OXYGEN DISSOCIATION CURVES

CARBON MONOXIDE POISONING

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Oxygen Dissociation Curves

Recall we had said earlier in the section that in humans the oxygen carrying capacity is 20 ml oxygen per 100 ml blood. The relationship of oxygen carrying capacity to surrounding oxygen concentration can be shown graphically by the **oxygen dissociation curves (ODC)** (Fig. 2.14) which give us information about the most important function of red blood cells and the haemoglobin contained within them which is, the affinity of haemoglobin for oxygen and its delivery to the tissues. These curves are obtained by subjecting blood samples to different partial pressures of oxygen. The percentage of oxyhaemoglobin saturation at different partial pressures of oxygen is plotted.

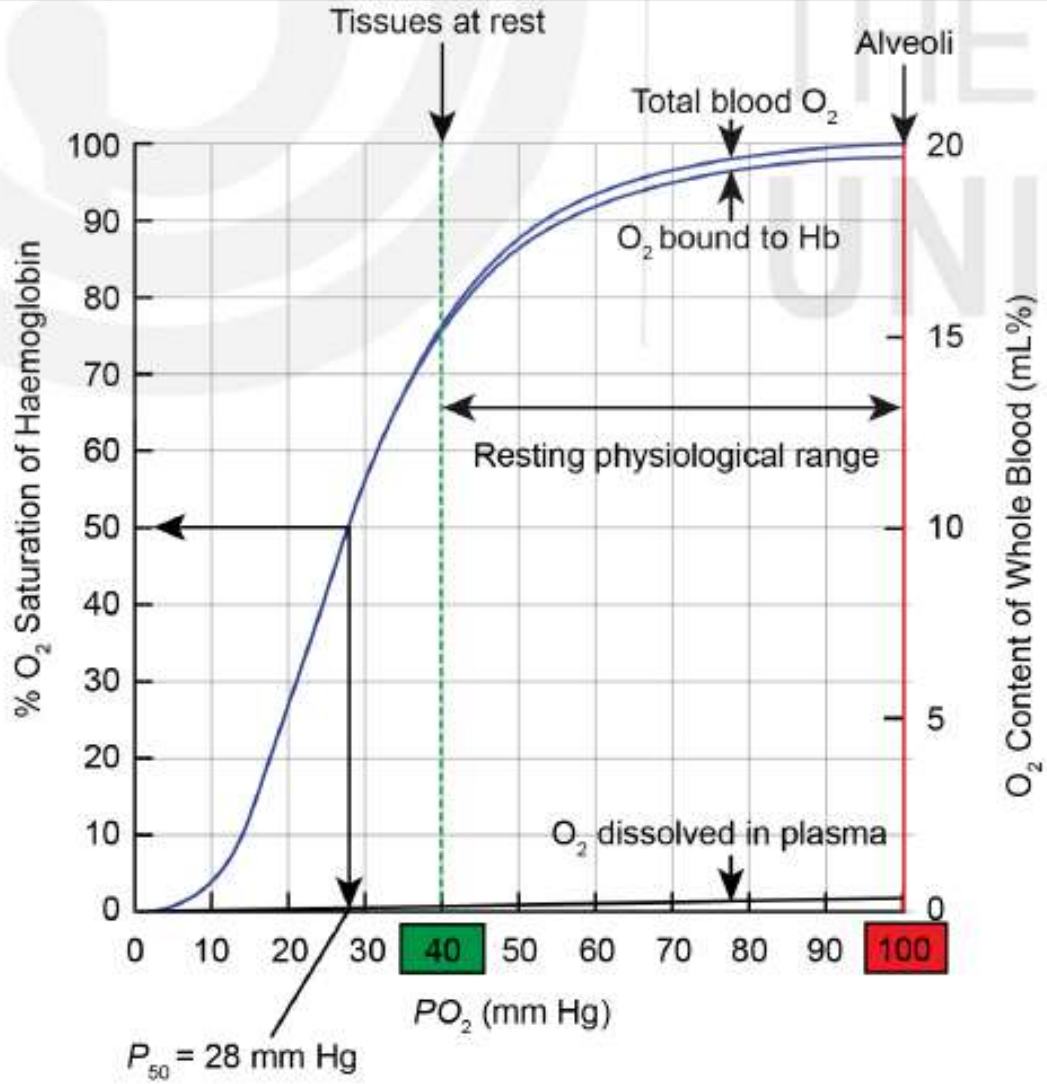

Fig. 2.14: Oxygen dissociation curve shows how haemoglobin's oxygen binding capacity depends on partial pressure of oxygen. Note that there is a 22% decrease in the percent of oxygen as blood passes from arteries to veins in the tissue. This results in unloading of approximately 5 ml of oxygen per 100 ml of blood.

The oxygen dissociation curve is S-Shaped or a sigmoid curve with the percentage of oxygen saturation of Hb shown on the Y (vertical) axis and the partial pressure of oxygen depicted on the X (horizontal) axis. You must remember that the amount of oxygen bound to hemoglobin i.e. the percentage O_2 saturation of hemoglobin at any time is related to partial pressure of O_2 that surrounds it. In the oxygen dissociation curve in Figure 2.14 we can see that that as Po_2 increases the oxygen saturation of haemoglobin also increases. We can see that total saturation of Hb occurs in the lungs where partial pressure of oxygen is above 95 mm Hg. We can also see that at 60 mm Hg partial pressure of oxygen the curve begins to flatten out even if Po_2 levels are increased sharply. The steep portion of the curve indicates that when Po_2 drops (in systemic capillaries of tissues) the oxygen is dissociated from Hb and is released to the tissue. The curve shows that changes in Po_2 values from arterial to venous blood result in 97-75 = 22% unloading when resting.

The PO_2 of oxygen when Hb is 50% saturated is about 28mmHg for healthy person and this point in graph is called P_{50}. In disease, the affinity of O_2 changes and the graph shifts to right or left.

Oxygen dissociation curve for a sample of blood is affected by several factors. The most important of them are:

1. Temperature
2. pH
3. CO_2
4. 2,3 – Diphosphoglycerate (DPG) –Organic phosphate

The importance of 2.3-DPG within the red blood cells is now recognized in blood banking. Old stored red cells lose their ability to produce 2.3-DPG which means that such cells will not unload their oxygen easily. Modern techniques for storage of blood, therefore, include the addition of energy substrates for respiration and phosphate sources needed for production of 213-DPG.

1. **Temperature :** Haemoglobin, at higher temperature gives up oxygen more readily and thus the dissociation curve shifts to the right (Fig 2.15). This is of physiological importance because increased temperature means higher metabolic rate or higher oxygen requirement by the organism.

2. **pH :** Another important factor that influences the oxygen dissociation curve is pH. An increase in carbon dioxide or other acids in the blood lowers the pH of the plasma and shifts the dissociation curve to the right (Fig. 2.15). At high carbon dioxide concentration more oxygen is unloaded at any given oxygen pressure. This effect is known as **Bohr effect,** after the Danish scientist who first described it. Therefore, as carbon dioxide enters the blood from respiring tissues it encourages the release of more oxygen. This is an important characteristic because it allows more oxygen to be released to the tissues which need it the most. More oxygen is loaded in the lungs and more is unloaded at the tissues as a result of **Bohr Effect,** than would be the case if only diffusion along the concentration gradient was responsible.

3. **Carbon dioxide :** Carbon dioxide lowers the oxygen affinity of haemoglobin even if the pH-is kept constant. This effect is due to the binding of carbon dioxide to the terminal amino groups of haemoglobin molecule forming carbaminohaemoglobin. This site is not the same site on the molecule where oxygen is bound.

4. **2, 3-diphosphoglycerate (DPG) :** The presence of organic phosphate namely 2,3-diphosphoglycerate (DPG), in the red blood cells helps to explain many peculiarities of the oxygen dissociation curve. Previously the red blood corpuscle was considered to be a bag full of haemoglobin with no metabolism of its own because of the absence of a nucleus. Now we know that it has an active carbohydrate metabolism and the RBC has a high content of ATP and 2, 3-diphosphoglycerate (DPG). 2, 3-diphosphoglycerate is a product of glycolysis and binds to the beta chain of the globin and reduces oxygen affinity. Experimentally it has been shown that pure haemoglobin has greater oxygen affinity than whole blood (the dissociation curve for pure haemoglobin is far to the left of the curve as compared to that for the whole blood) Fig. 2.15. If 2, 3-DPG is added to pure haemoglobin solution the oxygen affinity decreases and approaches that of whole blood.

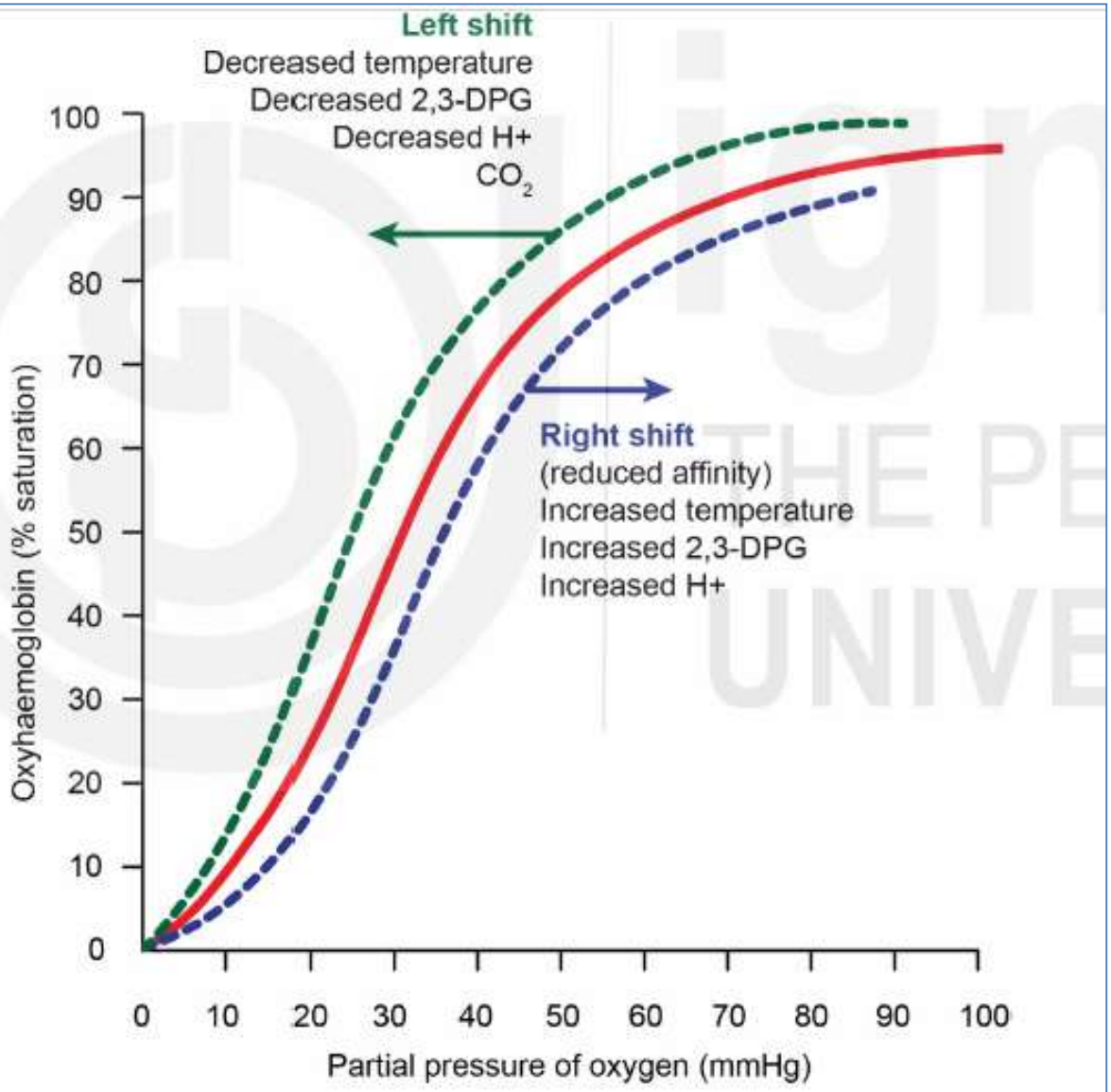

Fig. 2.15: The oxygen dissociation curve shifts to the right or left depending on temperature, carbon dioxide, pH, or 2,3-DPG levels . Due to Bohr effect oxyhaemoglobin surrenders its oxygen more readily in the presence of increasing acidity which is the case in metabolically active cells where more CO_2 is released.

We have learnt about the S shaped curve for haemoglobin. Let us now see how the oxygen dissociation curve of haemoglobin is different from the curve showing oxygen affinity in myoglobin. In myoglobin the haem reacts to oxygen independently. It does not show cooperativity binding as in the case of

haemoglobin. Fig. 2.16 shows the dissociation curve for myoglobin which in contrast to the curve for haemoglobin is rectangular. Myoglobin is described as middleman in the transfer of oxygen from blood to mitochondria within muscle cells. Myoglobin has a much stronger affinity for oxygen and stores oxygen in the muscles. It binds to oxygen at a much lower partial pressure than haemoglobin and dissociates from its bound oxygen only when the partial pressure of oxygen is very low as found in the mitochondria.

Fig. 2.16 also indicates that the myoglobin remains oxygenated until quite low levels of Po_2 in the surrounding fluids is reached. You can see from the figure that at 20 mm Hg the haemoglobin in the blood is about 30% saturated but the myoglobin in the muscles is above 80% saturated.

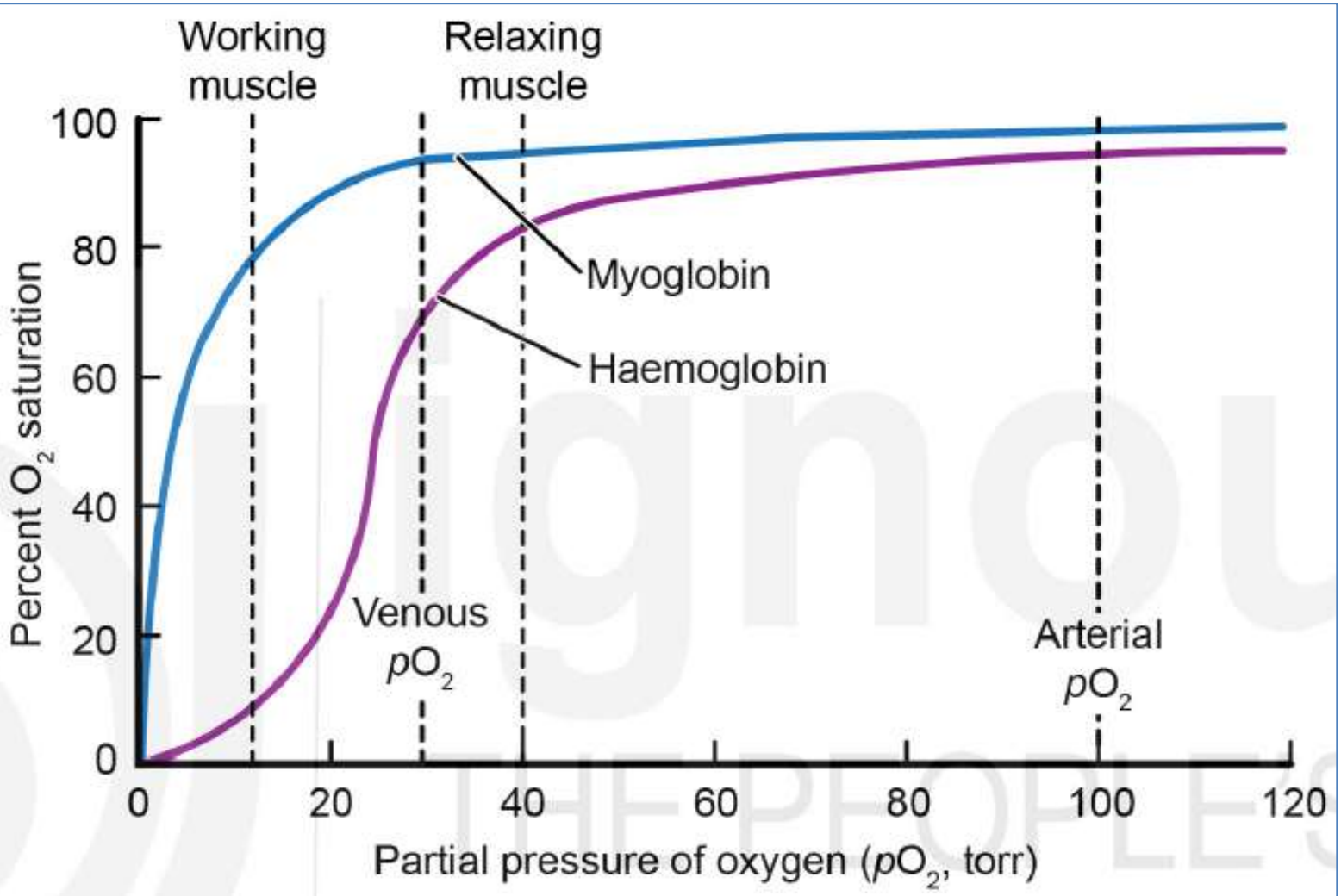

Fig. 2.16: A comparison of the dissociation curves for haemoglobin and for myoglobin. At the Po_2 of venous blood, the myoglobin retains almost all of its oxygen, indicating a higher affinity than haemoglobin for oxygen. The myoglobin does, however, release its oxygen at the very low PO2 values found inside the mitochondria.

CARBON MONOXIDE (CO) POISONING

The most common and widely distributed air pollutant is Carbon monoxide (CO). The physical properties of CO are the following:

- It is a colourless, odourless and tasteless gas
- Poorly soluble in water
- Slightly lower density than air

Carboxyhemoglobin is form when CO reacts with hemoglobin in human body and small amounts of carbon monoxide are also produced endogenously. 60 % of human activities are responsible for the annual global emissions of carbon monoxide, while 40% of the global emission is due to natural processes. The atmosphere has been estimated to be as high as 2600 million tonnes. Incomplete combustion of carbonaceous materials, anthropogenic emissions of carbon monoxide originate. The largest proportion of these emissions is produced as exhausts of internal combustion engines, especially by motor vehicles with petrol engines. Other common sources of CO emissions are following:

Toxicity of Carbon monoxide

The persistence period of Carbon monoxide is about a month, which can be transported long distances. It is not uniformly distributed around the Earth. This is one of the greenhouse gases, which has an influence on climate. CO has an ability to absorb infrared radiation that is escaping from the surface of the earth causing the atmosphere to warm up.

CO remains in the body for a long time - the half-life of CO in the body is about five hours. Increased levels of carbon monoxide reduce the amount of oxygen carried by hemoglobin in the body in red blood cells and also cause asphyxiation. The result is that vital organs, such as the brain, nerve tissues and the heart, do not receive enough oxygen to work properly. The effects depend on duration and concentration of carbon monoxide in the air. For example, breathing air which has 400 parts per million (ppm) of CO in it will cause a headache after one or two hours, but can kill some people after three hours. The older people, fetus, children and people with heart, circulatory, or lung disease are the most affected from the exposure to CO.

Carbon monoxide (CO) combines with haemoglobin in the blood 210 times as readily as oxygen to form carboxyhaemoglobin (COHb). On the other hand COHb dissociates less readily than oxygen. It effectively prevents haemoglobin from transporting oxyhaemoglobin to the cells of the brain and other vital organs.

The amount of COHb formed is dependent upon the CO concentration, the length of time exposed, and the rate of breathing. The effect of CO is more pronounced at higher altitudes and on persons suffering from cardiovascular disease, anaemic persons and smokers. Smokers have a rather high background level of COHb (about 5%) compared to non-smokers (about 0.5%). Studies have indicated that adverse health effects can be noted at COHb levels as low as 2.5%. A concentration of 20% COHb produces headache and other subjective symptoms. A 2.5% COHb level can be reached during an 8 hour exposure to a 15 ppm concentration of CO. Prolonged exposure to a 100 ppm concentration of CO can be fatal.

- Various industrial processes like power plants using coal, and waste incinerators.
- Petroleum-derived emissions have greatly increased during the past few decades.
- Some widespread natural nonbiological and biological sources, such as plants, oceans and oxidation of hydrocarbons, give rise to the background concentrations outside urban areas.
- In various indoor environments, space heaters fuelled with oil, gas or kerosene, gas stoves
- Some other combustion appliances, and tobacco smoking cause significant emissions of carbon monoxide.