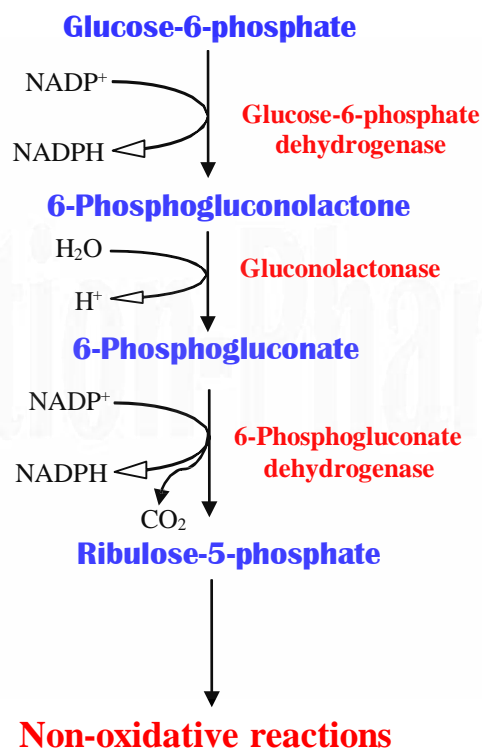


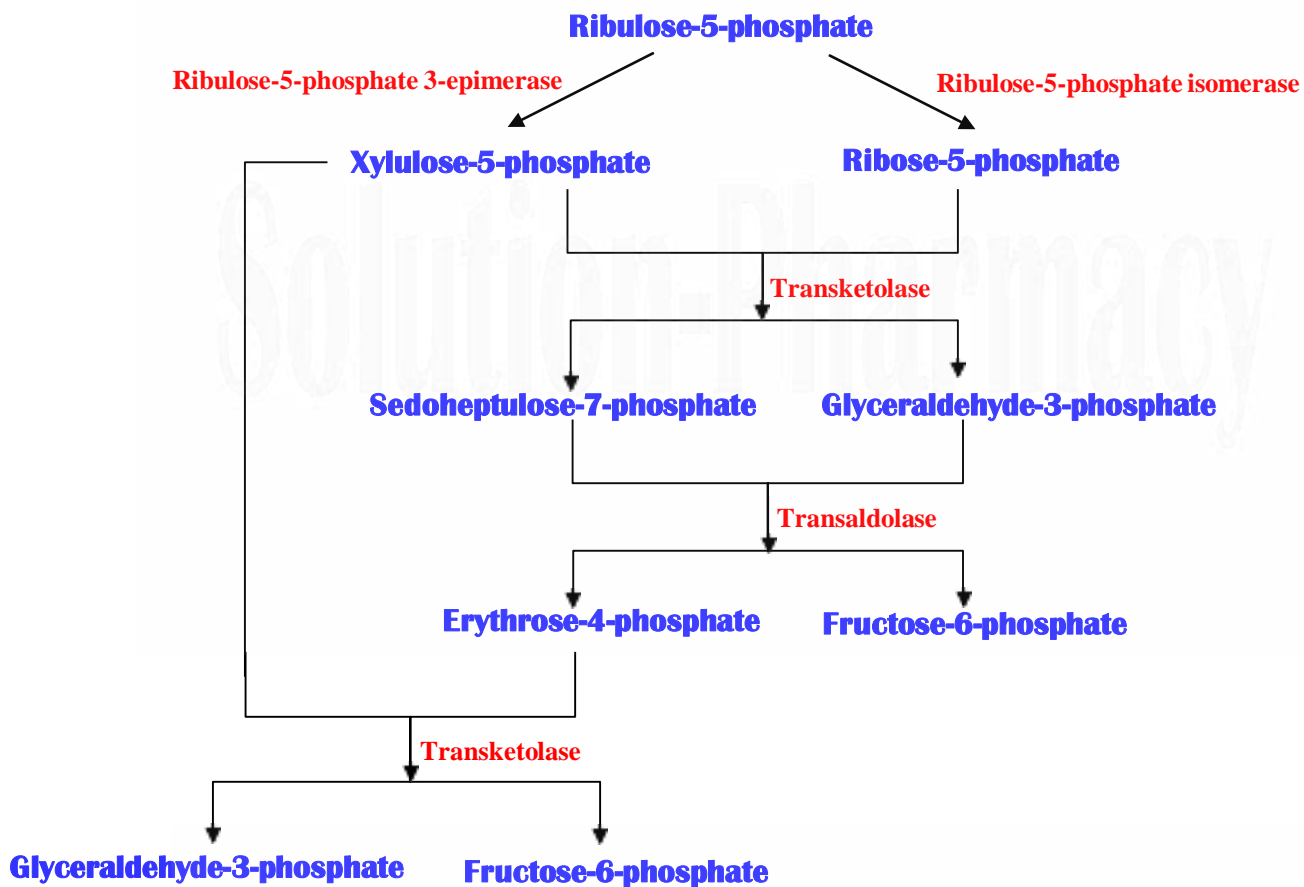
## Hexose Monophosphate Shunt

1. The Hexose Monophosphate Shunt is also known as **Pentose phosphate Pathway (PPP) or Phosphogluconate pathway.**
2. This is an alternative Glucose oxidation pathway.
3. The pentose phosphate pathway takes place in the **Cytosol.**
4. Its primary role is anabolic rather than catabolic.
5. Biosynthesis of **NADPH and Pentoses.**
6. Steroidogenic tissues, red blood cells and liver are the major sites of hexose monophosphate pathway.
7. The pentose phosphate pathway divided into two phases:
  - A. **Oxidative phase:** Each molecule of Glucose-6-Phosphate oxidized to Ribulose-5-Phosphate. It generates NADPH with the release of CO<sub>2</sub>.
  - B. **Non-oxidative phase:** Catalyzes the inter-conversion of 3, 4, 5 and 7- carbon sugars. Synthesize pentose-phosphate and other phosphate monosaccharides.

### Oxidative Stage of Pentose Phosphate Pathway



## Non-Oxidative Stage of Pentose Phosphate Pathway



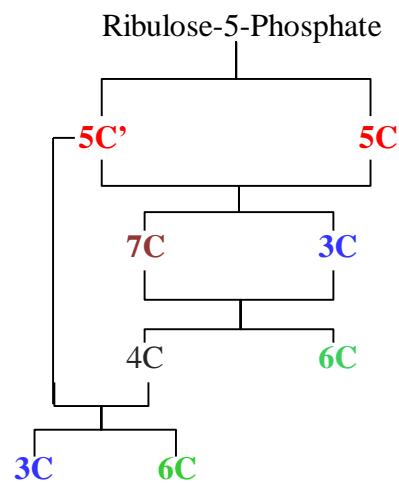
### Significance of HMP Shunt

1. It is a source of **NADPH and ribose-5-Phosphate**.
2. The NADPH is required for **the biosynthesis of fatty acid and steroids**, drug reduction (detoxification of drugs and foreign compounds), synthesis of certain amino acids involving the enzyme glutamate dehydrogenase, phagocytosis and as a cofactor for some non-synthetic enzymatic reactions.
3. The Ribose-5- Phosphate required for **nucleic acid biosynthesis (RNA and DNA)**.
4. NADPH involved in **Antioxidant (Free radical scavenging) reaction**. Gltathione mediated reduction of  $H_2O_2$ .
5. High concentration of NADPH in **lens of eye** is necessary to preserve the transparency of the lens.

6. In the Hexose MonoPhosphate Shunt Pathway, few molecules of **Glycolytic intermediates** (Glyceraldehyde-3-Phosphate and Fructose-6-Phosphate) are produced these are directly involves in Glycolysis.
7. NADPH is also required to preserve the **integrity of RBC membrane**.

**Trick to Remember Non Oxidative Pathway:**

1. **Glyceraldehyde-3- phosphate (3C)**
2. Erythrose -4-phosphate (4C)
3. **Xylulose-5- phosphate (5C')**
4. **Ribose-5- phosphate (5C)**
5. **Fructose-6- phosphate (6C)**
6. **Sedoheptulose-7- phosphate (7C)**  
 (5C'): (5C)  
 (7C): (3C)  
 (4C): (6C)  
 (5C'): (4C)  
 (3C): (6C)



## GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY (G6PD)

**Definition:** An X-linked genetic enzyme deficiency resulting in abnormal metabolism in red blood cell and can cause haemolysis usually after exposure to certain medications, foods, or even infections.

G6PD deficiency is a genetic abnormality that results in an inadequate amount of glucose-6-phosphate dehydrogenase (G6PD) in the blood. It is inherited as an X-linked recessive disorder. Glucose-6-phosphate dehydrogenase or G6PD, helps red blood cells (RBCs) function normally. This deficiency can cause **hemolytic anemia**, usually after exposure to certain medications, foods, or even infections.

### Pathophysiology

Normally red cells are protected from the action of free radicals by glutathione. NADPH produced in erythrocytes by pentose phosphate pathway is used to keep the glutathione in reduced state, reduced glutathione (GSH) which is essentially required to:

1. Preserve the integrity of RBC membrane.
2. Keep the ferrous ion ( $\text{Fe}^{2+}$ ) of hemoglobin in the reduced state so that accumulation of methemoglobin ( $\text{Fe}^{3+}$ ) is prevented, because accumulation of methemoglobin and peroxides in erythrocytes leading to hemolysis.
3. G6PD also protects red blood cells from potentially harmful byproducts, certain medications or an infection.

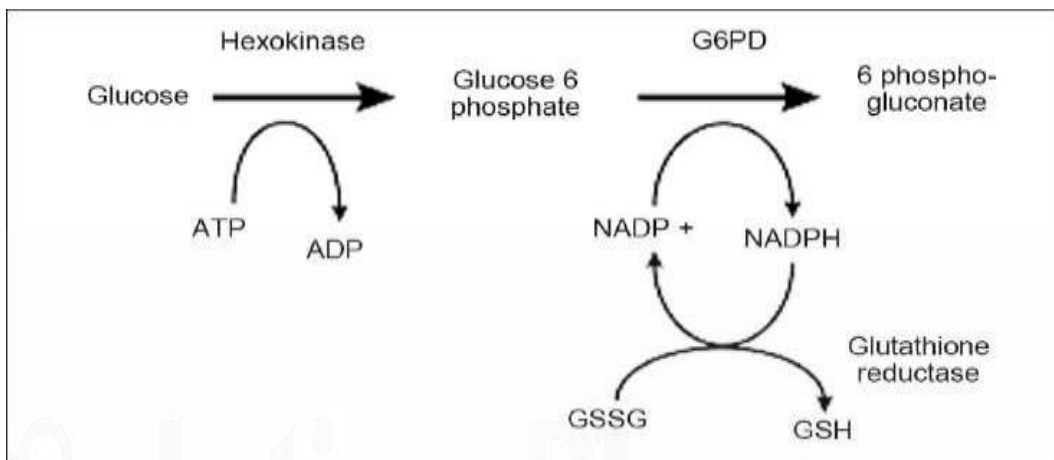


Figure 1: Pentose Phosphate pathway

HMP shunt is only means of providing NADPH in the erythrocytes.

Deficiency of G6PD impairs the synthesis of NADPH in RBC which maintain the reduced form of glutathione which is essential for RBC

G6PD deficiency causes breakdown of red blood cells, when the body is exposed to certain drugs or the stress of infection.

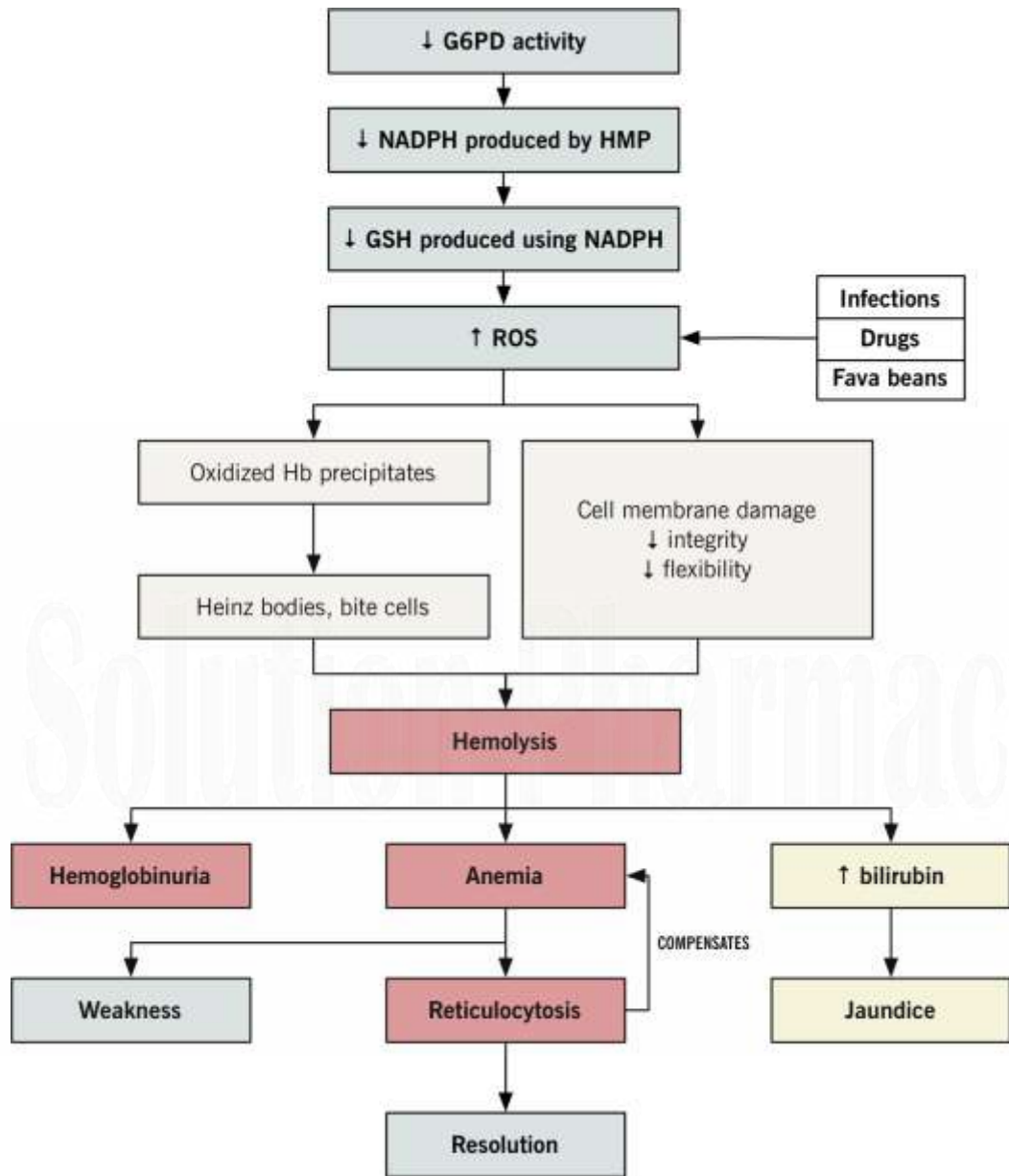
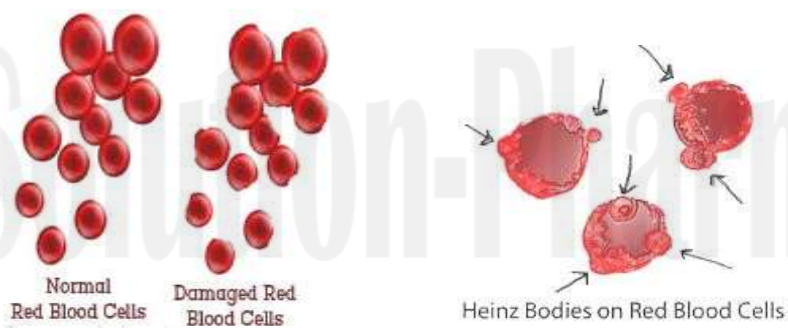


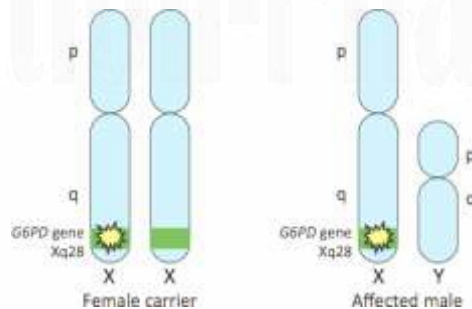
Figure 2: G6PD deficiency



\* ROS: Reactive oxygen species

## Causes

The defective gene that causes G6PD deficiency is on the X chromosome. Men have only one X chromosome, while women have two X chromosomes. In males, one altered copy of the gene is enough to cause G6PD deficiency. In females, however, a mutation would have to occur in both copies of the gene. Since it is unlikely for females to have two altered copies of this gene, males are affected by G6PD deficiency much more frequently than females. In people with G6PD deficiency, hemolytic anemia can occur after eating fava beans or certain legumes. It may also be triggered by infections or by certain drugs, such as antimalarials, sulfonamides, a medication used for treating various infections, aspirin, some nonsteroidal anti-inflammatory medications (NSAIDs).



## Symptoms

In more serious cases, a child may exhibit symptoms of hemolytic anemia (also known as a hemolytic crisis), including, rapid heart rate, shortness of breath, fever, fatigue, dizziness, paleness, jaundice, or yellowing of the skin and eyes particularly in new born, paleness (in darker-skinned kids, paleness is sometimes best seen in the mouth, especially on the lips or tongue), dark, tea-colored urine.

## Diagnosis

1. [Complete blood count](#) and [reticulocyte](#) count.
2. In active G6PD deficiency, [Heinz bodies](#) can be seen in [red blood cells](#) on a [blood film](#).
3. [Liver enzymes](#) (to exclude other causes of [jaundice](#)).
4. [Lactate dehydrogenase](#) (elevated in hemolysis and a marker of hemolytic severity) [Haptoglobin](#) (decreased in hemolysis).
5. A [direct antiglobulin test](#) (Coombs' test)
6. [Beutler fluorescent spot test](#) visually identifies [NADPH](#) produced by G6PD under [ultraviolet light](#). When the blood spot does not fluoresce, the test is positive.

## Treatment

Treatment for G6PD deficiency consists of removing the trigger that is causing symptoms. If the condition was triggered by an infection, then the underlying infection is treated accordingly. Medications that may be destroying red blood cells are also discontinued. Once G6PD deficiency has progressed to hemolytic anemia, treatment usually includes oxygen therapy and a blood transfusion to replenish oxygen and red blood cell levels.