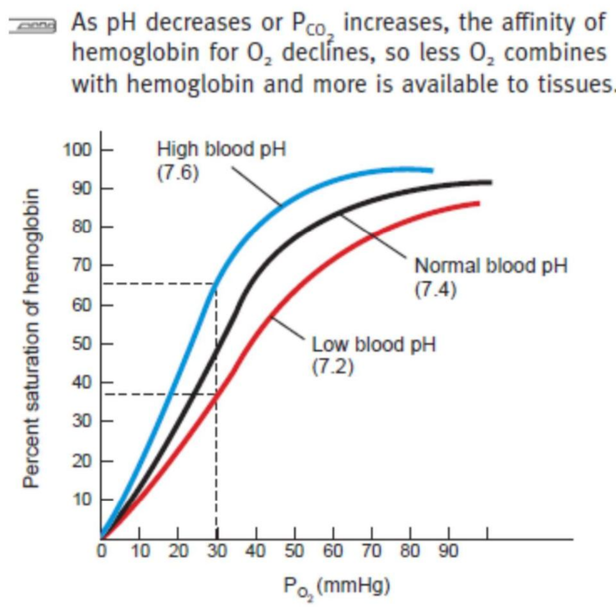
90% or more saturated with $O_2$. Thus, blood picks up a nearly full load of $O_2$ from the lungs even when the $PO_2$ of alveolar air is as low as 60 mmHg. The Hb–$PO_2$ curve explains why people can still perform well at high altitudes or when they have certain cardiac and pulmonary diseases, even though $PO_2$ may drop as low as 60 mmHg. Note also in the curve that at a considerably lower $PO_2$ of 40 mmHg, hemoglobin is still 75% saturated with $O_2$. However, oxygen saturation of Hb drops to 35% at 20 mmHg. Between 40 and 20 mmHg, large amounts of $O_2$ are released from hemoglobin in response to only small decreases in $PO_2$. In active tissues such as contracting muscles, $PO_2$ may drop well below 40 mmHg. Then, a large percentage of the $O_2$ is released from hemoglobin, providing more $O_2$ to metabolically active tissues.

### *Other Factors Affecting the Affinity of Hemoglobin for Oxygen*

Although PO2 is the most important factor that determines the percent $O_2$ saturation of hemoglobin, several other factors influence the tightness or **affinity** with which hemoglobin binds $O_2$. In effect, these factors shift the entire curve either to the left (higher affinity) or to the right (lower affinity).

The following four factors affect the affinity of hemoglobin for $O_2$:

**1. *Acidity (pH).*** As acidity increases (pH decreases), the affinity of hemoglobin for $O_2$ decreases, and $O_2$ dissociates more readily from hemoglobin. In other words, increasing acidity enhances the unloading of oxygen from hemoglobin.



(a) Effect of pH on affinity of hemoglobin for oxygen

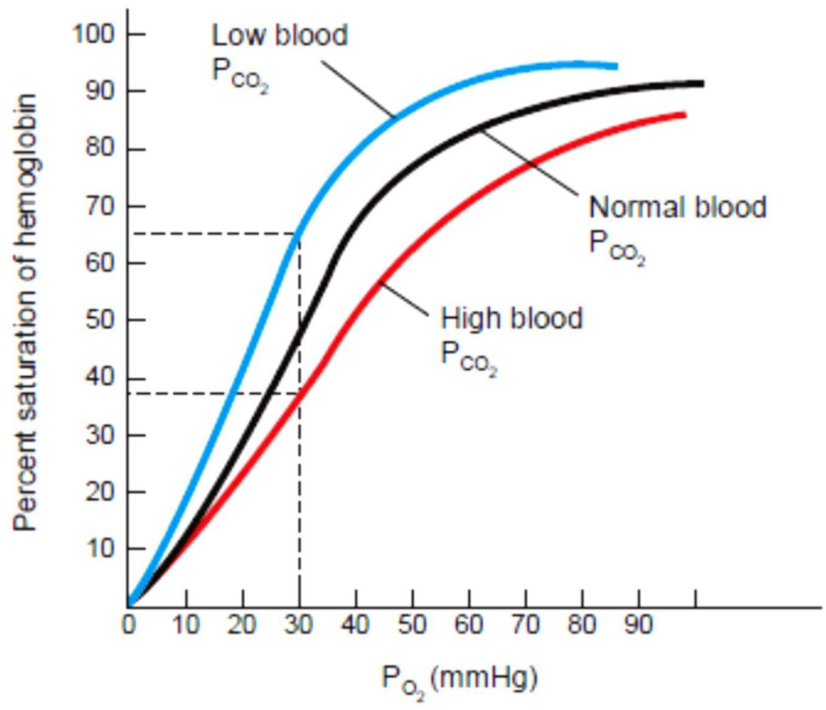
The main acids produced by metabolically active tissues are lactic acid and carbonic acid. When pH decreases, the entire oxygen–hemoglobin dissociation curve shifts to the right; at any given $PO_2$, Hb is less saturated with $O_2$, **- Bohr effect.** The Bohr Effect works both ways: An increase in PH in blood causes $O_2$ to unload from hemoglobin, and the binding of $O_2$ to hemoglobin causes unloading of H+ from hemoglobin. The explanation for the Bohr effect is that haemoglobin can act as a buffer for hydrogen ions ($H^+$). But when $H^+$ ions bind to amino acids in hemoglobin, they alter its structure slightly, decreasing its oxygen-carrying capacity.

Thus, lowered pH drives $O_2$ off hemoglobin, making more $O_2$ available for tissue cells. By contrast, elevated pH increases the affinity of hemoglobin for O2 and shifts the oxygen–hemoglobin dissociation curve to the left.

**2. *Partial pressure of carbon dioxide.*** $CO_2$ also can bind to hemoglobin, and the effect is similar to that of $H^+$ (shifting the curve to the right). As $PCO_2$ rises, hemoglobin releases $O_2$ more readily. $PCO_2$ and pH are related factors because low blood pH (acidity) results from high PCO2. As $CO_2$ enters the blood, much of it is temporarily converted to carbonic acid ($H_2CO_3$), a reaction catalyzed by an enzyme in red blood cells called *carbonic anhydrase (CA):*

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \overset{CA}{\rightleftharpoons} \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$

The carbonic acid thus formed in red blood cells dissociates into hydrogen ions and bicarbonate ions. As the $H^+$ concentration increases, pH decreases. Thus, an increased $PCO_2$ produces a more acidic environment, which helps release $O_2$ from hemoglobin. During exercise, lactic acid—a byproduct of anaerobic metabolism within muscles—also decreases blood pH. Decreased $PCO_2$ (and elevated pH) shifts the saturation curve to the left.




(b) Effect of $P_{CO_2}$ on affinity of hemoglobin for oxygen