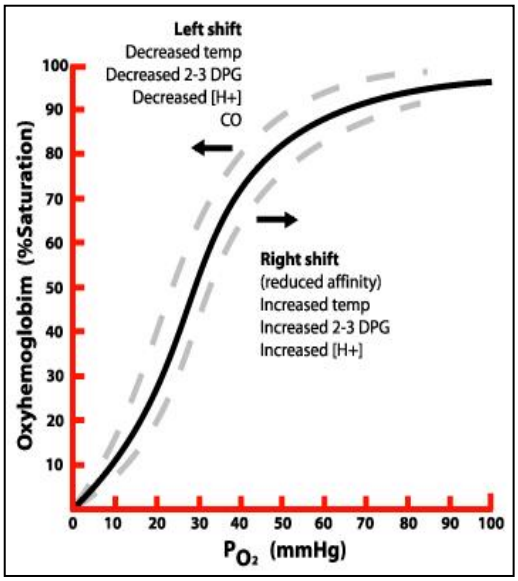
- Red blood cells membranes are composed of different proteins (mainly α/β spectrins & ankyrin) which stabilize the structure of the membrane and keep its integrity.
- **Mature RBCs**: have no internal organelles (no nucleus, no DNA/RNA, no mitochondria). They are flexible and biconcave in shape and have a lifespan of 120 days. They don't produce their own hemoglobin.
- **Myoglobin:**
  - It is a single globular protein (tertiary) which is composed of α-helical loops designated (A-H)
  - It is found in skeletal muscles and in muscles of the heart.
  - It has one heme group so it can carry one oxygen molecule only.
  - Myoglobin has a high affinity for oxygen.
  - Oxygen binds ferrous iron in the heme of myoglobin which is contained in a pocket formed by 2 polar histidines (63 & 94).
  - Its oxygen dissociation curve shape is hyperbolic & it is saturated with oxygen more rapidly.
  - It is amphipathic (containing both polar "on the surface" and non-polar "interior" portions).
- **Hemoglobin:**
  - It is a tetramer composed of 4 globin chains (2α2β) and is more complicated than myoglobin. The genes of α-chains are found on chromosome 16 while the genes of β-chains are found on chromosome 11.
  - It is exclusively found in red blood cells.
  - **Hemoglobin is composed of:**
    - ✓ *Heme*: which is a prosthetic group containing ferrous (Fe^{2+}) iron in its center that is hold by 4 nitrogenous bonds of the porphyrin rings and 2 additional bonds one on each side of the planar porphyrin ring (F8 & E7).
    - ✓ *Globin*.
  - Each globin contains one heme group, so the whole molecule has 4 heme groups. Therefore, 1 Hb can carry 4 oxygen molecules.
  - The oxygen dissociation curve is sigmoidal in shape with lower affinity to oxygen than myoglobin. Its saturation with oxygen is less rapid than myoglobin.
  - **Hemoglobin has two conformational states:**
    - ✓ *T "taut" state*: which is deoxygenated and has a lower affinity to oxygen. Therefore there are more salt bridges between αβ dimer 1 & αβ dimer 2.
    - ✓ *R "relaxed" state*: which is oxygenated and has a higher affinity to oxygen. Therefore there are less salt bridges between between αβ dimer 1 & αβ dimer 2.
  - **Allosteric effects**: ability of Hb to reversibly bind oxygen is affected by pO_2, pH, pCO_2 & 2,3-BPG. These are collectively called allosteric effectors because their interaction at one site on the hemoglobin molecule affects the binding of oxygen to heme groups at other sites on the molecule:
    - ✓ Binding of the first oxygen molecule enhances the binding of other oxygen molecules to other heme groups on the same molecule of Hb (this is called heme-heme interaction).
    - ✓ *pH*: as the acidity increases ($\uparrow H^+$, $\downarrow$pH) the oxygen dissociation curve will shift to the right favoring the T-conformational state.
    - ✓ *pO_2*: in the lungs ---> ↑ oxygen tension ---> Hb changes from T to R conformation. In the tissues ---> ↓oxygen tension ---> Hb changes from the R to T conformation.
    - ✓ *Bohr effect*: release of oxygen from Hb is enhanced when ↓pH & ↑pCO_2. Both result in decreased oxygen affinity of Hb and stabilize the T-form.
      ($CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3 + H^+$)
    - ✓ *↑2,3 BPG* ---> reduced affinity to oxygen and change in conformation from R to T.
    - ✓ *HbF*: has a higher affinity to oxygen than HbA because it lack the presence of 2,3BPG.
  - **Hemoglobin dissociation curve:**
    - ✓ ↑pCO_2 - ↑H^+ - ↑2,3BPG - ↑temp ---> all will lead to the shift of the curve to the right favoring the T-state which has a lower affinity to oxygen.



- **Sickle cell disease:**
  - Characterized by the presence of the abnormal HbS which result from the point mutation in the 6th amino acid position of the β-chain (valine instead of glutamic acid).
  - When there is decreased oxygen tension, HbS polymerizes into long, rope-like fibers. These intracellular fibers of the HbS will distort the erythrocytes resulting in rigid erythrocytes that will occlude blood flow in the capillaries. Therefore, microinfarcts will produce tissue anoxia resulting in severe pain.
- **G6PD deficiency:**
  - Acute hemolytic anemia is associated with fava beans (which contain vicine that will be converted to divicine and result in the production of free oxygen radicals that will cause hemolysis of the RBCs membranes and result in formation of Heinz bodies).
  - G6PD deficiency severity:
    - ✓ Moderate: 10-50%
    - ✓ Severe: < 10%
    - ✓ Very severe: < 2%