Disorders of Hemoglobin:

The genetic disorders of hemoglobin are divided into:

- Reduced rate of production of one or more of the globin chains, i.e., thalassemia.
- Structural change in a globin chain, e.g., sickle cell anemia.

The Thalassemias:

The thalassemias are a heterogeneous group of genetic disorders of hemoglobin synthesis, all of which result from a reduced rate of production of one or more of the globin chains of hemoglobin.

They are divided into α- or β-thalassemias, according to which globin chain is produced in reduced amounts.

In some thalassemias, no globin chain is synthesized at all, and these are called α^0- or β^0- thalassemias; in others, designated α^+- or β^+thalassemias, the globin chain is produced at a reduced rate.

Most thalassemias are inherited in a Mendelian recessive fashion. Heterozygotes are usually symptomless. More severely affected patients are either homozygote for α- or β-thalassemia or compound heterozygote.

Clinically, the thalassemias are classified according to their severity into major, intermediate and minor forms.

Thalassemia major is a severe, transfusion-dependent disorder. Thalassemia intermedia are characterized by anemia and splenomegaly, though not of such severity as to require regular transfusion. Thalassemia minor is the symptomless carrier state.

β-Thalassemias:

The β-thalassemias are the most important types of thalassemia because they are so common and usually produce severe anemia in their homozygous and compound heterozygous states.

β-Thalassemias major:

Hematological changes:

Hemoglobin values on presentation range from 2 to 8 g/dl.

The red cells show marked hypochromia, anisopoikilocytosis, and basophilic stippling. There are always some nucleated red cells in the peripheral blood.

There is a slight elevation in the reticulocyte count.

The bilirubin level is usually elevated and haptoglobins are absent.

Red cell survival is shortened.

The serum iron level rises progressively and most transfusiondependent children have a totally saturated iron-binding capacity. This change is mirrored by a high plasma ferritin level, and liver biopsies show an increase of iron in both the reticuloendothelial and parenchymal cells.

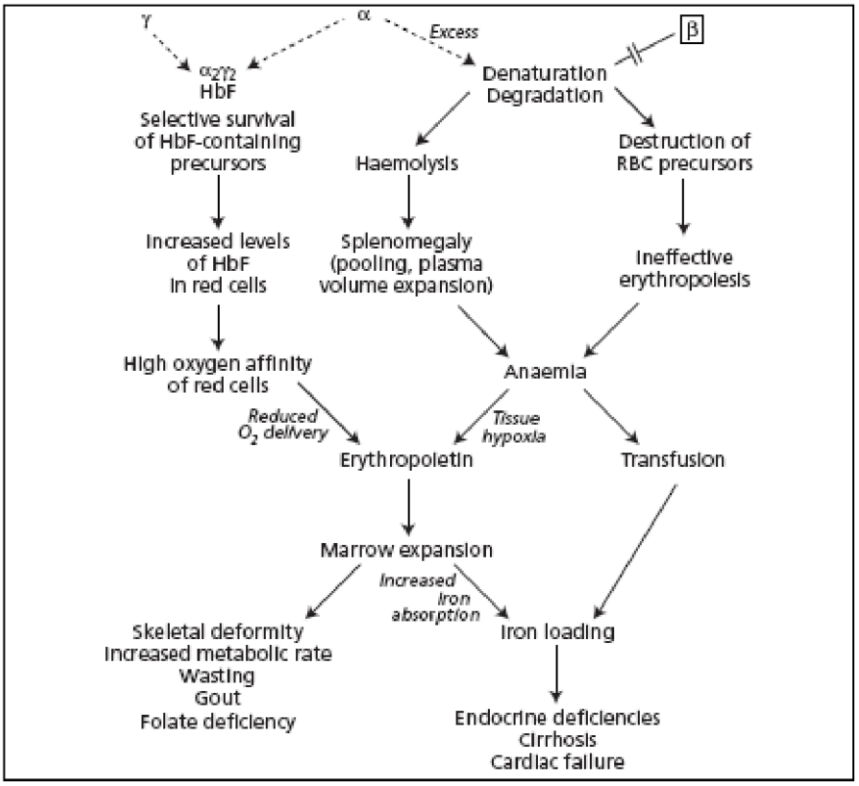
Hemoglobin changes (by Hemoglobin electrophoresis):

The HbF level is always elevated.

In β^+-thalassemia the level of HbF ranges from 30% to 90%.

In β^0-thalassemia, there is no HbA.

The HbA_2 level is of no diagnostic value.



The pathophysiology of β-thalassemia.

β-thalassemia minor (trait, heterozygous, carrier):

Carriers for β-thalassemia are usually symptom free except in periods of stress such as pregnancy, when they may become more anemic.

Haemoglobin values are in the 9–11 g/dl range.

The red cells show hypochromia and microcytosis with characteristically low red cell indices.

The reticulocyte count is normal.

The characteristic finding is an elevated HbA_2 level in the 4–7% range.