

compensated hemolytic disorder. As a result, the diagnosis may be delayed: in some cases, it is made, for instance, in a young woman during her first pregnancy, when the anemia may get worse. The delay in diagnosis may be caused in part by the fact that the anemia is often remarkably well tolerated because the metabolic block at the last step in glycolysis causes an increase in 2,3-bisphosphoglycerate (or DPG; [Fig. 100-1](#)), a major effector of the hemoglobin-oxygen dissociation curve; thus the oxygen delivery to the tissues is enhanced, a remarkable compensatory feat.

TREATMENT

Pyruvate Kinase Deficiency

The management of PK deficiency is mainly supportive. In view of the marked increase in red cell turnover, oral folic acid supplements should be given constantly. Blood transfusion should be used as necessary, and iron chelation may be required even in some patients who, though not receiving blood transfusion, may be developing iron overload (see “General Pathophysiology” above). About one-half of patients sooner or later undergo splenectomy, which usually provides a modest but significant increase in hemoglobin (paradoxically, often reticulocytes also increase considerably). Cholecystectomy may also be required. Some patients with severe disease have received bone marrow transplantation (BMT) from an HLA-identical PK-normal sibling. Prenatal diagnosis has been carried out in a mother who had already had an affected child. A clinical trial of a small molecule that is a specific PK ligand and may increase the stability and/or catalytic efficiency of mutant PK is currently ongoing. Rescue of inherited PK deficiency through lentiviral-mediated human PK gene transfer has been successful in mice. An oral small molecule allosteric activator of PK called *mitapivat* raised hemoglobin levels in about half of PK deficient patients in a small phase 2 study.

Other Glycolytic Enzyme Abnormalities All of these defects are rare to very rare ([Table 100-4](#)), and most of them cause HA with varying degrees of severity. It is not unusual for the presentation to be in the