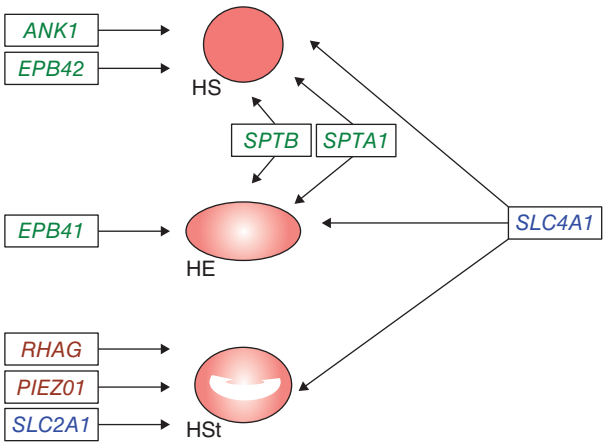

FIGURE 129-3 Hereditary spherocytosis (HS), hereditary elliptocytosis (HE), and hereditary stomatocytosis (HSt) are three morphologically distinct forms of congenital hemolytic anemia. It has emerged that each one can arise from mutation of one of several genes and that different mutations of the same gene can give one or another form. (See also Table 129-3.)

The variability in clinical manifestations that is observed among patients with HS is largely due to the different underlying molecular lesions (Table 129-3). Not only are mutations of several genes involved, but also individual mutations of the same gene can also give very different clinical manifestations. In milder cases, hemolysis is often compensated (see above), and this may cause variation in time even in the same patient, due to the fact that intercurrent conditions (e.g., pregnancy, infection) may cause decompensation. The anemia is usually normocytic, with the characteristic morphology that gives the disease its name. An increased mean corpuscular hemoglobin concentration (MCHC) on an ordinary blood count report should raise the suspicion of HS, because HS is almost the only condition in which this abnormality occurs. It has been apparent for a long time that the spleen plays a special role in HS through a dual mechanism. On one hand, like in many other HAs, the spleen itself is a major site of destruction; on the other hand, transit through the splenic circulation makes the defective red cells more spherocytic and, therefore, accelerates their demise, even though that may take place elsewhere.

When there is a family history, it is usually easy to make a diagnosis based on features of HA and typical red cell morphology. However, there may be no family history for at least two reasons. First, the patient may have a de novo mutation, i.e., a mutation that has taken place in a germ cell of one of his parents or early after zygote formation. Second, the patient may have a recessive form of HS (Table 129-3). In such cases, more extensive laboratory investigations are required, including osmotic fragility, the acid glycerol lysis test, the eosin-5′-maleimide (EMA)–binding test, and SDS-gel electrophoresis of membrane proteins; these tests are usually carried out in laboratories with special expertise in this area. Sometimes a definitive diagnosis can be obtained only by molecular studies demonstrating a mutation in one of the genes underlying HS (Table 129-3).

TREATMENT HEREDITARY SPHEROCYTOSIS

We do not have a causal treatment for HS; i.e., no way has yet been found to correct the basic defect in the membrane-cytoskeleton structure. Given the special role of the spleen in HS (see above), it has long been thought that an almost obligatory therapeutic measure was splenectomy. Because this operation may have more than trivial consequences, today we have more articulate recommendations, based on disease severity (having found out, whenever possible, about the outcome of splenectomy in the patient's relatives with HS), as follows. In mild cases, avoid splenectomy. Delay splenectomy until puberty in moderate cases or until 4–6 years of age in severe cases. Antipneumococcal vaccination before splenectomy is imperative, whereas penicillin prophylaxis after splenectomy is controversial. Along with splenectomy, cholecystectomy should not be regarded as automatic; it should be carried out, usually by the laparoscopic approach, when clinically indicated.

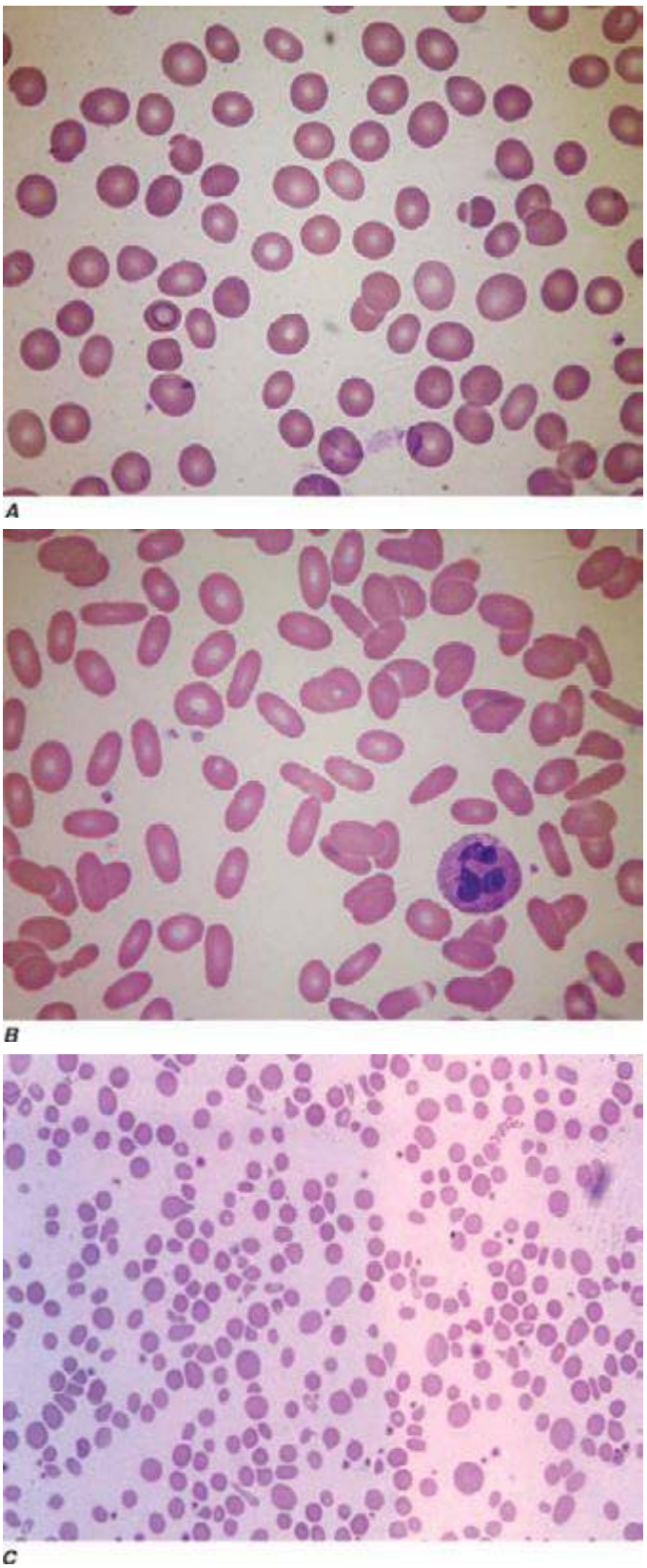

FIGURE 129-4 Peripheral blood smear from patients with membrane-cytoskeleton abnormalities. *A.* Hereditary spherocytosis. ***B.*** Hereditary elliptocytosis, heterozygote. ***C.*** Elliptocytosis, with both alleles of the α-spectrin gene mutated.