- A homozygous form, **thalassemia major** (also known as **Cooley anemia**), which results in a severe anemia that would lead to cardiac failure and death in early childhood without transfusion support

Pathophysiology

Normal postnatal Hgb is composed of two α- and two β-polypeptide chains. In β-thalassemia, there is a partial or complete deficiency in the synthesis of the β-chain of the Hgb molecule. Consequently, there is a compensatory increase in the synthesis of α-chains, and γ-chain production remains activated, resulting in defective Hgb formation. This unbalanced polypeptide unit is very unstable; when it disintegrates, it damages RBCs, causing severe anemia.

To compensate for the hemolytic process, an overabundance of erythrocytes is formed unless the bone marrow is suppressed by transfusion therapy. Excess iron from packed RBC transfusions and from the rapid destruction of defective cells is stored in various organs (**hemosiderosis**).

Diagnostic Evaluation

The onset of clinical manifestations in thalassemia major may be insidious and not recognized until the late infancy or early toddlerhood. The clinical effects of thalassemia major are primarily attributable to defective synthesis of HbA, structurally impaired RBCs, and shortened life span of erythrocytes (Box 24-3).

Box 24-3

Clinical Manifestations of Beta-Thalassemia

Anemia (Before Diagnosis)

Pallor

Unexplained fever

Poor feeding

Enlarged spleen or liver