KNOWLEDGE SHARING FOR RELAPSING MALARIA

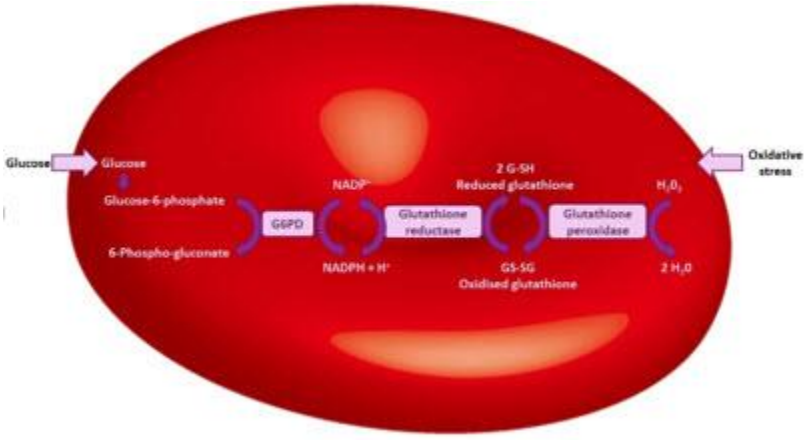
FACTSHEET

FOCUS ON: G6PD DEFICIENCY

Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that catalyses the first step in the pentose phosphate pathway. G6PD deficiency impairs the ability of the red blood cell to form NADPH (nicotinamide adenine dinucleotide phosphate), causing the cell to be susceptible to oxidative stress.

G6PD-deficient individuals can be exposed to oxidative stress, for example from food (e.g. fava beans) or medications, including 8-aminoquinoline antimalarial drugs. Oxidative stress leads to haemoglobin denaturation and ultimately cell rupture (lysis). If a person has a significant number of red blood cells rupture (haemolysis), they will become anaemic: when this causes clinical symptoms, such as tiredness and paleness, it is termed acute haemolytic anaemia. In severe cases, blood transfusion is needed.

Figure 1: The G6PD pathway protects red blood cells against oxidative stress.[1]



There are many different G6PD variants, at least 400, some of which are more common in specific populations. Different G6PD variants confer different degrees of severity of G6PD deficiency and not all variants have clinical relevance in malaria.

- Class 1 variants cause congenital non-spherocytic haemolytic anaemia.
- Class 2 variants cause severe enzyme deficiency (less than 10% of normal).
- Class 3 variants cause moderate to mild enzyme deficiency (10% to 60% of normal)
- Class 4 variants cause very mild or no enzyme deficiency (60% to 100% of normal)[2]

Clinically important phenotypic G6PD deficiency arises not because of a lack of enzyme production or poor catalytic activity, but because of variations in enzyme stability. Thus, young red blood cells that have just differentiated from reticulocytes will have higher G6PD enzyme levels than older red blood cells in which the enzyme will have degraded. In G6PD-deficient individuals, this process of enzyme degradation occurs more quickly than in G6PD-normal individuals, so on average the enzyme activity throughout their red blood cell population is lower. Note that it is the phenotype, in terms of average enzyme activity, rather than the genotype 'severity class' that determines the haemolytic risk for 8-aminoqunoline therapy. For more information please visit www.vivaxmalaria.org

[1] Red blood cell image: Database Center for Life Science (DBCLS)

[2] WHO Working Group (1989) Bull World Health Organ;67:601–611.