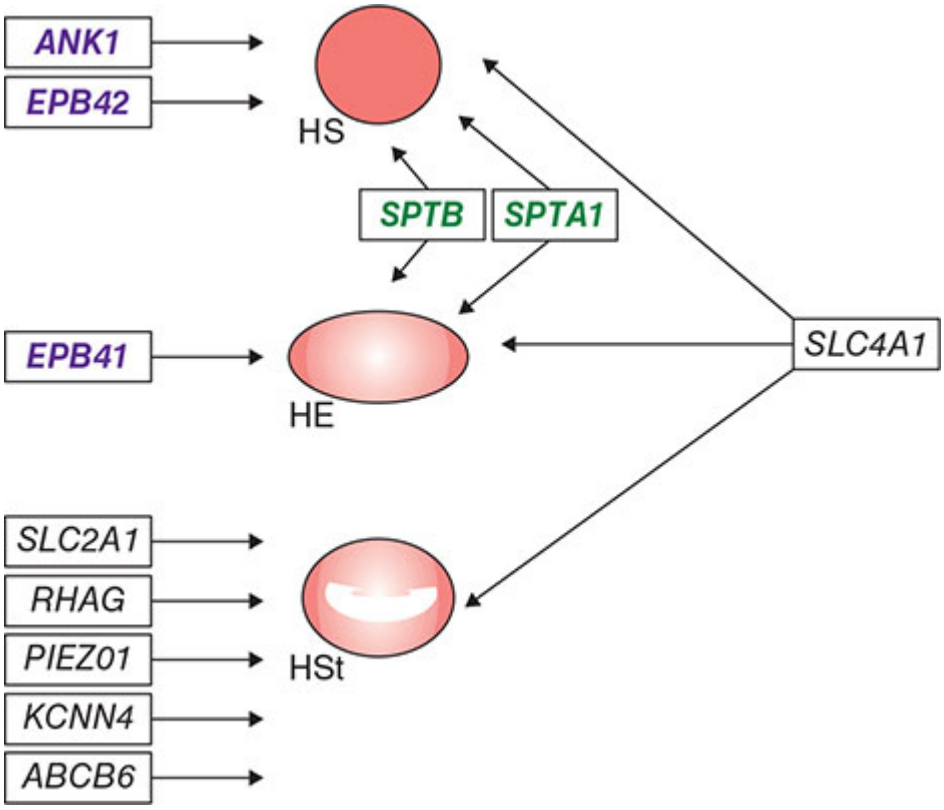

FIGURE 100-3 Hereditary spherocytosis (HS), hereditary elliptocytosis (HE), and hereditary stomatocytosis (HSt) are three morphologically distinct forms of congenital hemolytic anemia. It has emerged that each one can arise from mutation of one of several genes and that different mutations of the same gene can give one or another form. (See also Table 100-3.) Genes encoding membrane proteins are in *black*; genes encoding cytoskeleton proteins are in *green*; genes encoding proteins in the junctional and ankyrin complexes are in *purple*.

HEREDITARY SPHEROCYTOSIS This is most common among this group of HAs, with an estimated prevalence of 1:2000–1:5000 in populations of European ancestry. Its identification is credited to Minkowksy and Chauffard, who, at the end of the nineteenth century, reported families who had spherocytes in their peripheral blood **(Fig. 100-4*A*)**. In vitro studies revealed that the red cells were abnormally susceptible to lysis in hypotonic media; indeed, the presence of *osmotic fragility* became the main diagnostic test for HS. Today we know that HS, thus defined, is genetically heterogeneous; i.e., it can arise from a variety of mutations in one of several genes (Table 100-3). It has been also recognized that the inheritance of HS is not always autosomal dominant (with the patient being heterozygous);