6- O2-Hb dissociation curve, shift & significance

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Oxygen Transport by Blood

* **O_2 is carried by blood in two forms:**

***1) O_2 in physical solution*:** Nature: O_2 molecules dissolved in blood.

- Volume: it depends on O_2 tension according to *Henery's law*: (dissolved O_2 = PO_2 x 0.003). So,

  In arterial blood (with tension of 100 mmHg) = 0.3 ml/100 ml. and in venous blood (with tension 40 mmHg) = 0.13 ml/100 ml

- **Importance:** 1) It determines O_2 tension in the blood. 2) It is easy to be used by the tissue.

3) It determines the rate and direction of O_2 diffusion. 4)It determines the percentage saturation of haemoglobin with O_2.

2) *O_2 chemical form:*

- Nature: O_2 combines with the iron of haemoglobin while still in the ferrous state (It is called oxygenation not oxidation of Hb). - Hb combines with O_2 in steps HbO_2, HbO_4, HbO_6, and HbO_8
- Volume: 19 ml O_2/100 ml **arterial blood**. 14 ml O_2/100 ml **venous blood** (at rest)
- Importance: it is the main O_2 supply to tissues (however, the tissue utilize physical O_2 at first then chemical form)

O_2 -Dissociation Curve of Hemoglobin

- **Definition:** O_2 dissociation curve shows relationship between O_2 tension and percentage saturation of Hb at different O_2 tensions (Because the percentage saturation is not varied according to Hb. content in different persons).
- **Method:** 3 ml of blood in Tonometer are allowed to form thin layer on the wall and then exposed to different O_2 tensions and % saturation is calculated and plotted against the O_2 tensions in a cu

Physiological significance of the curve:

(a) At the lung and arterial blood: *If the blood is exposed to:*

- O_2 tension of 100 mmHg (normal alveolar O_2 tension) $\rightarrow$ 95% saturation .
- O_2 tension of 70 mmHg (alveolar tension at high altitude or diseased lung) $\rightarrow$ 90% saturation.
- So change of O_2 tension from 100 to 70 mmHg $\rightarrow$ mild change of % saturation. So the curve is nearly horizontal and saturation is easy and complete even with low O_2 tension at the lung to bind with more oxygen and carry it to tissue indicating that Hb has high affinity to O_2 at lungs.

(b) At the tissue and venous blood : *If the blood is exposed to:*

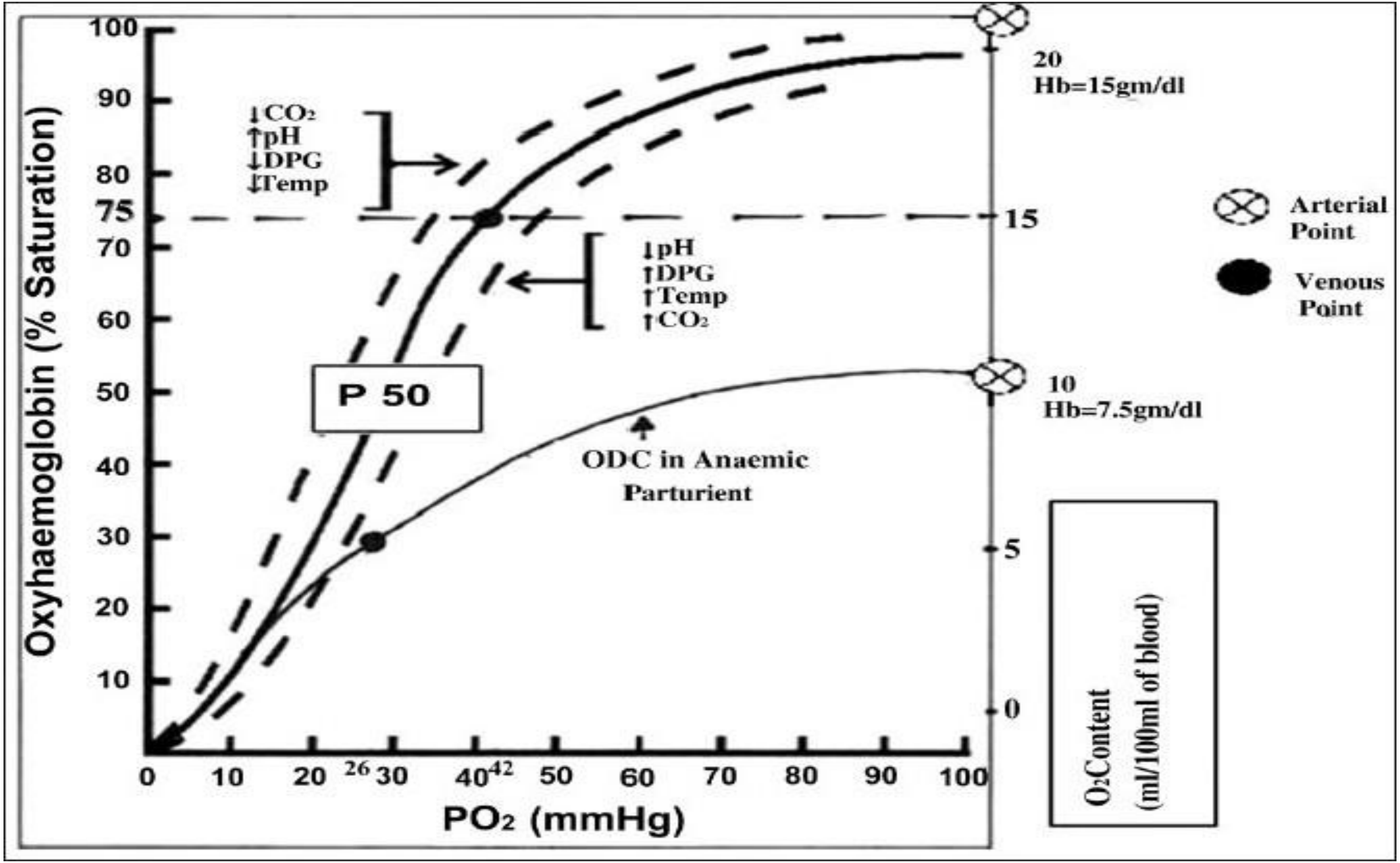
- O_2 tension of 40 mmHg (resting muscle& venous blood tension) → 70% saturation.
- O_2 tension of 25 mmHg (during exercise) → 40% saturation.
  - So, mild change in O_2 tension from 40 to 25 mmHg → large decrease in saturation from 70 to 40% to give oxygen to tissue, so the curve is nearly vertical (steep) at tissue & venous side due to low affinity of Hb to O_2 at lower O_2 tension.
- Also pressure difference between arterial and tissue O_2 is high (100-40 = 60 mmHg) → loss of 25% (95-70 = 25%) of O_2 carried by Hb at rest.

***(c) The curve is sigmoid or "S" shaped*:** because Hb contains 4 ferrous atoms and each one is saturated at certain O_2 tension & saturation of each one facilitates of the following one and so on .As there are 2 states of Hb: (1) Tense or "T" state when Hb gives $O_{2,}$ the "β" chains moves a part with decrease O_2 binding. (2) Relaxed or "R" state when Hb take O_2 the β chains move closer and favors more O_2 binding.

- ***Bohr Effect*:** *it is the decrease in O_2 affinity to hemoglobin when pH of the blood falls . It can attributed to the fact that reduced HB binds H^+ more actively than does oxyhemoglobin which causes unloading of O2 more easily.*

  i.e at lung level (↓ Co_2 & H^+) →↑ Hb affinity to O_2, and at tissue level (↑ Co_2 & H) →↓ Hb O_2 affinity to give it to tissue.

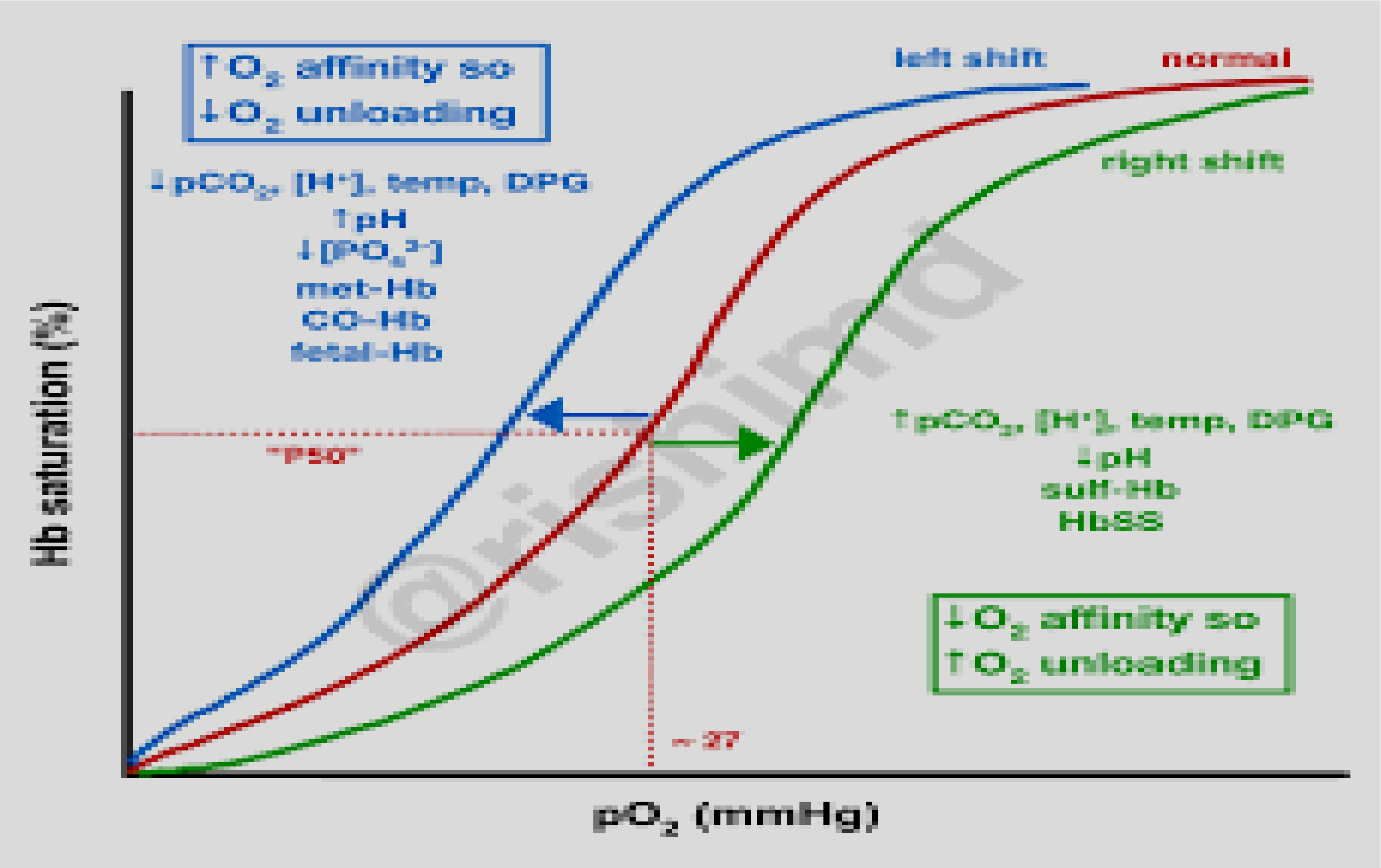
O_2-Hb curve *isn't between O_2 tension and O_2 content as this content is variable from person to other according to amount of hemoglobin. However, the percentage saturation isn't varied from one to another.*



Oxyhaemoglobin (% Saturation)
100
90
80
75
70
60
50
40
30
20
10
0
10
20
26
30
40
42
50
60
70
80
90
100
PO2 (mmHg)
↓CO2
↑pH
↓DPG
↓Temp
↓pH
↑DPG
↑Temp
↑CO2
P 50
ODC in Anaemic Parturient
20
Hb=15gm/dl
15
10
Hb=7.5gm/dl
5
0
Arterial Point
Venous Point
O2Content (ml/100ml of blood)

Shift of the O_2 dissociation curve

Shift to right	Shift to left
Meanings: It means that at any O_2 tension the Hb is less saturated with O_2 and give O_2 to tissue (↓ affinity or unloading)	It means that at any O_2 tension the Hb is more saturated with O_2 so give less O_2 to tissue (↑ affinity or loading)
Causes: (1) decrease O_2 (2) increase Co_2 (Bohr's effect) (3) increase H^+ (acidosis or ↓pH) (4) increase temperature (fever) (5) increase 2,3 DPG . (6) Pregnancy (7) Exercise (8) Anemia.	(1) increase O_2 (2) decrease Co_2 (3) decrease H^+ (alkalosis) (4) decrease temperature (5) decrease 2,3 DPG (6) Fetal Hemoglobin (7) CO poisoning. (8) Polycythemia.
Significance: This increase O_2 supply to active muscle during exercise.	This increases O_2 loading on Hb at the lung .



↑ O_2 affinity so
↓ O_2 unloading
left shift
normal
right shift
↓ pCO_2, $[H^+]$, temp, DPG
↑ pH
↓ $[PO_4^{2-}]$
met-Hb
CO-Hb
fetal-Hb
"P50"
~ 27
↑ pCO_2, $[H^+]$, temp, DPG
↓ pH
sulf-Hb
HbSS
↓ O_2 affinity so
↑ O_2 unloading
Hb saturation (%)
pO_2 (mmHg)

*(1) **Effect of 2,3 DPG:***

- *2,3 Diphosphoglycerate is formed in RBCs by **anaerobic glycolysis**, and combines to the reduced Hb leading to ↓ Hb affinity to O_2. 2,3 DPG increased in anemia, muscular exercise, high altitude, increase in thyroid hormone(hyperthyroidism), growth hormones and androgens and in chronic hypoxia → ↑O_2 supply to tissue*

- but in a stored blood →↓ 2,3 DPG →↓ O_2 supply to tissue of recipient. Also acidosis depress glycolysis and decrease 2,3DPG.

*(2) **Effect of fetal Hb in newly born:***

- *Adult Hb contains pair of (α) and pair of beta (B) polypeptides which combine with 2,3 DPG → ↓ Hb affinity to O_2.*
- *Fetal Hb contains pair of alpha (α) and pair of gamma (γ) which can't combine with 2,3 DPG so → ↑ Hb affinity to O_2. This facilitates movement of O_2 from mother to fetus and keeps high O_2 in fetal Hb to be used under need.*

*(3) **Effect of muscular exercise:***

- *Muscular exercise increases O_2 supply to tissue (muscles) by 50 times by the followings:*

1- ↑ cardiac output by 6 times (from 5 to 30 L/min).

2- VD of blood vessels of skeletal muscles (sympathetic and metabolic) →↑O_2 supply by 3 times.

3- ↑ coefficient of O_2 utilization by muscles, the muscle take 15 ml O_2 from total 19 ml O_2/100 ml of arterial blood due to (↓ O_2 in tissue & shift of O_2 dissociation curve to Rt. as before) →↑O_2 supply by 3 times.

** In **untreated diabetes** and **renal failure** there are shift to **right** due to associated **acidosis**.*

P50 of Hemoglobin & factors influencing

The P50 is the **oxygen tension** at which **hemoglobin** is **50% saturated**. **The normal P50 is 26.7 mm Hg**.

Shifting the curve to the left or right has little effect on the SO2 in the normal range where the curve is fairly horizontal; a much greater effect is seen for values on the steeper part of the curve.

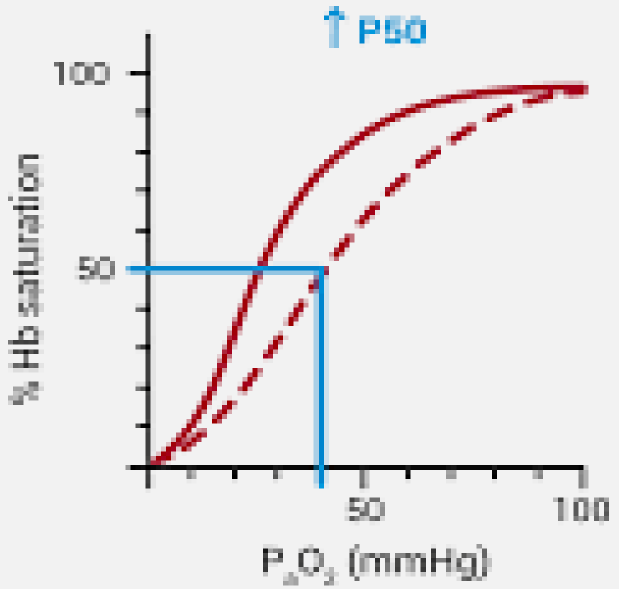
Shifting of the Oxy-hemoglobin dissociation curve:

A rightward shift increases P50 and lowers hemoglobin's affinity for oxygen, thus displacing oxygen from hemoglobin and releasing it to the tissues.

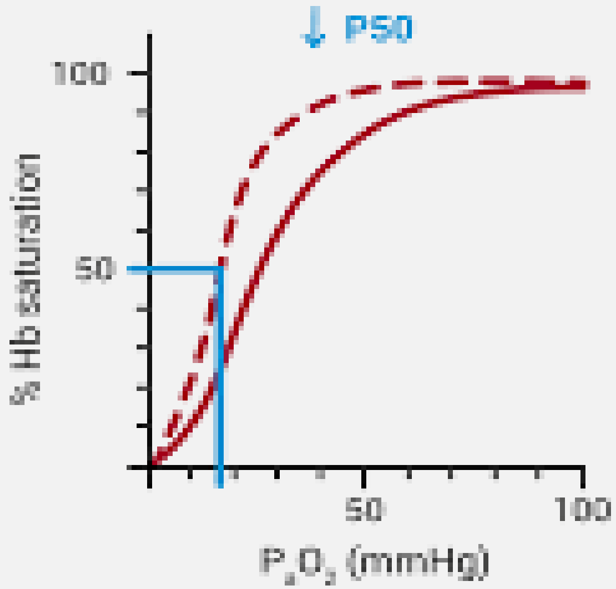
A leftward shift decreases P50 and increases hemoglobin's affinity for oxygen, thus reducing its availability to the tissues.

N.B: Met-hemoglobinemia causes a **left-ward shift** in the curve.

Shift to right



Shift to Left



Thank You