

**( Pentose phosphate pathway )**  
**Hexose monophosphate shunt**

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-The aim of this pathway is to produce NADPH and ( ribose-5-phosphate for nucleotide synthesis ) .

- The NADPH needed for fatty acid synthesis , cholesterol synthesis , glutathione reduction , neurotransmitter synthesis and detoxification reaction.

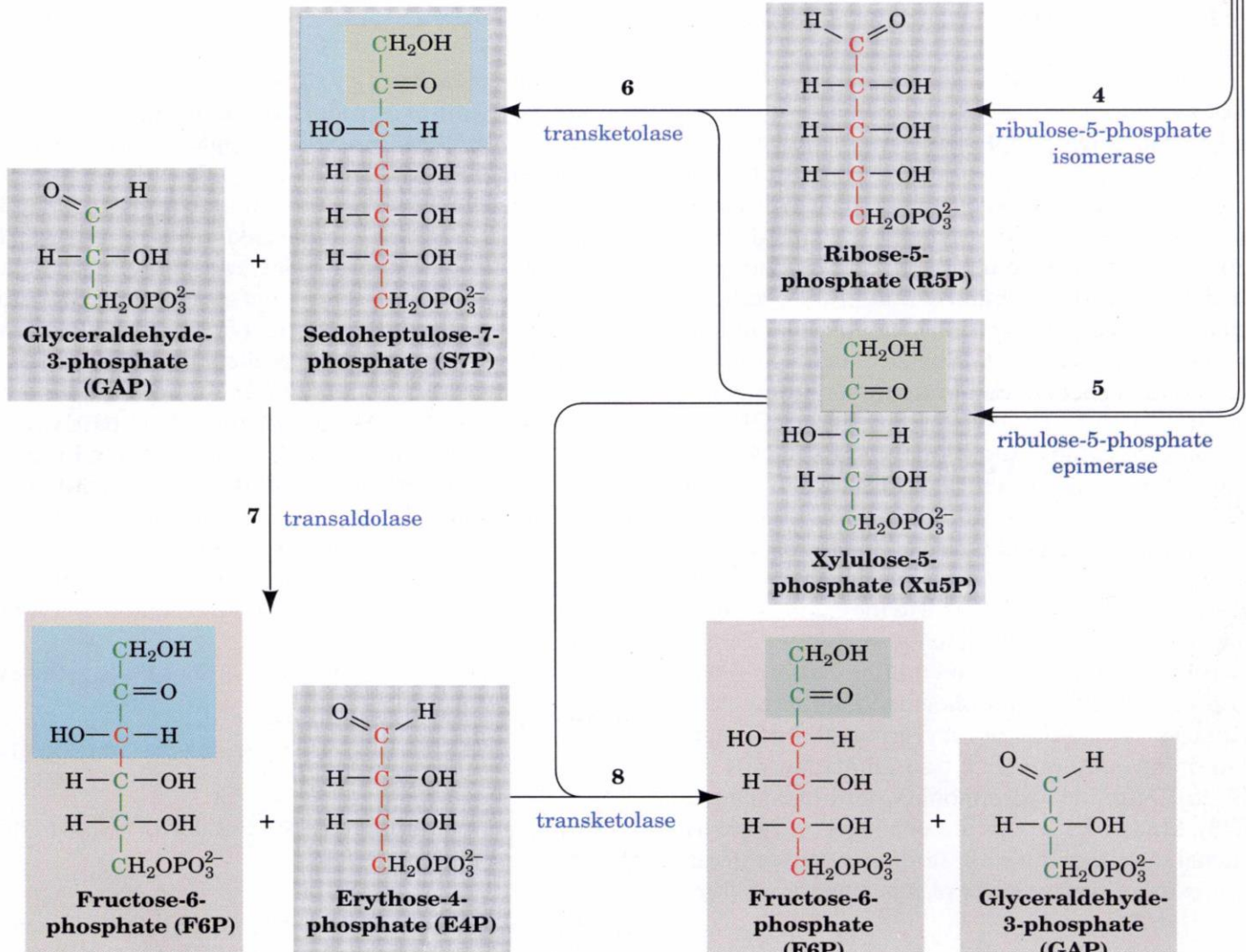
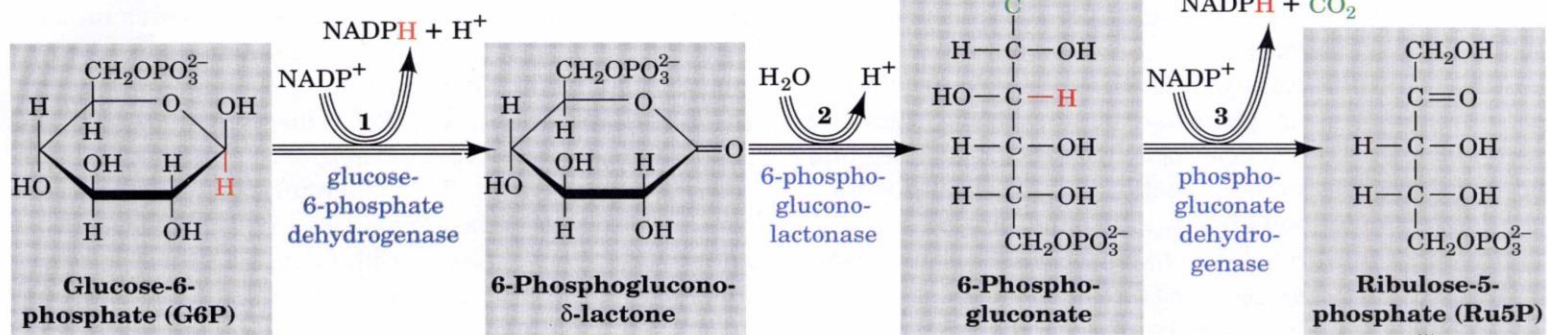
- NADPH is used in hydroxylation reaction during metabolism of phenyl alanine and tryptophan and also NADPH is used for synthesis of NO nitric oxide from arginine (NO acts as a neurotransmitter in brain ) (NO is a potent inhibitor of platelet aggregation also NO in macrophages is effective against viral , fungal protozoal infections ) (NO is a laughing gas used as anesthetic , causes smooth relaxation of vascular smooth muscles ) .

- HMP occurs in the liver , mammary gland , RBCs , adipose tissues , testis and adrenal cortex .

- This pathway is found in active tissues with rapid turnover ( so need more nucleic acid synthesis ) and in tissues which synthesize lipid and steroid .

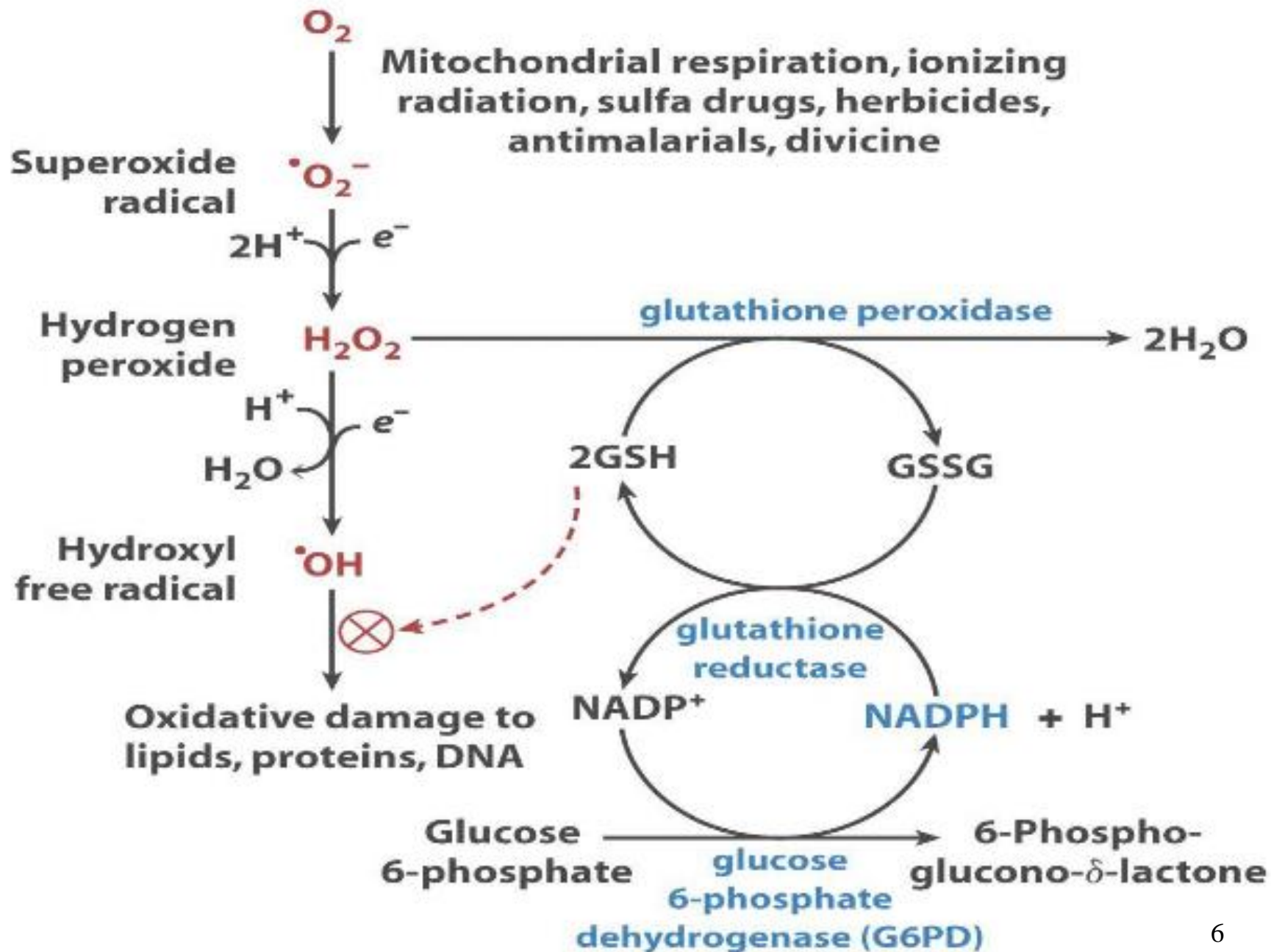
- The pathway has an oxidative phase, which is irreversible and generates NADPH, and a nonoxidative phase, which is reversible and provides ribose precursors for nucleotide synthesis.

- The PPP present in the cytosol, can account for the complete oxidation of glucose producing NADPH, CO<sub>2</sub> but not ATP.



# Why hemolysis occurs

1. In RBCs the pentose phosphate pathway provides NADPH for the reduction of oxidized glutathione catalyzed by the glutathione reductase .
2. Glutathione is a tripeptide consisting of glutamic acid , cysteine and glycine .
3. Reduced glutathione remove  $H_2O_2$  in a reaction catalyzed by glutathione peroxidase , since accumulation of  $H_2O_2$  may decrease the life span of the erythrocyte by causing oxidative damage to the cell membrane , leading to hemolysis .
4. Other reducing substance in the cell except NADPH as vitamin C and vitamin E .



- Reduced glutathione ( GSH ) protects the cell by destroying hydrogen peroxide and hydroxyl free radicals .
- Reduction of molecular oxygen yields superoxide anion radical .
- In erythrocytes , electrons from glutathione are used to keep cysteine residue in hemoglobin in the reduced state , and for reducing harmful reactive oxygen specie and hydroxyl free radicals that damage protein and lipids through oxidation induced cleavage reactions .

# ( G6PD deficiency )

In peoples with low G6PD , certain drugs will cause haemolytic anemia . Example of these drugs :

1. Antimalarial drugs ( Primaquine , Paraquine ) .
2. Sulfonamides ( Sulphacetamide , Sulphonamide , Sulphopyridine )
3. Analgesic ( Acetailid)
4. Antibacterial ( Nitrofurantone )

Notes :

- Fava beans can cause favism ( favism caused by G6PD defect ) .
- One of the active compound in the fava beans is called vicine ( a toxic glycoside that induces oxidative stress in erythrocytes ) .
- People having deficiency of G6PD cannot tolerate primaquine because their erythrocytes do not hold enough GSH to detoxify the reactive oxygen species produced by the compound .



# Laboratory Diagnosis :

The laboratory workup for glucose-6-phosphate deficiency includes the following :

- 1 . Measurement of G6PD activity .
- 2 . A complete blood cell ( CBC ) count with the reticulocyte count to determine the level of anemia .
- 3 . Indirect bilirubinemia occurs with excessive hemoglobin degradation and can produce clinical jaundice.
- 4 . Serum haptoglobin levels serve as an index of hemolysis and will be decreased .
- 5 . LDH is high and so is the unconjugated bilirubin , indicating that there is also extravascular hemolysis .<sup>9</sup>

# Notes :

- glutathione peroxidase, which destroy hydrogen peroxide and organic peroxides, requires selenium as a cofactor.
- G6PD is absent or only present in very small amount in muscle so this pathway not exist in muscle.
- NADPH is not utilized as source of energy because it can not oxidized directly in Respi – chain ( The aim of this pathway is not to produce ATP ) .
- Transketolase requires thiamine pyrophosphate ( TPP ) :  
chronic thiamine deficiency → defective transketolase and lead to Wernicke - karsakoff syndrome ( sytomes are chronic peripheral neuritis , beriberi , which may or not be associated with heart failure and edema ) .