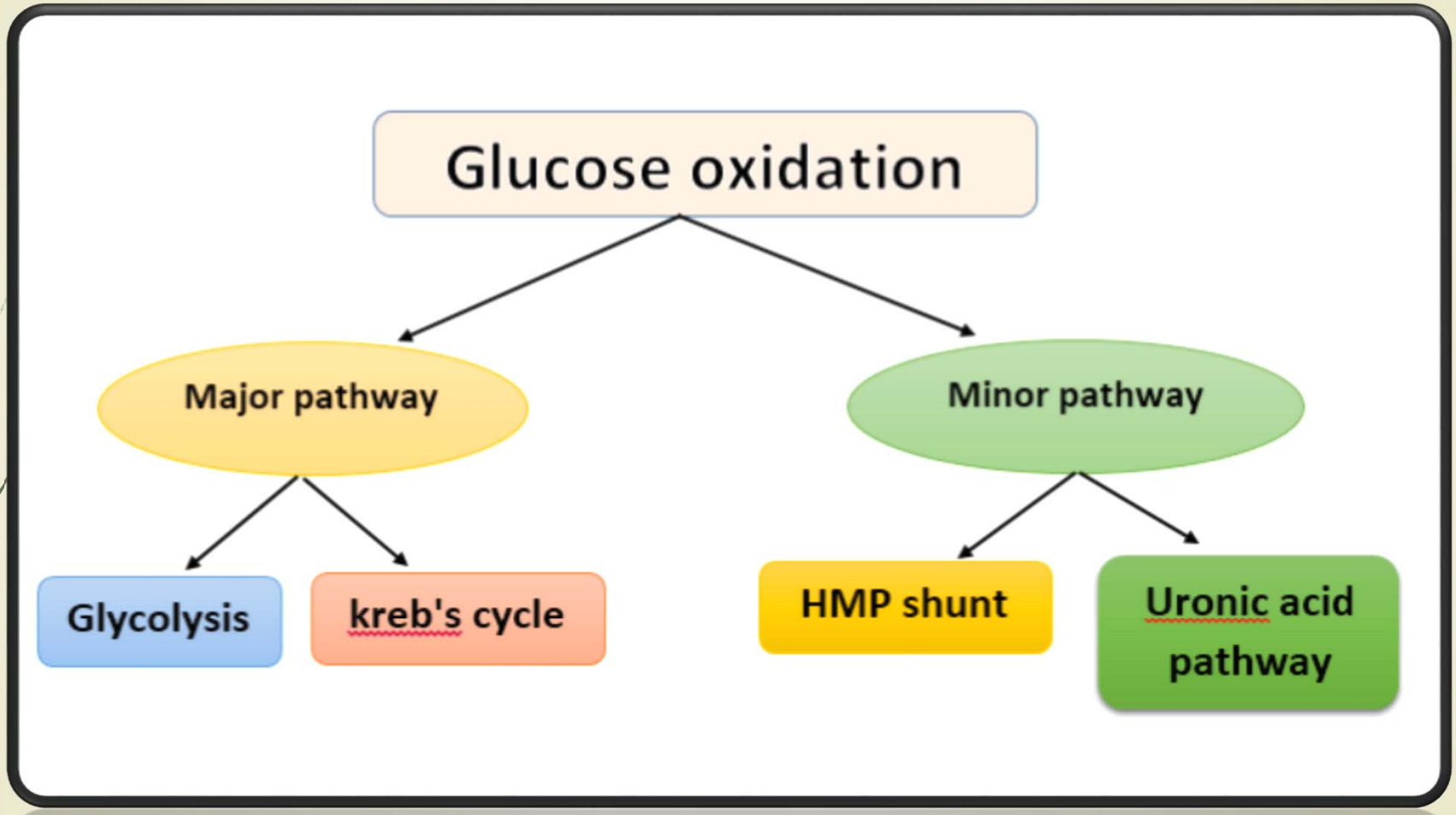
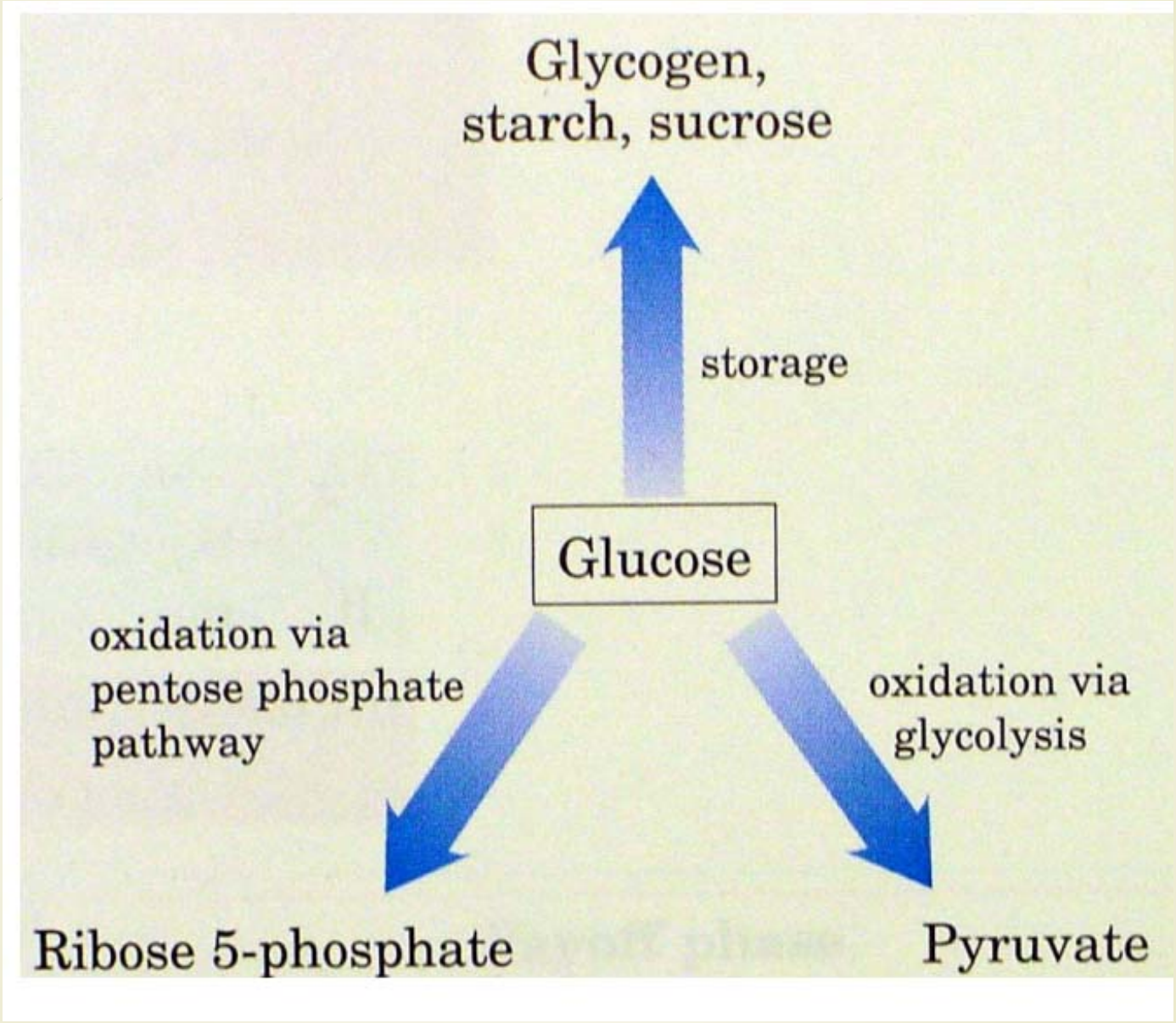
Oxidation of glucose


Glucose oxidation
Major pathway
Minor pathway
Glycolysis
kreb's cycle
HMP shunt
Uronic acid pathway


Glycogen,
starch, sucrose
storage
Glucose
oxidation via
pentose phosphate
pathway
oxidation via
glycolysis
Ribose 5-phosphate
Pyruvate

HMP shunt pathway

- Glycolysis and citric acid cycle are the common pathways by which animal tissues oxidise glucose to CO2 and H2O with the liberation of energy in the form of ATP.
- One of the most important alternative pathways is Hexose Monophosphate Shunt Pathway (HMP shunt).
- This pathway occurs in the extra-mitochondrial soluble portion of the cells.
- This occur in some cells as
- 1- liver.
- 2- adipose tissue.
- 3- supra renal cortex.
- 4- lactating gland mammary during lactation only.
- 5- RBCs.
- 6- Eye lens and retina.
- 7- thyroid gland.

- HMP shunt generates a different type of metabolic energy - the reducing power. Some of the electrons and hydrogen atoms of fuel molecules are conserved for biosynthetic purposes rather than ATP formation. This reducing power of cells is NADPH (reduced nicotinamide adenine dinucleotide phosphate).

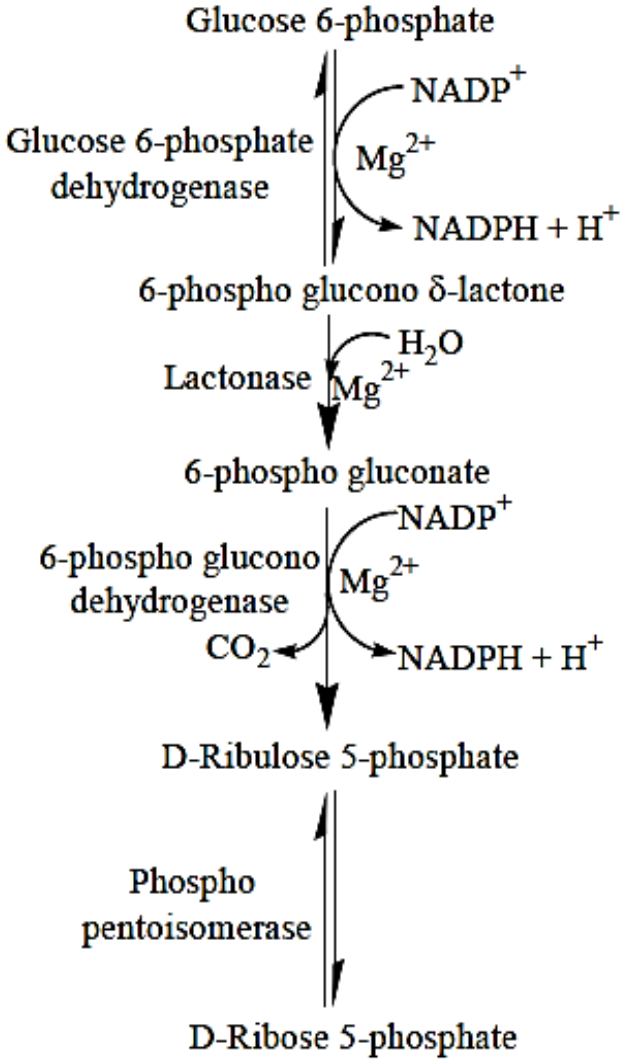


Fig. 3.3 Oxidative reactions of the hexose mono-phosphate pathway

Biological importance of HMP shunt

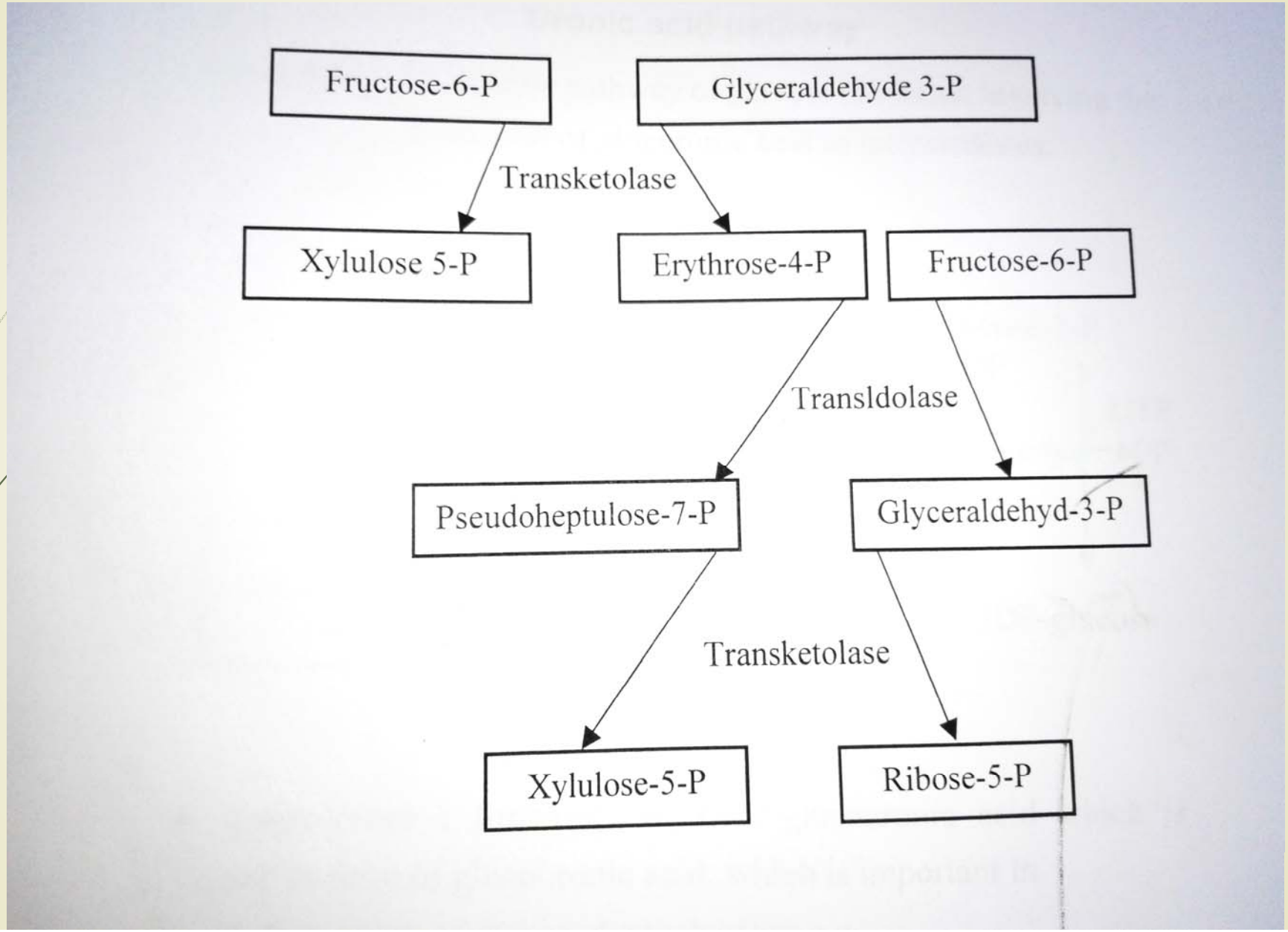
- 1- production of pentose-5-P which is essential for:
- Biosynthesis of RNA and DNA.
- Biosynthesis of nucleotides.
- Biosynthesis of coenzymes (eg FAD and NAD).
- 2- Production of NADPH which is important in:
- Biosynthesis of fatty acid, cholesterol, steroid hormones and galactolipid.
- 3- keep iron in Hb in ferrous state.
- 4- coenzyme in reductose and hydroxylase.

Regulation of HMP shunt pathway

- NADP concentration is the major factor in regulation of gluco-6-P reaction.
- NADPH is a competitive inhibitor.
- Key enzyme is G-6-P.
- This enzymes are activated by fed state, glucose, insulin, thyroxine and NADP but are inhibited during starvation, diabetes mellitus and with high NADPH.H+/NADP ratio.

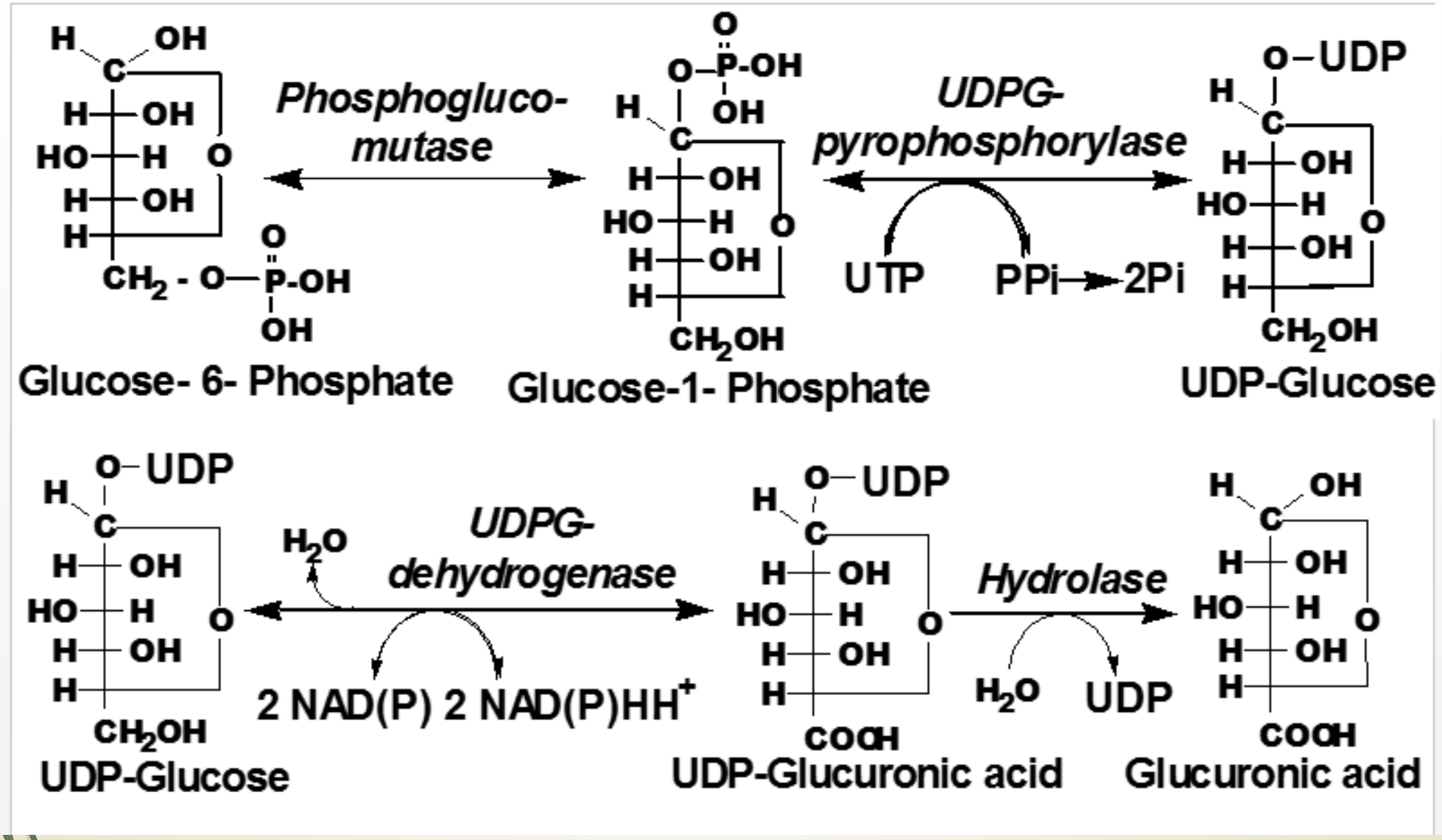
HMP-shunt in skeletal muscle

- Skeletal muscle contain very small a mount of glucose-6-P-dehyrogenase and 6- phospho gluconate dehydrogenase.
- Muscle tissue synthesis its ribose by several of the shunt using fructose-6-P and glyceraldehyde-3P(produced by glycolysis) and the enzymes transketolase and transaldolase.


Fructose-6-P
Glyceraldehyde 3-P
Transketolase
Xylulose 5-P
Erythrose-4-P
Fructose-6-P
Transldolase
Pseudoheptulose-7-P
Glyceraldehyd-3-P
Transketolase
Xylulose-5-P
Ribose-5-P

Uronic acid Pathway

- It is another minor alternative pathway for glucose oxidation by which glucuronic acid, ascorbic acid and pentoses are obtained from glucose.
- Like HMP shunt, it does not need nor generate ATP.
- Site:
- In cytosol of many tissues, especially liver, kidney and intestine.


Phosphogluco-
mutase
UDPG-
pyrophosphorylase
UTP
PPi
2Pi
Glucose- 6- Phosphate
Glucose-1- Phosphate
UDP-Glucose
UDP-Glucose
H2O
UDPG-
dehydrogenase
2 NAD(P) 2 NAD(P)HH+
Hydrolase
H2O
UDP
UDP-Glucose
UDP-Glucuronic acid
Glucuronic acid

Biological importance of Uronic Acid Pathway:

1-Production of UDP-glucuronic acid, which is the metabolically active form of glucuronic acid which enters in:

- Synthesis of mucopolysaccharides.
- Detoxification by conjugation: UDP-glucuronic acid is used to detoxify steroid hormones, drugs and toxins.
- Formation of conjugated bilirubin.
- 2-Formation of pentoses.
- 3-Formation of vitamin C in plants and animal.
- 4-formation of heparine sulfate for cell membrane receptors.
- 5- formation of heparine as anticoagulant.

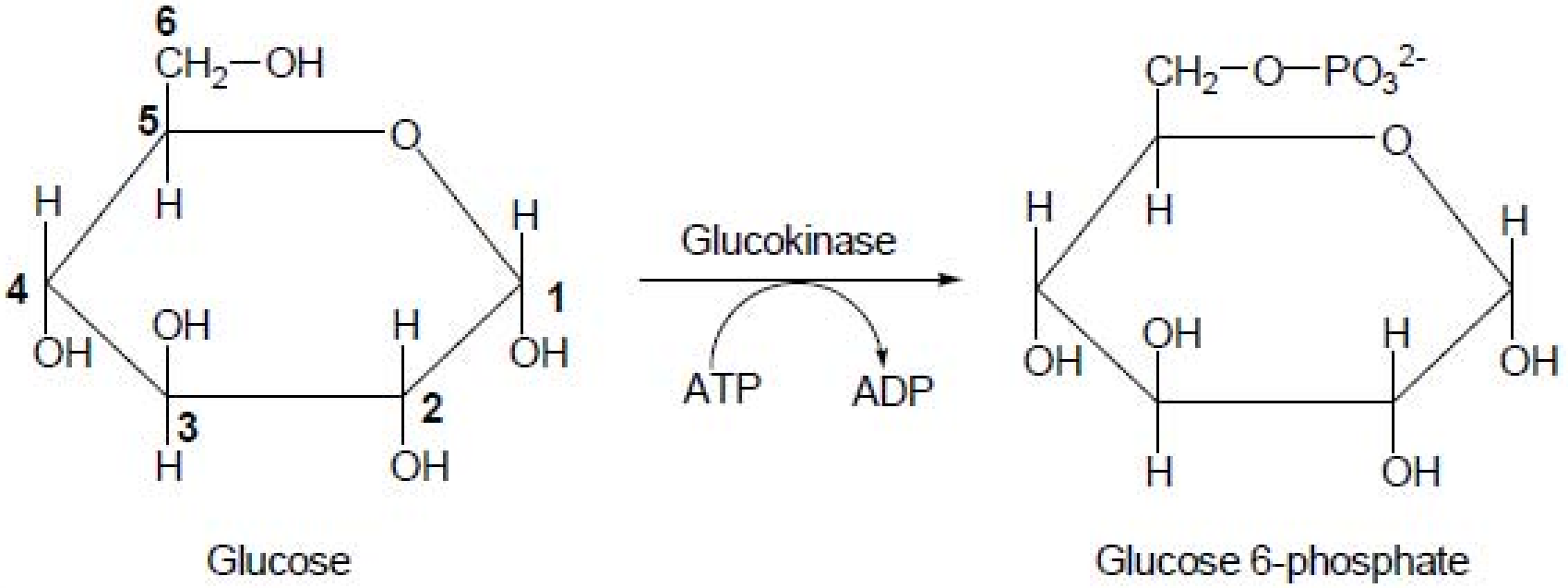
Glycogen

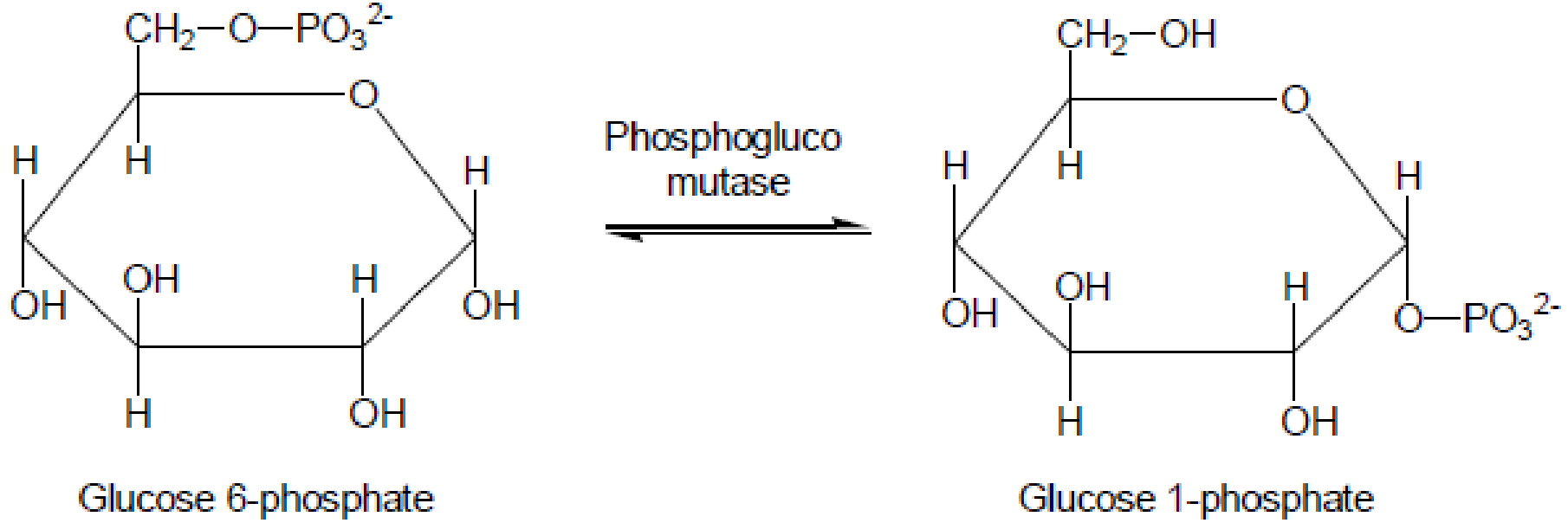
- **Glycogen** is the major storage form of carbohydrate in animals
- and corresponds to starch in plants. It occurs mainly in liver.
- **Glycogen biosynthesis**
- The process of biosynthesis of glycogen from glucose is known
- as glycogenesis.
- This occurs in all the tissues of the body but the major sites are liver and muscles.
- A considerable amount is synthesised in kidney also.

- **Why the cell can store glycogen but not glucose?**
- **Because when glucose increased, osmatic pressure in the cell increase, causing water movement toward the cell and leading to burst so when glucose accumulates in the cell, it will convert to glycogen which consists of branched series of glucose.**

REACTIONS OF GLYCOGENESIS

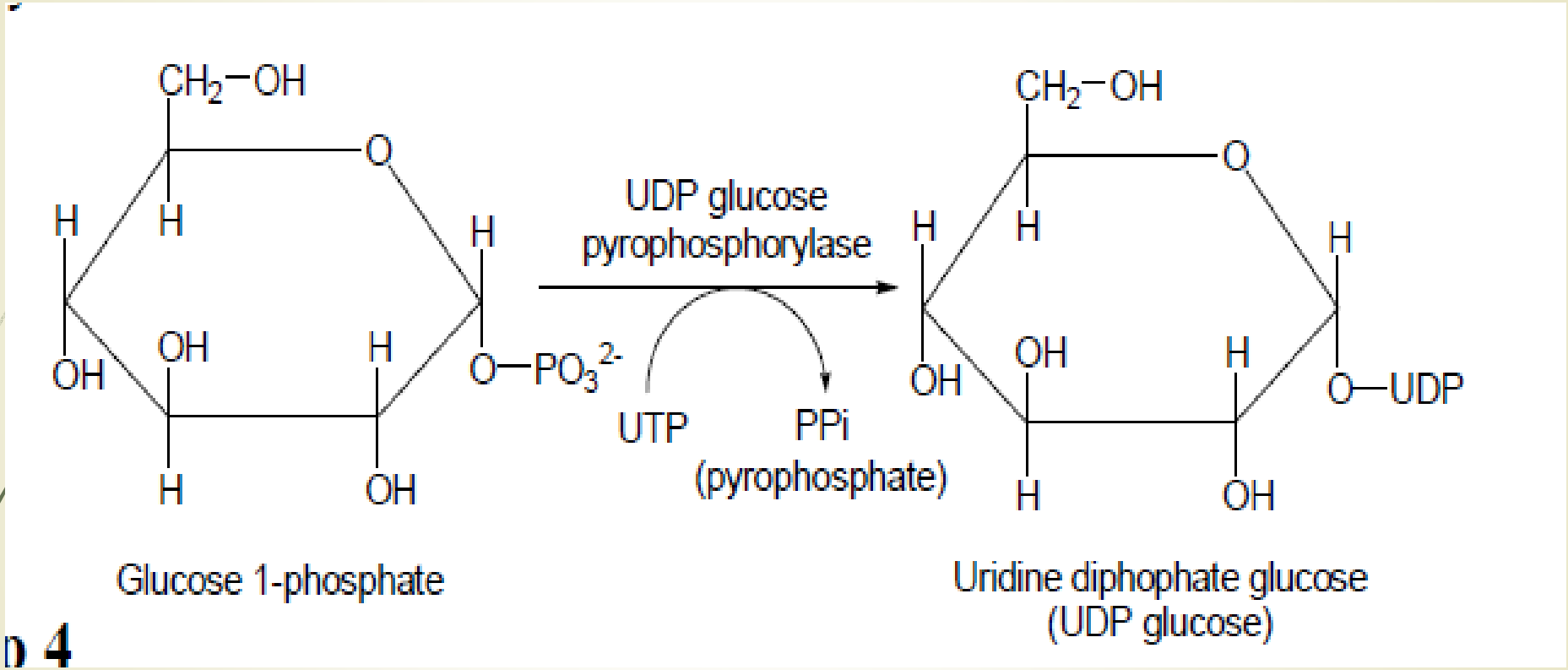
- Glycogen synthesis from of a D glucose
- The process occurs in the cytosol
- The process requires energy supplied by ATP and Uridine triphosphate (UTP).


6
CH2—OH
5
O
H
H
H
4
1
OH
OH
H
OH
3
2
H
OH
Glucose
Glucokinase
ATP
ADP
CH2—O—PO3 2-
O
H
H
H
OH
OH
H
OH
H
OH
Glucose 6-phosphate



Glucose 6-phosphate

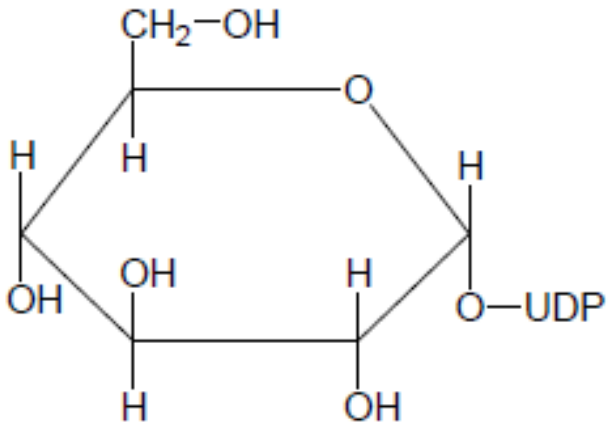
Glucose 1-phosphate



Glucose 1-phosphate

Uridine diphophate glucose
(UDP glucose)

4



Uridine diphophate glucose

(UDP glucose)

+

Glycogen chain (n)

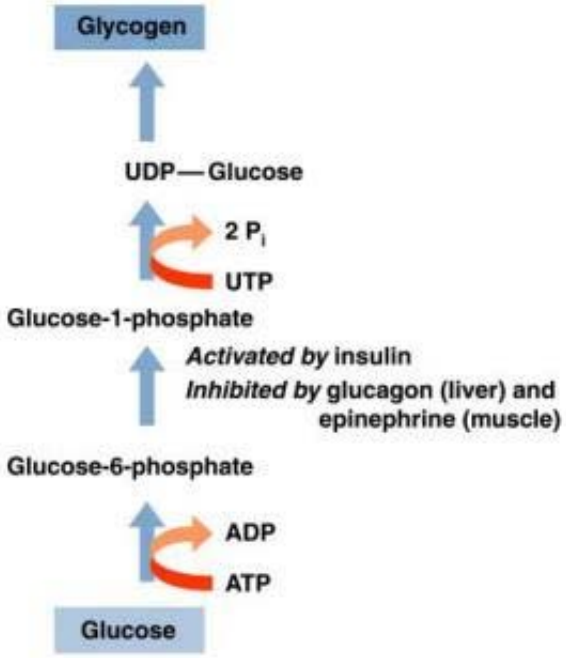
Glycogen synthase

Glycogen chain (n + 1)

+

UDP

Diagram of Glycogenesis



Glycogenolysis

- Degradation of glycogen When the blood sugar level falls (Hypoglycemia), glycogen stored in the tissues specially glycogen of liver and muscles may be broken down and this process of breakdown of glycogen is called glycogenolysis.

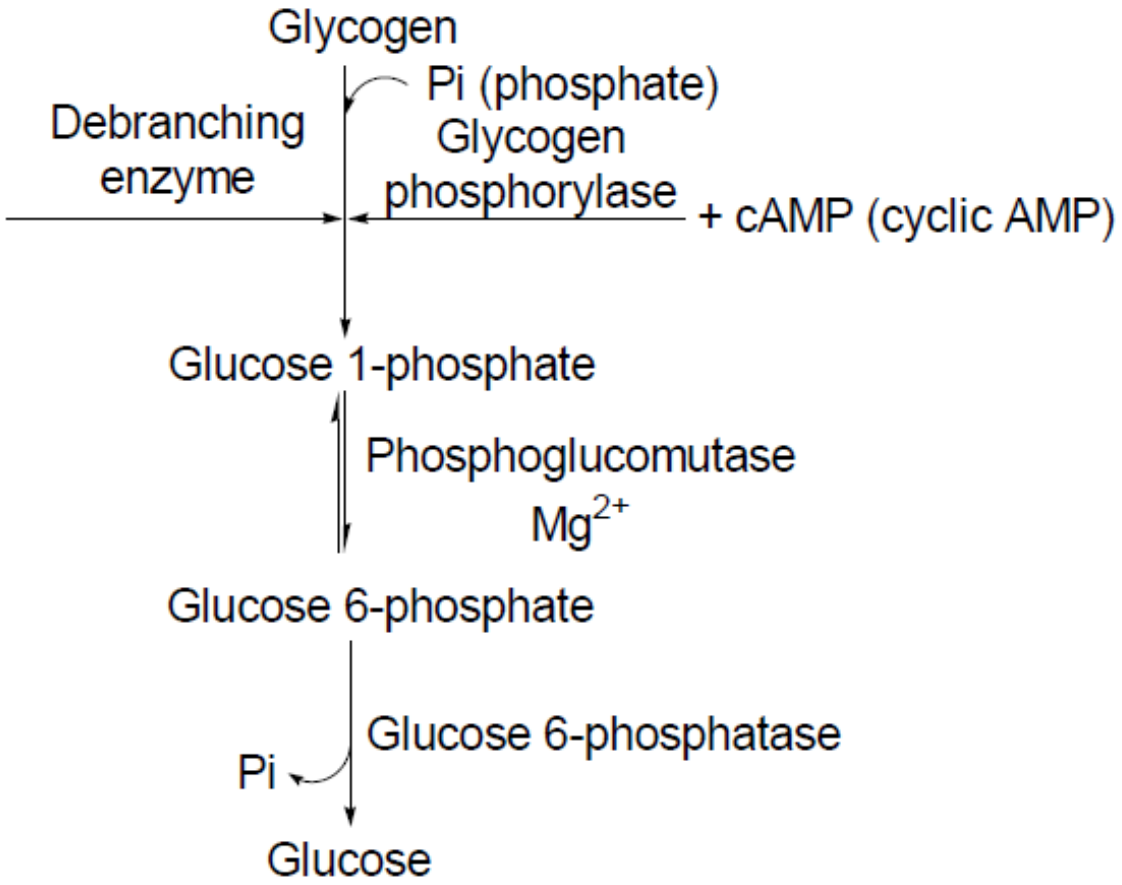


Fig.3.4 Glycogenolysis

Gluconeogenesis

- The synthesis of glucose from non-carbohydrate precursors is known as **gluconeogenesis.**
- The major site of gluconeogenesis is liver.
- It usually occurs when the carbohydrate in the diet is insufficient to meet the demand in the body, with the intake of protein rich diet and at the time of starvation, when tissue proteins are broken down to amino acids.

Gluconeogenesis and glycolysis

- Gluconeogenesis and glycolysis are opposing metabolic pathways and share a number of enzymes.
- In glycolysis, glucose is converted to pyruvate
- In gluconeogenesis pyruvate is converted to glucose.

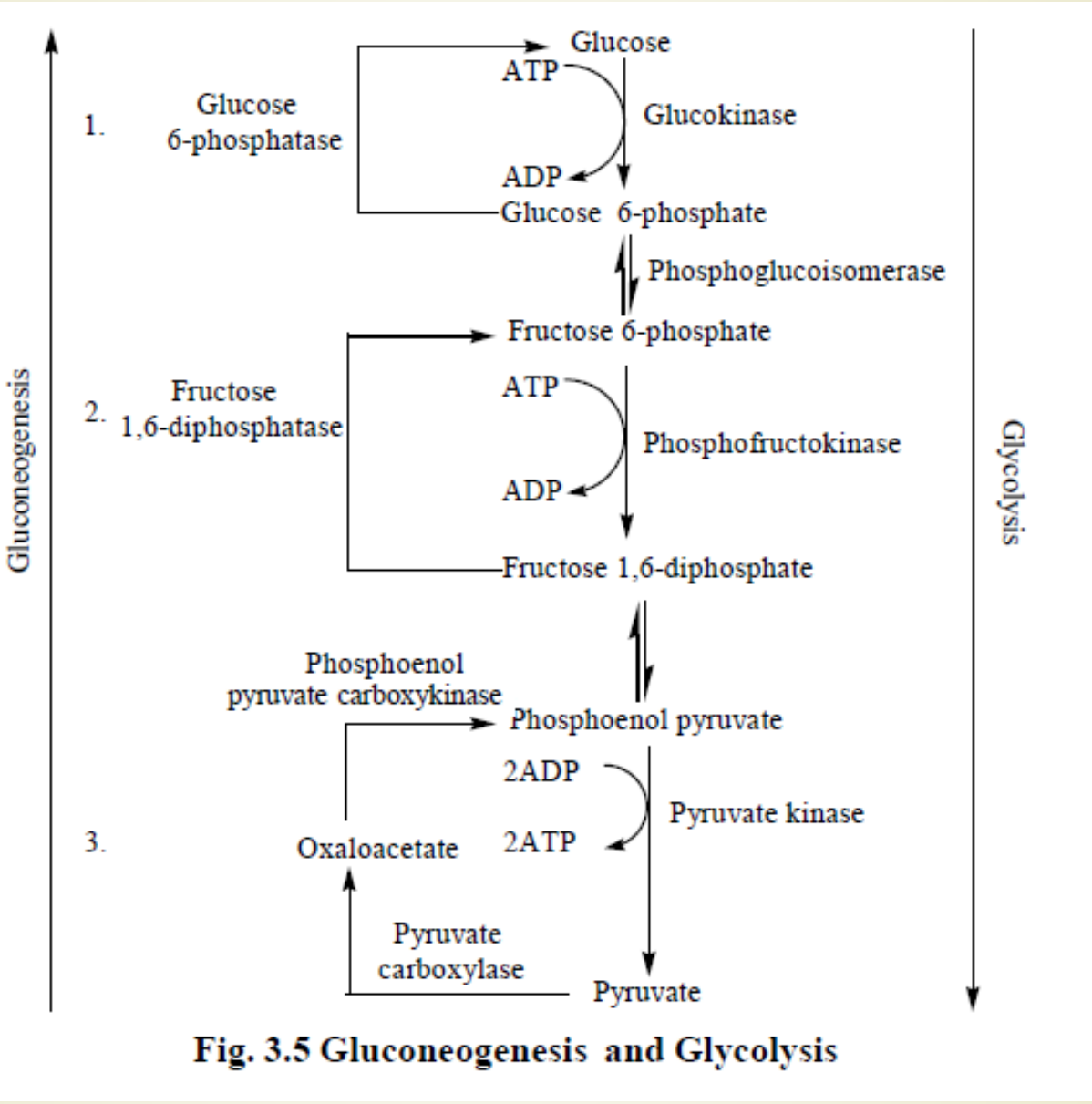


Fig. 3.5 Gluconeogenesis and Glycolysis

Gluconeogenesis of amino acids

- Amino acids which could be converted to glucose are called glucogenic amino acids.
- Most of the glucogenic amino acids are converted to the intermediates of citric acid cycle either by transamination or deamination.

Gluconeogenesis of Propionate

- Propionate is a major source of glucose in ruminants, and enters the main gluconeogenic pathway via the citric acid cycle after conversion to succinyl CoA.

Gluconeogenesis of Glycerol

- At the time of starvation glycerol can also undergo gluconeogenesis.
- When the triglycerides are hydrolysed in the adipose tissue, glycerol is released.
- Further metabolism of glycerol does not take place in the adipose tissue because of the lack of glycerol kinase necessary to phosphorylate it. Instead,
- glycerol passes to the liver where it is phosphorylated to glycerol 3-phosphate by the enzyme glycerol kinase.

Gluconeogenesis of lactic acid (Cori cycle)

- The liver and skeletal muscles exhibit a special metabolic cooperation as far as carbohydrates are concerned by the way of a cycle of conversions known as Cori cycle.

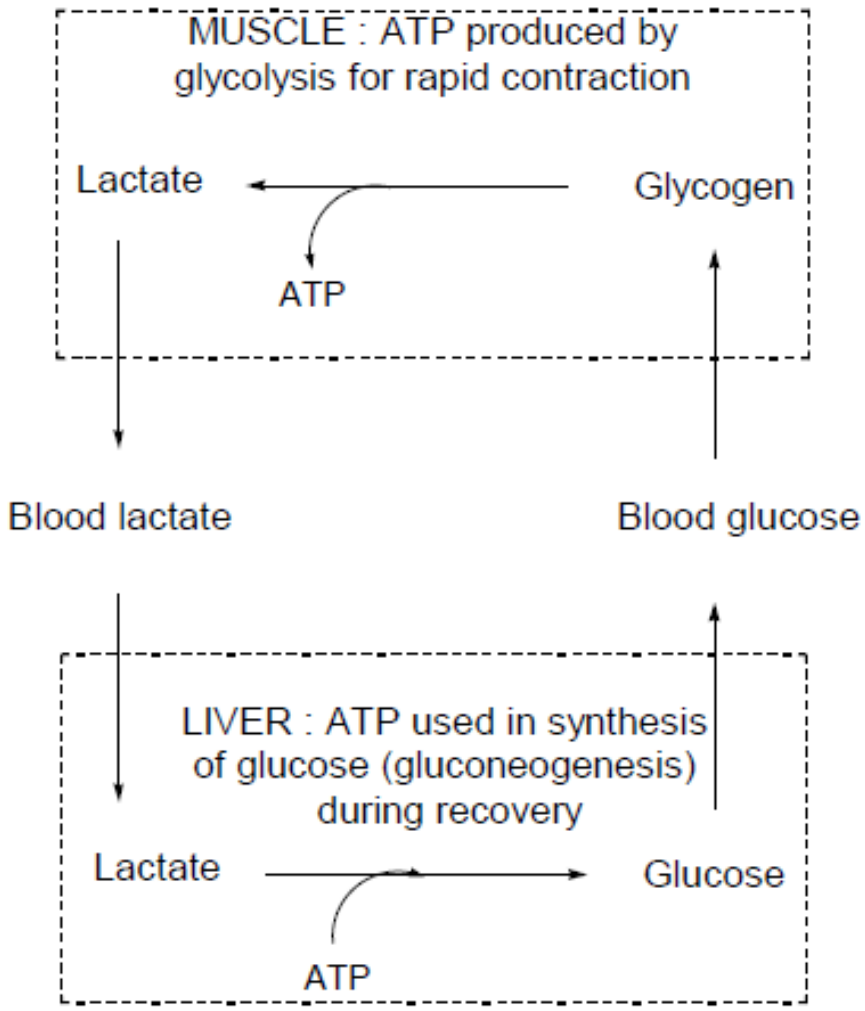


Fig. 3.6 Cori cycle

Glucose Tolerance Test (GTT)

- After a night without food, the patient drinks a test dose of 100 g of glucose dissolved in a glass of water.
- The blood glucose concentration is measured before the test dose and at 30 min intervals for several hours thereafter.
- A normal individual assimilates the glucose readily, the blood glucose rising to no more than about 80 to 120 mg/100 ml; little or no glucose appears in the urine.
- Diabetic individuals assimilate the test dose of glucose poorly; their blood glucose level far exceeds the kidney threshold (about 180 mg/100ml), causing glucose to appear in their urine.