mg for children 3 years and older) twice daily until age 5 years, and vaccination with pneumococcal vaccines are the main measures to prevent stroke and invasive pneumococcal infection. Folic acid, 1 mg daily, is given to prevent megaloblastic erythropoiesis; it is probably unnecessary in people with nutritious diets.

All women planning pregnancy should be screened for disorders of hemoglobin by blood counts, erythrocyte indices, and HPLC analysis of hemoglobin. Individuals with HbS or β thalassemia trait should have their partners tested. Only then is it possible to know the risks of a fetus having sickle cell disease (Table 98-2). Antenatal diagnosis using chorionic villus sampling is widely available.

Emerging Treatments Gene therapy has curative potential and requires neither matched donors nor immunosuppression. Autologous hematopoietic CD34+ stem cells are mobilized and modified ex vivo to produce an antisickling globin. These cells are reinfused following myeloablative conditioning. Phase 1/2 clinical trials have used lentivirus transduction of CD34+ cells with an antisickling β-globin or have interfered with the HbF-suppressive effects of BCL11A using CRISPR/Cas, zinc finger nucleases, or shRNA. These approaches have resulted in HbF or antisickling hemoglobin levels of nearly 50%, reduced hemolysis, total hemoglobin levels of >11 g/dL, and resolution of acute vasoocclusive events. It is too early to know their long-term safety or cure rate.

THALASSEMIA

Thalassemia is caused by reduced accumulation of either α- or β-globin chains causing a relative excess of the unaffected chain. Unbalanced globin synthesis is the hallmark of thalassemia and the proximate cause of its pathophysiology; unpaired globin chains damage the developing erythroblast. Like the HbS mutation and many other red cell traits, thalassemia reached polymorphic levels in tropical and subtropical populations because heterozygotes are protected from *Plasmodium falciparum* infection. Estimates are that 1–5% of the world's population carries a thalassemia mutation; in some locales, most people have a thalassemia mutation. These