Hemoglobinopathies and workup with anemia

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Hemoglobin structure

4 subunits

Protein (Globin)

Non protein (Heme)

Iron

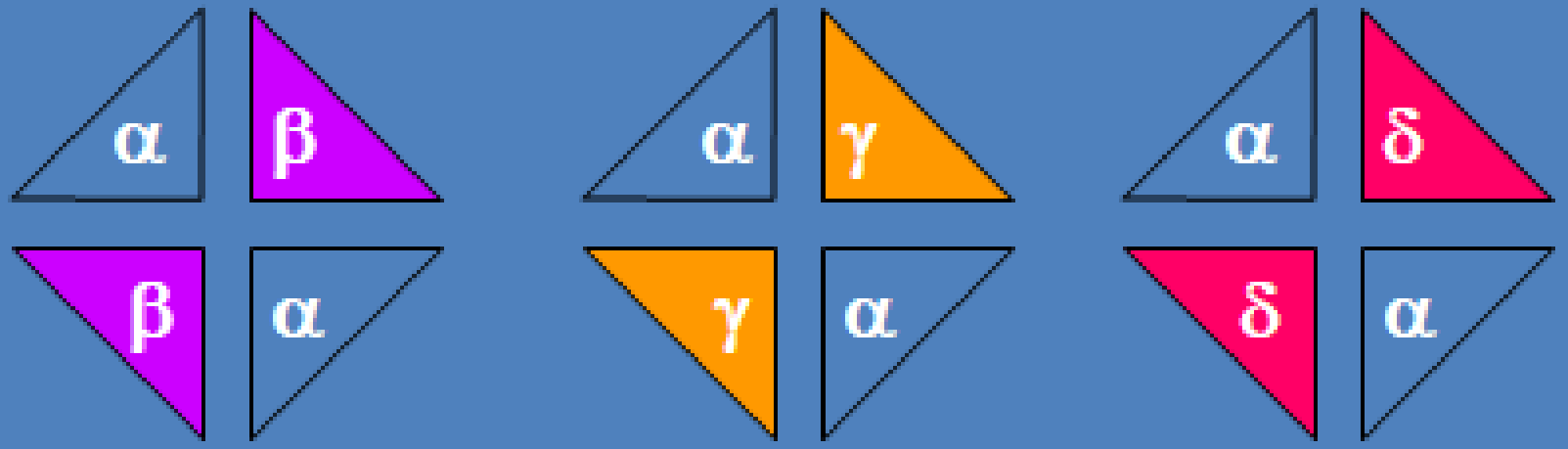
protoporphyrin

adult HbA 95%

Fetal Hb 1%

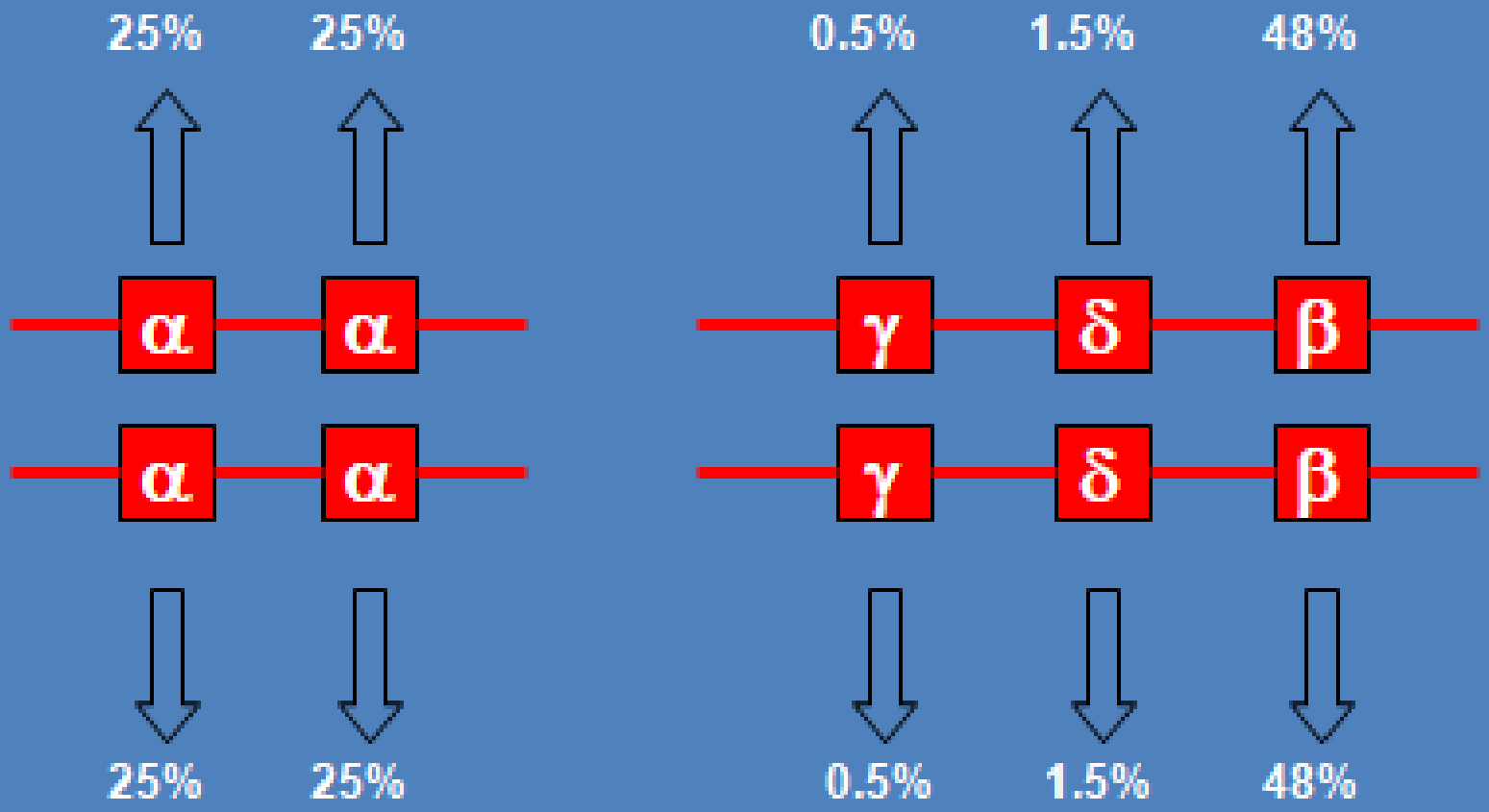
HbA2 1.5-3%

Hemoglobins in normal adults



HbA	HbF	HbA_2
98%	~1%	<3.5%

Hemoglobin synthesis

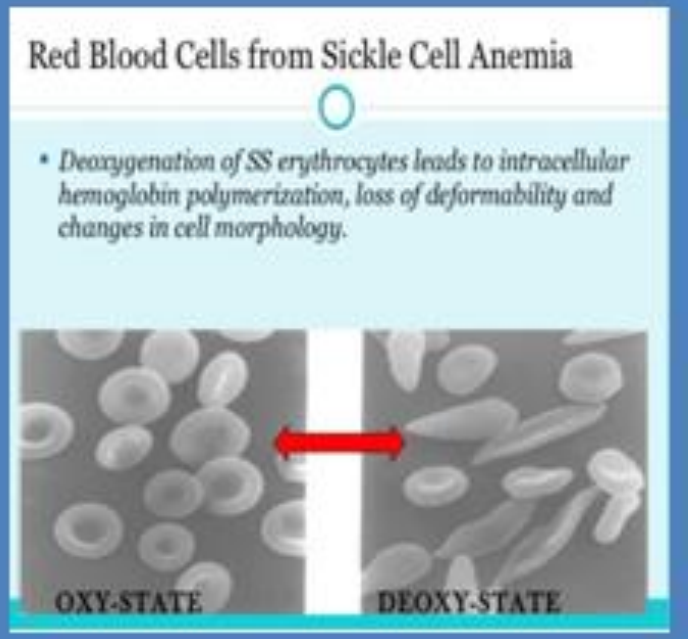


Sickle cell anemia

Sickle-cell anaemia

Is caused by a point mutation in the β-globin chain of haemoglobin, causing the hydrophilic amino acid glutamic acid to be replaced with the hydrophobic amino acid valine at the sixth position.

Red blood cells typically live 90–120 days, but sickle cells only survive 10–20 days.



- The Hb molecules in their deoxygenated state begin to aggregate with one anther to form long sickle shaped fiber

Sickle cell anemia

- Malaria
- Autosomal recessive both parents' carrier
- B globulin , HBB gene , chromosome 11
- GLU VAL number 6
- Deoxygenated polymerization (long fibers)
- Right shift dissociation curve
- Ca influx , K and H20 outflux dehydration
- HbA sickle HbF not sickle up to 6 months
- Hydroxyurea increase HbF and not sickle
- HbS > 60%
- deoxy HbS in vein and oxy in artery
- Extravascular anemia
- Vaso – occlusive crisis

Thalassemia alpha and beta

- Autosomal recessive
- Globin
- alpha chromosome 16 2 copies at 2 loci
- 1 locus asymptomatic
- 2 locus asymptomatic minor microcytic anemia misdiagnosed with iron deficiency
- 3 loci B4 tetramers HbH hemolytic anemia
- or Hb Barts gamma tetramers in fetals
- 4 loci not effective oxygenation hydrops fetalis

B minor is asymptomatic microcytic anemia

B major blood transfusion live max to 15 -25yrs

Thalassaemia

In health, equal quantities of α- and β-globin chains are produced. Abnormalities in the transcription of either α- or β-globin genes lead to the excessive production of the other chain, and these chains may precipitate, causing haemolysis and anaemia.

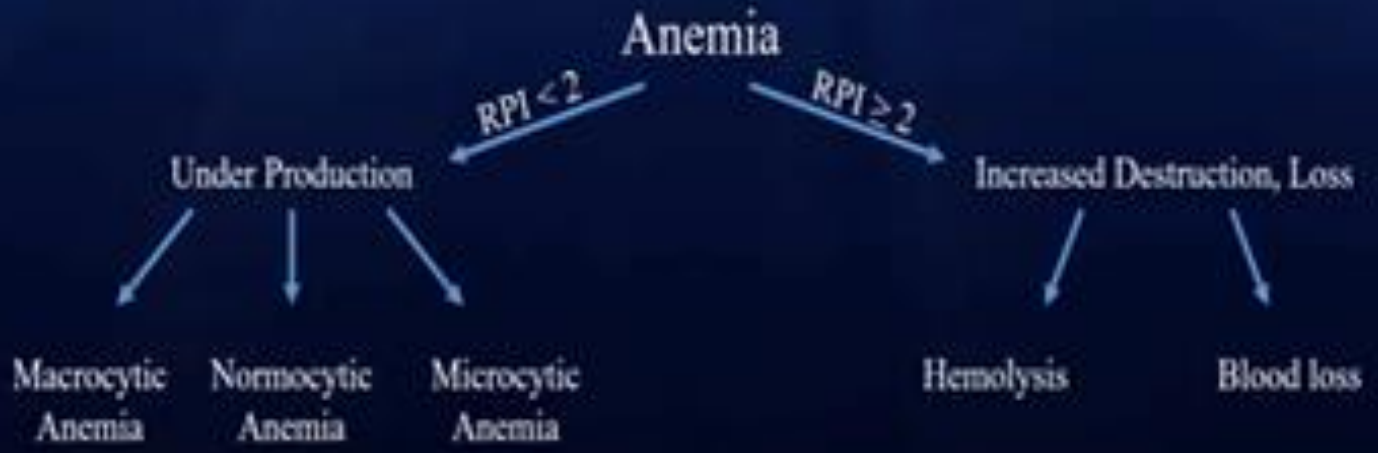
The gene for the α-globin chain is duplicated on each chromosome 16, so in health, four α-globin genes exist. α-Thalassaemia results from the deletion of between one and all four genes, with an associated variation in clinical severity. The deletion of all four genes is incompatible with life.

β-Thalassaemia is usually due to a single-gene mutation and results in the reduced production of β-globin chains. It normally becomes clinically apparent at between 3 and 6 months of age, when fetal haemoglobin begins to be replaced by HbA. The excess α-globin chains combine with the available β, δ, or γ chains, forming abnormal amounts of HbA_2 (δ-chains) and HbF (γ-chains

Art of Anemia Work-up

Kinetic approach

- Diagnosis by identifying the basic mechanism of the anemia.
- Start by looking at the RPI.



Morphologic approach

- Diagnosis by observation of cell changes.
- Start by looking at the MCV.