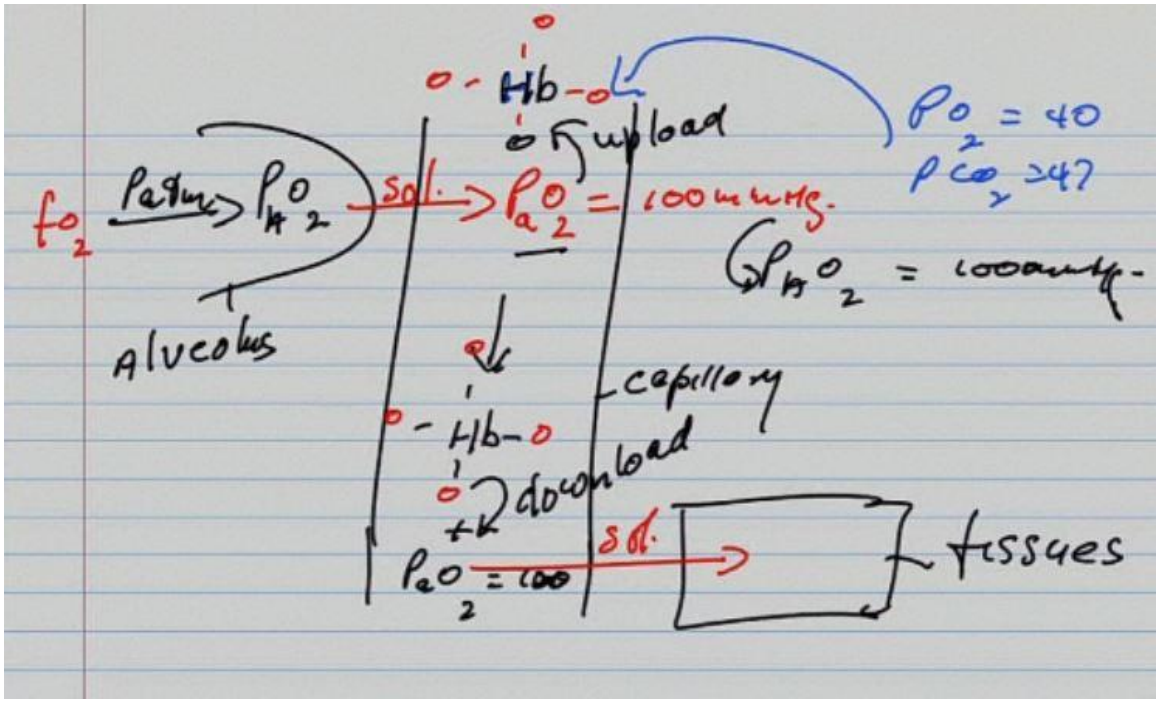
*The beginning of the video is easy and doesn't need notes.

---

*Oxygen doesn't go directly from alveoli to hemoglobin, it dissolves in plasma then from plasma it uploads to hemoglobin.

*Oxygen doesn't directly go from the hemoglobin to tissues; it dissolves in plasma then is downloaded to tissues.

*Oxygen must be dissolved in plasma in order to diffuse across membranes, and then it diffuses based on solubility.



Video #15
Transport of gases.
30th.11.2016

*The total oxygen ***(oxygen content)*** = 20% volume.
→I.e. 20 mL O_2 / 100 mL blood

*You need to be able to distinguish between oxygen content and P_{O2}.

*oxygen can be found either:
1) ***Dissolved in plasma***, which represents $P_{a\,O2}$ and accounts for 0.3% volume (0.3 mL O_2/100 mL blood), which gives us a partial pressure $P_{a\,O2}$ of 100 mmHg.
2) ***Attached to hemoglobin***, which accounts for 19.7% volume, i.e. most of the oxygen content, this volume that is carried by the hemoglobin depends on two factors **hemoglobin conc. [Hb]**, and on **hemoglobin saturation with oxygen**.

*Normally; [Hb]→ 13-15 grams.
****polycythemia*** → Decreased
****Anemia*** → Increased

*In polycythemia [Hb] increases, that means that the amount of oxygen carried by hemoglobin will increase, and that means that the total oxygen content will increase, this DOES NOT affect $P_{a\,O2}$ (stays normal).

*In anemia [Hb] decreases, that means that the amount of oxygen carried by hemoglobin decreases, and that means that the total oxygen content will increase; this DOES NOT affect $P_{a\,O2}$ (stays normal).

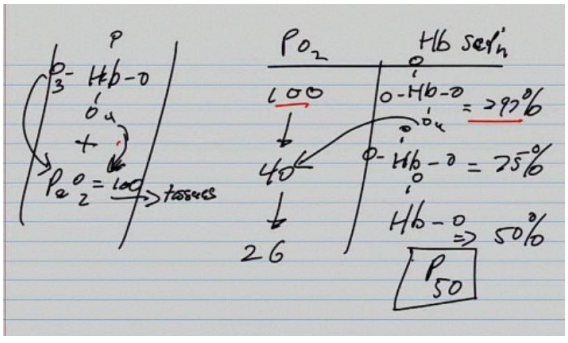
*Therefore in anemia, especially acute, we don't expect changes in the $P_{a\,O2}$, because we are not affecting it (dissolved in plasma).

Video #15
Transport of gases.
30th.11.2016

*The second factor that affects the amount of oxygen attached to Hb which is the hemoglobin saturation.
*Each hemoglobin molecule has the capacity to carry four oxygen molecules.
*When all of the four binging sites of hemoglobin are occupied with O_2 we say the Hb saturation is almost 100%.
*Each oxygen molecule of the four has different affinity towards Hb, recall the oxygen dissociation curve, so the last oxygen to bind (no. 4) will detach easier than the others and then 3 and so on (last to bind and first to detach).
*This is seen at different partial pressures of oxygen.
*At partial pressure 100 mmHg near the lungs, the fourth oxygen can't detach and become dissolved in plasma, due to high Partial pressure; plasma is fully saturated and prevents oxygen unloading.
*As the P_{O2} falls (to 40 mmHg), the fourth oxygen can detach, and the hemoglobin at this P_{O2} is 75% saturated.
*As P_{O2} continues to fall reaching 26 mmHg, the third oxygen will detach and the hemoglobin at this partial pressure (***P_{50}***) is 50% saturated.

*P_{50} is the pressure at which hemoglobin is 50% saturated, and it is the minimal saturation at which we can find Hb at physiological conditions and at extreme conditions (still physiological).

*If hemoglobin saturation reaches below 50% this is an indicator of ***hemolysis*** which is destruction of Hb.



*A graph plotted based on the previous table,

→ ***Hemoglobin-Oxygen Dissociation Curve***.

***Right shift (Decreased affinity)**

1) Increase in temperature
2) Increase in $[H^+]$ → Lower P_H
3) Increase in CO_2
4) increase in DPG's (Diphosphoglycerate, intermediate in hexose monophosphate shunt in the synthesis of five carbon sugars, this is found in patients with ***chronic polycythemia***.

*<u>Whenever we have right shift:</u>

→ Decrease in affinity

→ Increase in oxygen partial pressure P_{O2} that is dissolved in plasma

***Left shift (Increased affinity),** the exact opposite.

1) Decrease in temperature
2) Decrease in $[H^+]$→ Higher P_H
3) Decrease in CO_2
4) Decrease in DPG's

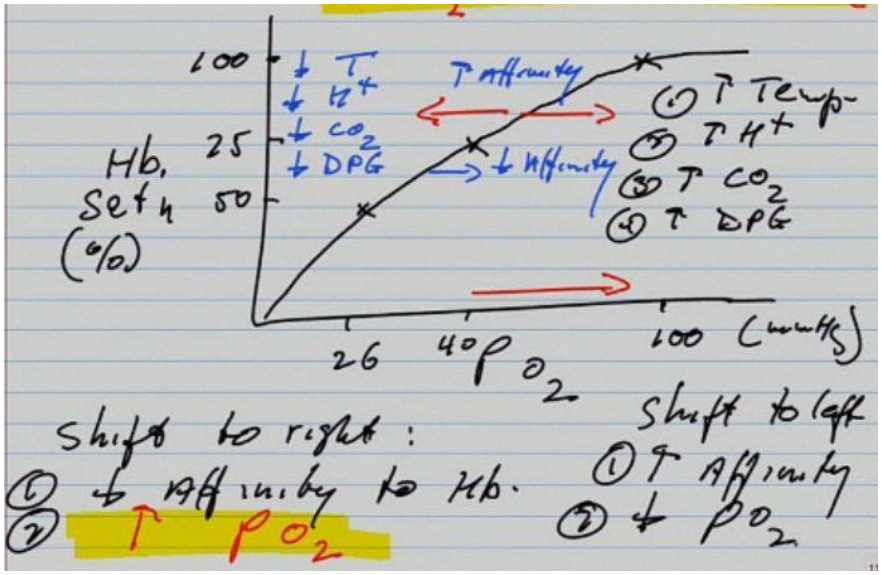
*<u>Whenever we have left shift:</u>

→ Increase in affinity

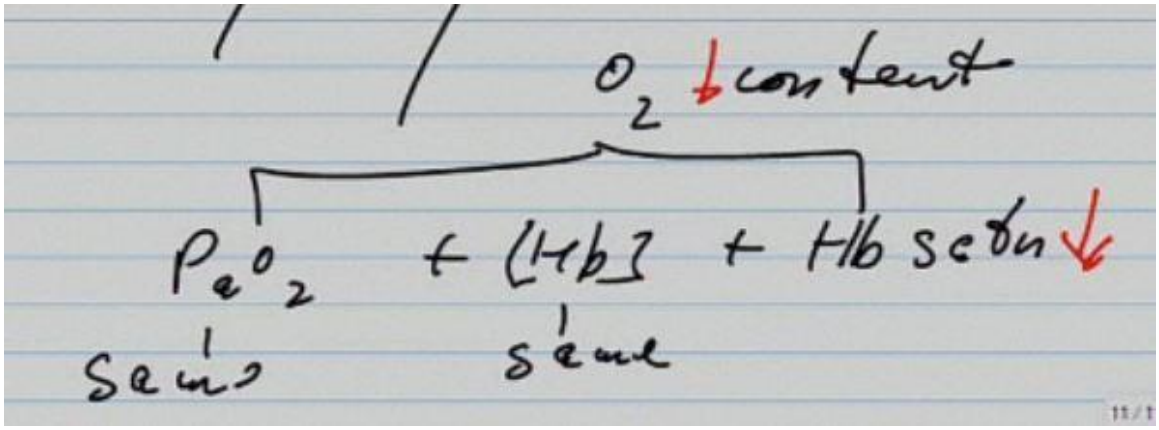
→ Decrease in P_{O2}

*A patient with hypothermia will have decreased P_{O2} and his capillaries will constrict; that's why he'll look pale.

Video #15
Transport of gases.
30th.11.2016

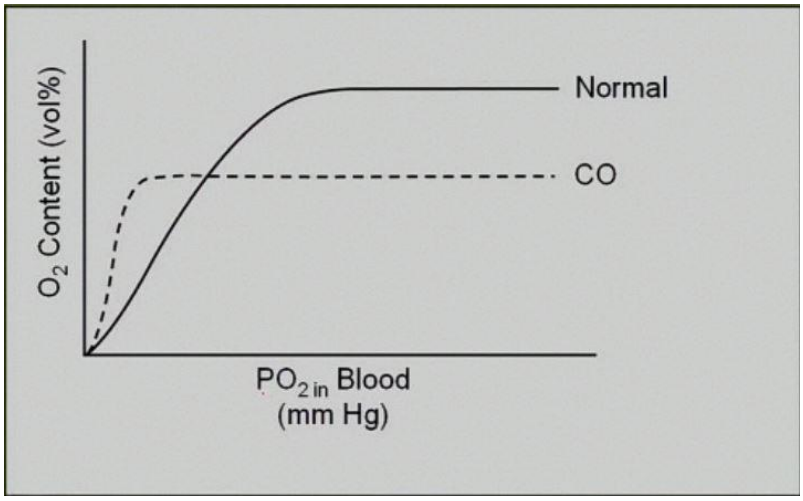


*In acute carbon monoxide poisoning the P_{O2} stays normal (100 mmHg), and the hemoglobin saturation decreases which accounts for decreased oxygen content.



*To diagnose that you should assess P_{50}.

*Pay attention that the Y-axis isn't Hb saturation but its oxygen content.



*The (plateau) is referred as the ***carrying capacity*** and it decreases with CO poisoning due to decrease in Hb saturation, of course without affecting the P_{O2}.

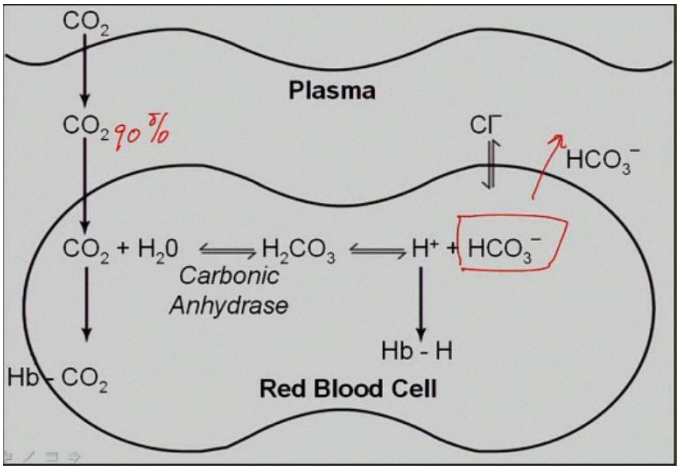
	PO_2	Hb Concentration	O_2 per g Hb	O_2 Content
Anemia	N	↓	N	↓
Polycythemia	N	↑	N	↑
CO poisoning (acute)	N	N	↓	↓
N = normal; O_2 per g Hb = % saturation				

Video #16
Transport of CO_2.
1st.12.2016

*5% of total CO_2 is ***dissolved in plasma***, responsible for the $P_{a\ CO2}$.

*5% of total CO_2 is carried as ***carbamino compounds***.

*90% of total CO_2 will ***diffuse into the red blood cell***, which will be which will be converted to HCO_3^-.



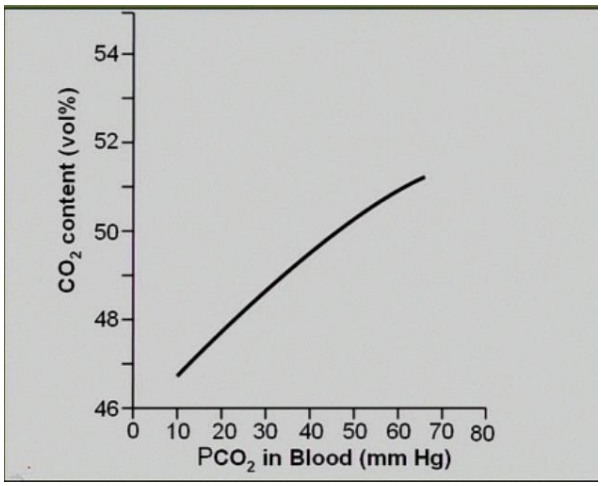
*The unleashed negative bicarbonate to plasma will create electrical imbalance in the plasma, Cl^- influx occurs to correct his imbalance a process called ***The Chloride Shift***.

*If a patient has ***hypochloremia*** his ability to exchange chloride ions with bicarbonate will be impaired, therefore his ability to transport bicarbonate will be impaired so the reaction in the figure will undergo right shift (accumulation of bicarbonate).

*Net result→ this patient will not be efficient in transporting CO_2, and will accumulate CO_2 in blood and will eventually develop or at risk of developing acidosis.

*That's why hypochloremia can yield an acidotic result.

Video #16
Transport of CO_2.
1st.12.2016



*As the P_{CO2} increases the CO_2 content increases.

*P_{CO2} is normal at about 40 mmHg (arterial CO_2 $P_{a\ CO2}$), and we can deduce the carbon dioxide content in the blood.

Video #16
Transport of CO_2.
1st.12.2016

Video #17
Regulation of alveolar ventilation.
1st.12.2016

*There are two groups of receptors involved in the regulation of ***alveolar*** ventilation:

1) ***Central chemoreceptors***

(I) Found in the medulla of the brain

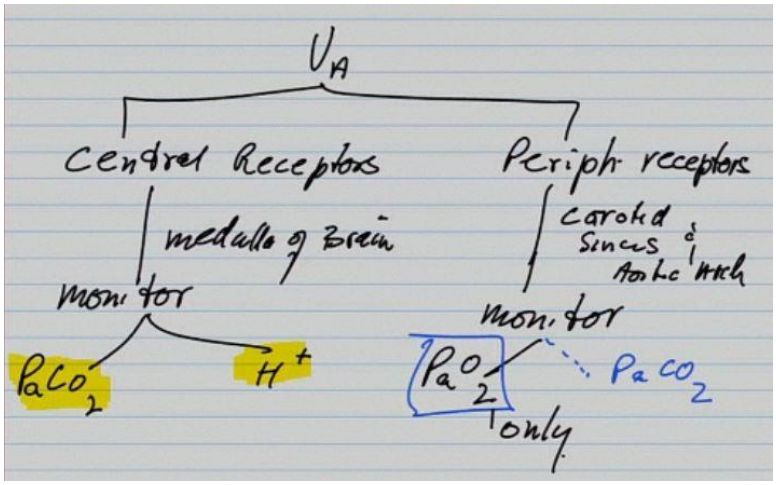
(II) Monitors $P_{a\,CO2}$ and H^+

2) ***Peripheral chemoreceptors***

(I) Found around the carotid sinus and aortic arch

(II) Monitor mainly $P_{a\,O2}$, and to a lesser extent $P_{a\,CO2}$.

*The peripheral receptors are the only ones responsible for monitoring the arterial oxygen $P_{a\,O2}$.

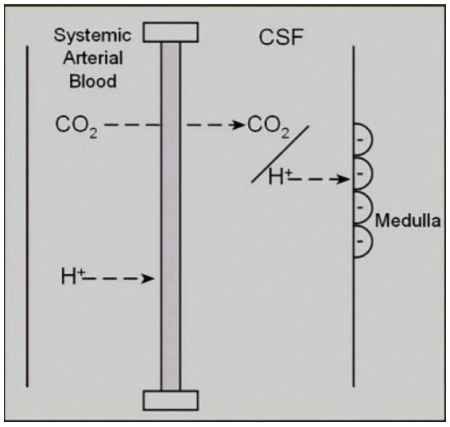


****Rule: Under normal circumstances, the central receptors are the main drive for alveolar ventilation V_A and do that by monitoring $P_{a\,CO2}$ mainly.***

****Exception: if we have a dramatic fall in $P_{a\,O2}$ of less than 80% or fall in F_{O2} less than 17%, the peripheral receptors take over control of alveolar ventilation V_A, regardless of what's happening in the $P_{a\,CO2}$.***

Video #17
Regulation of alveolar ventilation.
1st.12.2016

*CSF is the cerebro-spinal fluid.



***Carbon dioxide can easily diffuse across the BBB** and thereby stimulate the central receptors found in the medulla; **however H^+ cannot cross the BBB**, and therefore their presence in the CSF is coming from another source possibly an infection and not from the blood.

*If a patient has meningitis he will hyperventilate, due to excessive production of H^+ in the CFS and stimulation of the central receptors and resulting in hyperventilation.

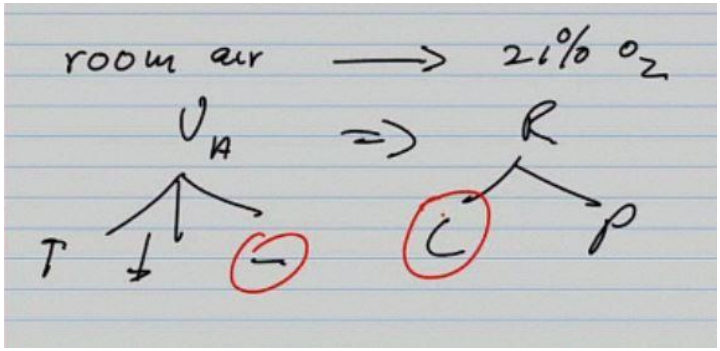
→A patient who over dosed morphine (a drug that suppresses the medulla) he will have hypoventilation, this will result in elevated $P_{a\,CO2}$ and as the central receptors are blocked by morphine they aren't responding to the increased partial pressure of CO_2.

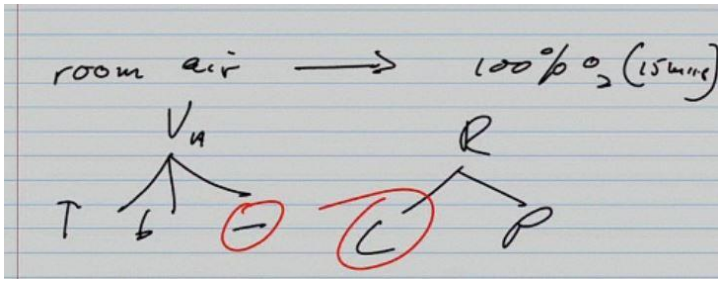
→Due to hypoventilation $P_{a\,O2}$ will decrease stimulating the peripheral receptors.

→The peripheral receptors are now the main drive for regulation of alveolar ventilation V_A.

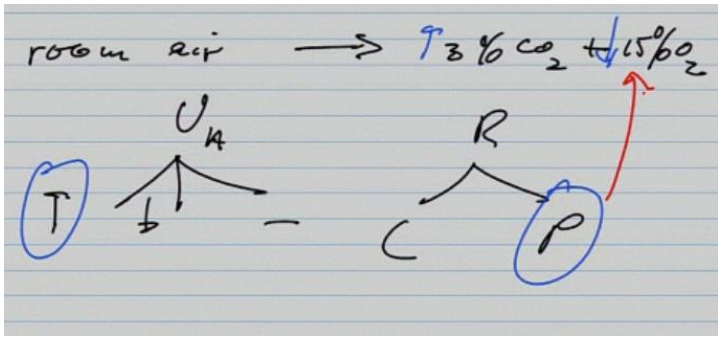
→If you correct $P_{a\,O2}$ you are removing the ventilatory drive via peripheral receptors, as if you stop peripheral receptors stimulation, patient will collapse.

*In ***anemia*** $P_{a\,CO2}$ and P_{O2} won't be affected, what decreases is the total oxygen content, therefore we ***won't have ventilatory response*** to this kind of hypoxia, this also applies to CO poisoning.





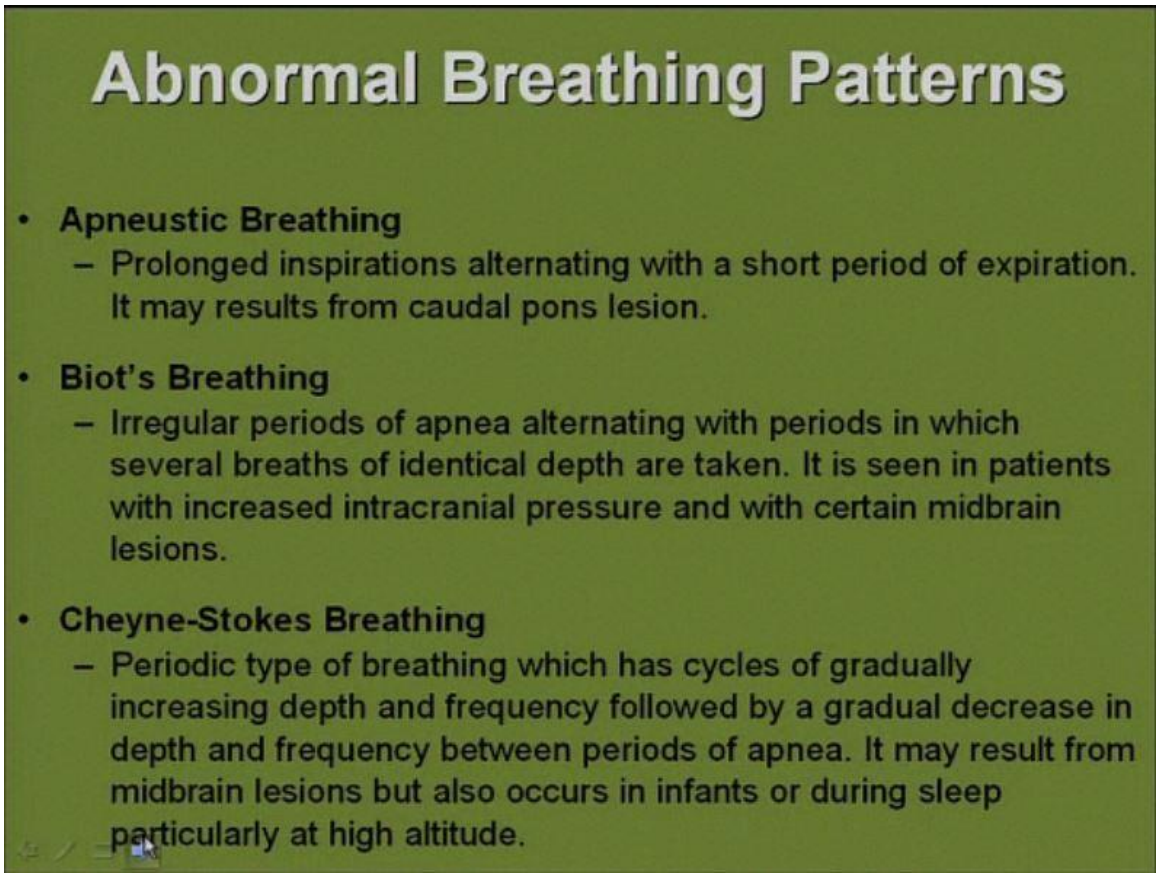
*In any case increasing P_{O2} doesn't affect peripheral receptors, its decreasing P_{O2} that stimulates the RR.



*rule and exception

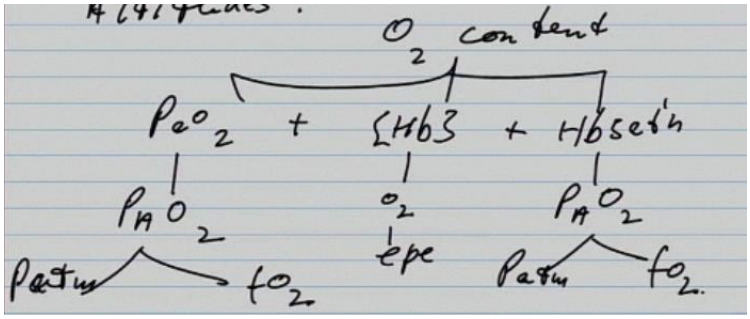
*__*Respiratory rhythm*__, expiration is longer than inspiration.

*If we have a stroke and damage in the medulla this results in abnormal breathing patterns.



Video #18
Unusual environments
1st.12.2016

*Recall:



*__Acclimatization__ is the process in which an individual organism adjusts to a gradual change in its environment (such as a change in temperature, humidity, photoperiod, or pH), allowing it to maintain performance across a range of environmental conditions.

Unusual Environments

High Altitude	Acute Changes	Acclimatization
PAO_2 and PaO_2	decrease	remains decreased
$PACO_2$ and $PaCO_2$	decrease	remains decreased
Systemic arterial pH	increase	decreases to normal via renal compensation
Hb concentration	no change	increases (polycythemia)
Hb % sat	decreased	remains decreased
Systemic arterial O_2 content	decreased	increases to normal

*Unusual factors,

(1) ***High altitudes***

(2) ***High pressure***

Video #18
Unusual environments
1st.12.2016

1) ***High altitudes:***

*At ***high altitudes*** P_{atm} decreases so $P_{A\,O2}$ decreases which is reflected to $P_{a\,O2}$, and as $P_{a\,O2}$ decreases hemoglobin saturation decreases, and as a result oxygen content decreases.

*If $P_{A\,O2}$ and $P_{A\,O2}$ decrease, this will stimulate ventilation by peripheral receptors which decrease $P_{A\,CO2}$ and $P_{a\,CO2}$.

*Acclimatized→ Think P_H, 3-4 weeks.

*In acclimatization $P_{A\,O2}$ and $P_{A\,O2}$ will still decreased because the reason of this is P_{atm} which will not change, and so $P_{A\,CO2}$ and $P_{a\,CO2}$ will remain decreased, and so ***hyperventilation will stay***.

*P_H will return to normal because of decreased bicarbonate production by the kidney.

*When oxygen content decreases, this will stimulate ***erythropoietin*** release from the kidney which is a factor involved in ***erythropoiesis***, so hemoglobin concentration will increase and that is called ***physiological polycythemia***.

*as the hemoglobin saturation is affected by P_{atm} and not controlled by the body it will also decrease at high altitudes.

*Oxygen content returns normal in acclimatization.

2) ***High pressure:***

*For example at deep sea diving.

*At sea level (760 mmHg) Nitrogen is insoluble and can't diffuse across membranes to the blood.

*An increase in pressure gasses including nitrogen solubility increases due to the fact that pressure is directly proportional to solubility, so nitrogen will diffuse to the blood and will dissolve in the plasma (increased P_{N2}).

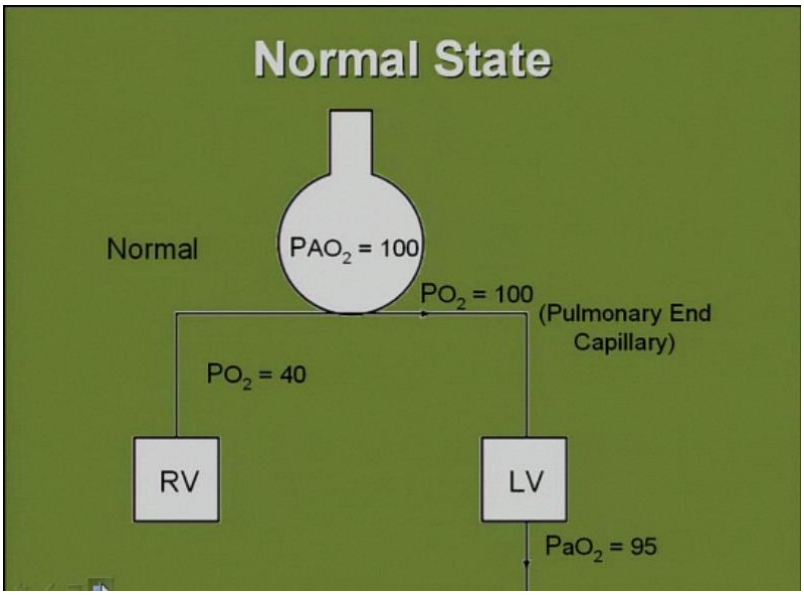
*The presence of nitrogen in the plasma is not a problem by itself, however, sudden loss of pressure (loss of solubility) which results in undissolving of nitrogen from the plasma forming ***nitrogen bubbles*** in the plasma resulting in what we call ***nitrogen narcosis*** which is no different that air embolism, this is called ***Caisson's disease.***

*There should be re-pressurizing to what's called the ***shelf*** redissolve nitrogen, and then we can slowly release nitrogen.

Video #19
Hypoxia
1st.12.2016

*__A-a difference__ is an important parameter to decide whether someone has hypoxia or not, and is the difference between alveolar oxygen and arterial oxygen.

*As we know that the arterial oxygen should be equal to the alveolar if we have a perfect lung, in our bodies this is not always the case and some of the oxygen will not be sharply equal and we have A-a difference of 5-10 mmHg.



*__Hypoxia__ is decrease in P_{O2} and is considered severe if P_{O2} is less than 80%.

*Possible causes of hypoxia:
1) Hypoventilation, decreased V_A, and treatment is to give O_2
2) Diffusion impairment, e.g. Fibrosis
3) Perfusion limited situation, e.g. Pulmonary shunt

*$\dot{V}/Q$ __Ventilation-Perfusion mismatch__ is not a pathology by itself because it occurs in all of the above mentioned cases, and will be discussed separately.

Video #19
Hypoxia
1st.12.2016

*Characteristics of ***hyperventilation***:
1) $P_{a\,O2}$ Decrease.
2) A-a difference is zero

*Characteristics of ***diffusion impairment***:
1) $P_{a\,O2}$ Decrease
2) A-a difference > zero

*A-a difference when greater than zero rules out hypoventilation.

*Characteristics of ***pulmonary shunt***:
1) $P_{a\,O2}$ Decrease
2) A-a difference > zero

****Atelectasis*** is an example of pathology with pulmonary shunt.

→To differentiate between diffusion impairment and pulmonary shunt, we give 100% O_2 for 15 minutes, and then we measure the arterial blood gases and observe the change in $P_{a\,O2}$.

→ ***If there's significant increase of $P_{a\,O2}$ (of more than 10 mmHg increase)***, which means the high pressure oxygen that we gave was able to get across, this tells us that the problem is ***diffusion impairment,*** at which there's problem in the alveolar wall and if we increase pressure of O_2 will force the oxygen to cross the impairment so we observe significant increase in arterial partial pressure of oxygen.

→ ***if there's no significant increase of $P_{a\,O2}$ (of less than 10mmHg increase)***, that tells me that the problem is ***pulmonary shunt*** (diffusion limited situation) as seen in atelectasis at which we have collapsed alveoli and no matter how much pressure we apply oxygen will not reach the blood and therefore we won't observe significant increase in $P_{a\,O2}$.

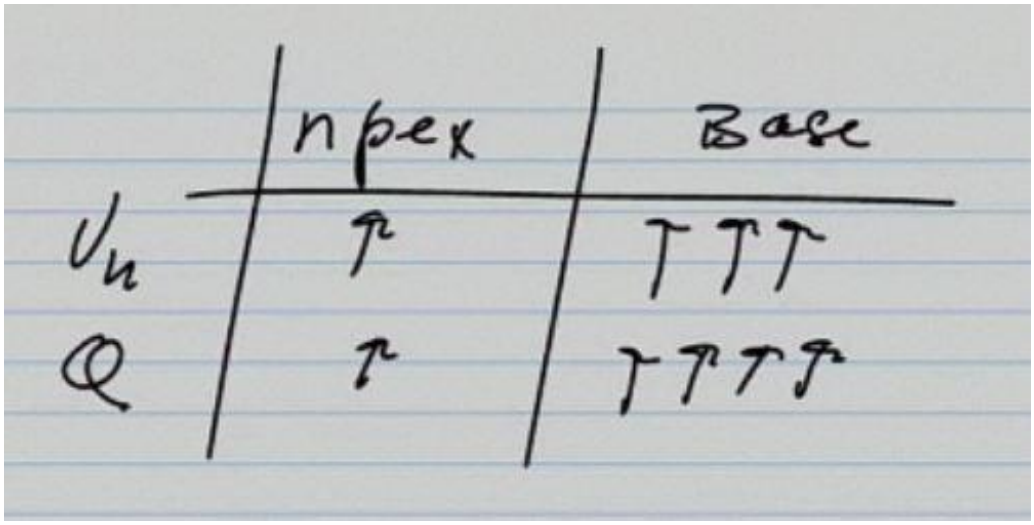
Video #20
Ventilation perfusion mismatch
2nd.12.2016

*V/Q in a perfect lung is 1 in the ideal case at which every milliliter of air is matched with every mL of blood perfusing that alveoli, usually it's around 80% as we don't have perfect lung.

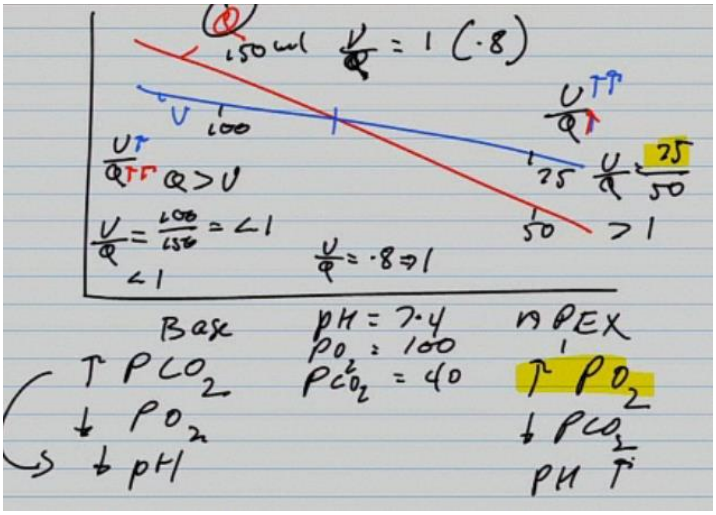
*we can divide the lung functionally as apex and base.

→ Larger portion of the air will flow to the base due to the effect of gravity.

→ Larger portion of blood will also go to the base more than the apex, due to the gravity.



Video #20
Ventilation perfusion mismatch
2nd.12.2016



*As mentioned the base receives more ventilation and more perfusion.

*Somewhere in the middle of the curve at which two lines intersects ventilation and perfusion are equal at which $^{V}/_{Q} = 0.8$, the P_H will be 7.4, P_{O2} is 100 and P_{CO2} is 40 (arterial blood gases are normal); because of the perfect exchange being able to get rid of all CO_2 and to bring in O_2 and to stabilize P_H.

→***At the base:*** doing the ventilation-perfusion ratio in the base which has more blood than air (relatively, as blood is heavier and more affected by the gravity than air) so the V/Q ratio will be < 1 in other words, in the base the perfusion is greater than ventilation so we have net surplus of blood.

The blood coming to the base is venous blood, rich in CO_2, excess carbon dioxide that isn't being matched with ventilation to get rid of.

So at the base, there will be ***increased P_{CO2}*** (net retention of CO_2 and ***decreased P_{O2}*** as all the oxygen that is coming is taken to the blood (relative short in oxygen supply), oxygen is not matching high perfusion, and due to increase in carbon dioxide there will be ***lower P_H***.

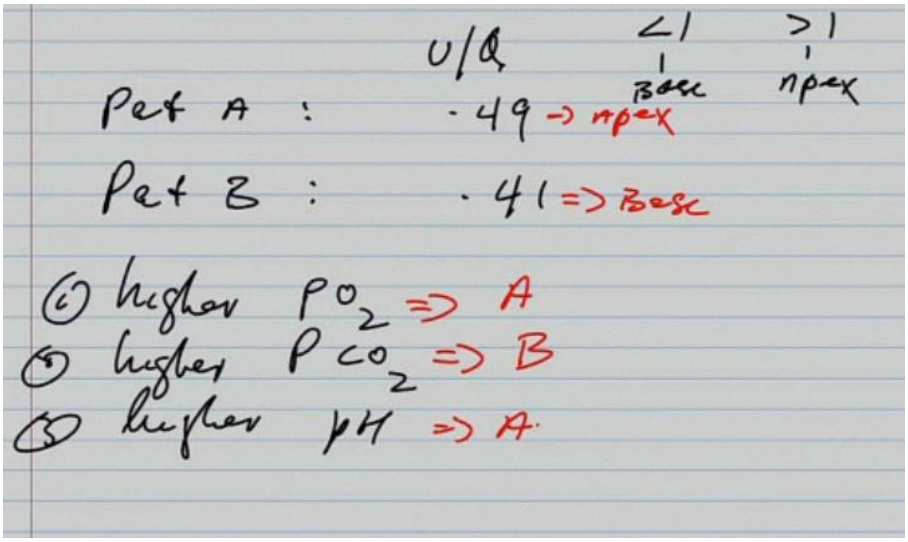
Video #20
Ventilation perfusion mismatch
2nd.12.2016

→***At the apex:*** doing V-Q match, we have more ventilation than we have perfusion; V/Q will be > 1, so we have surplus of air (ventilation) we have more air than blood coming to the apex and so we have surplus of oxygen (relative excess of oxygen supply).

This explains why ***Tuberculosis (Tb)*** goes to the apex, because of the physiological mismatch that is taking place. So at the apex, there will be ***increased P_{O2}***, and there will be ***decreased P_{CO2}*** because all of the blood that is going to the apex will be able to get rid of its CO_2, and therefore at the apex we will have ***decreased P_H***.

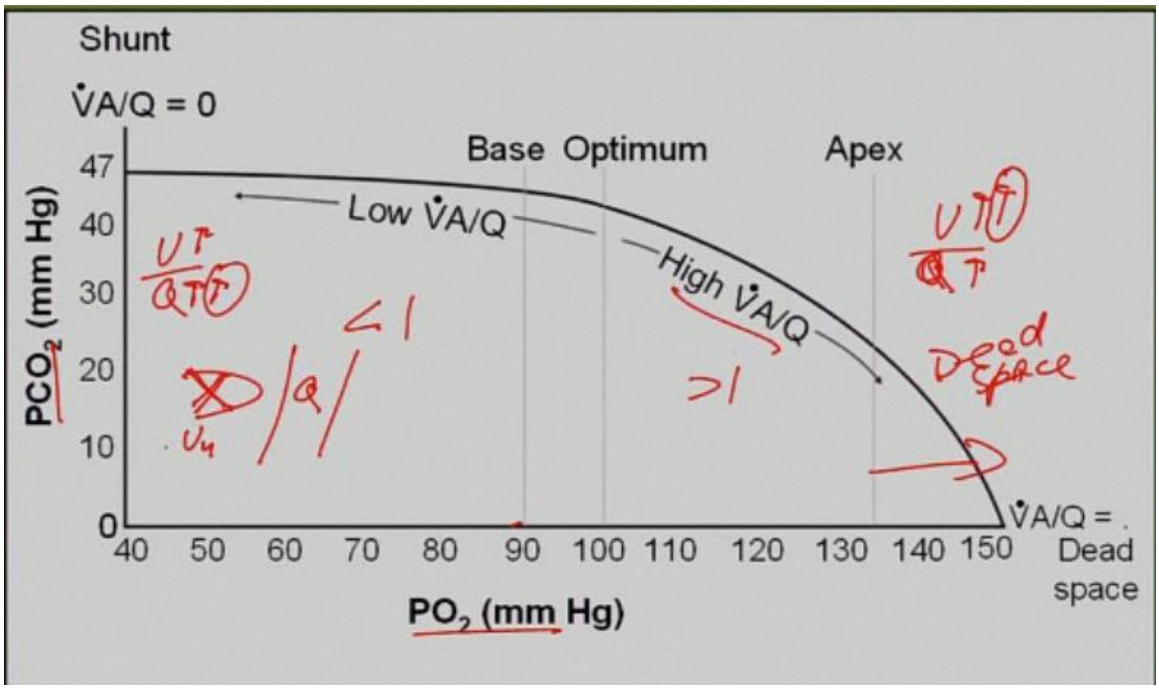
*The base is to CO_2.

*The apex is to O_2.



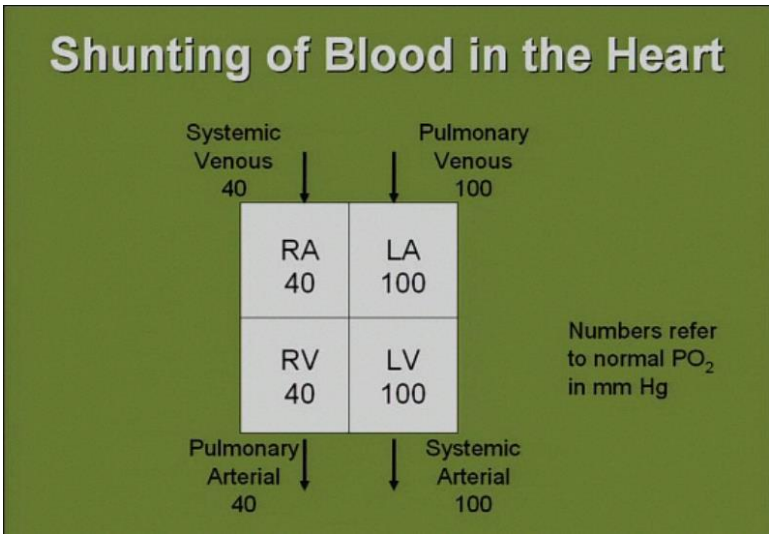
Video #20
Ventilation perfusion mismatch
2nd.12.2016

*If someone inhales a peanut, it will obstruct ventilation and of course not perfusion, this will decrease the V/Q ratio, as we are moving more base so P_{O2} decreases, P_{CO2} increase, P_H will decrease and the flow will decrease due to ***hypoxic vasoconstriction***.



*At the base there is ***shunt-like situation***.
*At the apex there is ***dead space-like situation.***

Video #21
Shunting blood in the heart and its effect on oxygen content and distribution.
2nd.12.2016



Consequences of Three Different Left-to-Right Shunts

	Atrial Septal Defect	Ventricular Septal Defect	Patent Ductus (newborn)
Systemic arterial PO_2	no change	no change	no change
Right atrial PO_2	↑	no change	no change
Right ventricular PO_2	↑	↑	no change
Pulmonary arterial PO_2	↑	↑	↑
Pulmonary blood flow	↑	↑	↑
Pulmonary arterial pressure	↑	↑	↑