



**FIGURE 12.1.** Sickle-cell anemia can be caused by a single-base change in the coding sequence of the gene that encodes one of the proteins (hemoglobin A) that makes up hemoglobin, resulting in the glutamic acid to valine substitution at the 6th amino acid position in the mutant-form hemoglobin S in sickle-cell disease. A schematic diagram of this is shown in which the normal  $\beta$  subunit (in blue) is present in the normal hemoglobin (HbA) and an abnormal  $\beta$  subunit (in red) is in the sickle-cell form of hemoglobin (HbS). When present, the altered hemoglobin molecule causes red blood cells to occasionally form a sickle shape, especially when under low oxygen levels. This in turn can lead to major phenotypic consequences such as the blocking of small blood vessels.