Hemoglobinopathies and workup with anemia

Dr. ARWA RAWASHDEH

Hemoglobin structure

280 million in RBc x 5 million /ml = I quadrillion Hb

4 subunits

Protein (Globin) ribosomes thalassemia and sickle cell anemia

Non protein (Heme) mitochondria, fe2+ , Fe 3+ Met Hb

Iron

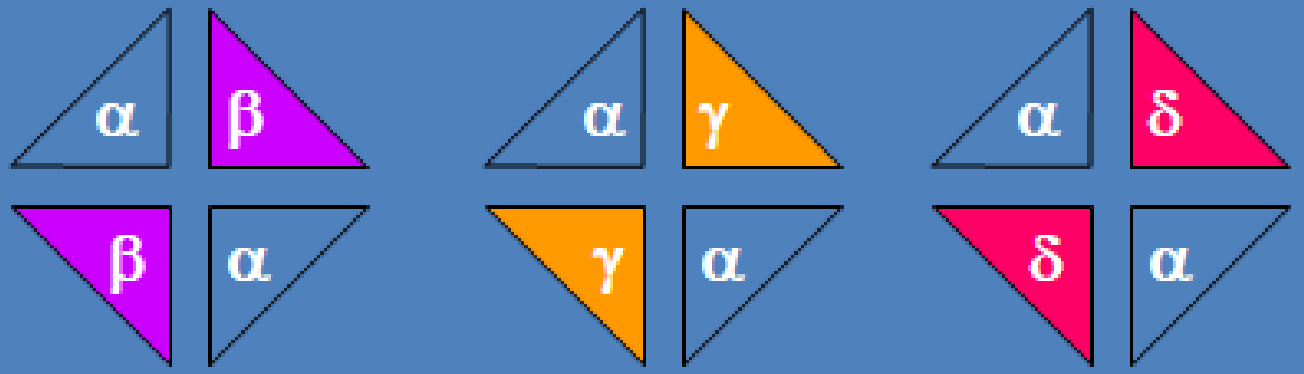
protoporphyrin sideroblastic

adult HbA 95%

Fetal Hb 1%

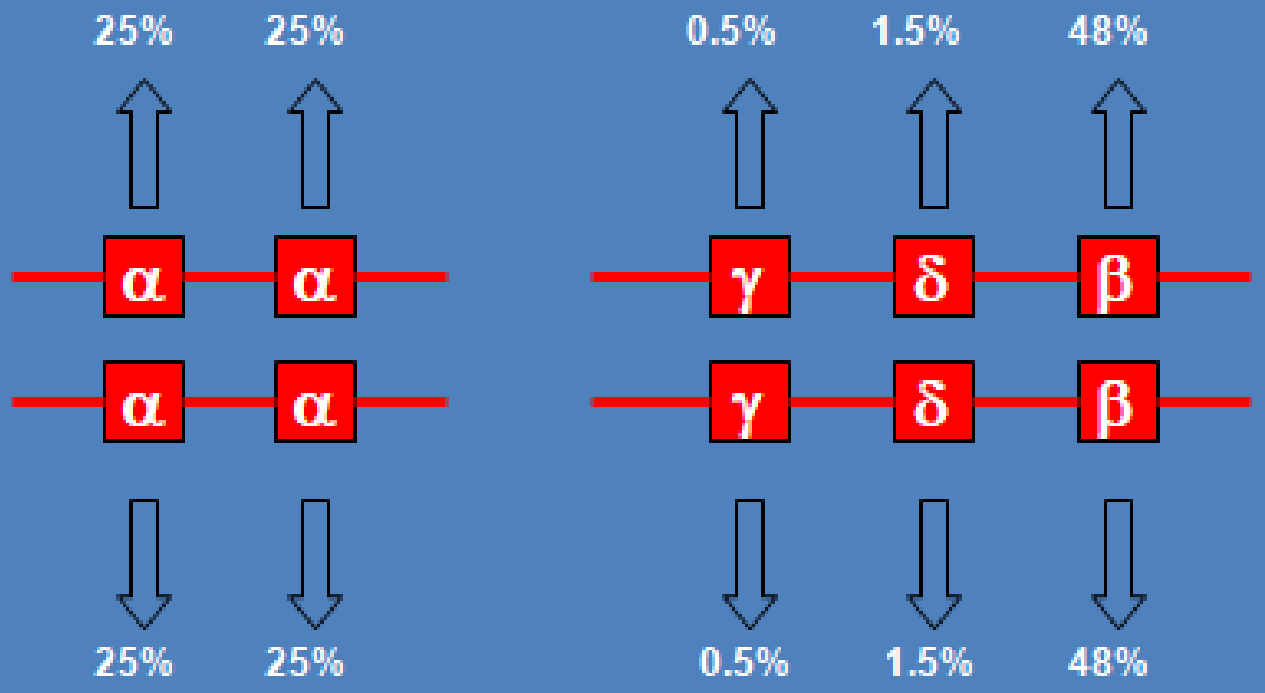
HbA2 1.5-3%

Hemoglobins in normal adults



HbA	HbF	HbA_2
98%	~1%	<3.5%

Hemoglobin synthesis



Sickle cell anemia

Autosomal recessive both parents' carrier

B globulin , HBB gene , chromosome 11

GLU VAL number 6

Deoxygenated polymerization (long fibers)

Ca influx , K and H2O outflux dehydration

HbA sickle HbF not sickle up to 6 months

Drug Hydroxyurea increase HbF and not sickle

HbS > 60% or increase deoxy Hb Conc ; volume depletion, acidosis, hypoxemia

deoxy HbS in vein and oxy in artery

Extravascular anemia

Vaso – occlusive crisis

Thalassemia alpha and beta

Microcytic anemia	Thalassa: sea, emia: blood	Autosomal recessive: mom and dad carrier 25%, 50%, 25% normal	Heme; Fe iron deficiency anemia and chronic inflame. Protoporphyrin sideroblastic anemia	Globin: thalassemia alpha and bet
Low Hb and chain synthesis unbalanced hem tetramers (insoluble) ineffective erythropoiesis	alpha chromosome 16 2 copies at 2 loci= 4 gene to alpha	1 locus asymptomatic trait	2 loci asymptomatic minor microcytic anemia misdiagnosed with iron deficiency	3 loci B4 tetramers HbH hemolytic anemia blood transfusion
	4 loci not effective oxygenation hydrops fetalis (die in the uterus) or Hb Barts gamma tetramers in fetals	B minor is asymptomatic microcytic anemia chromosomes 11	B major blood transfusion live max to 15 -25yrs hemochromatosis	

Thalassaemia

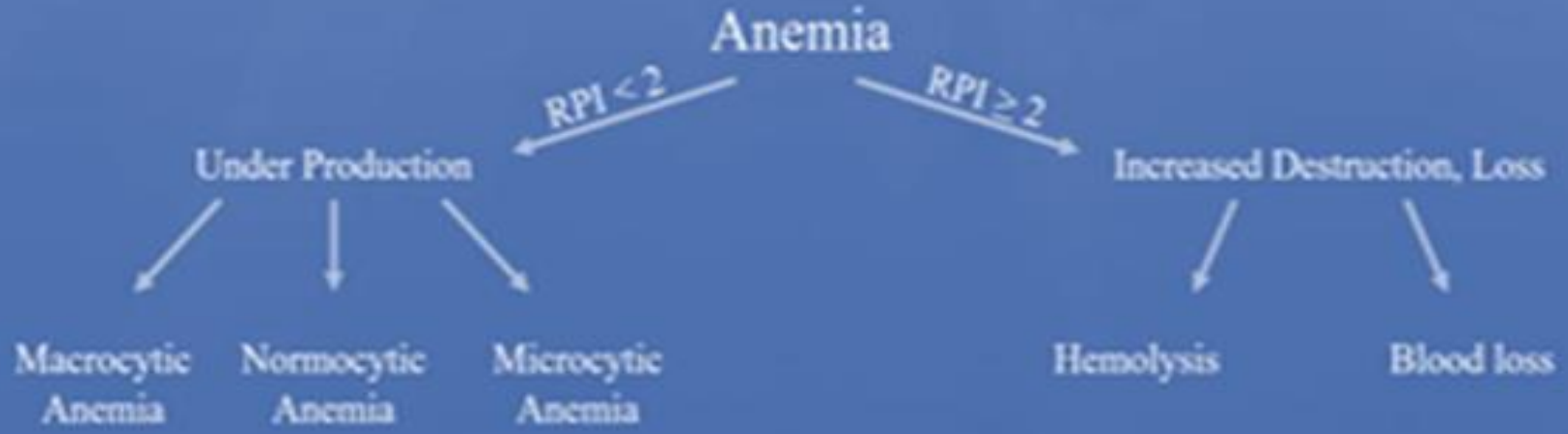
In health, equal quantities of α- and β-globin chains are produced. Abnormalities in the transcription of either α- or β-globin genes lead to the excessive production of the other chain, and these chains may precipitate, causing haemolysis and anaemia.

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

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.