- **Binding of 2,3-BPG to deoxyhemoglobin**
  - The binding **decreases the O2 affinity** of Hb by binding to deoxyhemoglobin
  - HbO2 + 2,3-BPG <--> Hb-2,3-BPG + O2
- **Binding site of 2,3-BPG**
  - One molecule of 2,3-BPG binds to **a pocket, formed by the two β globin chains**, in the center of the deoxyhemoglobin tetramer
    - This pocket contains **several positively charged amino acids** that form ionic bonds with the negatively charged phosphate groups of 2,3-BPG
- **Shift of the oxygen dissociation curve**
  - In RBC, the presence of 2,3-BPG significantly reduces the affinity of hemoglobin for oxygen, shifting the oxygen-dissociation curve to the right
  - This reduced affinity enables hemoglobin to release oxygen efficiently **at the partial pressures found in the tissues**
- **Response of 2,3-BPG levels to chronic hypoxia or anemia**
  - In **chronic hypoxia**, such as COPD like emphysema, or at high altitudes; where circulating hemoglobin may have difficulty receiving receiving sufficient oxygen.
  - In **Chronic anemia;** elevated 2,3-BPG levels **lower the oxygen affinity of Hb**, permitting greater unloading of oxygen in the capillaries of the tissues
- **Roles of 2,3-BPG in transfused blood**
  - Stored blood displays an abnormally high oxygen affinity and fails to unload its bound oxygen properly in the tissues; Hb deficient in 2,3-BPG thus **acts as the oxygen "trap**" rather than as an oxygen transport system
  - Transfused RBC are able to restore their depleted supplies of 2,3-BPG in 6-24 hours. However, severely ill patients may be compromised if transfused with large quantities of such 2,3-BPG-"stripped" blood

- **Binding of CO2**
  - Most of the CO2 produced in metabolism is hydrated and transported as **bicarbonate ion**
    - However, some CO2 is carried as carbamate bound to the N-terminal amino groups of hemoglobin (forming carbaminohemoglobin)

$$Hb - NH_2 + CO_2 \leftrightarrow Hb - NH - COO^- + H^+$$

- The binding of CO2 **stabilizes the T or deoxy form of hemoglobin,** resulting in **a decrease in its affinity for oxygen** and **a right shift in the oxygen-dissociation curve**
- In the lungs, CO2 **dissociates from the Hb** and is released in the breath