Glucose-6-phosphate dehydrogenase deficiency

Jayden was born to African American parents. When he was 4 years old, they stayed for a week at his grandmother’s house. Suddenly, his parents noticed that he began to tire easily and became out of breath with a racing heart rate. He also turned yellow and had dark urine. Concerned, his parents took him to the doctor where they performed a series of tests. They found that he had severe anemia and a high bilirubin level. The doctor ordered a G6PD screen, and it came back positive. Jayden had Glucose-6-phosphate dehydrogenase deficiency.

Typically hemoglobin levels remain normal when adequate nutrients, particularly iron, are present. Iron in the ferrous state is inserted into a porphyrin ring, and heme is formed. This heme is an essential part of red blood cells, necessary to carry oxygen to cells around the body. It is synthesized within cells which will become red blood cells. When the body doesn’t have enough red blood cells, anemia occurs. The most common anemia is iron-deficiency anemia where iron stores are so low that the red blood cell count is decreased. However, there are other reasons people become anemic. One of these is a lack of the glucose-6-phosphate dehydrogenase enzyme.

Glucose-6-phosphate dehydrogenase deficiency, or G6PD is a condition common to people of Mediterranean and African descent. Those with G6PD have normal red blood cell function until a trigger happens in diet, medications, or environment. Their red blood cell count is normal because most of glucose-6-phosphate is changed by phosphoglucoisomerase as part of the glycolysis reaction. However, part of the glucose-6-phosphate typically enters an alternate pathway, the phosphate shunt pathway, through the G6PD enzyme. This produces NADPH. The NADPH created is frequently used in the glutathione system, which reduces Hb-Fe$^{3+}$ to Hb-Fe$^{2+}$, decreasing the effect of oxidizing agents.

![Figure 1: Pentose Shunt Pathway](image-url)
When a patient is exposed to a trigger, many of the patient’s red blood cells are exposed to excessive oxidative stress. The patient’s red blood cells accumulate Heinz bodies (denatured haemoglobin precipitates) that damage the cell. This causes an abnormal amount of red blood cell destruction which leaves the patient anemic and with high levels of bilirubin. This can be dangerous if the exposure is severe. Some of the triggers include: infection, ingestion of fava bean, moth balls, and certain medications. Symptoms include jaundice, back pain, and anaemia.

There are several genes identified that contribute to glucose-6-phosphate dehydrogenase synthesis. These genes are located on the X chromosome. This makes glucose-6-phosphate dehydrogenase deficiency more common among men than women. There are also several different levels of the disease ranging from a severe chronic non-spherocytic haemolytic anemia to increased activity of the G6PD enzyme. There is an association between G6PD deficiency and malaria. It seems as if people with this enzyme deficiency are somewhat resistant to malaria, though this effect is more pronounced in men than in women.

Jayden has had G6PD deficiency since birth, but had never been exposed to a trigger. When his parents researched the disease, they guessed that the trigger was the mothballs that Jayden had been exposed to when playing in the closets at his grandmother’s house. Once Jayden has recovered from his anemia, he will be able to live a normal life. However, he will need to be extra careful to avoid the things that may trigger a haemolytic reaction.

Questions:
1. Why is this disease so common in the Mediterranean and Africa?
2. How are individuals affected by this disease able to live a normal life?
3. Why are red blood cells affected more than other body cells?
4. Why is G6PD more common in men than women.

References: