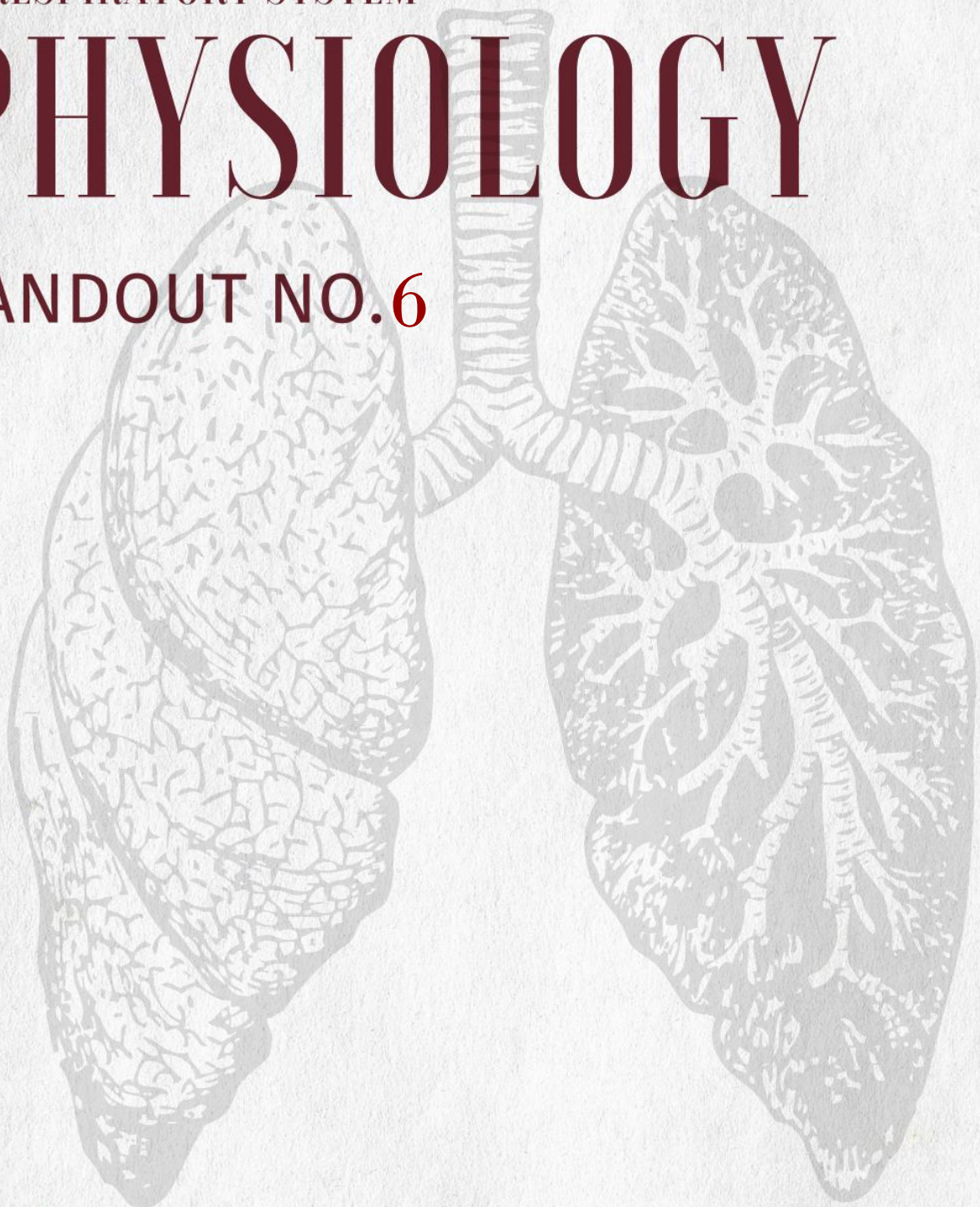
RESPIRATORY SYSTEM

PHYSIOLOGY

HANDOUT NO.6



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Ventilation- perfusion ratio

Color code
slides
doctor
important
Additional info

Bronchial Circulation

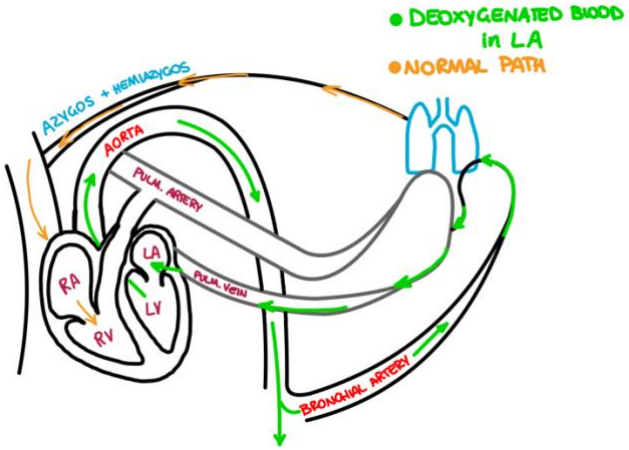
-When we talk about Bronchial Circulation, which is the blood supplying the bronchi and the bronchioles, it:

1. Arises from the aorta, the arterial side of the circulation.
2. Part of systemic circulation (oxygenated), not form pulmonary circulation.
3. The bronchial artery Receives about 1-2% of left ventricular output.
4. Mainly Supplies the supporting tissues of the lungs, including the connective tissue, septa, and bronchi, keeping the non-alveolar part of the lung oxygenated.
5. There are two drainage options, about 50% of the bronchial veins drain into the right atrium through the azygos and hemi-azygos veins, while the other 50% empty into the pulmonary veins, which lead to the left atrium. This results in a small mixture of blood in the left atrium, where approximately 2% of the blood is venous (deoxygenated) and 98% remains arterial (oxygenated). Cardiac veins (Thebesian veins) in addition to the bronchial veins contribute to **deoxygenated** blood reaching both the left and right chambers of the heart.

So, a question the doctor has for us is: since the blood pumped out from the left ventricle is originally from 2 sites:

- Right ventricle > pulmonary artery > pulmonary capillaries > **pulmonary veins**. Let's say 5L come from here
- And a small quantity of blood, 2%, comes from the bronchial veins

Does that mean that the left ventricular output is equal or more than the right ventricular output? (from the slide: The blood flow into left side is greater by 2%...do you think left ventricular output is equal to right ventricular output?



Extra: The blood leaving the left ventricle into the aorta is considered part of the systemic circulation, because this blood goes to various organs before eventually returning to the right atrium. However, a small portion of this blood eventually reaches the bronchial artery. This is an important blood supply to the lungs as it helps keep the non-alveolar tissue supplied with oxygen. Most of the blood in the bronchial artery empties into the pulmonary vein, which then returns to the left atrium. This way, the bronchopulmonary circulation essentially bypasses the alveoli. You may be asking yourself; how does the bronchopulmonary circulation get oxygenated then? Well, it doesn't technically get oxygenated. What happens is the deoxygenated bronchopulmonary circulation mixes with the oxygenated blood in the pulmonary vein. The oxygen content of the pulmonary vein is much higher than the deoxygenated content of the bronchial arteries. So, the two circulations mix, and the total oxygen content remains quite high. This means that the mixed blood can travel back to the systemic circulation and still have enough oxygen to adequately oxygenate the tissues, including the bronchopulmonary circulation. It's also important to know that a small portion of blood from the bronchial arteries can actually return to the right atrium by traveling through the azygos and hemiazygos veins.

- ***Let's compare the pulmonary circulation with the systematic circulation:***

Pulmonary Pressures

– Pulmonary artery pressure and systemic pressures are not the same. Here pulmonary artery pressures are:

• systolic 25 mmHg

• diastolic 8 mmHg

• mean 14/15 mmHg

• capillary 7-10 mmHg

• Left Atrial and Pulmonary Venous Pressures = 2 (1-5) mmHg (estimated)

• Pulmonary wedge pressure = 5 mmHg (usually its 2 to 3 mmHg greater than the left atrial pressure)

Difference between pulmonary & systemic capillaries

	Pulmonary capillary	Systemic capillary
Pc	10 mm Hg	30 mm Hg
Πc	28 mmHg	28 mmHg
Pi	- 5 mmHg	Zero
Πi	14 mmHg*	7 mmHg

- **Pc**: The hydrostatic pressure is 10 mmHg in the **pulmonary capillary**, while its 30mmHg in the **systematic capillary**.
  Why 30? This is because the pressure on the arterial end of the systematic capillary is 40 mmHg, and 20mmHg on the venous end. The value in between is measured, hence, it is 30mmHg.
- **Πc**: is the same in both capillaries, 28 mmHg (it opposes filtration, favours reabsorption)
- **Pi**: the interstitial pressure in the pulmonary circulation is **–**5mmHg (negative = subatmospheric), while it is 0 in the systematic circulation(under normal conditions).
  However, in certain organs like the kidneys or liver, the presence of a surrounding capsule can create positive interstitial pressure (greater than zero), this is because the capsule's rigidity exerts mechanical resistance preventing outward expansion, leading to positive interstitial pressure.So in many areas of the systemic circulation, interstitial pressures may fluctuate between slightly positive and slightly negative values, often canceling each other out on average
- **Πi**: in the pulmonary circulation is 14mmHg, which in this case is a lot.
  This is used to indicate the concentration of proteins in the interstitial fluid by measuring the proteins concentration in the lymph that comes from the lungs(the protein conc. in the lymph mirrors that in the interstitial fluid).
  However, some books indicate it with a question mark (?) and others use another value. Here let's consider it 14mmHg.

-Finally, if we sum up the pressures of the pulmonary circulation, we get a net filtration pressure of +1 mmHg, which is in favour of **filtration** (moving towards the lung), and the extra fluid that enters the lung due to this filtration can be removed by the lymphatics.

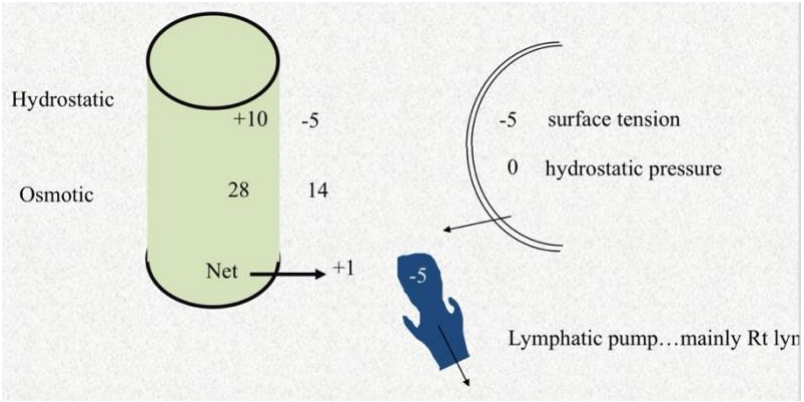
Outward Forces

– Pulmonary capillary pressure 10 mmHg

– Interstitial colloid osmotic pressure 14 mmHg

– Negative interstitial pressure 5 mmHg

– Total 29 mmHg

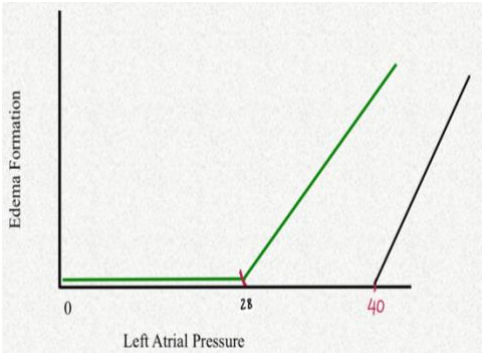


Inward Forces

– Plasma osmotic pressure 28 mmHg

- **Net filtration pressure 1 mmHg**
- **Lymphatic vessels take care of this extra filtrate**
- There is plenty lymphatics which empty in the right lymphatic duct to prevent the occurrence of pulmonary edema. The left apex empties in the thoracic duct. =Pulmonary edema safety factor.

Lymphatics drainage importance



Here we can see the filtrate will be pumped by the highly effective lymphatic drainage. Actually, if due to Left heart failure the pulmonary capillary P reaches 28 mmHg (equals blood colloid osmotic pressure P) :(21 mm Hg above normal) pulmonary edema **would not develop**. (21 mm Hg is a safety factor). That is true in case of acute state, however, in chronic conditions (> 2 WKS) the lung become even more resistant to pulmonary edema and a pulmonary capillary hydrostatic Pressure of 40- 45 develop without significant pulmonary edema.

Extra: In left heart failure, the pulmonary capillary pressure can rise to 28 mmHg (which equals the blood's colloid osmotic pressure). This increase of 21 mmHg above normal is considered a safety factor because it doesn't cause pulmonary edema (fluid buildup in the lungs). The lymphatic system helps manage the extra fluid effectively. In the acute stage, the body can handle this pressure increase without significant edema. However, in chronic conditions (lasting more than 2 weeks), the lungs adapt and become more

resistant to edema. As a result, the pulmonary capillary pressure can rise to 40-45 until edema happens!

Causes of pulmonary edema (which is life threatening edema)

– left heart failure (most common cause)

– damage to pulmonary membrane which increases the membrane permeability:

infection or noxious gas such as, chlorine, sulfur dioxide

• Safety factor

– negative interstitial pressure

– lymphatic pumping

Now we will talk about V/Q ratio:

Blood Perfusion

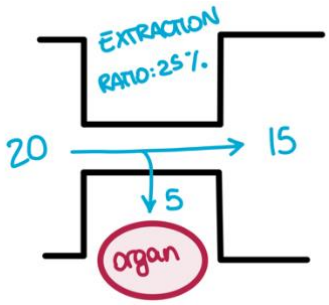
Let's revisit one of the primary functions of the respiratory system: **gas exchange.** The efficiency of this process in the lungs is largely determined by the **ventilation-perfusion (V/Q) ratio**, which ensures a balance between airflow to the alveoli and blood flow in the pulmonary capillaries. In contrast, the systemic organs listed in the following chart demonstrate varying levels of oxygen demand and extraction, reflecting the unique metabolic needs and blood flow patterns of each tissue.

Tissue	Blood flow (ml/g/min)	A-V O_2] difference (Vol %)	Flow ml/min	O_2 consumption ml/min
Heart	0.8	11	250	27
Brain	0.5	6.2 (25-30% Extraction)	750-900	
Skeletal Muscle	0.03	6	1200	70
Liver	0.6	3.4 Reconditioner organ		
SKIN	0.1			
Kidney	4.2	1.4 Reconditioner organ	1250	18
Carotid bodies	20	0.5 Reconditioner organ	0.6	

- Let's dig deep with the explanation of some points (make sure to check the table while understanding the points) :

- **Blood flow** is the amount of blood that enters a determined organ, based on the weight of the organ itself. If a heart weights 300g and we have a flow (coronary flow) of 250 mL/min (which increases during exercise reaching 500-1000), the blood flow will be 250/300=0.8 mL/g/min.

- **A-V O2 difference** (arterio-venous oxygen **concentration** difference) is mainly based on the changes that affect the venous side of the circulation, since the O2 concentration that reaches all of the organs remains the same. **But what does it represent and how can we calculate it?** This difference represents the extraction ratio, which is the quantity of oxygen that is being extracted from the circulation by the organ. If we have an arterial conc. of 20 and a venous conc. of 15, we can determine that the extraction is 25% -> $\frac{arterial-venous}{arterial} * 100\ \%$, pay attention that this is the concentration of O2, not pO2.



- In the heart, the A-V difference is 11, knowing that the arterial O2 is always 20ml/dl (the concentration of O2 in any organ, any artery, is always the same), the venous will be 9(it differs between organs) , we can conclude that the heart extract most of the oxygen deliverd to it, so it can't stand ischemia .
- There are **essential organs** and **reconditioning organs** in the body. Essential organs, like the skeletal muscles, receive only as much blood as they need. For example, muscles usually receive around 1 liter of blood, but during exercise, they may require up to 10 liters. On the other hand, reconditioning organs receive much more blood than their metabolic needs, which is why the **A-V O2 difference** (arterio-venous oxygen difference) is **small** in these organs. This is because they extract less oxygen from the blood compared to essential organs.
- For instance, when discussing the arterial-venous oxygen concentration difference (A-V difference), take the kidneys as another example, we notice a really low value of 1.4. This low value is due to their **reconditioning function:** not all the blood they receive is metabolically essential, as a significant portion is used for filtration and maintenance of homeostasis. This contrasts with organs like skeletal muscles, where blood flow is tightly matched to metabolic demand, and the A-V difference can vary significantly, especially during exercise, as muscles extract only the oxygen they need.
- To distinguish a **reconditioning organ** from a **non-reconditioning organ**, we can observe the A-V difference: reconditioning organs generally have lower values. The lowest A-V difference is seen in the carotid bodies (0.5), which receive a substantial blood flow relative to their size (20 ml/g/min). The kidneys follow with the second-lowest A-V difference (1.4), despite receiving a much smaller blood flow (4.2 ml/g/min).
- In the muscles, which is 40% of your weight, for example you weigh 70kg then it is 28,000 grams, to calculate blood flow, 1000 /28,000 = 0.03 ml/g/min compared to much more in the kidneys and carotid bodies.

-The composition of alveolar air reflects the harmony by which respiratory & cardiovascular systems are working: Ventilation: Perfusion Ratio (V/Q).

Ventilation perfusion ratios:

The ratio of alveolar ventilation to pulmonary blood flow = 0.84 (4.2 L/min ÷ 5 L/min).

• When the ventilation (V) is zero, but there is adequate perfusion (Q) of the alveolus, the V/Q is zero.

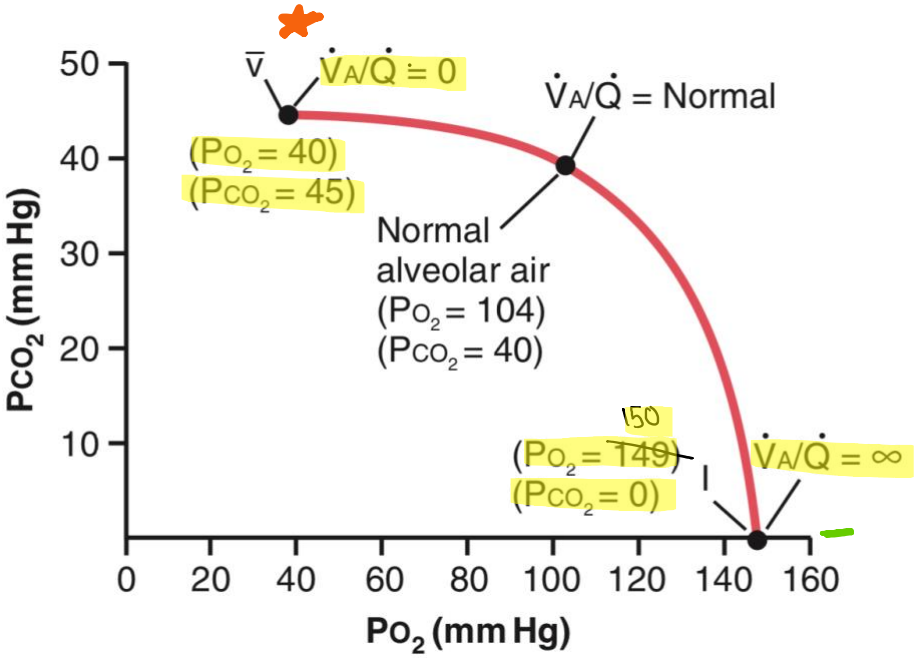
• when there is adequate ventilation, but zero perfusion, the ratio V/Q is infinity.

• At a ratio of either zero or infinity, there is no exchange of gases through the respiratory membrane of the affected alveoli

- The harmony we normally should have in the body is a lung that is **both well perfused and ventilated**. If you remember, we have an alveolar ventilation of 4.2 L/min and a cardiac output of 5L/min. Therefore, the ratio of alveolar ventilation to pulmonary blood flow (V/Q ratio) = 0.84 (4.2 L/min ÷ 5 L/min), that we usually either approximate to 0.8 or just indicate as > or < than 1. However, even normally to some extent, and especially in many lung diseases, some areas of the lungs are well ventilated but have almost no blood flow, whereas other areas may have excellent blood flow but little or no ventilation. Let's discuss the two conditions:

1. If we take into consideration a part of the lung that is well ventilated but not perfused, we will notice a V/Q ratio of infinite (number/ 0 = infinite), the PO2 is 150 and PCO2 is zero. In this case we consider this situation as **wasted ventilation,** with as an example, the pulmonary embolism (PE) because it blocks blood flow to a part of the lung while ventilation (air supply) continues.
2. While if we consider the second case, good perfusion and no ventilation, we will have a V/Q ratio of 0 (0/n=0), so alveolar PO2 =40, PCO2=45 (as the venous!).Here we have **wasted perfusion**. Don't get confused! We said in previous lectures that in cases of low O2 levels, vasoconstriction will happen to the pulmonary capillaries, but here we are describing the beginning of the hypoxia.

In either of these conditions, gas exchange through the respiratory membrane is seriously impaired, and the person may suffer severe respiratory distress despite both normal total ventilation and normal total pulmonary blood flow, but with the ventilation and blood flow going to different parts of the lungs.

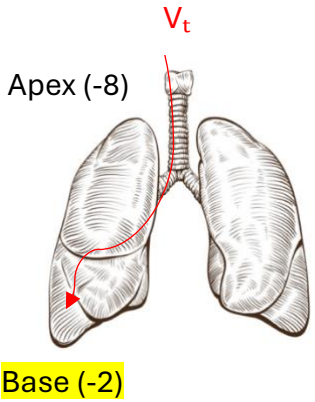


- physiologic shunt-> The total amount of shunted blood per minute, which is a direct connection between arteries and veins without the capillary presence, that will cause the blood to not be ventilated. So there is 2% of shunted blood that reaches the left atrium is deoxygenated blood, plus 1-2% of bronchial circulation , that leads to venous admixture (pollution), which means that the arterial blood is polluted with venous blood. So we don't expect the PO2 to be 100, since some of the blood is not oxygenated during its passage through the lungs.
- physiologic dead space: Alveolar wasted volume + anatomical dead spaces

There are regional differences in the intra-pleural pressure, it is not (-4) everywhere like we learned earlier. The pressure at the apex is (-8) and (-2) at the base in the standing position.

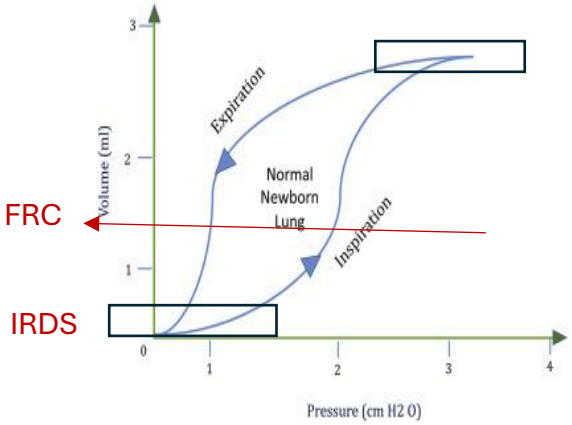
(-8) means that the alveoli are inflated (highly negative surrounding pressure). While in the base, the alveoli are partially inflated. So, the apical alveoli have a low compliance while the basal alveoli have a high compliance.

This variation in compliance indicates that when we take a breath (V_t), most of the inhaled air (ventilation) goes to the **base** of the lung because the apical alveoli are already inflated.



- Recall the **compliance curve**
  - ✓ The top of the lung is already inflated, you can't inflate already inflated alveoli.

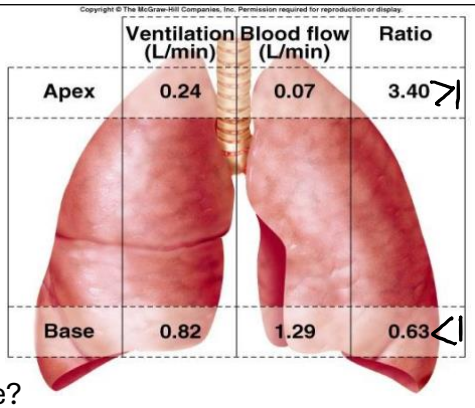
- ✓ While at the bottom the risk of IRDS becomes of concern because we cannot reopen totally collapsed, closed alveoli. Compliance is the highest in the middle of the curve (FRC)



Recap:

1) V apex < V base
2) Q apex < Q base; the lung is about 30cm high, and the heart is positioned somewhat in the center between the two lungs, and when the person is standing erect it is much easier to pump blood with gravity than against it (so it is easier to the heart to pump blood to the base , it is harder to the apex)
3) V/Q ratio apex > VQ ratio base

Numbers are not to be memorised



Functionally:

- Alveoli at apex are underperfused (overventilated).
- Alveoli at the base are underventilated (overperfused).

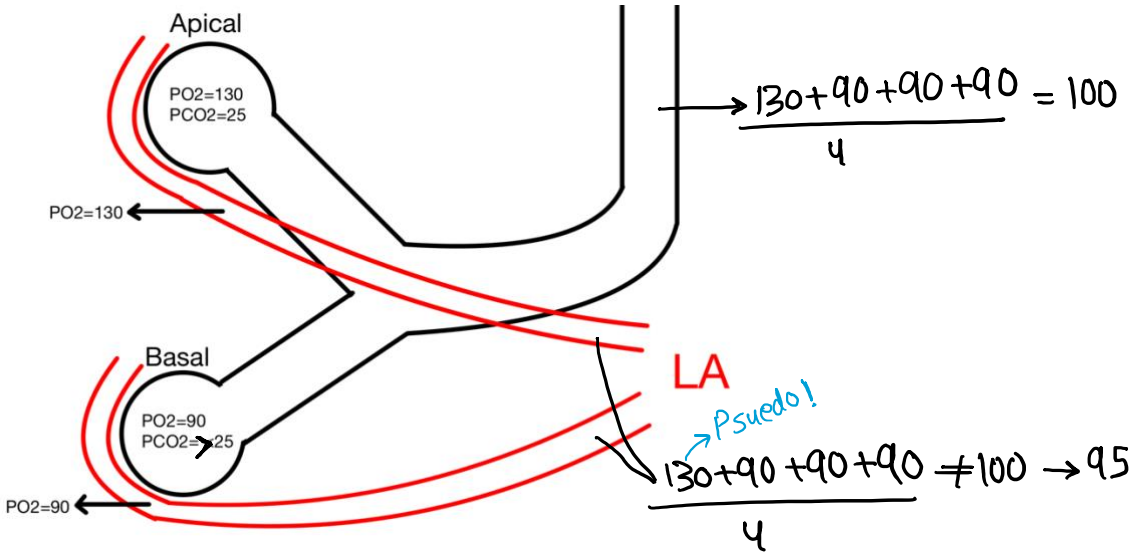
While the ventilation at the base is higher, perfusion is too so the V/Q ratio is less than 1, while it is more than 1 in the apex.

If we look at an apical alveolus, how much will the PO2 & PCO2 be?

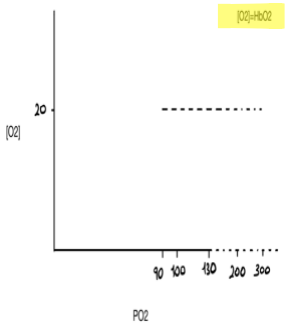
Will the PO2 be 100, more than 100 or less? It'll be more, specifically 130mmHg and the PCO2 will be 25mmHg (in standing individual)

As for a basal alveolus, the PO2 will be 90mmHg and the PCO2 will be higher than at the apex.

Now during expiration, the air we exhale from the apex is one 3rd of the air we exhale from the base (a ratio of 1:3, the ventilation at the base is 3 times more than in the apex). This means that we exhale 130mmHg of O2 from the apical alveoli along with 3 times 90mmHg of O2 from the basal alveoli, 130+90+90+90 divided by 4 to calculate the mixed expired O2 and it equals to 100mmHg.



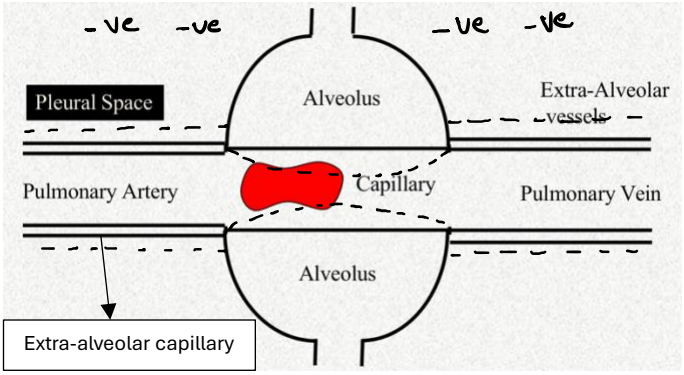
Alveolar capillaries end up at the left atrium (LA). What will the PO2 in the apical alveolar **capillary** be? 130mmHg, the exact same as the alveolar PO2, there's no difference between the two. This is because O2 isn't diffusion limited, it's rather perfusion limited. The same goes for **basal** alveolar capillaries, with a PO2 of 90mmHg.



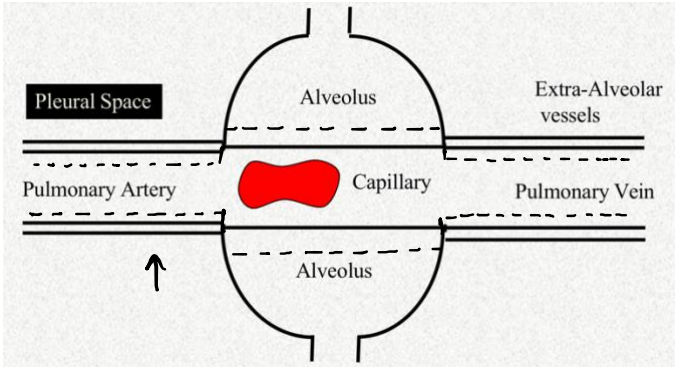
Now if we were to calculate the mixed PO2 arriving at the LA, we'll find that it equals 95mmHg, it's the same equation as the mixed expired O2 (air) but it doesn't apply to blood (زبطت بالهواء لكن ما زبطت بالدم), actually the 130mmHg is pseudo here. In fact, it's only 100mmHg.

But why is that? The hyperventilated blood (high pO2 in the apex capillaries) isn't able to correct for the hypoventilated blood (in the basal capillaries), this is ought to the Hemoglobin being already saturated with O2 at 100mmHg, hence the plateau in the graph. So, the 130mmHg isn't 30% more oxygen to be up-taken (because the hemoglobin is already saturated!)

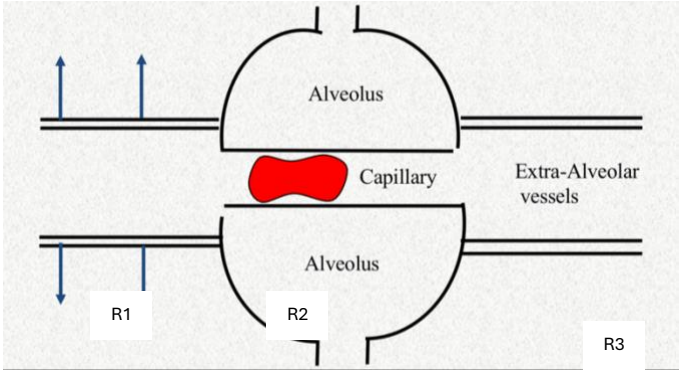
When the total lung capacity (TLC) increases too much, a more negative intrapleural pressure is needed leading to an extra-alveolar capillary's vasodilation, and when the TLC is achieved inside the alveolus , the alveolus compresses the adjacent part of the capillary(decreasing the radius of the intra-alveolar part of the capillary), this results in a decreased resistance in the extra-alveolar capillary but an increased resistance in the alveolar segment of the capillary.



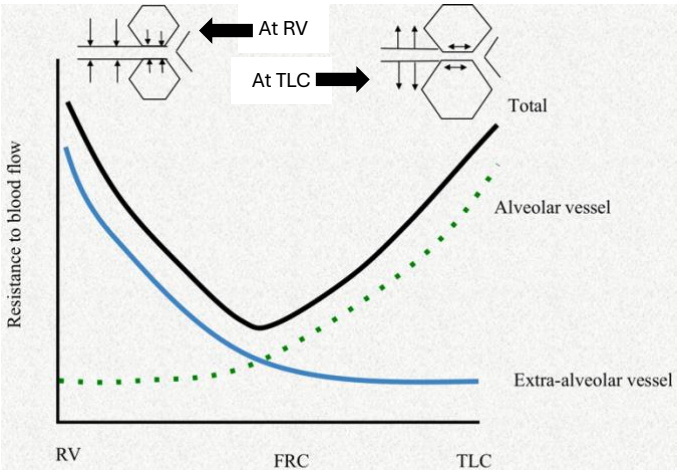
In case of the residual volume (RV), the opposite will happen. Because the alveolar pressure will be less than normal (less air in the alveolus so the compression on the intra-alveolar segment will be less), and less negative intrapleural pressure will be (compressing force) , thus distending the alveolar segment and decreasing the alveolar segment's resistance with an opposing increase in the extra-alveolar vessel's resistance.



Pleural pressure (-) … during inflation … alveolar capillary is compressed, and the extra-alveolar vessel is expanded, the intrapleural pressure is negative. (normal)



The total resistance is the sum of a **series** of resistances, R_t=R1+R2+R3. This represents the pulmonary vascular resistance.

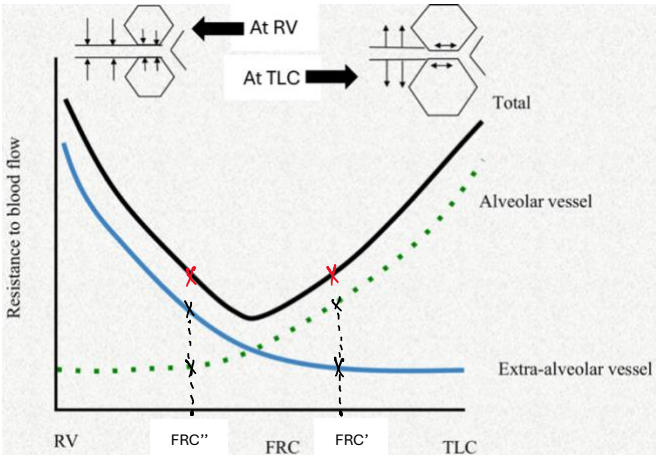


As you can see in the attached graph, the resistance of the alveolar vessel (intermittent line) increases when the alveoli compresses it (increase in alveolar volume) during inhalation (towards TLC), increasing the vessel's resistance.

In extra-alveolar vessels (blue line), as the volume of the alveoli decreases (towards RV), the pressure surrounding the vessel become less negative, compressing the vessel itself, increasing its resistance. In contrast, when the volume inside the alveolus increases, as in TLC, expansion of the intrapleural pressure happens and the resistance decreases.

To calculate the total resistance (R_t, red X), we simply add both the alveolar and the extra-alveolar vessels' resistances.

-At the FRC, both resistances are equal, and the total vascular resistance is **minimum**.



In pathological conditions, such as emphysema (FRC'), the alveolar vessel resistance is increased (due to the overly compliant alveoli's compression) while the extra-alveolar vessel resistance is decreased. However, the total resistance is increased.

A case of restrictive lung disease (fibrosis), there is collapsing which yields a lower FRC (FRC"), where the alveolar vessel pressure is decreased and the extra-alveolar vessel resistance is, in turn, increased.

We conclude that whether there's an increase in FRC (like in COPD) or a decrease (like in fibrosis, restrictive lung disease), they both correlate with an increase in R. But to maintain the flow (F=Pa/R) constant, we compensate by increasing arterial pressure (Pa). Increasing Pa increases afterload on the heart, leading to cor pulmonale (RVHF).

People living in the Andes (hypoxic environment, when we get up 5.5 km the pO2 =80, which is very low) develop pulmonary hypertension and ultimately cor pulmonale. Women of the Andes must give birth at a lower altitude so the baby can survive.

Version 2:

- **P9:** in the lung picture, intrapleural P next to the base= -2 (instead of -4)
- **P13:** extra-alveolar vessel resistance is increased (instead of decreased)