# BIOCHEMISTRY

## Fourth Class-First Couse


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# The pentose phosphate pathway

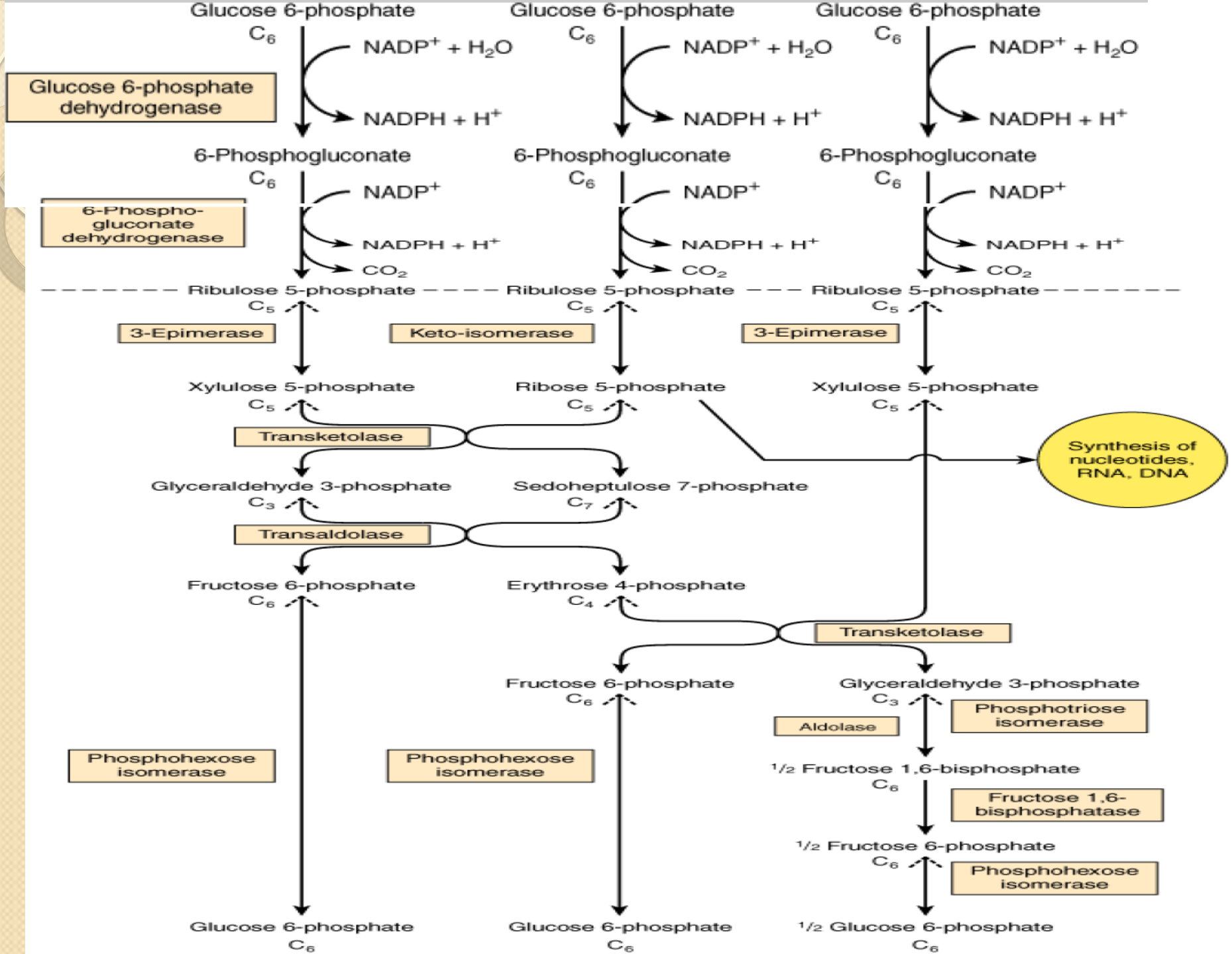
## BIOMEDICAL IMPORTANCE

The pentose phosphate pathway is an alternative route for the metabolism of glucose. It does not lead to formation of ATP but has two major functions:

I) the formation of **NADPH for synthesis of fatty acids and steroids, and**

# THE PENTOSE PHOSPHATE PATHWAY FORMS NADPH & RIBOSE PHOSPHATE

The pentose phosphate pathway (hexose monophosphate shunt) is a more complex pathway than glycolysis (Figure 21–1). Three molecules of glucose 6-phosphate give rise to three molecules of CO2 and three 5-carbon sugars. These are rearranged to regenerate two molecules of glucose 6-phosphate and one molecule of the glycolytic intermediate, glyceraldehyde 3-phosphate. Since two molecules of glyceraldehyde 3-phosphate can regenerate glucose 6-phosphate, the pathway can account for the complete oxidation of glucose.


Glucose 6-phosphate
C6
NADP+ + H2O
Glucose 6-phosphate dehydrogenase
NADPH + H+
6-Phosphogluconate
C6
NADP+
6-Phospho-gluconate dehydrogenase
NADPH + H+
CO2
Ribulose 5-phosphate
C5
3-Epimerase
Keto-isomerase
Xylulose 5-phosphate
Ribose 5-phosphate
Transketolase
Glyceraldehyde 3-phosphate
C3
Sedoheptulose 7-phosphate
C7
Transaldolase
Fructose 6-phosphate
C6
Erythrose 4-phosphate
C4
Synthesis of nucleotides, RNA, DNA
Phosphohexose isomerase
Aldolase
Phosphotriose isomerase
1/2 Fructose 1,6-bisphosphate
Fructose 1,6-bisphosphatase
1/2 Fructose 6-phosphate
1/2 Glucose 6-phosphate

## REACTIONS OF THE PENTOSE PHOSPHATE PATHWAY OCCUR IN THE CYTOSOL

Like glycolysis, the enzymes of the pentose phosphate pathway are cytosolic. Unlike glycolysis, oxidation is

achieved by dehydrogenation using **NADP + , not NAD + , as the hydrogen acceptor. The sequence of reactions of**

the pathway may be divided into two phases: an **oxidative nonreversible phase and a nonoxidative**

**reversible phase. In the first phase, glucose 6-phosphate undergoes dehydrogenation and decarboxylation to**

yield a pentose, ribulose 5-phosphate. In the second phase, ribulose 5-phosphate is converted back to glucose 6-

phosphate by a series of reactions involving mainly two enzymes: **transketolase and transaldolase (see Figure**

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### The Oxidative Phase Generates NADPH

Dehydrogenation of glucose 6-phosphate to 6-phosphogluconate occurs via the formation of 6-

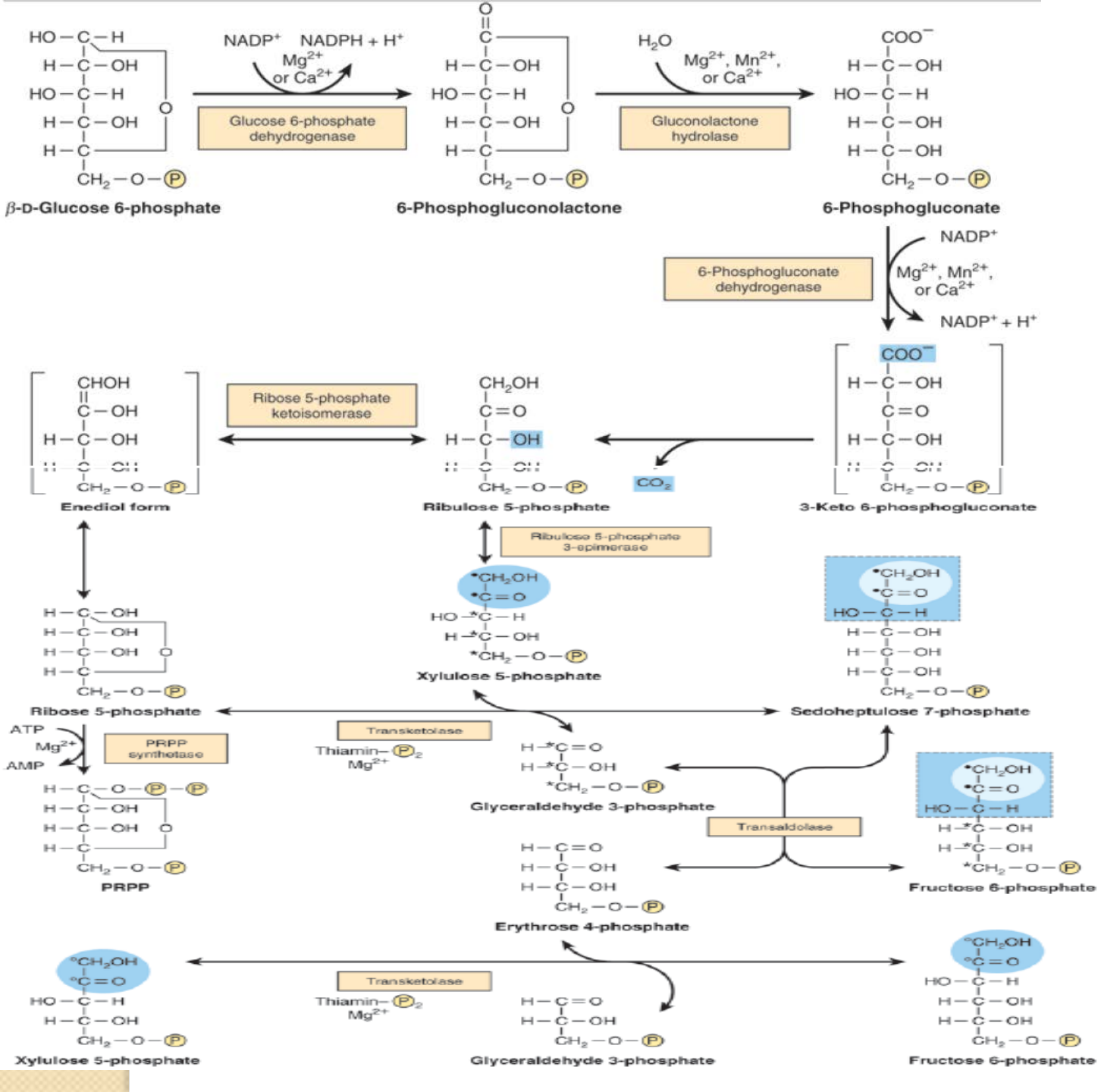
phosphogluconolactone catalyzed by **glucose 6-phosphate dehydrogenase, an NADP-dependent enzyme**

(Figures 21–1 & 21–2). The hydrolysis of 6-phosphogluconolactone is accomplished by the enzyme

**gluconolactone hydrolase. A second oxidative step is catalyzed by 6-phosphogluconate dehydrogenase,**

which also requires NADP+ as hydrogen acceptor. Decarboxylation follows with the formation of the ketopentose

ribulose 5-phosphate.

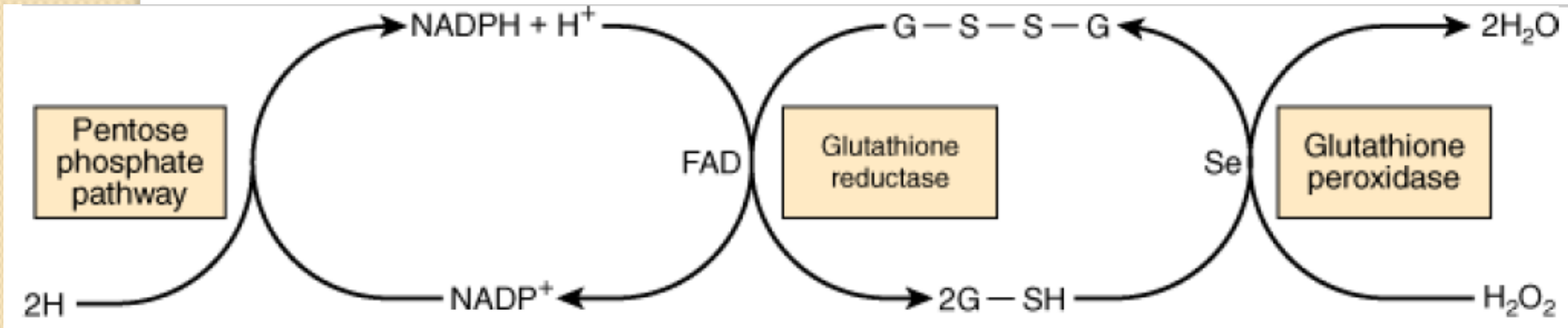

β-D-Glucose 6-phosphate
NADP+ NADPH + H+
Mg2+ or Ca2+
Glucose 6-phosphate dehydrogenase
6-Phosphogluconolactone
H2O
Mg2+, Mn2+, or Ca2+
Gluconolactone hydrolase
6-Phosphogluconate
NADP+
Mg2+, Mn2+, or Ca2+
NADP+ + H+
6-Phosphogluconate dehydrogenase
3-Keto 6-phosphogluconate
CO2
Enediol form
Ribose 5-phosphate ketoisomerase
Ribulose 5-phosphate
Ribulose 5-phosphate 3-epimerase
Xylulose 5-phosphate
Ribose 5-phosphate
Sedoheptulose 7-phosphate
ATP
Mg2+
AMP
PRPP synthetase
PRPP
Transketolase
Thiamin–P2
Mg2+
Glyceraldehyde 3-phosphate
Transaldolase
Fructose 6-phosphate
Erythrose 4-phosphate
Transketolase
Thiamin–P2
Mg2+
Xylulose 5-phosphate
Glyceraldehyde 3-phosphate
Fructose 6-phosphate

## THE PENTOSE PHOSPHATE PATHWAY & GLUTATHIONE PEROXIDASE PROTECT ERYTHROCYTES AGAINST HEMOLYSIS

In red blood cells the pentose phosphate pathway provides NADPH for the reduction of oxidized glutathione

catalyzed by **glutathione reductase, a flavoprotein containing FAD. Reduced glutathione removes H2 O2 in a** reaction catalyzed by **glutathione peroxidase, an enzyme that contains the selenium analogue of cysteine**

(selenocysteine) at the active site (Figure 21–3). The reaction is important, since accumulation of H2 O2 may decrease the life span of the erythrocyte by causing oxidative damage to the cell membrane, leading to hemolysis.




Role of the pentose phosphate pathway in the glutathione peroxidase reaction of erythrocytes. (G-S-S-G, oxidized glutathione; G-SH, reduced glutathione; Se, selenium-containing enzyme.)