Treatment Options for Sickle Cell Disease

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KEYWORDS

• Sickle cell disease • Hydroxyurea • Transfusion
• Hematopoietic stem cell transplant • Fetal hemoglobin

KEY POINTS

- Hydroxyurea is well tolerated and effective in reducing the number of sickle cell–related complications in all ages of people with HbSS and HbSβ^0thalassemia.
- Erythrocyte transfusions have a limited number of indications in treating people with sickle cell disease.
- The overall survival for matched sibling donor hematopoietic stem cell transplantation exceeds 90%, but less than 20% of people with sickle cell disease have a matched sibling donor available.

INTRODUCTION

Since the description of the first case of sickle cell disease (SCD) in 1910 by James Herrick and Ernest Irons, much has been learned about the disorder and improvements in care have increased survival in childhood.[1] Despite these advances, the average life expectancy for individuals with SCD has not changed in the past 30 years and remains half that of the average American.[2,3]

SCD is used to describe individuals who have hemoglobin S (HbS) as the predominant form of hemoglobin. HbS is caused by a single point mutation in the beta globin gene substituting a hydrophobic valine amino acid for glutamic acid at position 6 of the beta chain, making HbS molecules much more likely to polymerize in states of dehydration or acidosis. HbS polymerization causes the characteristic sickle shape change and downstream effects of sickling that include anemia, vaso-occlusion, cell adhesion, and vasoconstriction (**Fig. 1**). Inability of rigid, sickled cells to pass through the microvasculature leads to hypoxia of the tissues and painful vaso-occlusive episodes (VOE). Intrasplenic sickling leads to eventual splenic autoinfarction, which is responsible for an increased risk of infection with encapsulated organisms in individuals with SCD. Sickled erythrocytes and reticulocytes have adhesion proteins on

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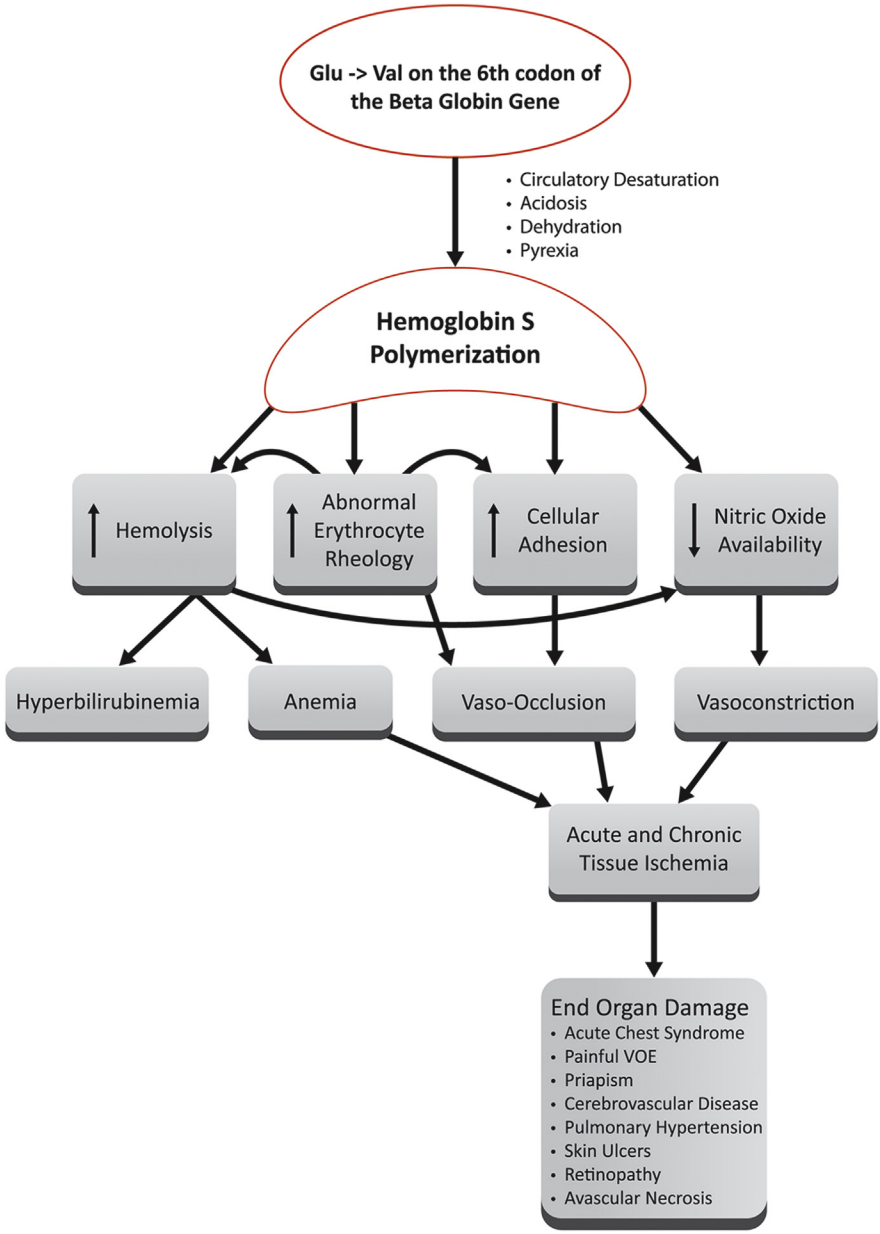

Fig. 1. Sickle cell pathophysiology. The pathophysiology of sickle cell disease is complex and stems from the polymerization of HbS that occurs during periods of hypoxemia, dehydration, acidosis, and pyrexia. Polymers of sickle hemoglobin cause the characteristic shape change of the erythrocyte and lead to hemolysis, abnormal rheology, cellular adhesion, and decreased nitric oxide availability. These changes result in anemia, vaso-occlusion, and vasoconstriction that are the cause of SCD-associated end organ damage. VOE, vaso-occlusive episode. (*From* Meier ER, Rampersad A. Pediatric sickle cell disease: past successes and future challenges. Pediatr Res 2017;81(1-2):249–58; with permission.)