mutations can affect any globin gene, but clinically, β and α thalassemia are the most important. With nearly 500 unique thalassemia-causing mutations *(www.globin.bx.psu.edu)* that can interact with each other and with hemoglobinopathies, thalassemia syndromes are remarkably diverse. Where resources permit and the mutation is known, genetic counseling can be provided and antenatal diagnosis is possible.

HbE (β^{27} glu-lys) is a common variant whose biosynthesis is reduced because the site of the mutation alters its mRNA processing. Its reduced biosynthesis leads to a deficit of β^{E}-globin chains and features of β thalassemia. Hemoglobin Constant Spring is caused by a mutation of the termination codon of *HBA2* that leads to the synthesis of an elongated α-globin chain that is unstable and suboptimally synthesized. This variant therefore behaves as an α thalassemia variant.

β THALASSEMIA

■ EPIDEMIOLOGY

Once known as Mediterranean anemia, because of the concentration of cases in Italy, Greece, and other countries bordering the Mediterranean Sea, or as Cooley's anemia after the physician first describing cases, β thalassemia is common in most areas of the world where malaria was endemic. Effective programs of screening, counseling, and antenatal diagnosis have reduced the birth of new cases from the Mediterranean region. The bulk of new patients now are of Asian, Middle Eastern, and Indian origin. About 40,000 β thalassemia patients are born yearly. In the United States there are ~1000 cases of severe β thalassemia.

■ CLASSIFICATION

β^{0} Thalassemia mutations totally prevent the accumulation of any globin from the affected gene; β^{+} thalassemia mutations cause minor or extreme reductions in β-globin synthesis. β Thalassemia major and β thalassemia intermedia are now categorized as transfusion-dependent and non-transfusion-dependent based on the number