OXYGEN TRANSPORT (CARRIAGE) BY THE BL00D

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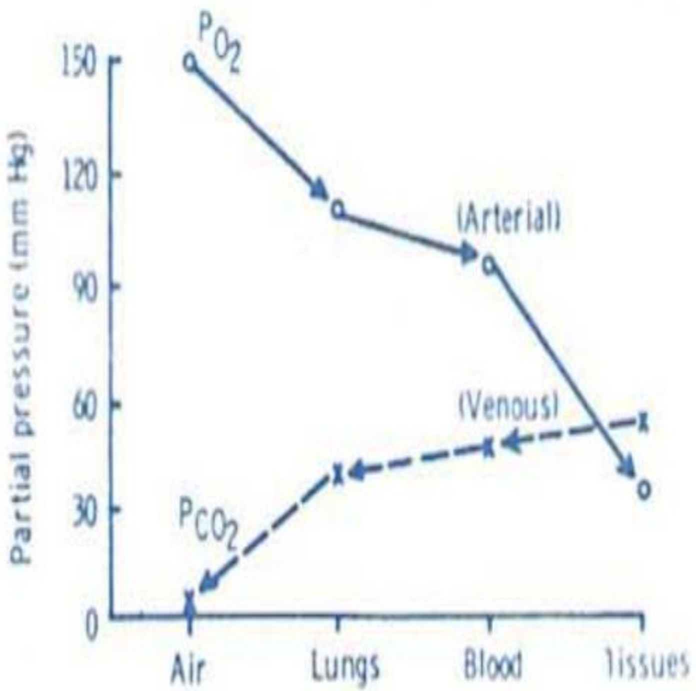
CBU SCHOOL OF MEDICINE

- According to the level of P02, *oxygen flows downhill* from the alveolar air to the blood then into the tissues

- 0xygen supply to the tissues is the function of the *respiratory and cardiovascular systems,* and the amount delivered depends on:

(a) The amount of 02 that enters the lungs
(b) The efficiency of gas exchange in the lungs
(c) The capacity of the blood to carry 02
(d) The rate of blood flow to the tissues.



Directions of O_2 and CO_2 diffusion in the body.

OXYGEN IN THE BLOOD

- Oxygen is present in the blood in the following 2 forms:

(I) In physical solution (i.e. dissolved in the plasma and blood cells): This is normally *a very small amount* but it is important because:

(a) It determines the PO2: in the blood, which in turn determines the direction and rate of flow of 02 as well as the degree of saturation of haemoglobin with *02*

(b) It is the only stimulant to the peripheral chemoreceptors

(2) In chemical combination with haemoglobin (Hb): This constitutes the majority of the blood O2 content, so it is essential for supplying adequate amounts of O2 to the tissues both during rest and exercise.

- *Hb increases the 02 carrying capacity of the blood about 70 times.* 02 combines loosely to Hb, and is also easily dissociated from it, and these processes occur *very rapidly* (in less than 0.0I second).

- The Hb molecule contains *4 ferrous atoms,* each of which can reversibly bind to one 02 molecule *without changing the ferrous state,* so this binding is a form of *oxygenation and not oxidation.*

- Therefore, each Hb molecule can bind 4 02 molecules. The saturation of Hb with 02 occurs gradually in 4 steps as follows :

$$Hb_4 + O_2 \rightarrow Hb_4O_2 + O_2 \rightarrow Hb_4O_4 + O_2 \rightarrow Hb_4O_6 + O_2 \rightarrow Hb_4O_8$$

When fully saturated, each gram of Hb carries about 1.34 ml of oxygen

❑The following table shows the normal (P), % Hb saturation with 02 and volumes of 02 & C02 in ml/ dL (100 ml) in arterial & venous blood at rest.

	O_2 volume (ml / dL)		CO_2 volume (ml /dL)	
Arterial blood : *P_{O2} 95 mmHg, P_{CO2} 40 mmHg and Hb saturation with O_2 97 %*	**dissolved**	**combined**	**dissolved**	**combined**
	0.3	19.5	2.6	46.4
Venous blood : *P_{O2} 40 mmHg, P_{CO2} 46 mmHg and Hb saturation with O_2 75 %*	**dissolved**	**combined**	**dissolved**	**combined**
	0.1	15.1	3	49.7

Notice that **normally at rest**, *the arterial blood contains about 19.8 ml O_2 / dL while the venous blood contains only 15.2 ml O_2 / dL*, which indicates that **each 100 ml of arterial blood supplies the tissues with 4.6 ml O_2**.

❑OXYGEN CONTENT: This is the volume of 0 2 (in ml) present in *chemical combination* (i.e bound to Hb) in I00 ml blood.

❑OXYGEN CAPACITY: This is the maximal volume of 02 (in ml) that can be carried in chemical combination by I00 ml blood (i.e. when Hb is completely saturated with oxygen).

❑OXYGEN % SATURATION: This is the % saturation of Hb with 0 2, and it is calculated as follows:

$$O_2 \text{ \% saturation} = \frac{\text{oxygen content}}{\text{oxygen capacity}} \times 100$$

❑COEFFICIENT OF OXYGEN UTILIZATION: This is the % of 02 in the arterial blood that is taken by the tissues, and it is calculated as follows :

$$\text{Coefficient of } O_2 \text{ utilization} = \frac{\text{arterial } O_2 \text{ content - venous } O_2 \text{ content}}{\text{arterial } O_2 \text{ content}} \times 100$$

** The average normal values for the P_{O2} and O_2 content in the arterial and venous blood *during rest* are shown in the above table (page 65).

** Since there is normally about 15 gm Hb / ml blood and each gm combines with about 1.34 ml O_2, then **the normal O_2 capacity of blood** =

15 x 1.34 = 20 ml O_2 / 100 ml blood (approximately)

The coefficient of O_2 utilization **at rest** = $\frac{19.5 - 15.1}{19.5} \times 100$ = about 25 %.

During exercise, this coefficient increases to ***75 % or more***. It is to be noted that the venous blood always contains an amount of O_2 (even in the most severe exercises), so it is commonly called **mixed venous blood**.

THE PHYSIOLOGIC SHUNTS

- These are *normal shunts* that allow drainage of some systemic venous blood into the pulmonary venous blood (which is arterial blood after equilibration with the alveolar air). This systemic venous blood is derived from :

l. The bronchial veins, which drain some of their blood into the pulmonary capillaries and veins.

2. The coronary veins, which drain some of their blood directly into the left side of the heart via the *thebesian veins*

- As a result of these physiologic shunts, the P02 and % saturation of Hb with 02 in the systemic arterial blood (about 95 mmHg and 97 % respectively) are *normally slightly less* than their corresponding values in the blood that has equilibrated with alveolar air at the venous ends of the pulmonary capillaries (about 97 mmHg and 97.5% respectively).

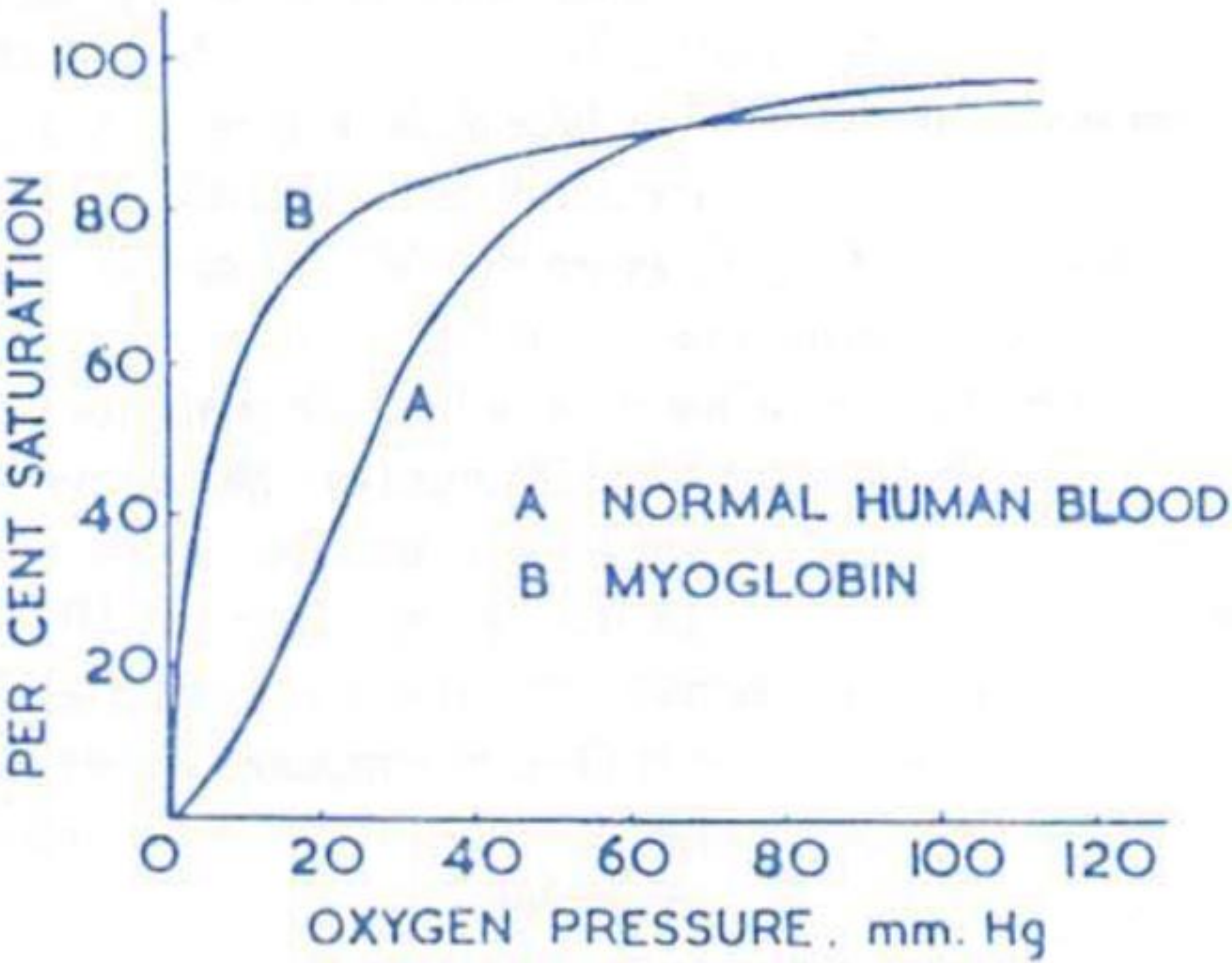
THE 02 Hb DlSSOCIATION CURVE

- This curve shows the relation between the 02 pressure and the% saturation of Hb with 02.

- It is constructed by placing small volumes of blood in several tonometers (special glass containers), and exposing each tonometer to a particular 02 pressure at 37 °C.

- Enough time is allowed for equilibration then the blood is analyzed to determine its 02 content.

- The % saturation of Hb with 02 is calculated and then plotted against the 02 pressure. The curve is normally sigmoid in shape i.e. S-shaped



The O_2 dissociation curve for blood Hb (A) and myoglobin (B).

Cause of the sigmoid shape of the 0 2 Hb dissociation curve

- The Hb molecule is formed of *4 haem units,* so it is called Hb_4. Each unit is an iron-containing porphyrin that consists of one ferrous atom attached to 4 pyrrole rings, and *can combine with one oxygen molecule (02).*

- This combination occurs *in steps,* and when a unit is oxygenated, the affinity of the other units to 02 increases. This is because oxygenation of the haem units changes the shape of the Hb molecule from the *Tense or T state* (= state of less affinity to 02) to the *Relaxed or R state* (= state of increased affinity to 02).

- The facilitation of binding of 02 to Hb as a result of previous 02 binding is known as the cooperative effect of 02, and this is the cause of the sigmoid shape of the 02 - Hb dissociation curve.

Physiological significance of the 0 2 Hb dissociation curve

1. At 02 pressure of 100 mmHg, Hb is almost 100% saturated with 02. This indicates that at the normal arterial PO2 (about 95 mmHg), Hb is nearly fully saturated with 02 (about 97 %) which helps adequate supply of 02 to the tissues.

2. At 0 2 pressure of 70 mmHg, Hb is about 93 % saturated with 02. This indicates that the alveolar or arterial PO2 can be lowered by about 1/3 without much decrease in the % saturation of Hb with 02 (as occurs in high altitudes and the pulmonary diseases that cause alveolo-capillary block).

3. At 02 pressure of 40 mmHg, Hb is about 75 % saturated with 02. This is the *02 pressure in the venous blood during rest,* and the 0 2 content in this blood is about 15.2 ml %.

- This indicates that the *tissues extract 4. 6 ml of O2 from each 100 ml blood.* Since about 5.5 litres of blood perfuse the tissues each minute at rest (= the cardiac output), they will obtain *250 ml O2 per minute,* which is adequate for their needs.

4. At 0 2 pressures between 40 and 20 mmHg, *the curve becomes steep* meaning that the slightest decrease in 0 2pressure results in marked desaturation of Hb (i.e. marked decrease in the % saturation of Hb with 02).

❑This effect is useful in muscular *exercise* in which the arterial PO2 decreases below 40 mmHg due to the increased 0 2 consumption by the active muscles, resulting in more desaturation of Hb (i.e. more *0 2* is unloaded or dissociated from Hb and delivered to the active muscles)

5. At lower 02 pressures than 20 mmHg, 02 dissociation from Hb is insignificant and consequently, the released amount of 02 to the tissues becomes minimal. In this case, the tissues require an additional source of 02, and this is supplied by the *myoglobin* present in the muscles

*** If the curve is analyzed in the opposite direction (i.e. from left to right, it will show *the phases of 02 binding to Hb at various 0 2 pressures,* and n this case, it may be called the *O2 association curve*

MYOGLOBIN

- This is a red oxygen-carrying pigment found in skeletal muscles, spec ally those specialized for prolonged contraction (i.e. the slow muscles that are rich in red fibres).

- Its molecular weight is 1/4 that of Hb (16700), and its molecule contains *only one haem unit that contains one ferrous atom and can bind only one oxygen molecule (O2) .*

- The myoglobin 02 dissociation curve lies to the left of the Hb *0 2 disso*ciation curve and is in the form of *rectangular hyperbola*. *This* indicates that myoglobin retains (or stores) 0 2 when the 0 2 pressure is high and releases it only at low 02 pressures.

- It performs a *complementary function to blood Hb* because the steep part of its curve comes after that of the Hb curve (thus at low 0 2 pressures, myoglobin can release its 0 2 content to the tissues at a time the release of 02 from the blood Hb becomes minimal).

FACTORS THAT AFFECT (SHIFT) THE 02 HB DISSOCIATION CURVE (= FACTORS THAT AFFECT THE AFFINITY OF HB FOR 0 2)

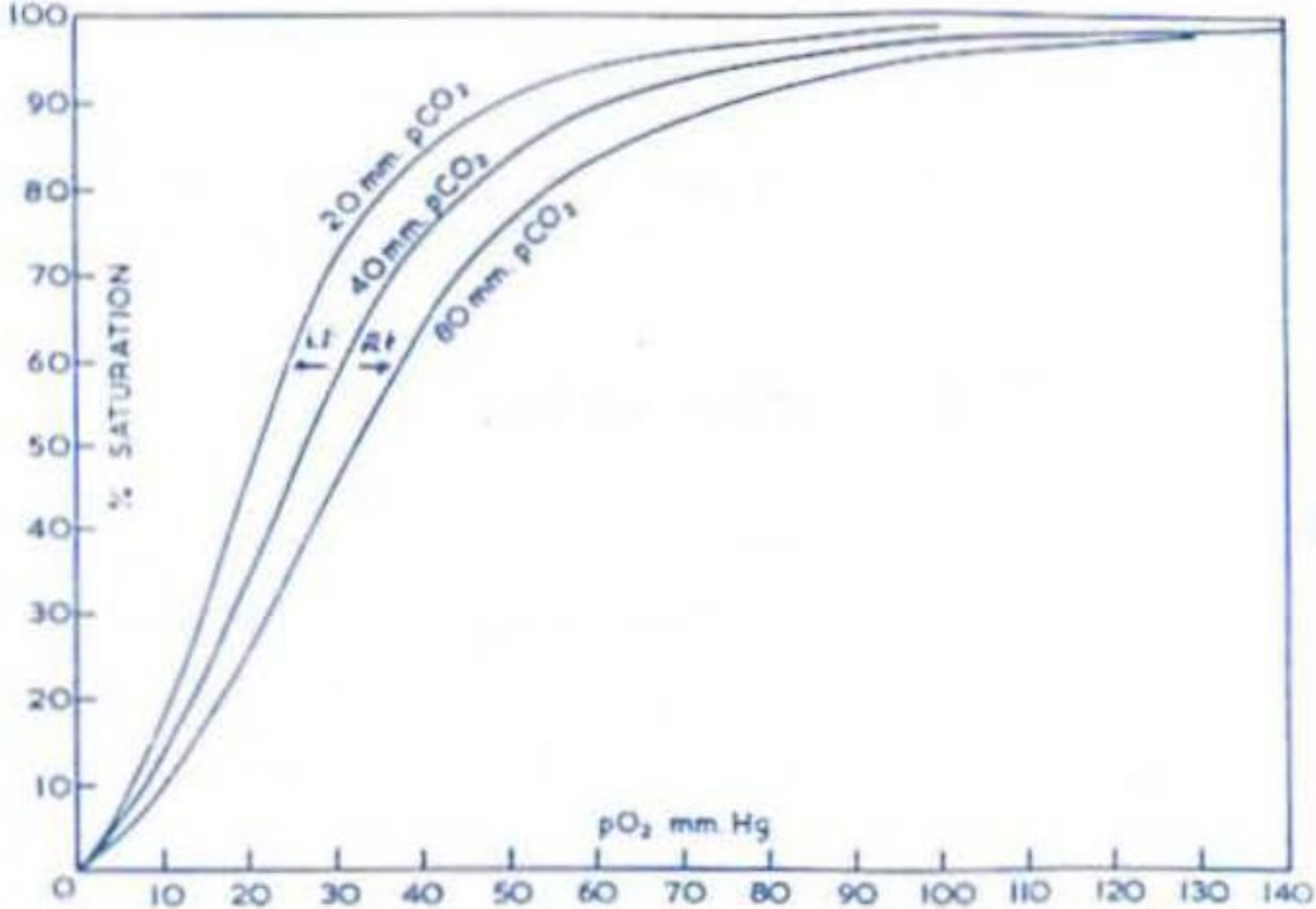
- The 02 Hb dissociation curve may be shifted to the right or to the left. When the curve is shifted to the right, the% saturation of Hb with 02 is decreased at any given 0 2 pressure, indicating decreased affinity of Hb for 02

i.e. more 02 dissociation from Hb & a greater delivery of 02 to the tissues). On the other hand, shift of the curve to the left produces opposite effects

The P_{50}

- This is the 02 pressure at which Hb is 50 % saturated with 02. it is *an index for shifts of the O2-Hb dissociation curve. The normal P50 at* rest *is about 26 mmHg.*

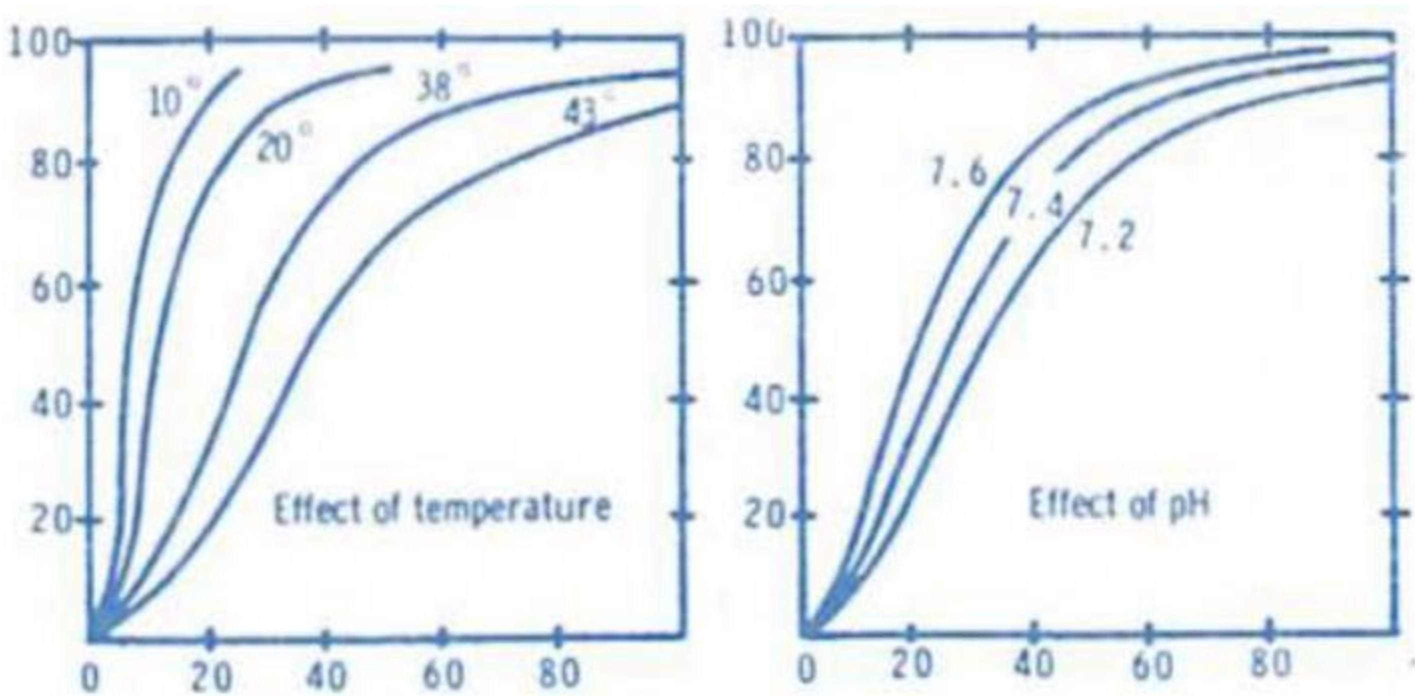
- It *increases when the curve is shifted to the right* (i.e. when the Hb-02 affinity is decreased) while it is *decreased when the curve is shifted to the left* (i.e. when the Hb-02 affinity is increased).



Effects of changes in the arterial P_{CO2} on the O_2-Hb diss. curve.

FACTORS THAT SHIFT THE CURVE TO THE RIGHT

- These factors convert the Hb molecule *from the R form to the T form* (i.e.from the state of more affinity to 02 to the state of less affinity to 02) resulting in more 02 dissociation from Hb and its delivery to the tissues
- The most important of these factors include the following :



Effects of changes in the temperature (left) and blood pH (right) on the O_2-Hb dissociation curve.

1. An increase in H+ concentration (i.e. drop of the blood pH or acidosis). This effect is called Bohr's effect.
2. An increase in the arterial PC02. This shifts the curve to the right secondary to lowering of the blood pH (so it is also a Bohr's effect)
3. An increase in the body temperature.
4. An increase in the 2,3 DPG inside the red blood cells (see next slide).
5. An increase in Hb concentration (e.g in pregnancy and polycythaemia).

*** The first 4 factors act during muscular exercise, helping more 02 dissociation from Hb and greater delivery of 02 to the active muscles.

Role of 2-3 DPG in 02-Hb dissociation

- 2-3 DPG (2-3 diphosphoglycerate) is formed as a product of glycolysis in the Red blood cells. It combines with beta polypeptide chains of Hb A and converts Hb to the T form, which favours release of O2 from Hb as follows :

$$HbO_2 + 2\text{-}3\ DPG \rightarrow Hb.\ 2\text{-}3\ DPG + O_2$$

- Accordingly, when the 2-3 DPG increases, the affinity of Hb to 02 decreases and the curve is shifted to the right. On the other hand, if its concentration decreases, the affinity of Hb to 02 increases and the curve is shifted to the left.

Factors that increase 2-3 DPG synthesis

1. Alkalosis e.g. at high altitudes.
2. Muscular exercise.
3. Anemia and other causes of hypoxia (e.g chronic lung diseases).
4. Some hormones (e.g. thyroxine, the growth hormone and androgens).

- The increase in 2-3 DPG at high altitudes antagonizes the effect of the developed alkalosis to shift the 02-Hb dissociation curve to the left, and shifts the curve to the right (which increases *02* delivery to the tissues)

Factors that decrease 2-3 DPG synthesis

1. Blood storage for long periods.
2. Acidosis [however, during exercise, 2-3 DPG increases in spite of the tendency to acidosis, probably as a result of the temporary hypoxia that occurs in the active muscles due to the increased 02 consumption].

FACTORS THAT SHIFT THE CURVE TO THE LEFT

- These factors convert the Hb molecule*, from the T form to the R form* (i.e. from the state of less affinity to 0 2 to the state of more affinity to 02) resulting in less 0 2 dissociation from Hb and less delivery of 02 to the tissues

- The most important of these factors include the following:

1. A decrease in H+ concentration (i.e. rise of the blood pH or alkalosis).
2. A decrease in the arterial PCO2.
3. A decrease in the body temperature.
4. A decrease in the 2,3 DPG inside the red blood cells. This commonly occurs in *stored blood for long periods*.
5. A decrease in Hb concentration e.g in anaemia.
6. *Carbon monoxide poisoning*.
7. *Fetal blood*.

**** Hb must be kept inside the red blood cells to be concentrated.* In cases of haemolysis, it escapes into the plasma where it is diluted, resulting in shift of the 02-Hb dissociation curve to the left.

❑This is *a serious condition because Hb will be unable to release its 02 content (although it is fully saturated with 02) except at very low 02* pressures.

***Fetal blood contains Hb F (fetal Hb), the molecule of which contains a *pair of alpha polypeptide chains and a pair of gamma polypeptide chains* (instead of the alpha and beta polypeptide chains present in Hb A, refer to notes on blood).

❑*2-3 DPG does not bind to Hb F* because 2-3 DPG can combine *only with the beta polypeptide chain of the Hb A* (see previous slides), which are lacking in HbF. For this reason, the *affinity of HbF to 02 is high,* which results in:

(a) Shift of the 02-Hb dissociation curve to the left
(b) Facilitation of transfer of 02 from the mother to the fetus (in whom 02 dissociation from Hb is favoured by the relatively low PO2 at the fetal tissues)