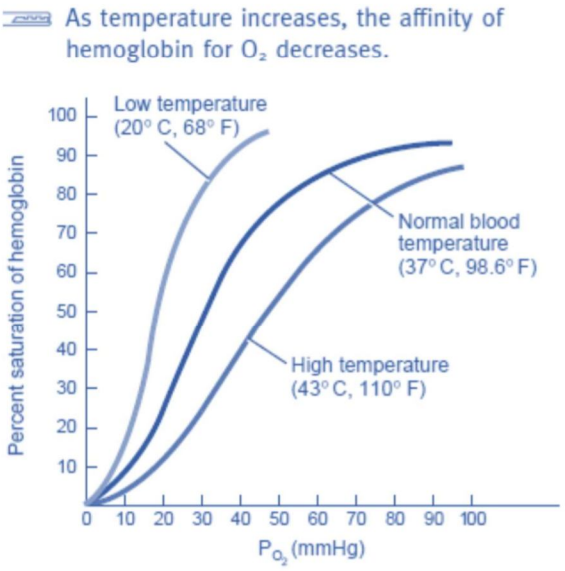
Transport of Gases-III

3. *Temperature.* Within limits, as temperature increases, so does the amount of O_2 released from hemoglobin. Heat is a byproduct of the metabolic reactions of all cells, and the heat released by contracting muscle fibers tends to raise body temperature. Metabolically active cells require more O_2 and liberate more acids and heat. The acids and heat in turn promote release of O_2 from oxyhemoglobin. Fever produces a similar result. In contrast, during hypothermia (lowered body temperature) cellular metabolism slows, the need for O_2 is reduced, and more O_2 remains bound to hemoglobin (a shift to the left in the saturation curve).



4. *BPG.* It is a substance found in red blood cells called **2, 3-bisphosphoglycerate (BPG),** decreases the affinity of hemoglobin for O_2 and thus helps unload O_2 from hemoglobin. BPG is formed in red blood cells when they break down glucose to produce ATP in a process called glycolysis. When BPG combines with hemoglobin by binding to the terminal amino groups of the two beta globin chains, the hemoglobin binds O_2 less tightly at the heme group sites. The greater the level of BPG, the more O_2 is unloaded from hemoglobin. Certain hormones, such as thyroxine, human growth hormone, epinephrine, norepinephrine, and testosterone, increase the formation of BPG. The level of BPG also is higher in people living at higher altitudes. 2,3-BPG is very plentiful in red cells. It is a highly charged anion that binds to the β chains of deoxyhemoglobin. One mole of deoxyhemoglobin binds 1 mol of 2,3-BPG. In effect,

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

In this equilibrium, an increase in the concentration of 2,3-BPG shifts the reaction to the right, causing more O_2 to be liberated.

Because acidosis inhibits red cell glycolysis, the 2,3- BPG concentration falls when the pH is low. Conversely, thyroid hormones, growth hormones, and androgens can all increase the concentration of 2,3- BPG and the P50 . Exercise has been reported to produce an increase in 2,3- BPG within 60 min (although the rise may not occur in trained athletes). Th e P 50 is also increased during exercise, because 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. Finally, at low PO_2 values, the oxygen-

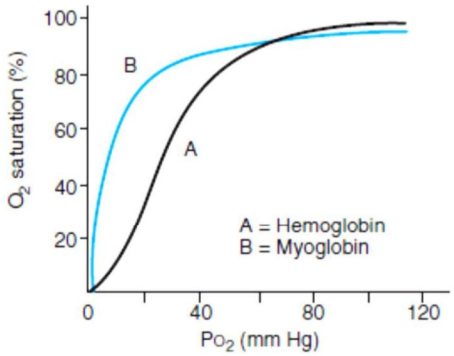
hemoglobin dissociation curve is steep, and large amounts of O_2 are liberated per unit drop in Po_2.

Effects of 2,3-BPG on Fetal & Stored Blood

The affinity of fetal hemoglobin (hemoglobin F) for O_2, which is greater than that for adult hemoglobin (hemoglobin A), facilitates the movement of O_2 from the mother to the fetus. The cause of this greater affinity is the poor binding of 2,3- DPG by the γ polypeptide chains that replace β chains in fetal hemoglobin. Some abnormal hemoglobins in adults have low P 50 values, and the resulting high O_2 affinity of the hemoglobin causes enough tissue hypoxia to stimulate increased red cell formation, with resulting polycythemia. It is interesting to speculate that these hemoglobins may not bind 2,3-BPG. Red cell 2,3-BPG concentration is increased in anemia and in a variety of diseases in which there is chronic hypoxia. This facilitates the delivery of O2 to the tissues by raising the PO_2 at which O_2 is released in peripheral capillaries. In banked blood that is stored, the 2,3-BPG level falls and the ability of this blood to release O_2 to the tissues is reduced. This decrease, which obviously limits the benefit of the blood if it is transfused into a hypoxic patient, is less if the blood is stored in citrate–phosphate–dextrose solution rather than the usual acid–citrate–dextrose solution.

Myoglobin. It is an iron-containing pigment found in skeletal muscle. Myoglobin resembles hemoglobin but binds 1 rather than 4 mol of O_2 per mole protein. The lack of cooperative binding is reflected in the myoglobin dissociation curve, a rectangular hyperbola rather than the sigmoid curve observed for haemoglobin. The left ward shift of the myoglobin O_2 binding curve when compared with haemoglobin demonstrates a higher affinity for O_2, and thus promotes a favorable transfer of O_2 from hemoglobin in the blood.

Comparison of dissociation curves for hemoglobin and myoglobin . The myoglobin binding curve (B) lacks the sigmoidal shape of the hemoglobin binding curve (A) because of the single O_2 binding site in each molecule. Myoglobin also has greater affinity for O_2 than hemoglobin (curve shifted left) and thus can release O_2 in muscle when PO_2 in blood is low (eg, during exercise).



The steepness of the myoglobin curve also shows that O_2 is released only at low PO_2 values (eg, during exercise). The myoglobin content is greatest in muscles specialized for sustained contraction. The muscle blood supply is compressed during such contractions, and myoglobin can continue to provide O_2 under reduced blood flow and/or reduced PO_2in the blood.