G6PD:

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a genetic disorder that occurs almost exclusively in males. This condition mainly affects red blood cells, which carry oxygen from the lungs to tissues throughout the body. In affected individuals, a defect in an enzyme called glucose-6-phosphate dehydrogenase causes red blood cells to break down prematurely. This destruction of red blood cells is called hemolysis.

The most common medical problem associated with glucose-6-phosphate dehydrogenase deficiency is hemolytic anemia, which occurs when red blood cells are destroyed faster than the body can replace them. This type of anemia leads to paleness, yellowing of the skin and whites of the eyes (jaundice), dark urine, fatigue, shortness of breath, and a rapid heart rate. In people with glucose-6-phosphate dehydrogenase deficiency, hemolytic anemia is most often triggered by bacterial or viral infections or by certain drugs (such as some antibiotics and medications used to treat malaria). Glucose-6-phosphate dehydrogenase deficiency is also a significant cause of mild to severe jaundice in newborns. Many people with this disorder, however, never experience any signs or symptoms and are unaware that they have the condition.

Glucose-6-phosphate dehydrogenase deficiency results from mutations in the G6PD gene. This gene provides instructions for making an enzyme called glucose-6-phosphate dehydrogenase. This enzyme is involved in the normal processing of carbohydrates. It also protects red blood cells from the effects of potentially harmful molecules called reactive oxygen species, which are byproducts of normal cellular functions. Chemical reactions involving glucose-6-phosphate dehydrogenase produce compounds that prevent reactive oxygen species from building up to toxic levels within red blood cells.

If mutations in the G6PD gene reduce the amount of glucose-6-phosphate dehydrogenase or alter its structure, this enzyme can no longer play its protective role. As a result, reactive oxygen species can accumulate and damage red blood cells. Factors such as

infections, certain drugs, or ingesting fava beans can increase the levels of reactive oxygen species, causing red blood cells to be destroyed faster than the body can replace them. A reduction in the number of red blood cells causes the signs and symptoms of hemolytic anemia.

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

The G6PD gene, 18□k base (kb) long and is located on chromosome Xq28, consists of 13 exons and 12 introns. The complete coding sequence is 1548 base pair (bp) long and encodes 514 amino acids. Mutations throughout the *G6PD* gene lead to a deficiency in protein functions. Based on their biochemical and physicochemical characteristics, over 400 variants of G6PD have been reported. However, based on the type of mutations, those protein variants resulted from only ~140 different mutations. Glucose-6-phosphate-dehydrogenase deficiency is the most common pentose monophosphate pathway enzyme deficiency that has been reported to affect 400 million people globally with the highest incidence in African, Mediterranean, and South Asian populations.