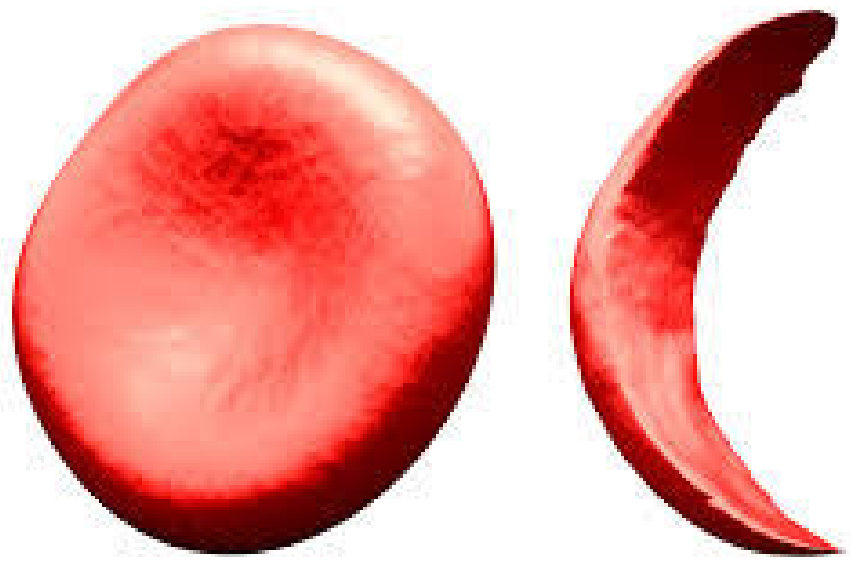
Hemoglobinopathies



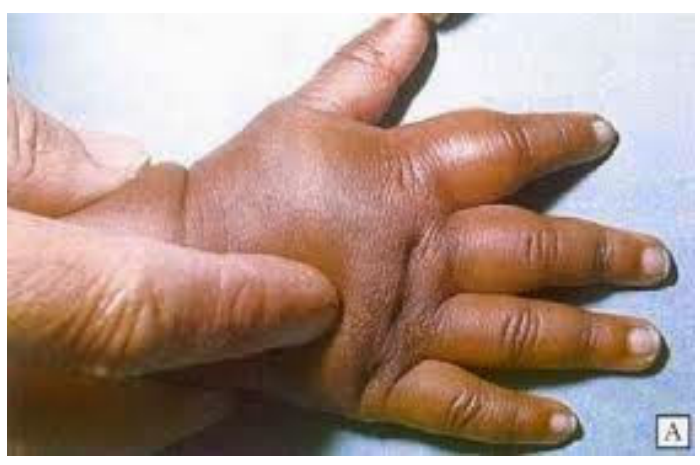
Learning Objectives

- Hemoglobinopathies (Abnormal Hb variants)
- Different Hemoglobin combinations-Nr and Abn

Sickle Cell Trait ($\alpha_2\beta_1\beta_1^{6\ glu\text{-}val}$)

- Sickle cell trait is the **heterozygous form** of the disease
- Represents a combination of HbA and HbS.
- Individuals with HbS trait are usually asymptomatic or have mild anemia.

Pathophysiology of Sickle Cell Disease



HbC ($\alpha_2\beta^C_2$) - • Modification - Glutamic acid to lysine at β6

HbD ($\alpha_2\beta^d_2$) - • Modification - Glutamic acid to glutamine at β121

HbE ($\alpha_2\beta^e_2$) - • Modification - Glutamic acid to lysine at β26

Hb Abnormal variants- Quantitative Abnormality

- Decreased or absent synthesis of a particular globin chain (**structurally normal**)
- i.e. Thalassemias

Thalassemia

- Common in population of African descent, Southeast Asian, Italians, Middle Eastern

- Two types-

α- thalassemia (Reduced production of α- globin chains-HbH or Hb Bart's)
β- thalassemia (Reduced production of β- globin chains-Cooley's Anemia)

α-THALASSEMIA

- **α-THALASSEMIA Trait (Minor):** α - / α α, - α / - α

α-THALASSEMIA

- **α-THALASSEMIA Major** (β_4, HbH disease): - - / - α,
- **Hemoglobin Barts** (γ_4, y-globin tetramer, lethal):
  With four-gene deletion: - -/- -

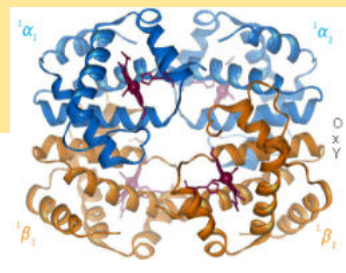
β-THALASSEMIA

- One or both β -globin genes have mutations that cause partial (β +) or total loss (β ^{0}) of β - chain production.

- Decreased synthesis of β -globin chains disturbs the balance between the two chains and α-chains precipitate - producing membrane damage and early destruction.

Normal Hb combinations/compounds

Oxyhemoglobin



- Hb reacts with four molecules of O_2 to form Hb_4O_8.

$Hb_4 + O_2 \rightarrow\leftarrow Hb_4O_2$, $Hb_4O_2 + O_2 \rightarrow\leftarrow Hb_4O_4$, $Hb_4O_4 + O_2 \rightarrow\leftarrow Hb_4O_6$, $Hb_4O_6 + O_2 \rightarrow\leftarrow Hb_4O_8$

Carbaminohemoglobin

Carbaminohemoglobin is a compound of hemoglobin with CO_2 (carbon dioxide), and is one of the forms in which carbon dioxide is transported in the blood at tissue level.

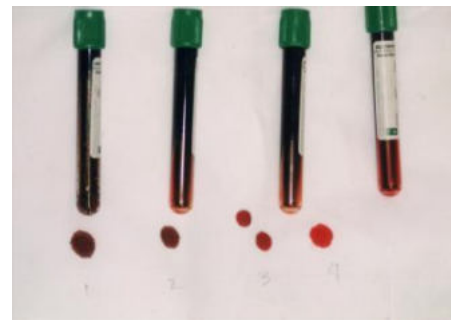
10% of carbon dioxide is carried in blood this way, bound to the globin protein.

Abnormal Hb compound-Methemoglobinemia

•When Fe^{++} is oxidized to Fe^{+++} form in Hemoglobin, this is called as Methemoglobin.

• The affinity of oxygen is impaired in ferric form of iron and binding of oxygen to methemoglobin results in an increased affinity for oxygen in the remaining heme sites that are in ferrous state within the same tetrameric hemoglobin unit.

Methemoglobinemia



Sign and Symptoms by Methemoglobin formation % :

- Less than 10% metHb - No symptoms
- 10-20% metHb –
- >50% metHb -

Treatment

Carboxy-hemoglobin

Carbon monoxide is a colourless, odourless, and tasteless gas that is lighter than air and can be fatal to life.

It has a greater **affinity for hemoglobin** (≈ 200 times) than oxygen **does**. It displaces oxygen and quickly bind to Hb

SOURCES

Carboxy-hemoglobin

CLINICAL SIGNS

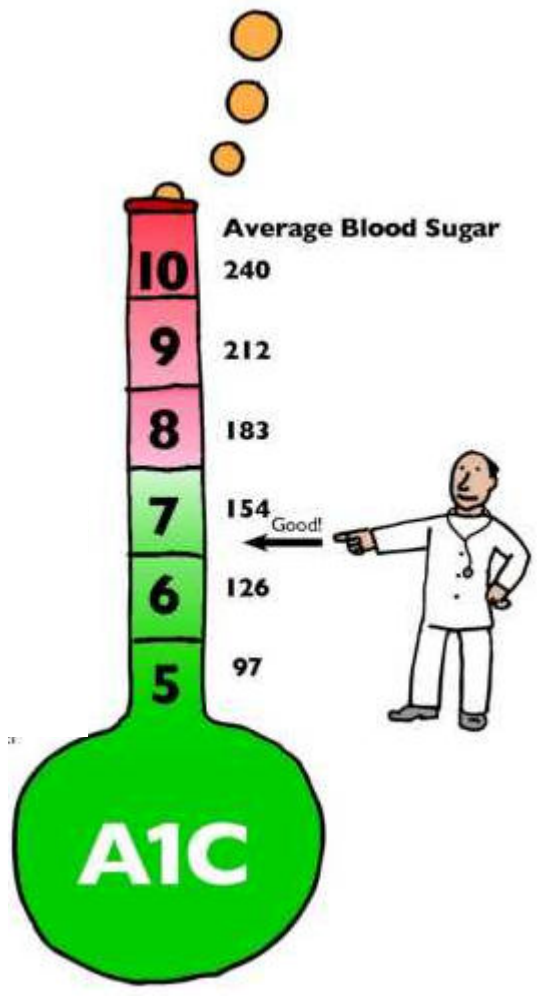
The signs of carbon monoxide poisoning vary with concentration and length of exposure.

TREATMENT

Glycated hemoglobin

A very minute amount of hemoglobin A is continuously and slowly binds with glucose irreversibly and **Non enzymatically** with each β chain. This is known as 'Glycated Hemoglobin' or $HbA1_c$.

A higher glucose concentration results in more HbA_{1c}.
The normal reference range is approximately **4–5.9%**



Self Asessment

Sickle cell trait is the ……of the disease, which has mild anemia.

Decreased or absent synthesis of a particular globin chain that is structurally ……

Thalassemis major has severe anemia, the type is ……..due to enhanced hemolysis

Hemoglobin Barts has a …… and cannot release oxygen to tissues.

β -thalassemia major is also called …… and Microcytic hypochromic anemia

Thank you