

# RESPIRATORY SYSTEM

Physiology



Sheet



Slide

Number:

9

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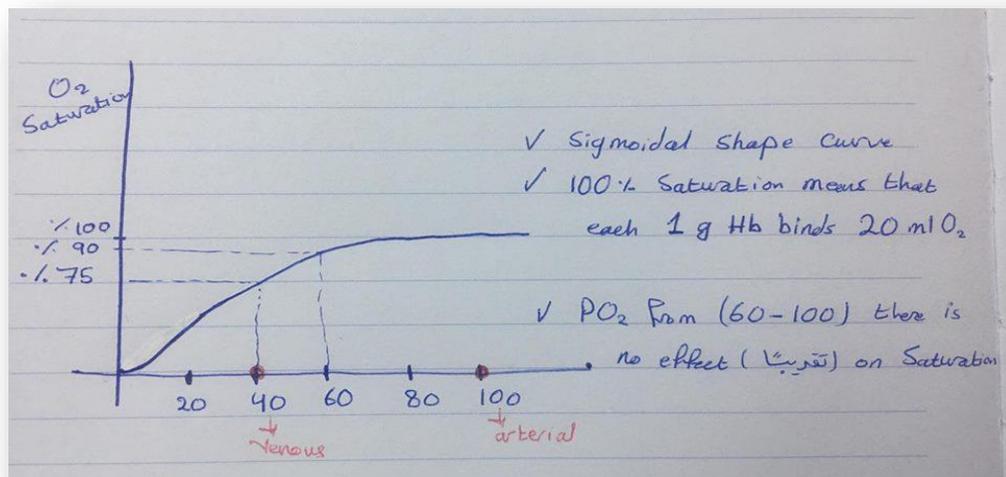
-Yanal shafaqouj

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 O<sub>2</sub> concentration as it moves in the body:

1-Arterial concentration of O<sub>2</sub> of the whole blood = 20.3 (20 binding with Hb and 0.3 dissolved in plasma ) “100% saturated”



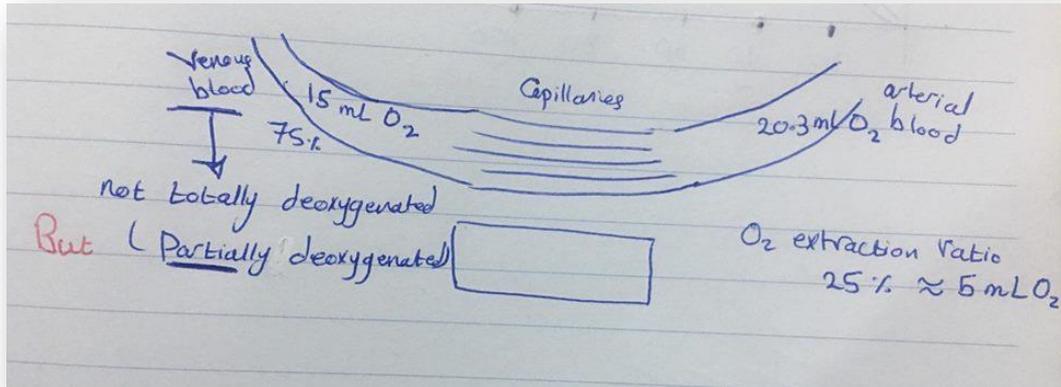
2-As the blood moves in vessels, it gets utilized by cells. Cells utilize **25%** of the arterial O<sub>2</sub> concentration. This cell's O<sub>2</sub> utilization ratio is called Oxygen extraction ratio.

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

3-At the end, venous blood contains 15 ml of O<sub>2</sub> in each 100ml, according to the following equation:

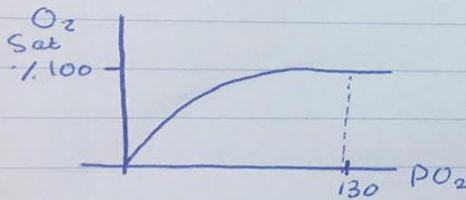
$$\text{Venous blood O}_2 \text{ conc} \text{ "100ml"} = \text{Arterial blood O}_2 \text{ conc/100ml} - \text{O}_2 \text{ extracted by cells from 100ml of blood}$$

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



✓ important notes by Doctor. Yanal

Blood derived from apex of lung has  $PO_2 = 130$  mmHg  
(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

$$\Rightarrow (\text{Henry law}) \quad O_2 \text{ in plasma} = PO_2 \times \text{Solubility}$$

$$130 \times 0.003 = 0.39$$

$$(\text{when } PO_2 = 100 \Rightarrow O_2 \text{ in plasma} = 0.3)$$

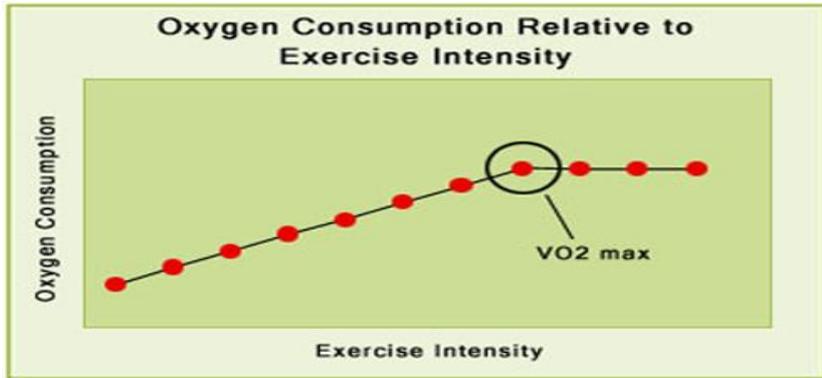
So, it's not much increment)

✓ in case of  $O_2 \Rightarrow$  hyperventilated lung was unable to correct hypoventilated lung because of the shape of  $O_2$  curve (sigmoidal)

✓ in case of  $CO_2 \Rightarrow$  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 O<sub>2</sub> 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 O<sub>2</sub> CONSUMPTION BY CERTAIN TISSUES DURING EXERCISE, BOTH CARDIAC OUTPUT AND EXTRACTION RATIO INCREASE.**

	A	B	
PO <sub>2</sub>	100	100	✓ Person "A" is better than "B" because our target is O <sub>2</sub> concentration which is higher in person "A" due to higher Hb concentration
O <sub>2</sub> Saturation	100%	100%	
Hb	15	7.5	
[O]	20	10	

✓ Both A and B, their lungs have done their jobs  
PO<sub>2</sub> for both = 100

### **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 O<sub>2</sub> in the blood is transported as.  $\alpha_2 \beta_2$ .

#### Hb Type

**Adult (A) HbA :  $\alpha_2 \beta_2$**

**Fetal (P) HbF :  $\alpha_2 \gamma_2$**

**Sickle (S) HbS :  $\alpha_2 \beta_2^s$**

Each Hb molecule can attach and carry up to four oxygen molecules (Highest saturation of O<sub>2</sub>(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.

<b>PO2</b>	<b>O2 sat</b>	<b>Notes</b>
<b>100 mmHg Arterial</b>	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 <sub>2</sub> is more than 2000mmHg we theoretically won't need RBC but this amount of oxygen is toxic and cannot be achieved
<b>60 mmHg</b>	90% 18 mL	Ascending to high altitudes will decrease the atmospheric pressure , P <sub>A</sub> O <sub>2</sub> and P <sub>a</sub> O <sub>2</sub>  The percentage of oxygen outside is always constant at 21% but P <sub>H<sub>2</sub>O</sub> will be more with the same contribution of 47mmHg  Any increased ascending will result in major changes and stimulation of the respiratory centers.
<b>40 mmHg Venous</b>	75% 15 mL	15 mL is what remains after cells extracts their needs (25% or 5 mL)
<b>26 mmHg</b>	50%	P <sub>50</sub> (%50 of the Hb is bound to O <sub>2</sub> )

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

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:

$$1.34([\text{Hb}]) = 1.34(15) = 20 \text{ mL O}_2/100 \text{ mL blood} = 20 \text{ vol\%}.$$

This volume represents the “carrying capacity” of the blood.

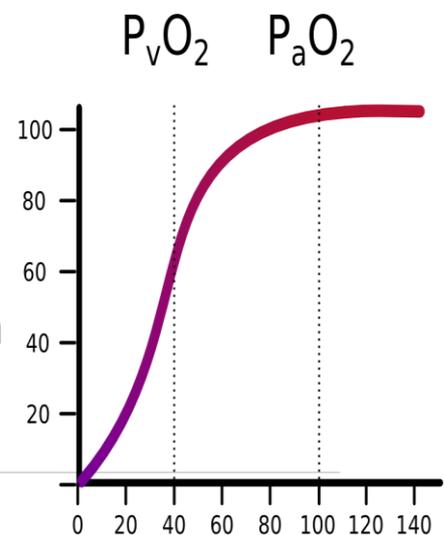
	Hb CONCENTRATION	% O2 SAT OF Hb	DISSOLVED O2 (Pao2)	TOTAL O2 CONTENT
CO poisoning	Normal	↓ (CO competes with O2)	Normal	↓
Anemia	↓	Normal	Normal	↓
Polycythemia	↑	Normal	Normal	↑

\*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

Hemoglobin % Saturation



amount, albeit small, is what determines the partial pressure of O<sub>2</sub>(P<sub>O2</sub>) in the blood. It will also influence the amount of oxygen that binds to Hb; as P<sub>O2</sub> increases, oxyHb increases (but not linearly!!).

*Extra note: we plot P<sub>O2</sub> against percentage of saturation rather than O<sub>2</sub> content because the content is affected by – in addition to P<sub>O2</sub>- amount of Hb, affinity of O<sub>2</sub> to HB and tissue O<sub>2</sub> 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 O<sub>2</sub> and Hb.*

We said that as P<sub>O2</sub> increases so does oxyHb. One might assume that the curve between P<sub>O2</sub> and saturation of O<sub>2</sub> is then linear, however that is not the case. We find the curve to be **sigmoidal** 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: P<sub>O2</sub> of arterial blood=100mmHg, P<sub>O2</sub> of venous blood=40mmHg and 60 mmHg.

At 100mmHg (which stands for 20ml of O<sub>2</sub>{1.34\*15}) the percent of saturation is approximately 100%, and at 60mmHg (which stands for 18ml of O<sub>2</sub>) is 90%. Notice how a decrease of 40mmHg in P<sub>O2</sub> resulted in only a slight decrease in O<sub>2</sub> saturation as well as content. This can be explained by looking at the curve: the P<sub>O2</sub> 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 P<sub>O2</sub> will cause only a small change in % of saturation. *Extra note: This happens due to the higher affinity of O<sub>2</sub> to hemoglobin at higher partial pressure values.* This also indicates that this drop in P<sub>O2</sub> will not drastically impair O<sub>2</sub> 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 O<sub>2</sub> levels are decreased; O<sub>2</sub> transport will be normal because, again, the percentage of saturation is still near 100% despite P<sub>O2</sub> 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<sup>+</sup>} will affect our physiology greatly, and may kill) . Only O<sub>2</sub> 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.

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

Below PO<sub>2</sub> 60mmHg , the respiratory center in the brain is stimulated to increase ventilation , while above PO<sub>2</sub> 100mmHg there is no stimulation to decrease ventilation as the saturation will still the same (Plateau )

( this is not applied to CO<sub>2</sub> as the curve is linear )

So, we know what happens if PO<sub>2</sub> drops to below 60mmHg, but what happens if we increase it to more than 100mmHg?

Remember that blood derived from the apex has PO<sub>2</sub> 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 O<sub>2</sub> 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 O<sub>2</sub> at 130 mmHg  
“increases” = 130,  $130 \times 0.003 = 0.4$

The dissolved O<sub>2</sub> at 100 mmHg=  
 $100 \times 0.003 = 0.3$

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 O<sub>2</sub> saturation, as it already has one near 100% that cannot be exceeded due to the sigmoidal curve. So, **hyperventilated** lung was unable to correct (compensate) the **hypoventilated** lung.

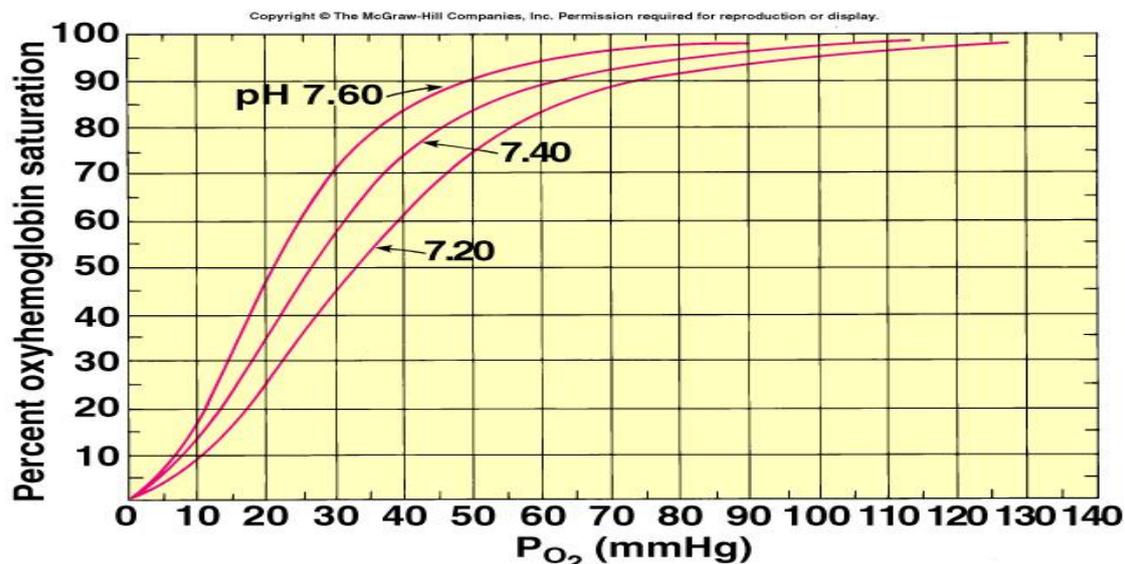
We can conclude that **oxygen** is a gas that **cannot compensate** for itself due to its sigmoidal curve.

Question: does a linear curve allow for such compensation?

Yes, such compensation is seen with CO<sub>2</sub>. If we mix the blood from a hyperventilated lung with high release of CO<sub>2</sub> (low CO<sub>2</sub> in alveolar space) and blood from a hypoventilated lung with high CO<sub>2</sub> in alveolar space), we will find CO<sub>2</sub> to be increased because it follows a linear curve (any increase in PCO<sub>2</sub> will be met by an equal increase in percent of saturation). **CO<sub>2</sub> is then a self-compensatory gas.**

This partially answers why V/Q ratio inequality (or venous admixture) affects O<sub>2</sub> and doesn't affect CO<sub>2</sub> (compensate for itself); because of the shape of the curve: sigmoidal vs linear.

### Shifts in Hb–O<sub>2</sub> Dissociation Curve



The following factors shift the curve to the right:

- Increased CO<sub>2</sub> (Bohr effect)
- Increased hydrogen ion (decrease pH)
- 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 P<sub>O<sub>2</sub></sub> of 100 mm Hg is still close to 100% saturation. The opposite chemical changes shift the curve to the left.

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 O<sub>2</sub> molecules and has higher affinity for each subsequent O<sub>2</sub> 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 O<sub>2</sub> (facilitates unloading of O<sub>2</sub> to tissue)- increases P<sub>50</sub> (higher P<sub>o2</sub> required to maintain 50% saturation).
- Shifting the curve to the left - decreases O<sub>2</sub> unloading - renal hypoxia – increases EPO synthesis - compensatory erythrocytosis.
- Fetal Hb has higher affinity for O<sub>2</sub> 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 O<sub>2</sub>; normal Hb amount in blood is 15 g/dL. O<sub>2</sub> binding capacity ≈ 20.1 mL O<sub>2</sub>/dL of blood.
- With decrease Hb there is decrease O<sub>2</sub> content of arterial blood, but no change in O<sub>2</sub> saturation and P<sub>aO2</sub>.

*STUDY WELL.. GOOD LUCK*

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

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