DIAGNOSIS

Heterozygous β thalassemia, also known as β thalassemia trait and β thalassemia minor, has mild or no anemia but microcytic/hypochromic erythrocytes with minimal or no increase in reticulocyte count. After recognizing these hematologic abnormalities and excluding iron deficiency, finding an elevated level of HbA_2 and perhaps HbF by HPLC is sufficient to establish this diagnosis. The hematologic characteristics of this heterozygous carrier state are listed in **Table 98-4**. Sometimes, the spleen is enlarged. Before genetic counseling and antenatal diagnosis are considered after carrier identification by red cell indices and quantitation of HbA_2, the thalassemia-causing mutation should be identified. This is the key to preventing homozygotes or compound heterozygotes with transfusion-dependent thalassemia.

TABLE 98-4 β Thalassemias

CLASSIFICATION	HEMOGLOBIN (g/dL)/ MCV (fL)	HEMOGLOBIN FRACTIONS (%)	CLINICAL FEATURES
β Thalassemia trait	100–140 (10–14)/60–80	HbA: 94 HbF: 1–2 HbA_2: 4–6	Heterozygosity for β^+ or β^0 thalassemia mutations; "silent" carriers can have normal HbA_2 and red cell indices.
Non-transfusion-dependent β thalassemia (thalassemia intermedia)	70–120 (7–12)/65–80	HbA: 60–90 HbF: 10–40 HbA_2: 4–6	Defined by infrequent or no transfusion requirement; caused by many different genotypes including homozygosity for "mild" β^+ mutations, combinations of β and α thalassemia, homozygous β thalassemia with high HbF producing capacity, and many others. Iron loading, thromboembolic disease, and pulmonary hypertension are major clinical events.
Transfusion-dependent β thalassemia (thalassemia major)	20–40 (2–4)/50–80	HbA: 0–5 HbF: 90–100 HbA_2: 2–5	Caused by many different genotypes including homozygosity and compound heterozygosity for β^0 and β^+ mutations, combinations of β and α thalassemia; transplantation curative; iron chelation required.
HbE-β thalassemia	50–80 (5–8)/60–70	HbE: 50–70 HbF: 30–50	Common in SE Asian populations; in some parts of the word, the most prevalent severe thalassemia; in HbE-β^0 thalassemia, only HbE and HbF are found; in HbE-β^+ thalassemia, HbA is present. Transfusion dependence depends in part on the thalassemia mutation.
δβ Thalassemia and hemoglobin Lepore	110–120 (11–12)/65–75	HbA: 70 HbF: 7–13 HbA_2: 2	Rare; deletions removing the δ- and β-globin genes cause δβ thalassemia; Lepore hemoglobins are fusion globin chains; values are for heterozygotes; homozygotes have 100% HbF with hemoglobin 10–11 g/dL.
Gene deletion HPFH	120–140 (12–14)/75–85	HbA: 70 HbF: 15–30 HbA_2: 2	Rare; large deletions removing the δ- and β-globin genes; values are for heterozygotes; homozygotes, who are asymptomatic, have 100% HbF without anemia.

Note: Laboratory results are averages in adults.

The more severe forms of β thalassemia are hemolytic anemias with hypochromia, microcytosis, reticulocytosis, marked anisocytosis, and poikilocytosis with variable numbers of circulating nucleated red cells **(Fig. 98-5)**.