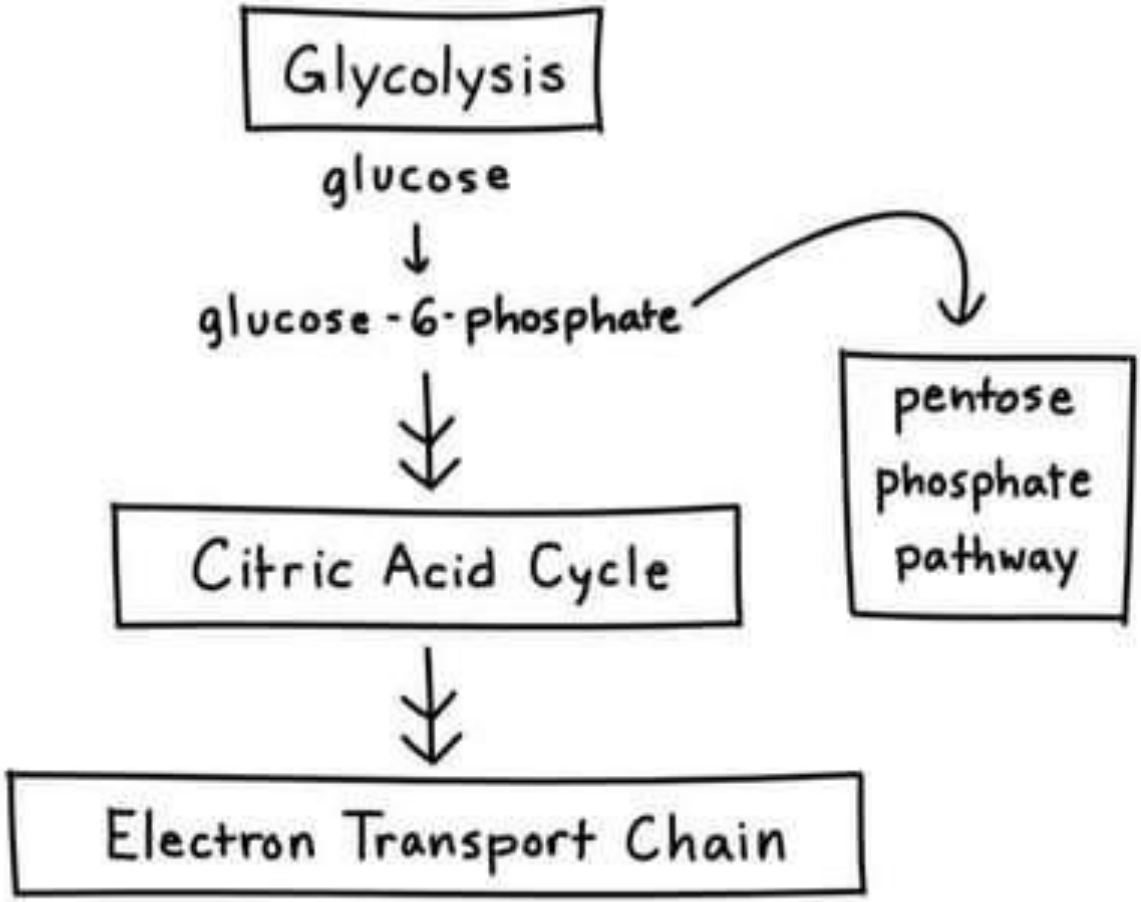
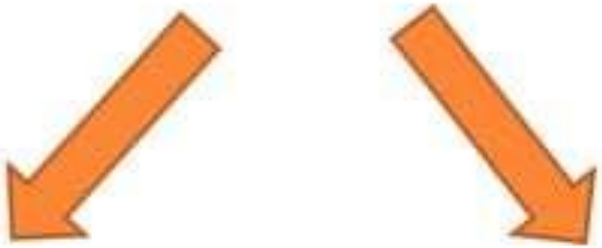
# Pentose Phosphate Pathway

- Pentose phosphate pathway is also called Hexose monophosphate pathway/ HMP shunt/ Phosphogluconate pathway.
- It is an alternative route for the metabolism of glucose.
- It is more complex pathway than glycolysis.
- It is more anabolic in nature.
- It takesplace in **cytosol**.
- The tissues such as liver, adipose tissue, adrenal gland, erythrocytes,testes and lactating mammary gland are highly active in HMP shunt.
- It concern with the biosynthesis of **NADPH** and **pentoses.**


Glycolysis
glucose
glucose-6-phosphate
pentose phosphate pathway
Citric Acid Cycle
Electron Transport Chain

# Phases in PPP pathway

- **Pentose Phosphate pathway** starts with glucose and it is a multi-steps reaction.
- There are two distinct phages in the pathway.



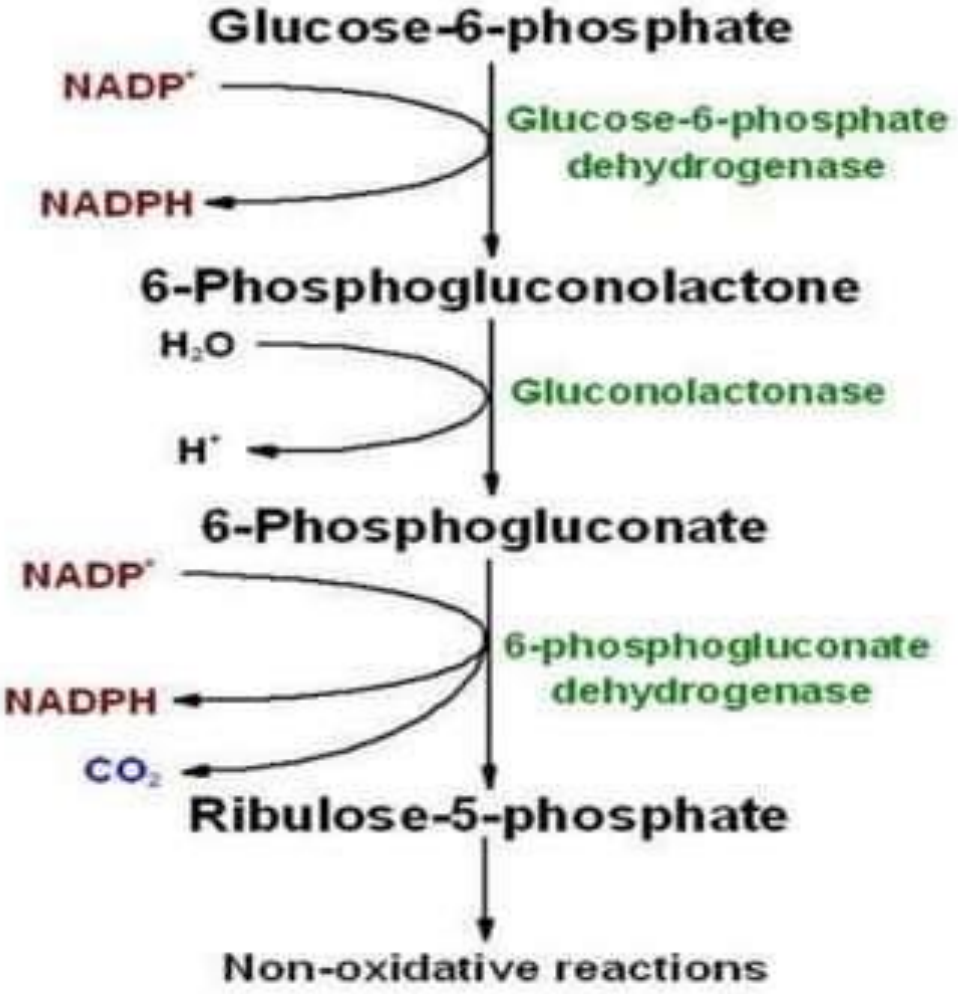
**The first is Oxidative phase, in which NADPH is generated.**

**The second is the Non-oxidative synthesis of 5-carbon sugars.**

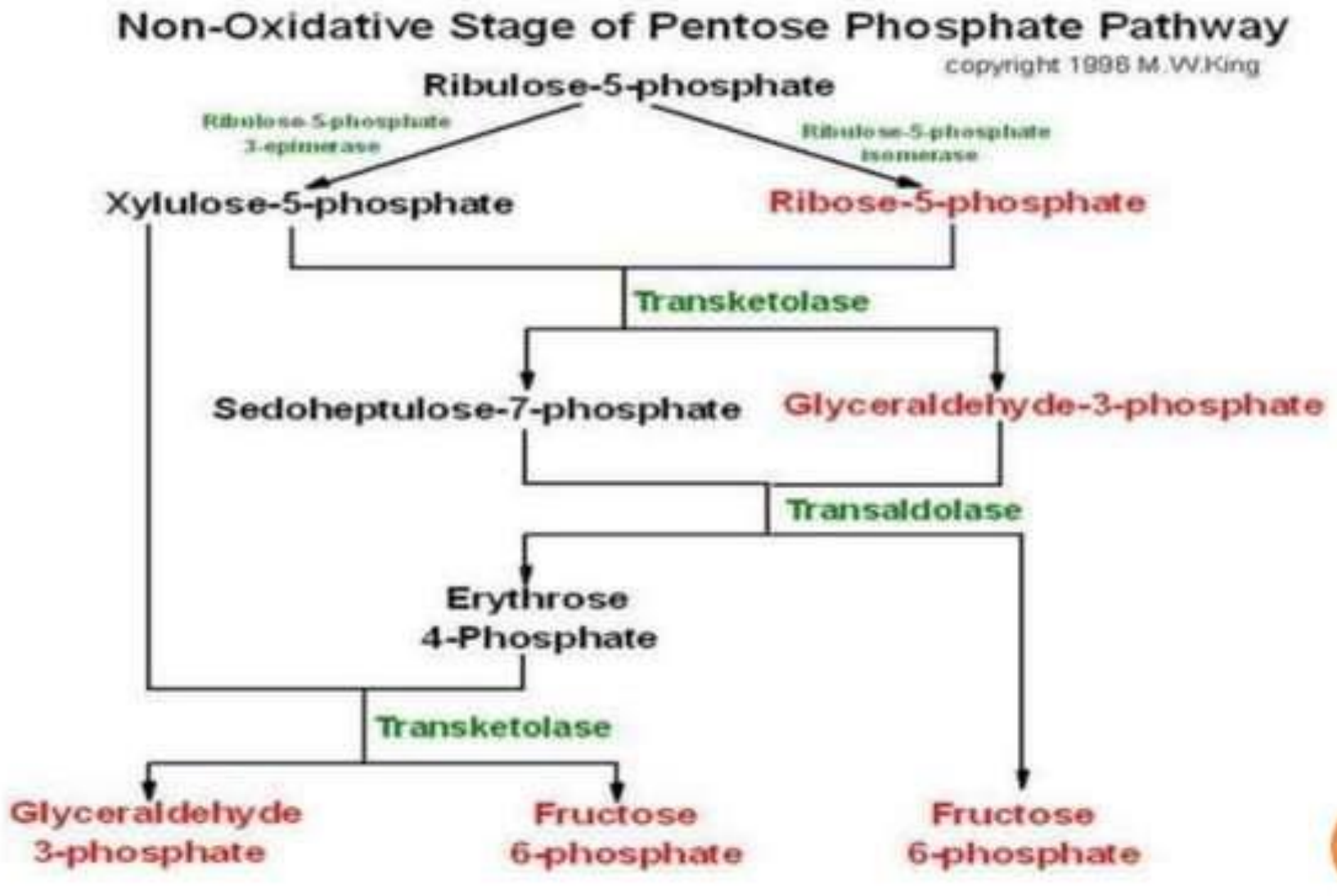
## Oxidative phase

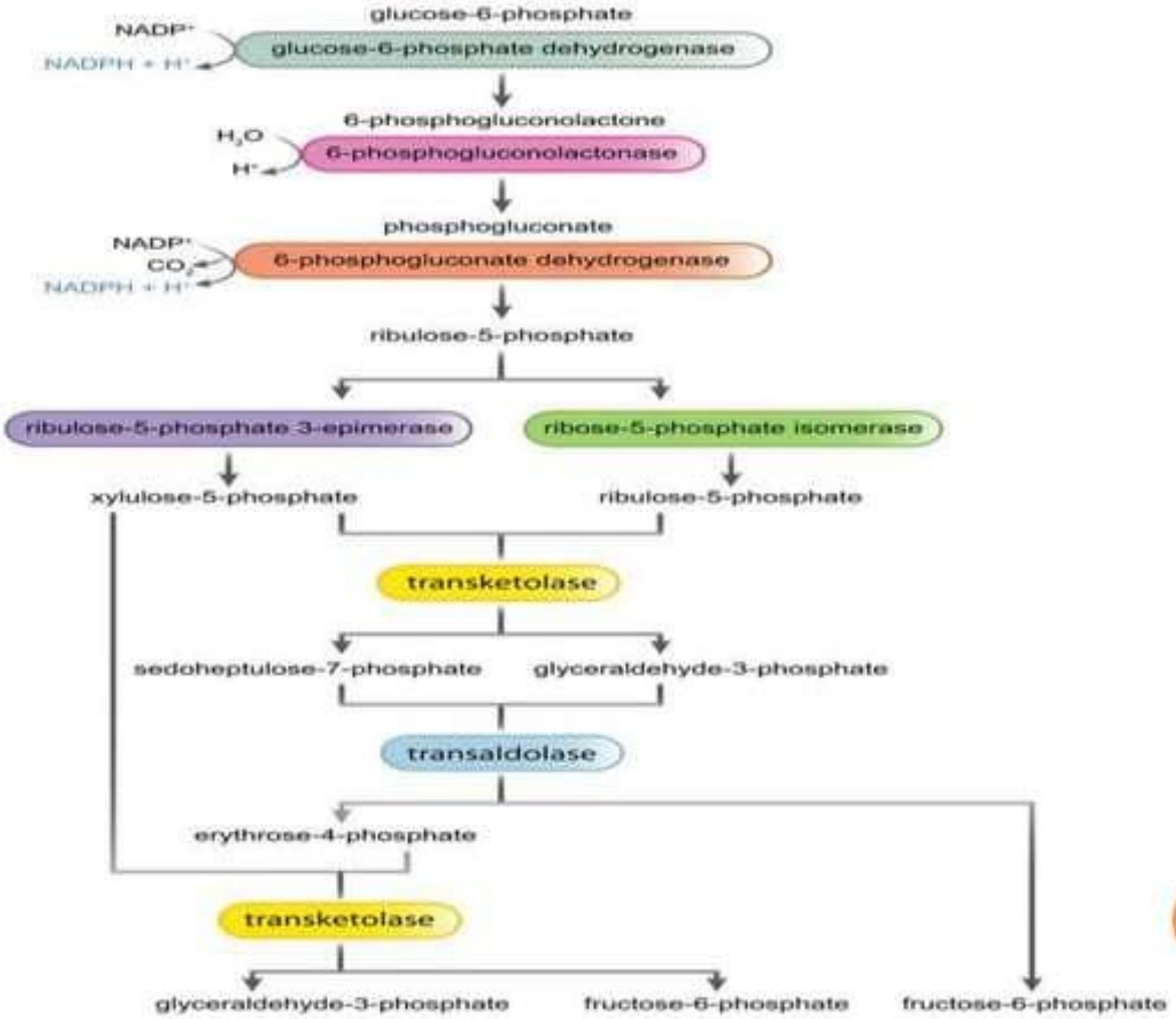
- **Irreversible** phase.
- **Dehydrogenation** of glucose 6- phosphate to 6- phosphogluconate catalyzed by glucose 6-phosphate dehydrogenase.
- Followed by **hydrolysis** of 6-phosphoglucolactone catalyzed by 6- phospho- glucnate dehydrogenase.
- **Decarboxylation** follows with the formation of the keopentose ribulose 5-phosphate.
- both this step requires **NADP+** as hydrogen acceptor.

# Oxidative Stage of Pentose Phosphate Pathway



# Non-oxidative phase




glucose-6-phosphate
NADP+
NADPH + H+
glucose-6-phosphate dehydrogenase
6-phosphogluconolactone
H2O
H+
6-phosphogluconolactonase
phosphogluconate
NADP+
CO2
NADPH + H+
6-phosphogluconate dehydrogenase
ribulose-5-phosphate
ribulose-5-phosphate 3-epimerase
ribose-5-phosphate isomerase
xylulose-5-phosphate
ribulose-5-phosphate
transketolase
sedoheptulose-7-phosphate
glyceraldehyde-3-phosphate
transaldolase
erythrose-4-phosphate
transketolase
glyceraldehyde-3-phosphate
fructose-6-phosphate
fructose-6-phosphate

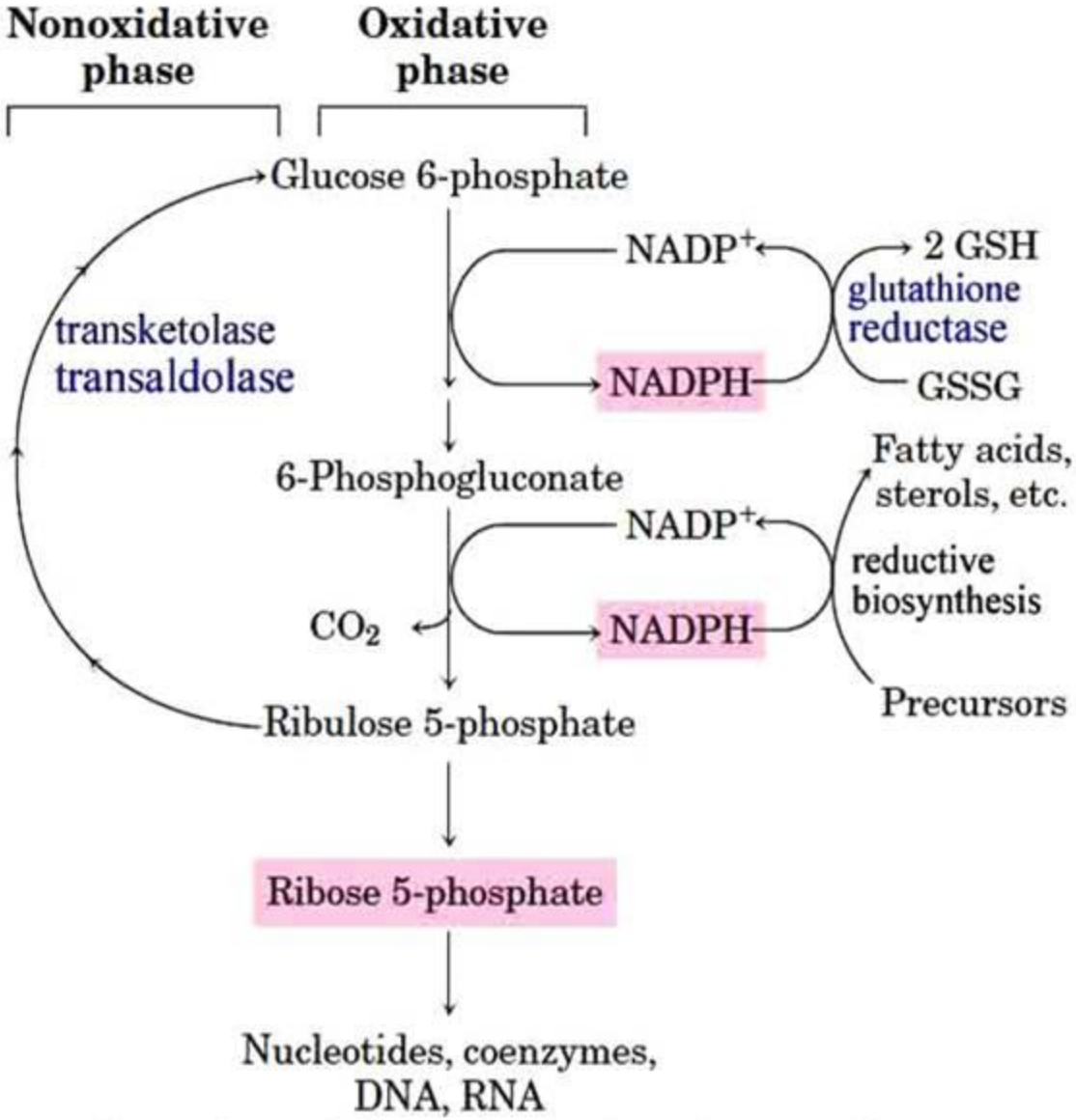
## Biological significance

A) Importance of NADPH

1) NADPH is used in the synthesis of certain aminoacids involving the enzyme glutamate dehydrogenase.
2) it is used for the biosynthesis of fatty acids and steroids.
3) The NADPH keeps the glutathione of RBC in reduced state to preserve the integrity of RBC membrane.
4) The NADPH keeps the ferrous(Fe2+) iron of hemoglobin in reduced state.
5) The process phagocytosis requires NADPH.
6) It is required for the detoxification of drugs.

**B) Importance of pentoses**

1) The pentose and its derivatives are used for the synthesis of nucleic acids(DNA, RNA) & many nucleotides(ATP, NAD+, coA).
2) When an organism growing on pentose sugar(5c),this pathway is used to produce carbohydrates for cell wall synthesis.




**Overview of the pentose phosphate pathway**

*(Lehninger Principles of Biochemistry (5E, 2008) Nelson and Cox, WH Freeman and company)*

# Regulation of HMP Shunt

- **The hexose monophosphate shunt (HMP shunt) is regulated by the levels of NADP+ and NADPH in the cell, and by the activity of the key regulatory enzymes G-6-PD and 6-phospho-gluconate dehydrogenases:**

- **NADP+ levels**

  High levels of NADP+ activate G-6-PD, which promotes the HMP shunt when the cell needs more R5P or NADPH.

- **NADPH levels**

  High levels of NADPH inhibit G-6-PD, which slows down the pathway when there is enough NADPH.

- **Enzyme activity**

  The activity of the enzymes is activated by glucose, insulin, thyroxine, and inhibited by starvation.

- **Carbohydrate diets**

  High carbohydrate diets enhance the activities of both dehydrogenases and the rate of the pathway