RS MODULE
PHYSIOLOGY (LECTURE 5)
O_2-Hb Dissociation Curve

BY

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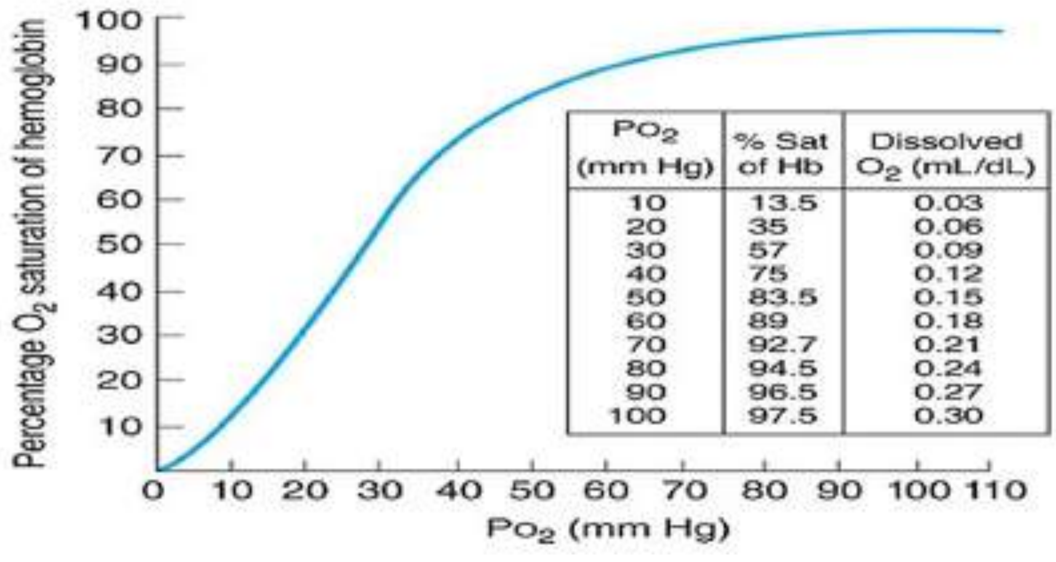


Po_2 (mm Hg)	% Sat of Hb	Dissolved O_2 (mL/dL)
10	13.5	0.03
20	35	0.06
30	57	0.09
40	75	0.12
50	83.5	0.15
60	89	0.18
70	92.7	0.21
80	94.5	0.24
90	96.5	0.27
100	97.5	0.30

Transport of Oxygen in Blood

OXYGEN DELIVERY TO THE TISSUES

Oxygen delivery:

- It is the volume of oxygen delivered to the systemic vascular bed per minute.
- It is the product of the cardiac output and the arterial oxygen concentration.

▪ The ability to deliver O_2 in the body depends on both the respiratory and the cardiovascular systems.

▪ O_2 delivery to a particular tissue depends on:

- The amount of O_2 entering the lungs.
- The adequacy of pulmonary gas exchange.
- The capacity of the blood to carry O_2.
- The rate of blood flow to the tissue.

The oxygen is present in blood in two forms:

(1) Dissolved in the plasma and erythrocyte cytosol (physical solution). It is normally a very small amount but important (it determines PO_2 in blood and the degree of saturation of Hemoglobin with O_2).

(2) Reversibly combined with hemoglobin molecules in the erythrocytes (chemical combination). It constitutes the majority of O_2 content in blood. It is essential for supplying adequate amounts of O_2 to tissues.

Therefore, hemoglobin (Hb) can exist in one of two forms: deoxyhemoglobin (Hb) and oxyhemoglobin (HbO_2).

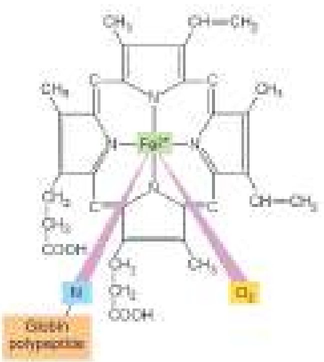
Total amount of oxygen carried by hemoglobin in the blood depends on:

- Hemoglobin in each liter of blood.
- The percent saturation of hemoglobin.

In a blood sample containing many hemoglobin molecules, the fraction of all the hemoglobin in the form of **oxyhemoglobin is expressed as the percent hemoglobin saturation:**

Percent Hb saturation = $\dfrac{O\,2\ bound\ to\ Hb\ (O2\ content)}{Maximal\ capacity\ of\ Hb\ to\ bind\ O2}\ x\ 100$

Maximal capacity of Hb to bind O2 = O2 carrying capacity of blood.



Maximal capacity of Hb to bind O_2 and Oxygen Content of Blood

Maximal capacity of Hb to bind O_2:

- ✓ **When Hb is fully saturated: each gram (g) of normal hemoglobin binds 1.34 mL of O_2.**
- ✓ The hemoglobin concentration in normal blood is about 15 g/dl.
- ✓ Therefore, **1 dl (100 ml) of blood contains 20.1 ml (1.34 ml × 15) of O_2 bound to hemoglobin when the hemoglobin is 100% saturated = Maximal capacity of Hb to bind O_2.**

- ❑ **The amount of dissolved O_2 is a bout 0.3 ml/dl (arterial blood).**
- ❑ **In vivo, the hemoglobin in the blood at the ends of the pulmonary capillaries is about 97.5% saturated with O_2 (PO_2 = 100 mm Hg).**
- ❑ **Because of a slight admixture with venous blood that bypasses the pulmonary capillaries (i.e, physiological shunt), the hemoglobin in systemic arterial blood is only 97% saturated.**

O_2 content:

It is the volume of O_2 (ml) present in chemical combination (bound to Hb) in 1dl of blood.

- Oxygen content of blood can be calculated by the following formula:

O_2 content = % saturation × O_2 binding capacity + dissolved oxygen.

- **The arterial blood O_2 content** = about 19.8 ml of O_2/dl: 19.5 ml bound to hemoglobin and 0.3 ml in solution.
- **In venous blood :**
  - ✓ **The hemoglobin is 75% saturated.**
  - ✓ The total O_2 content is about 15.2 ml/dl: 15.1 ml bound to hemoglobin and 0.12 ml in solution.

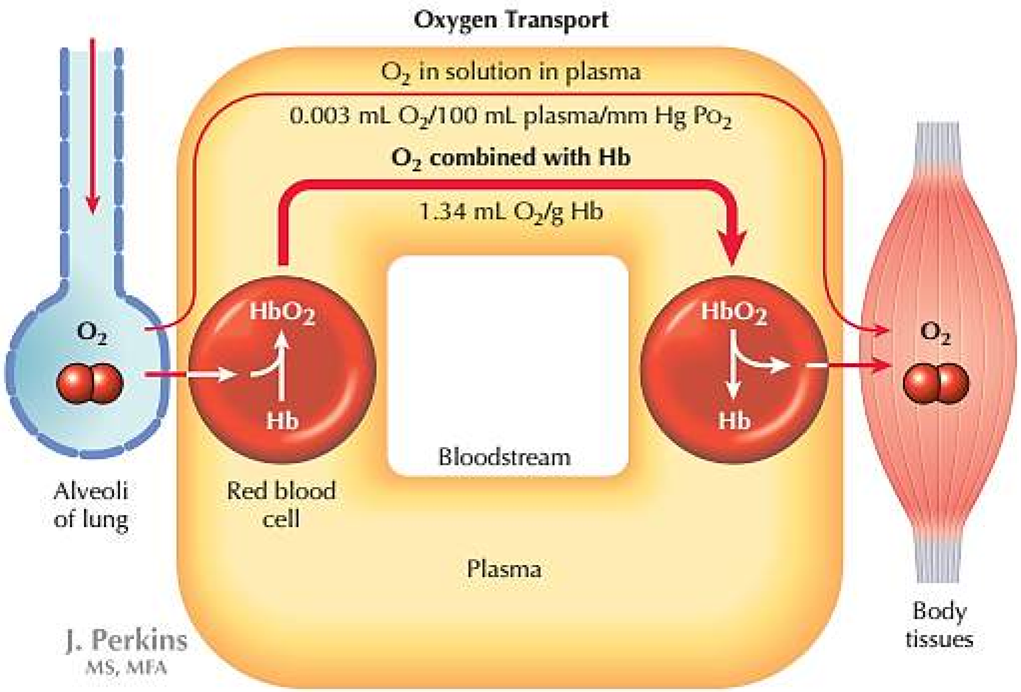


Figure 15.1 **Oxygen Transport** Oxygen diffuses into the blood flowing through alveolar capillaries and is transported to tissues, where it diffuses out of the blood along its concentration gradient. Transport of oxygen in the blood is mainly in the form of oxygen combined with hemoglobin, with only a minor portion carried in the form of dissolved oxygen.

Arteriovenous Oxygen Gradient and Oxygen Consumption

- **Arteriovenous difference in oxygen content of blood is about 4.6 ml. Thus, at rest the tissues remove about 4.6 ml of O_2 from each deciliter (dl) of blood passing through them.**

- Based on this arteriovenous difference in oxygen content of blood and cardiac output, oxygen consumption can be estimated. Thus,
- O_2 consumption = $[a - v]O_2 \times$ cardiac output.
- **In this way, about 250 ml O_2 /minute is transported from the blood to the tissues at rest.**

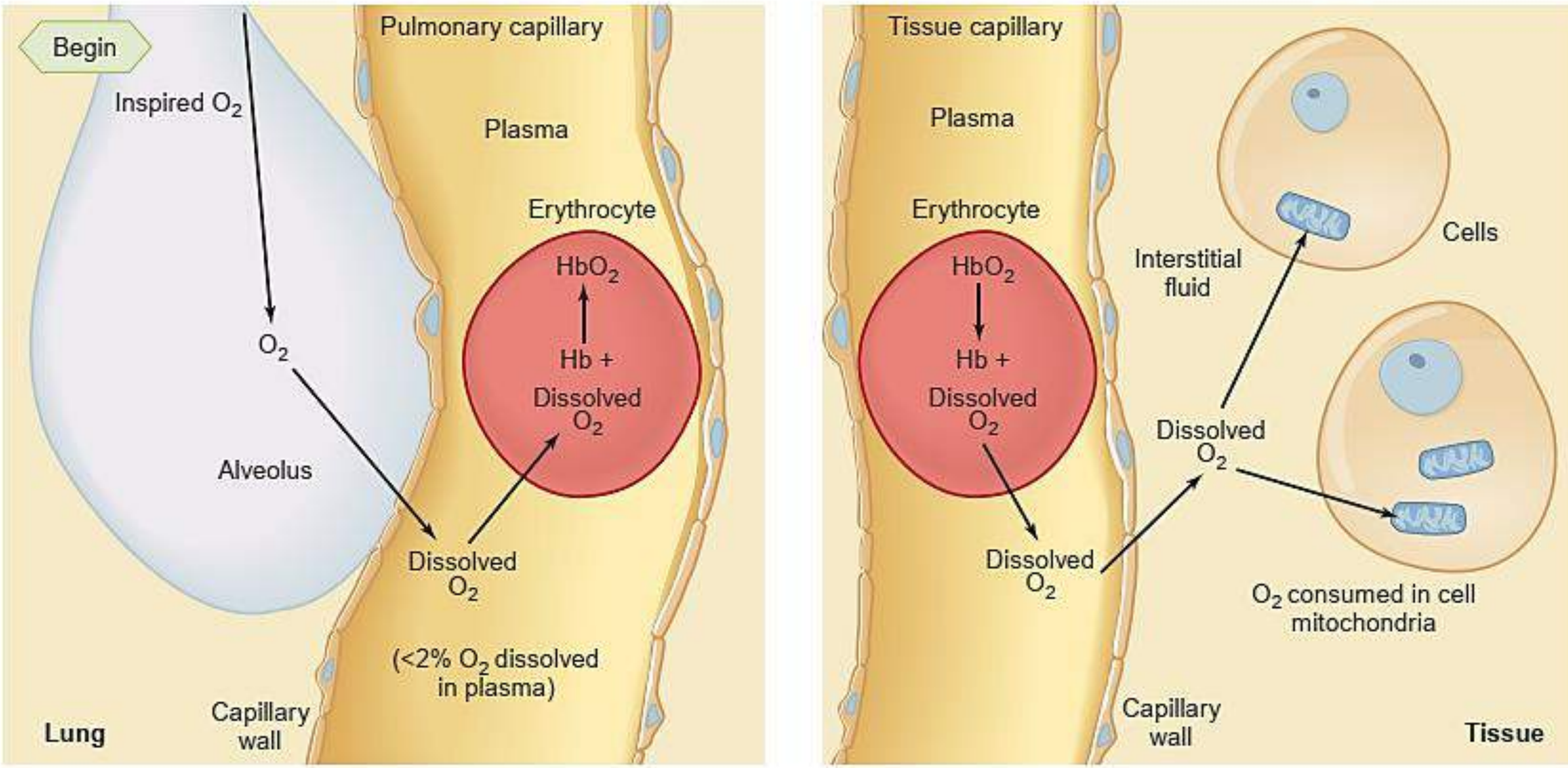
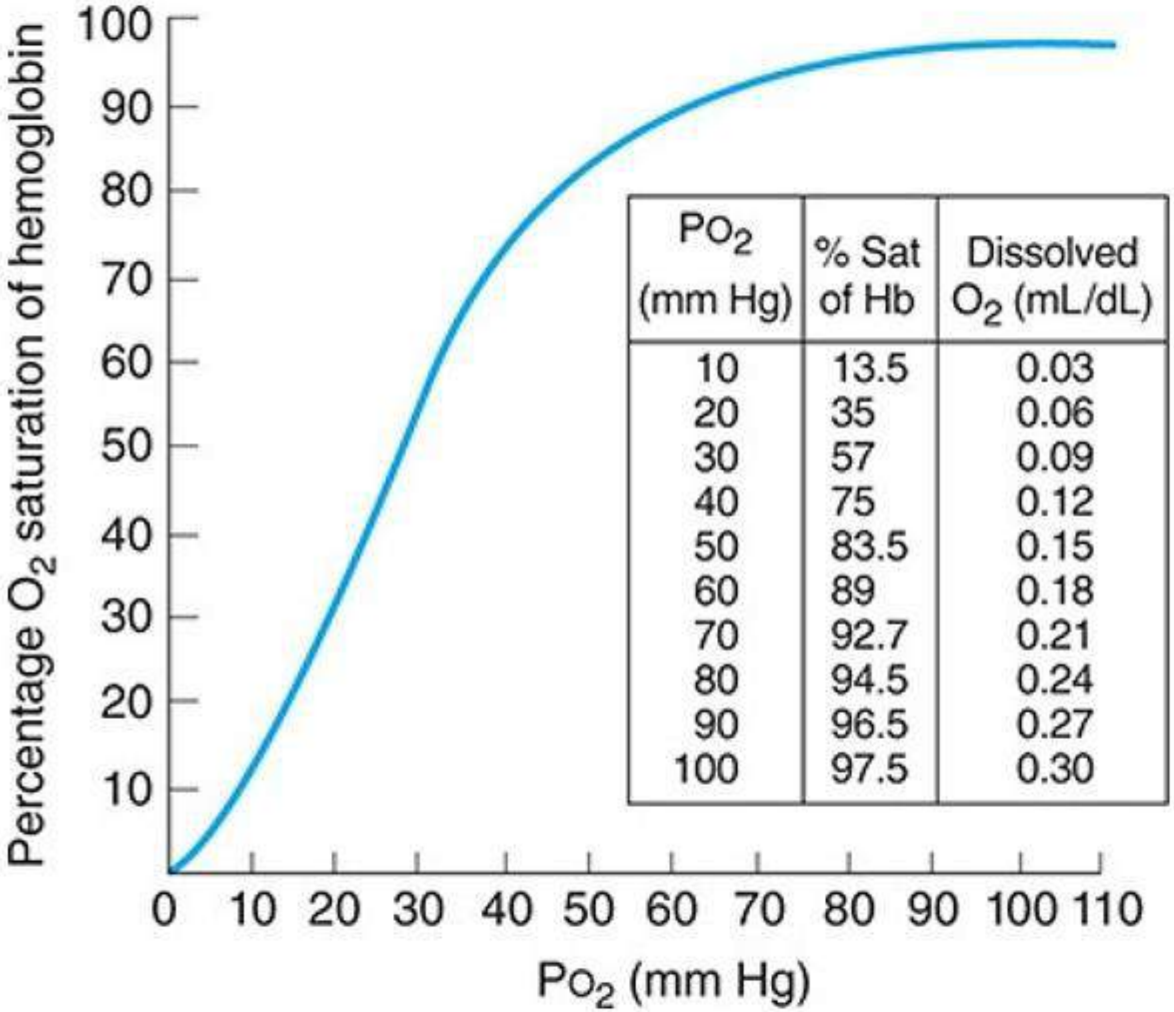


Figure 13.28 AP|R Oxygen movement in the lungs and tissues. Movement of inspired air into the alveoli is by bulk flow; all movements across membranes are by diffusion.

The oxygen–hemoglobin dissociation curve

- **It describes the relationship between the percentage O_2 saturation of hemoglobin (SaO_2) to the PO_2.**
- At PO_2 of 100 mm Hg (arterial blood), hemoglobin is actually, 97.5% saturated with oxygen and at PO_2 40 mm Hg (venous blood), hemoglobin is 75% saturated.
- **This curve has a characteristic sigmoid shape (S-shaped)** due to the T–R configuration interconversion.
- Combination of the first heme in the Hb molecule with O_2 increases the affinity of the second heme for O_2, and oxygenation of the second increases the affinity of the third, and so on, so that the affinity of Hb for the fourth O_2 molecule is many times that for the first. (cooperative binding of O_2 to hemoglobin).



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Oxygen–hemoglobin dissociation curve

Significance of O2-Hb dissociation curve

Due to the sigmoid shape:

- ✓ **In the lungs, blood will become fully saturated with oxygen over a wide range of PO_2, due to the flat upper portion of the oxygen-hemoglobin dissociation curve.**
- ✓ **PO_2 can fall substantially without greatly affecting the degree of saturation of hemoglobin: at PO_2 of 70 mm Hg, SaO_2 is still about 93% as occurs in high altitude and pulmonary diseases that cause alveolo-capillary block.**
- ✓ **On the other hand, at the lower PO_2 levels in tissue capillaries : A small decrease in PO_2 results in dissociation of relatively large amounts of oxygen (marked decrease in SaO_2) due to the steep portion of the curve, facilitating oxygen delivery to the tissues.** Thus, small changes at low PO_2 lead to large changes in SaO_2. This effect is useful in **muscular exercise**.

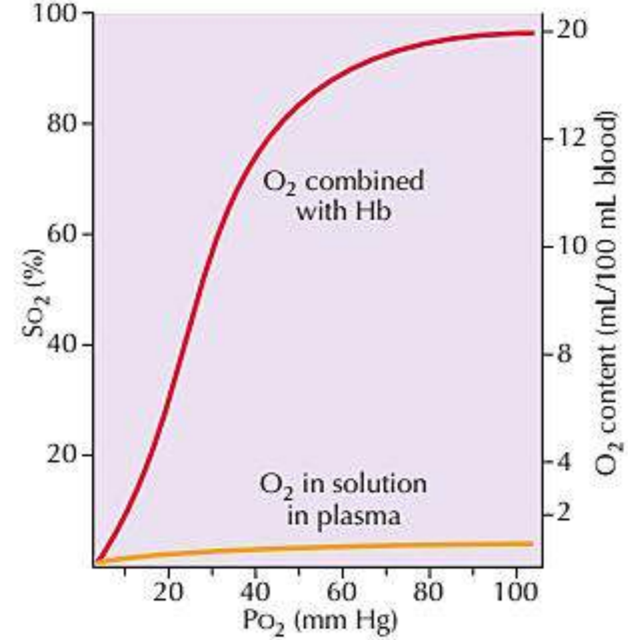
FACTORS AFFECTING THE OXYGEN– HEMOGLOBIN DISSOCIATION CURVE

- ✓ **Factors affecting the affinity of Hb for O_2 (shift of O_2-Hb dissociation curve)**
- ✓ Three important conditions affect the oxygen–hemoglobin dissociation curve:
  - **The pH.**
  - **The temperature.**
  - **The concentration of 2,3-diphosphoglycerate (DPG; 2,3-DPG).**
- ✓ **A rise in temperature or 2,3- DPG or a fall in pH (increased PCO_2) shifts the curve to the right…….decreased affinity of Hb to O_2.**
- ✓ **Shift to the right : Means that at any given PO_2, hemoglobin has less affinity for oxygen (SaO_2 is decreased). When the curve is shifted in this direction…….decreased affinity of Hb to O_2 and enhanced O_2 delivery to tissues.**
- ✓ **The pH of blood falls as its CO_2 content increases, so that when the PCO_2 rises, the curve shifts to the right.**

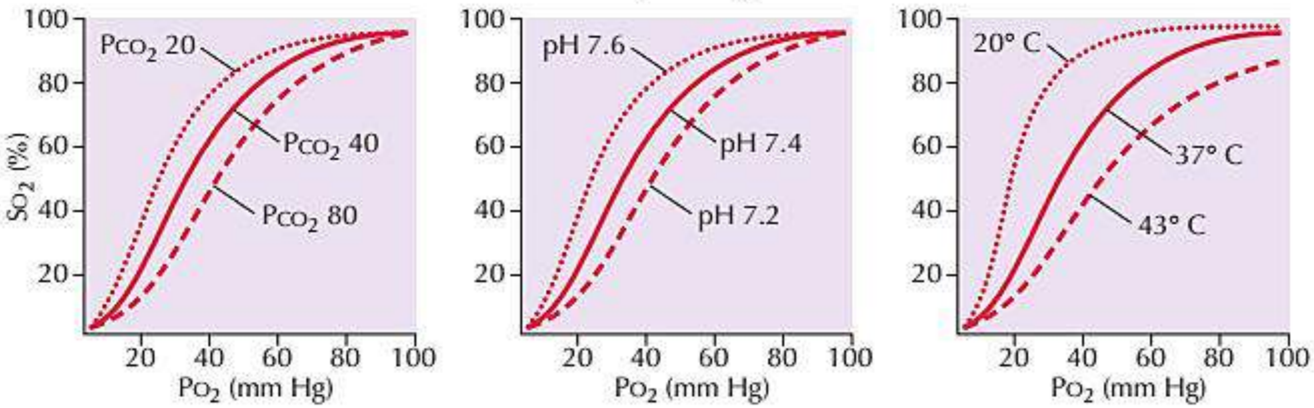
- ✓ Conversely, **a fall in temperature or 2,3- DPG or a rise in pH (decreased PCO_2) shifts the curve to the left……….increased affinity of Hb to O_2 (SaO_2 is increased).**
- ✓ **Carbon monoxide poisoning and fetal Hb (HbF)………shift of O_2-Hb dissociation curve to left.**
- ✓ **Shift to the left: Means that at any given PO_2, hemoglobin has a greater affinity for oxygen (SaO_2 is increased) and less delivery of O_2 to tissues.**
- ✓ **A convenient index for comparison of such shifts is the P_{50}.**
- ✓ **P_{50}** : **It is the PO_2 at which hemoglobin is half saturated with O_2. It is about 26 mmHg.**

- o The higher the P_{50}, the lower the affinity of hemoglobin for O_2 (shift to right).
- o The lower P_{50}, higher the affinity of hemoglobin for O_2 (shift to left).

Oxyhemoglobin Dissociation Curve
(at pH 7.4, P_{CO_2} 40 mm Hg, 37° C)



Effects of P_{CO_2}, pH, and Temperature on O_2 Dissociation Curve



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- ✓ The decrease in O_2 affinity of hemoglobin when the pH of blood falls or PCO_2 rises is called the Bohr's effect.
- ✓ **Most of the unsaturation of hemoglobin that occurs in the tissues is secondary to the decline in the PO_2.**
- ✓ **2,3-DPG :**

- o It is very plentiful in red blood cells. It is formed from 3- phosphoglyceraldehyde, which is a product of glycolysis.
- o It binds to the β chains of HbA.

$$HbO_2 + 2,3\text{-}DPG \rightleftarrows Hb - 2,3\text{-}DPG + O_2$$

- o In this equilibrium, an increase in the concentration of 2,3-DPG shifts the reaction to the right, causing more O_2 to be liberated.
- o **High altitude, hypoxia, muscular exercise and some hormones (thyroid hormones, growth hormones, and androgens), can all increase the concentration of 2,3-DPG.**

During exercise:

- **The temperature rises in active tissues and CO_2 and metabolites accumulate, lowering the pH.**
- In addition, much more O_2 is removed from each unit of blood flowing through active tissues because the tissue **PO_2 declines……(Shift of O_2-Hb dissociation curve to right)**
- Finally, at low PO_2 values, the oxygen–hemoglobin dissociation curve is steep, and large amounts of O_2 are liberated.

HBF

- Oxygen delivery to the fetus involves transfer of oxygen from maternal blood to fetal blood across the placenta.
- Fetal blood contains a form of hemoglobin known **as fetal hemoglobin (hemoglobin F) that has higher affinity for oxygen than adult hemoglobin (hemoglobin A)**, facilitating transfer of oxygen from maternal to fetal blood.
- **Thus, the oxygen-hemoglobin dissociation curve for hemoglobin F is shifted to the left**, compared with the dissociation curve for hemoglobin A.
- **At a given PO_2, oxygen saturation of hemoglobin F will be higher than that of hemoglobin A.**
- Hemoglobin F is replaced by hemoglobin A within the first 3 months of life.

Effect of Carbon Monoxide on Oxygen Binding to Hemoglobin

- Carbon monoxide is a colorless, odorless gas.
- It is one of the more common causes of sickness and death due to poisoning.
- Its most striking pathophysiological characteristic is **its extremely high affinity—210 times that of oxygen—for the oxygen-binding sites in hemoglobin.**
- For this reason, **it reduces the amount of oxygen that combines with hemoglobin in pulmonary capillaries** by competing for these sites.
- **It also exerts a second deleterious effect: It alters the hemoglobin molecule so as to shift the oxygen–hemoglobin dissociation curve to the left**, thus **decreasing the unloading of oxygen from hemoglobin in the tissues**.


Thank you