and frequency of transfusions required to sustain a good quality of life.

Pathophysiology Single nucleotide changes are the most common β thalassemia mutations, but gene deletions also occur. A partial listing of the classes of mutations causing β thalassemia include mutations in the promoter elements affecting gene transcription causing mild and sometimes silent β^+ thalassemia; mutations in the junctions between exons and introns that affect mRNA processing causing β^0 and β^+ thalassemia; introduction of alternative splice sites into introns or exons usually causing β^+ thalassemia; 3′ end-processing sequence mutations preventing RNA polyadenylation leading to mild or silent β^+ thalassemia; mutations preventing initiation of translation causing β^0 thalassemia; and introduction of stop codons that prematurely terminate translation (nonsense mutations) producing reading frameshifts and resulting in truncated globin mRNA and β^0 thalassemia.

In β thalassemia, the deficit in β-globin chain synthesis allows α-globin chains to accumulate in excess. Without a non-α-globin chain partner in dimer and tetramer formation, unpaired α-globin chains are unstable, cannot form a tetramer, and precipitate within the developing erythroblast, causing membrane lipid oxidation and damage. The predominant cause of anemia is intramedullary destruction of erythroid precursors, known as ineffective erythropoiesis. Reduced deformability and phosphatidyl serine exposure also cause extra- and intravascular hemolysis of those erythrocytes that gain entrance into the circulation. In poorly treated β thalassemia, severe anemia leads to bone marrow expansion; hepatosplenomegaly; iron accumulation in liver, heart, and endocrine organs; pulmonary hypertension; and thromboembolic disease.

Frightening pictures of children with severe β thalassemia permeate the literature. These examples of near-terminal disease should be relegated to history because treatment with transfusion and iron chelation can prevent their occurrence and hematopoietic stem cell transplantation can “cure” patients who have suitable donors.