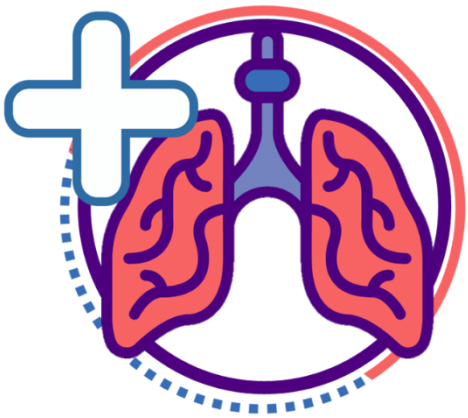

RESPIRATORY SYSTEM

Physiology

Sheet Slide

Number:	9
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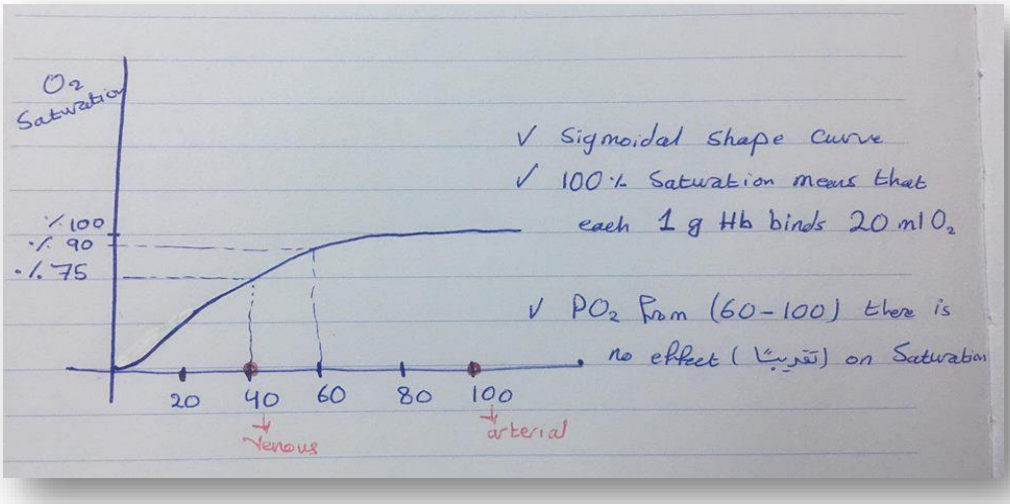
In this sheet, the discussed topics include Oxygen in blood, Binding of Oxygen to Haemoglobin (Hb) and Oxygen–Hb Dissociation Curves.

Oxygen in blood

Changes in O2 concentration as it moves in the body:

1-Arterial concentration of O2 of the whole blood = 20.3 (20 binding with Hb and 0.3 dissolved in plasma) "100% saturated"



2-As the blood moves in vessels, it gets utilized by cells. Cells utilize **25**% of the arterial O2 concentration. This cell's O2 utilization ratio is called Oxygen extraction ratio.

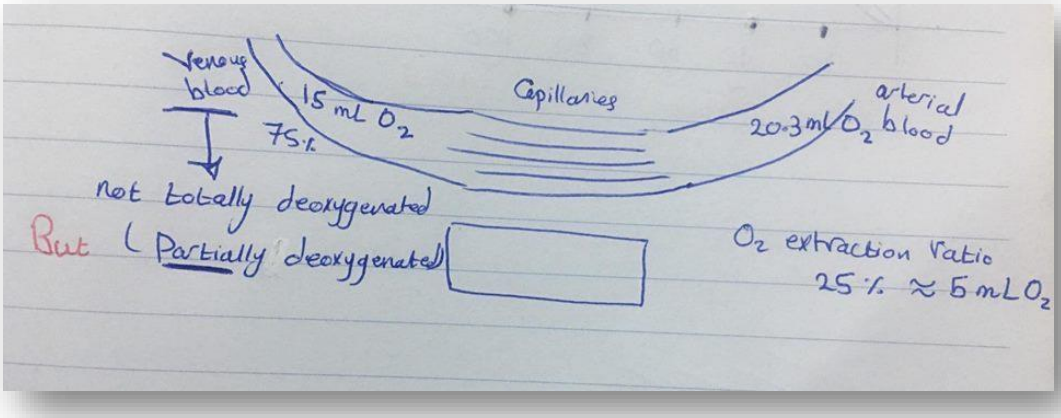
Cells extract 5 ml of the 20 ml that were originally in arterial blood

3-At the end, venous blood contains 15 ml of O2 in each 100ml, according to the following equation:

Venous blood O2 conc"100ml" =Arterial blood O2 conc/100ml - O2 extracted by cells from 100ml of blood

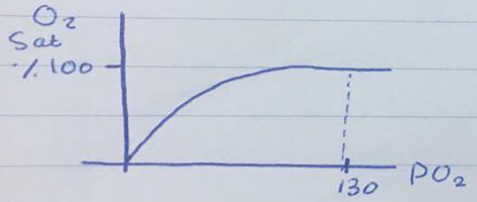
that's why saying that venous blood is deoxygenated is wrong, since it is actually 75% saturated. **IT'S partially oxygenated**.

General basic notes :



✓ important notes by Doctor. Yanal

Blood derived from apex of lung has PO_2 = 130 mm Hg
(100% Saturated)



PO_2 = 130 mmHg does not mean that O_2-Saturation in Hb increases (20 ml O_2 / 100 ml blood) but O_2-dissolved in plasma increases

⇒ (Henry law) O_2 in plasma = PO_2 x Solubility

130 x 0.003 = 0.39

(when PO_2 = 100 ⇒ O_2 in plasma = 0.3

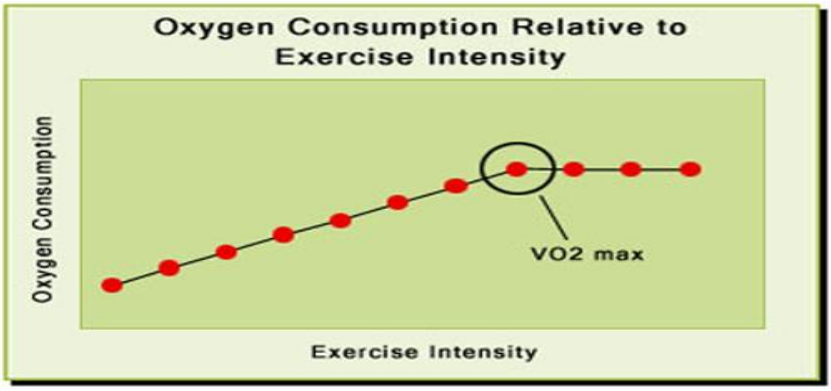
So, it's not much increament)

✓ in Case of O_2 ⇒ hyperventilated lung was unable to Correct hypoventilated lung because of the shape of O_2 curve (sigmoidal)

✓ in Case of CO_2 ⇒ hyperventilated lung was able to Correct hypoventilated lung because of the shape of CO_2 curve (linear)

-At rest, oxygen consumption is **250ml/min**. During exercise oxygen consumption increases till it reaches a certain point called VO2 max.

VO2 max is the maximum oxygen consumption during maximum exercise.



Note:The VO2 max may reach 5L in athletes during exercise, but only reaches 3.5L for normal people under the stress of exercise

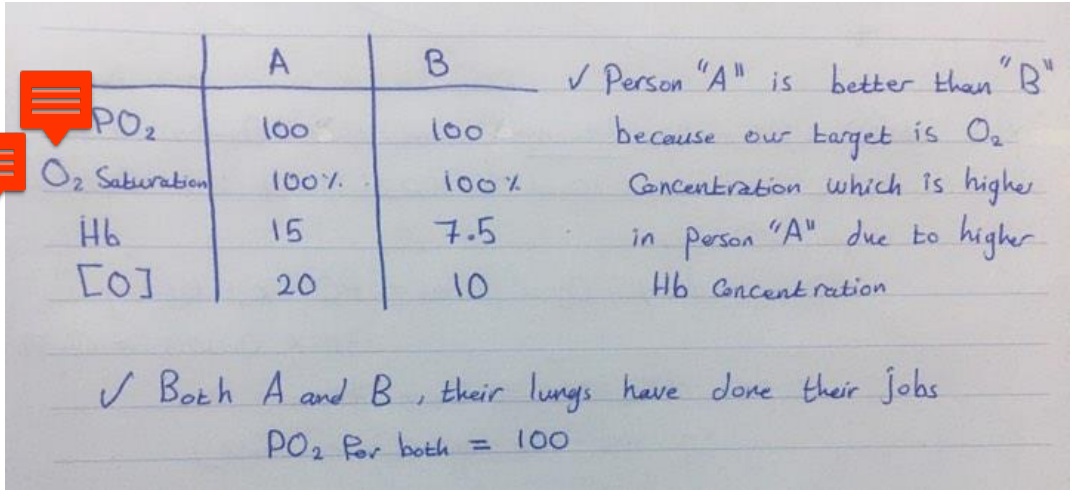
-The cardiac output at rest equals 5L, while at mild exercise it reaches approximately 12L. Those litres reach the organs as the following in rest and exercise: "important"

Organ	**Rest 5L**	**Exercise 12L**
Skeletal muscle	1L *"20%"*	8L *"66%"*
Brain	1L	1L"CONSTANT"
GIT	1L	0.5 L
Kidneys	1L	0.5
Others	1L coronary circulation receive almost 250ml	The left of the 12L. coronary circulation receive almost 500ml

The reason why O2 concentrations that reach organs change during exercise is that blood goes to the “easy” place when there is a dilation in the vessel it flows when there’s constriction it doesn’t and so on .

And those dilations and constrictions happens due to sympathetic and parasympathetic stimulations and local mediators.

TO INCREASE THE O2 CONSUMPTION BY CERTAIN TISSUES DURING EXERCISE, BOTH CARDIAC OUTPUT AND EXTRACTION RATIO INCREASE.



Binding of Oxygen to Hemoglobin (Hb)

The oxygen from the alveoli is transported in the blood in two forms: **a dissolved form** in the plasma, which represents a very small amount, and a chemically bound form to hemoglobin forming **oxy-Hb**, which the majority of O2 in the blood is transported as. α2 β2.

Hb Type

Adult (A) HbA :α2β2

Fetal (P) HbF : α2 γ2

Sickle (S) HbS :α2β2s

the percentage of saturation , takes the total number of oxygen binding sites into consideration , ex: in each hemoglobin there are 4 binding places , when 1 O is bound this hemoglobin is 25% saturated , when two O atoms are bound , its 50% saturated , when 3 is bound its 75% saturated….

Each Hb molecule can attach and carry up to four oxygen molecules (Highest saturation of O2(100%)). Binding sites on Hb have different affinities for oxygen. Also, the affinity of a site can and does change as oxygen is loaded or unloaded from the Hb molecule and as the chemical composition of the plasma changes.

PO2	O2 sat	Notes
100 mmHg Arterial	100% 20 mL	Exceeding the 100% is not efficient so don't try to make the pressure >100mmHg The additional oxygen above the 100 is in the dissolved form not the bound, and it's not sufficient to make a change. If the PO_2 is more than 2000mmHg we theoretically won't need RBC but this amount of oxygen is toxic and cannot be achieved
60 mmHg	90% 18 mL	Ascending to high altitudes will decrease the atmospheric pressure , P_AO_2 and P_aO_2 The percentage of oxygen outside is always constant at 21% but PH_2O will be more with the same contribution of 47mmHg Any increased ascending will result in major changes and stimulation of the respiratory centers.
40 mmHg Venous	75% 15 mL	15 mL is what remains after cells extracts their needs (25% or 5 mL)
26 mmHg	50%	P_{50} (%50 of the Hb is bound to O2)

Most of the oxygen in systemic arterial blood is oxygen attached to Hb. The only significant form in which oxygen is delivered to systemic capillaries is oxygen bound to Hb.

Hemoglobin O2 Content

Hemoglobin concentration :
in males : 14-16 g/dl
In females :12-14 g/dl

The number of mL of oxygen carried in each 100 mL of blood in combination with Hb depends on the Hb concentration [Hb]. Each gram of Hb can combine with 1.34 mL of O2.

If the [Hb] is 15 g/100 mL (15 g%), then the maximal amount of O2 per 100 mL (100% saturation) in combination with Hb is:

1.34([Hb]) = 1.34(15) = 20 mL O2/100 mL blood = 20 vol%.

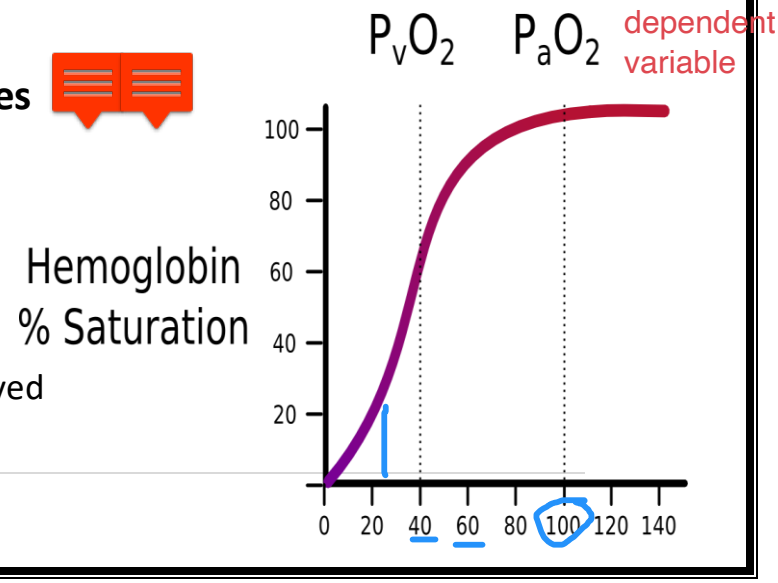
This volume represents the "carrying capacity" of the blood.

	Hb CONCENTRATION	% O2 SAT OF Hb	DISSOLVED O2 (Pao2)	TOTAL O2 CONTENT
CO poisoning	Normal	↓ (CO competes with O2)	Normal	↓
Anemia	↓	Normal	Normal	↓
Polycythemia	↑	Normal	Normal	↑

*Hb Concentration Effects

Oxygen–Hb Dissociation Curves

On the X-axis will be the partial pressure of O2(PO2), while the Y-axis will carry the percentage of saturation with oxygen. The dissolved



amount, albeit small, is what determines the partial pressure of O2(PO2) in the blood. It will also influence the amount of oxygen that binds to Hb; as PO2 increases, oxyHb increases (but not linearly!!).

Extra note: we plot PO2 against percentage of saturation rather than O2 content because the content is affected by – in addition to P02- amount of Hb, affinity of O2 to HB and tissue O2 consumption. The percentage of saturation however is only affected by the partial pressure. So, by using it we can eliminate all other factors and reach a more accurate understanding of the relationship between O2 and Hb.

We said that as PO2 increases so does oxyHb. One might assume that the curve between PO2 and saturation of O2 is then linear, however that is not the case. We find the curve to be **sigmodal** instead (like lung compliance curve) and it has several phases: phase 1, 2 and 3. We will point three values of importance on the X-axis: PO2 of arterial blood=100mmHg, PO2 of venous blood=40mmHg and 60 mmHg.

At 100mmHg (which stands for 20ml of O2{1.34*15}) the percent of saturation is approximately 100%, and at 60mmHg (which stands for 18ml of O2) is 90%. Notice how a decrease of 40mmHg in PO2 resulted in only a slight decrease in O2 saturation as well as content. This can be explained by looking at the curve: the PO2 of 60mmHg corresponds to a point on the horizontal line of the curve or the "plateau" phase, which means as we move along this line(to the right) any change in PO2 will cause only a small change in % of saturation. *Extra note: This happens due to the higher affinity of O2 to hemoglobin at higher partial pressure values.* This also indicates that this drop in PO2 will not drastically impair O2 transport to tissue (as long as it is within physiologic limits), which is of great importance to people who climb or live at higher altitudes where O2 levels are decreased; O2 transport will be normal because, again, the percentage of saturation is still near 100% despite PO2 decreasing.

It should be noted that, a decrease to almost half the original concentration without drastically impairing the function doesn't occur anywhere else in the body (for example a minimal change in {K+} will affect our physiology greatly, and may kill) . Only O2 can drop from 100 to 60mmHg without a change in the function, which we explained why by interpreting the sigmoidal curve. Had the curve been linear, such effect would be present.

What happens if the PO2 became 200mmHg instead of 100 mmHg ? 

However, if the PO2 decreases to below 60mmHg and we reach the **steep part** of the curve (phase 2), any change in PO2 will be met with an equal one in the percent of saturation (this part of the curve is somewhat like a linear one).

Below PO2 60mmHg , the respiratory center in the brain is stimulated to increase ventilation , while above PO2 100mmHg there is no stimulation to decrease ventilation as the saturation will still the same (Plateau)

(this is not applied to CO2 as the curve is linear)

So, we know what happens if PO2 drops to below 60mmHg, but what happens if we increase it to more than 100mmHg?

Remember that blood derived from the apex has PO2 that equals 130mmHg. By looking at the curve, we can see that at this value the percent of saturation is still 100%. So, despite increasing the amount of available oxygen **by 30mmHg**, the percentage remained the same. This is because at 100% saturation, all available Hb molecule are bound to 4 molecules of oxygen (remember this is what saturation means) and so the additional O2 molecules have no place to bind to and will not be able to affect the percentage. (the box elaborates what happens in numbers).

OxyHb is the same = 20ml.(already saturated)

The dissolved O2 at 130 mmHg "**increases"** = 130, 130*0.003=0.4

The dissolved O2 at 100 mmHg= 100*0.003=0.3

Which means that 0.3 has become 0.4, such increase is almost nothing and is negligible.

This means that adding blood of 130mmHg (like the apex) to blood of 90mmHg (like the base) won't cause the latter to have a massive increase in O2 saturation, as it already has one near 100% that cannot be exceeded due to the sigmoidal curve. So, **hyper**ventilated lung was unable to correct (compensate) the **hypo**ventilated lung.

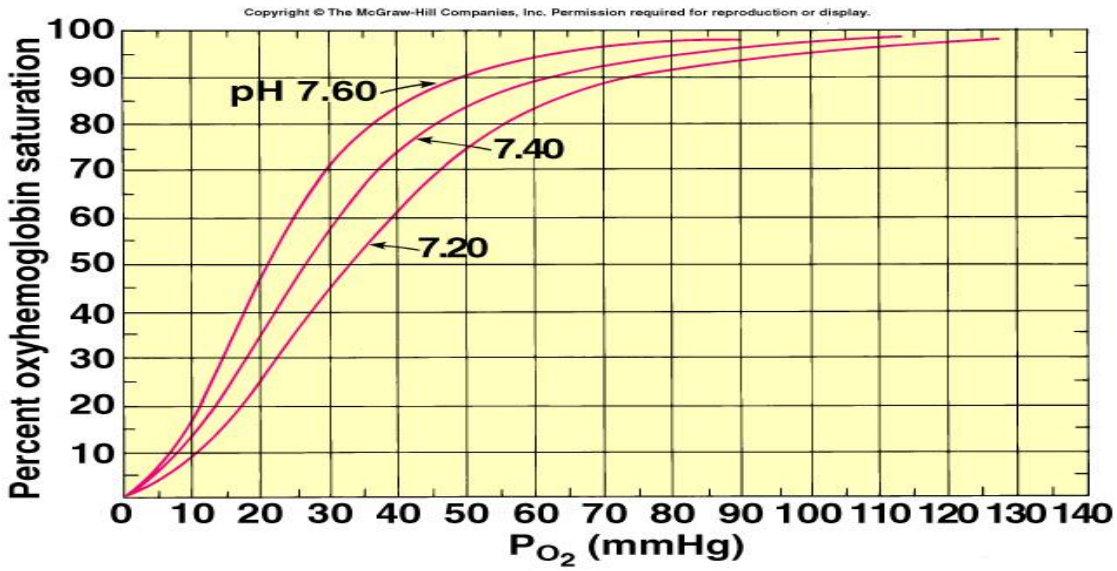
We can conclude that **oxygen** is a gas that **cannot compensate** for itself due to its sigmoidal curve.

Question: does a linear curve allow for such compensation?

Yes, such compensation is seen with CO2. If we mix the blood from a hyperventilated lung with high release of CO2 (low CO2 in alveolar space) and blood from a hypoventilated lung with high CO2 in alveolar space), we will find CO2 to be increased because it follows a linear curve (any increase in PCO2 will be met by an equal increase in percent of saturation). **CO2 is then a self-compensatory gas**.

This partially answers why V/Q ratio inequality (or venous admixture) affects O2 and doesn't affect CO2 (compensate for itself); because of the shape of the curve: sigmoidal vs linear.

Shifts in Hb–O2 Dissociation Curve



The following factors shift the curve to the right:

- Increased CO2 (Bohr effect)
- Increased hydrogen ion (decrease pH) , acidosis
- Increased temperature
- Increased 2,3-bisphosphoglycerate (2,3-BPG)

In each case, the result can be explained as a reduced affinity of the Hb molecule for oxygen. However, carrying capacity is not changed, and systemic arterial blood at a PO2 of 100 mm Hg is still close to 100% saturation. The opposite chemical changes shift the curve to the left.

Decreased CO2 , temperature , hydrogen ions -which also means alkalosis or increased ph , decrease 2,3 BPG.

also fetal hemoglobin , which is alpha 3 gamma 2 , is shifted towards the left, since no 2,3 BPG is present

Stored blood loses 2,3-bisphosphoglycerate, causing a left shift in the curve, while hypoxia stimulates the production of 2,3-bisphosphoglycerate, thereby causing a right shift.

NOTES

- Oxygen-hemoglobin dissociation curve…Sigmoidal shape due to positive cooperativity (ie, tetrameric Hb molecule can bind 4 O2 molecules and has higher affinity for each subsequent O2 molecule bound). Myoglobin is monomeric and thus does not show positive cooperativity; curve lacks sigmoidal appearance.
- Shifting the curve to the right – decreases Hb affinity for O2 (facilitates unloading of O2 to tissue)- increases P50 (higher Po2 required to maintain 50% saturation).
- Shifting the curve to the left - decreases O2 unloading - renal hypoxia – increases EPO synthesis - compensatory erythrocytosis.
- Fetal Hb has higher affinity for O2 than adult Hb (due to low affinity for 2,3-BPG), so its dissociation curve is shifted left.
- Normally 1 g Hb can bind 1.34 mL O2; normal Hb amount in blood is 15 g/dL. O2 binding capacity ≈ 20.1 mL O2/dL of blood.
- With decrease Hb there is decrease O2 content of arterial blood, but no change in O2 saturation and Pao2.

STUDY WELL.. GOOD LUCK

WE FALL..WE BREAK..WE FAIL..

BUT THEN, WE RISE..WE HEAL..WE OVERCOME.