

(ISCs), which are sickle erythrocytes that are forever deformed because of permanent membrane damage regardless of whether HbS remains polymerized. Damaged sickle erythrocytes are responsible for initiating the vasoocclusive, hemolytic, and inflammatory features of the disease shown in Fig. 98-3.

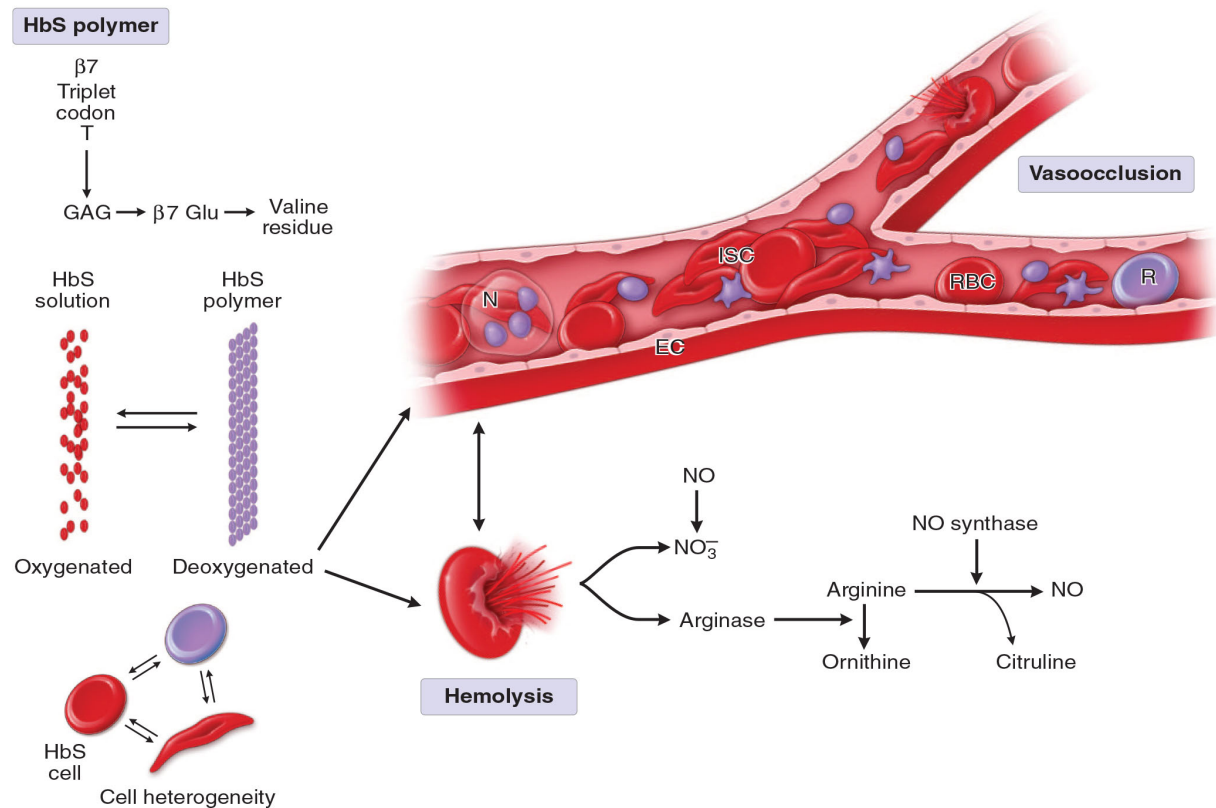


FIGURE 98-3 Pathophysiology of sickle cell disease. HbS is in solution when oxygenated but reversibly polymerizes when deoxygenated. Polymerization is dependent on the 30th power of hemoglobin concentration. In the sickle cell, this means that small changes in hemoglobin concentration or cell hydration can have large effects on polymerization. Polymerization begins seconds to minutes following deoxygenation. Erythrocyte deformation, or sickling, is initially reversible, but after an undetermined number of cell sickling events, the cell becomes irreversibly deformed. These are known as irreversibly sickled cells (ISCs). Their membrane is permanently damaged, although depending on their oxygen (O_2) content, HbS could be in solution. Sickie erythrocytes lead to the clinical and laboratory phenotypes of disease. Sickie cells interact with endothelial cells and other blood cells, occluding flow in small and sometimes large vessels and causing the many complications thought to be a result of vasoocclusion. Sickie cells also live <20 days (normal ~120 days) hemolyzing intra- and extravascularly. Intravascular hemolysis depletes haptoglobin and hemopexin while liberating