Tishk International University
Faculty of Applied Science
Department of Nutrition and Dietetics
2nd Grade

Carbohydrate Metabolism

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Objectives

- Chemistry of carbohydrates
- Functions of carbohydrates
- Digestion and absorption of Carbohydrates
- Glycolysis
- Gluconeogenesis
- Glycogen Metabolism (Glycogenolysis and glycogenesis)
- Pentose phosphate pathway

Introduction

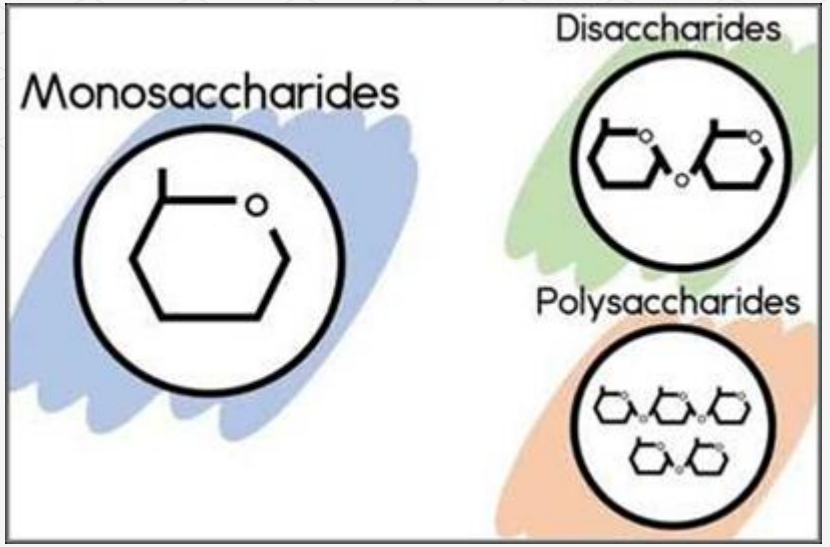
- Carbohydrates are the most abundant macromolecules in nature.
- They are the main source and storage of energy in the body. They serve also as structural component of cell membrane.
- The general molecular formula of carbohydrate is CnH2nOn or (CH2O)n. Chemically, they contain the elements Carbon, hydrogen and oxygen. Thus they are Carbon compounds that contain large quantities of Hydroxyl groups.
- Carbohydrates in general are polyhydroxy aldehydes or ketones or compounds which give these substances on hydrolysis.

Classification and Structure

Classification

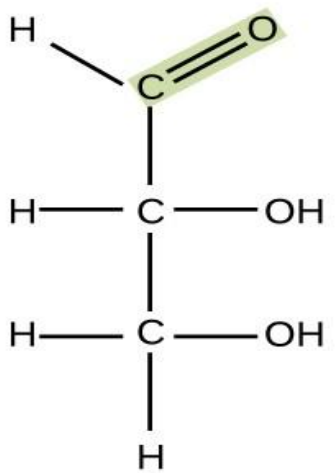
There are three major classes of carbohydrates

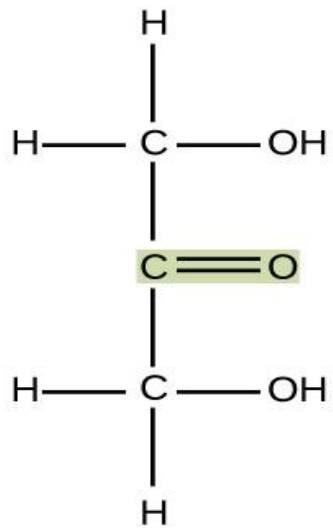
- Monosaccharides (Greek, mono = one)
- Oligosaccharides (Greek, oligo= few) 3-10 monosaccharide units.
- Polysaccharides (Greek, Poly = many) >10 monosaccharide units.

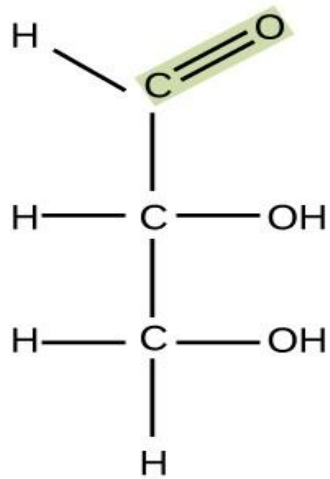


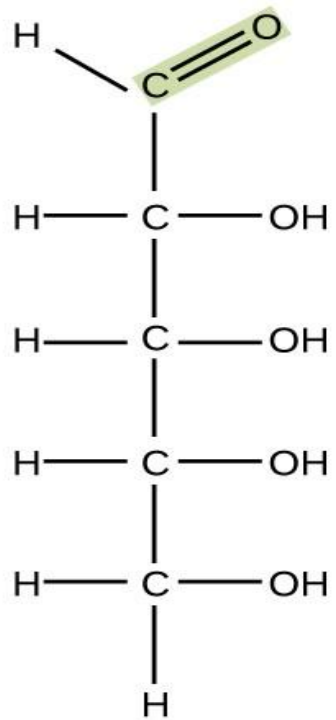
Monosaccharides

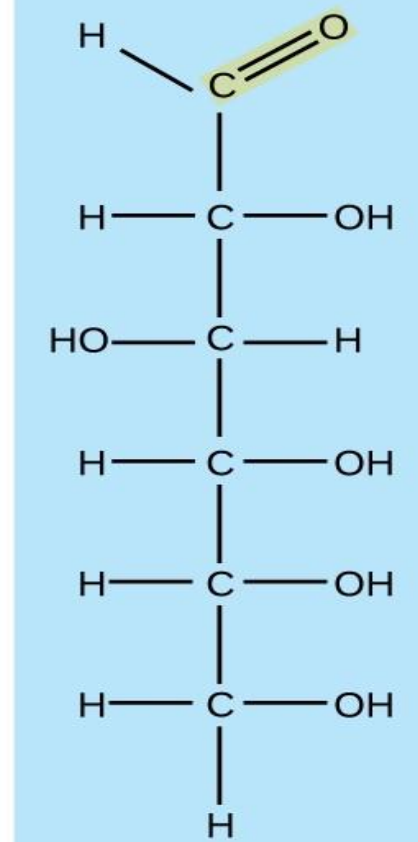
aldose	ketose	triose	pentose	hexose
glyceraldehyde	dihydroxyacetone	glyceraldehyde	ribose	glucose











Functions of Carbohydrates

Carbohydrates have a wide range of functions.

1) They provide energy; act as storage molecules of energy.

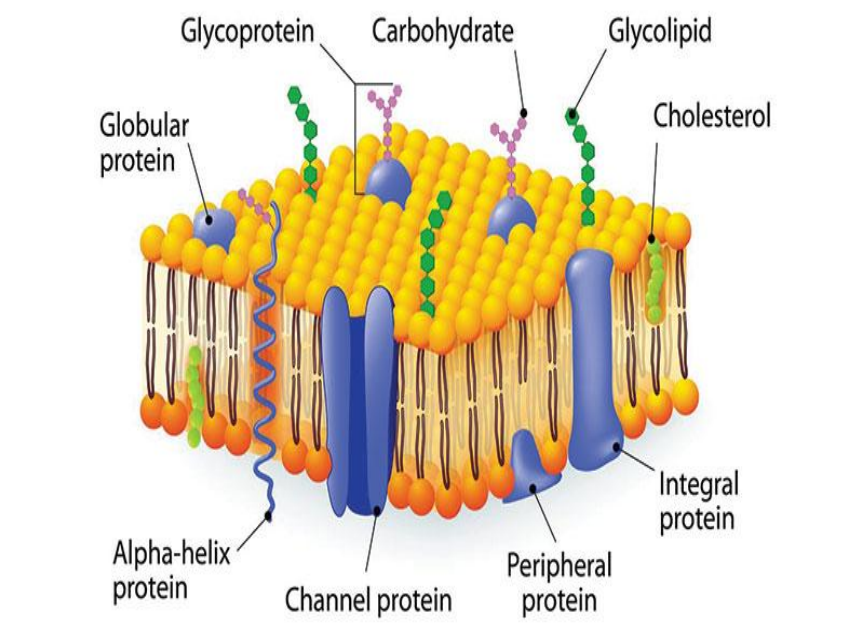
2) Serve as cell membrane components and mediate some forms of communication between cells.

* Absence of a single enzyme like **lactase** causes discomfort and diarrhea.

*The failure of Galactose and fructose metabolism due to deficient enzymes leads to turbidity of lens proteins (Cataract).

* Blood glucose is controlled by different hormones and metabolic processes.

People suffer from Diabetes if the insulin hormone is less or not functioning well, such people are prone to atherosclerosis, vascular diseases, and renal failure.



Digestion and absorption of Carbohydrates

Dietary carbohydrates principally consist of the polysaccharides: starch and glycogen. It also contains disaccharides: sucrose, lactose, maltose and in small amounts monosaccharides like fructose and pentoses. Liquid food materials like milk, soup, fruit juice escape digestion in mouth as they are swallowed, but solid foodstuffs are masticated thoroughly before they are swallowed.

1 Digestion in Mouth

Digestion of carbohydrates starts at the mouth, where they come in contact with saliva during mastication. Saliva contains a carbohydrate splitting enzyme called salivary amylase (ptyalin).

Action of ptyalin (salivary amylase).

It is α - amylase, requires Cl- ion for activation and optimum pH 6-7. The enzyme hydrolyzes α(1,4) glycosidic linkage at random, from molecules like starch, glycogen and dextrins, producing smaller molecules maltose, glucose and disaccharides maltotriose. Ptyalin action stops in stomach when pH falls to 3.0

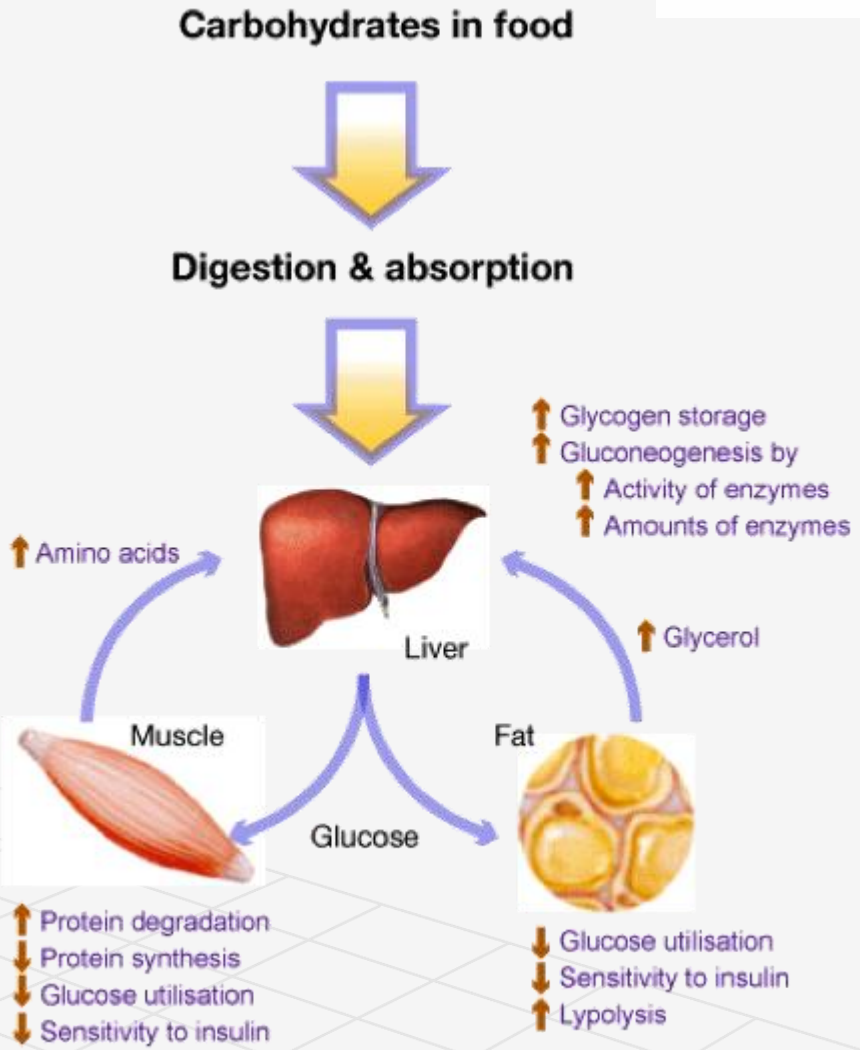
Starch or glycogen $\xrightarrow{\alpha\text{ -Amylase}}$ Glucose, Maltose And Maltotriose

2 Digestion in Stomach

No carbohydrate splitting enzymes are available in gastric juice. HCl may hydrolyze some dietary sucrose to equal amounts of glucose and fructose.

3 Digestion in Duodenum

Food reaches the duodenum from stomach where it meets the pancreatic juice. Pancreatic juice contains a carbohydrate-splitting enzyme pancreatic amylase.



Action of pancreatic Amylase

It is also an α - amylase, optimum pH 7.1. Like ptyalin it also requires Cl- for activity. The enzyme hydrolyzes α-(1,4) glycosidic linkage situated well inside polysaccharide molecule. Other criteria and end products of action are similar of ptyalin.

Digestion in Small Intestine

Action of Intestinal Juice

a. pancreatic amylase: It hydrolyzes terminal α-(1,4), glycosidic linkage in polysaccharides and Oligosaccharide molecules liberating free glucose molecules.

b. Lactase : It is a β- glycosidase, its pH range is 5.4 to 6.0. Lactose is hydrolyzed to glucose and galactose.

Lactose $\xrightarrow{lactase}$ Glucose + Galactose

C. Maltase : The enzyme hydrolyzes the α -(1,4) glycosidic linkage between glucose units in maltose molecule liberating two glucose molecules. Its pH range is 5.8 to 6.2.

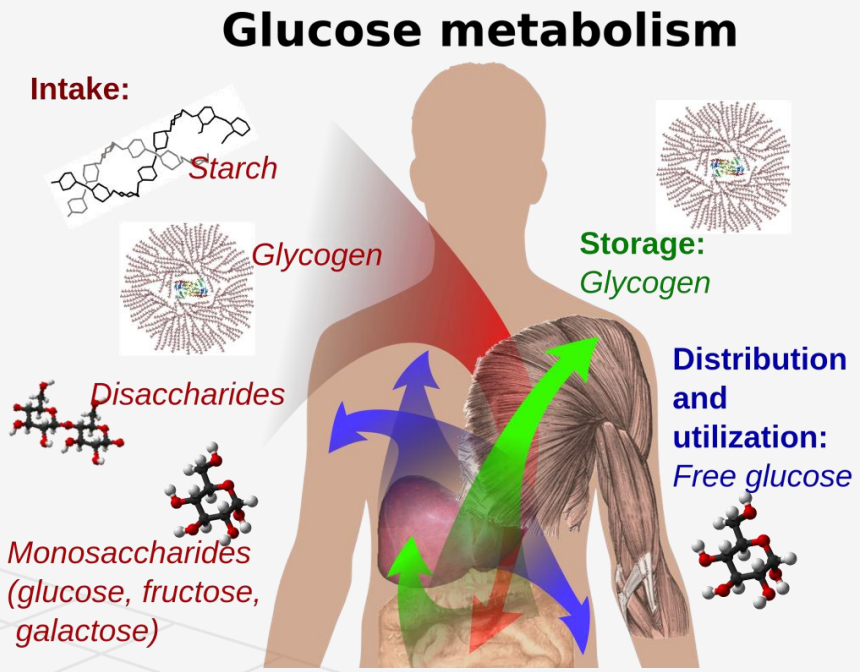
Maltose —*maltase*→ Glucose + Glucose

D. Sucrase : PH ranges 5.0 to 7.0. It hydrolyzes sucrose molecule to form glucose and fructose.

Sucrose —*Sucrase*→ Glucose + fructose

Absorption of Carbohydrates

- Products of digestion of dietary carbohydrates are practically completely absorbed almost entirely from the small intestine.
- Absorption from proximal jejunum is three times grater than that of distal ileum. It is also proved that some disaccharides, which escape digestion, may enter the cells of the intestinal lumen by “pinocytosis” and are hydrolyzed within these cells.
- No carbohydrates higher than the monosaccharide can be absorbed directly in to the blood stream.



Mechanism of Absorption:

Two mechanisms are involved;

1. Simple Diffusion

This is dependent on sugar concentration gradients between the intestinal lumen. Mucosal cells and blood plasma. All the monosaccharides are probably absorbed to some extent by simple 'passive' diffusion.

2. "Active "Transport Mechanisms

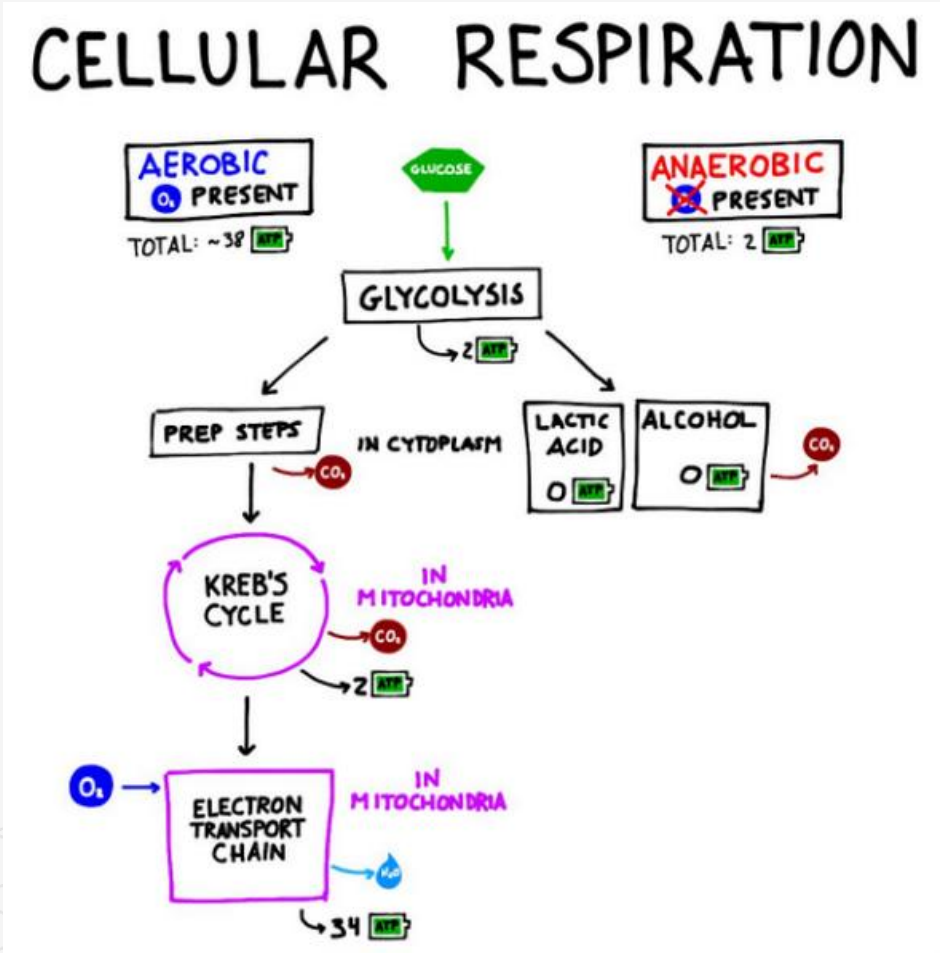
- Glucose and galactose are absorbed very rapidly and hence it has been suggested that they are absorbed actively and it requires energy.

Fructose absorption is also rapid but not so much as compared to glucose and galactose but it is definitely faster than pentoses. Hence fructose is not absorbed by simple diffusion alone and it is suggested that some mechanism facilitates its transport, called as" ***facilitated transport***"

Glycolysis

Oxidation of glucose or glycogen to pyruvate and lactate is called glycolysis.

It occurs virtually in all tissues. Erythrocytes and nervous tissues derive its energy mainly form glycolysis. This pathway is unique in the sense that it can utilize O2 if available ('aerobic') and it can function in absence of O2 also ('anaerobic')



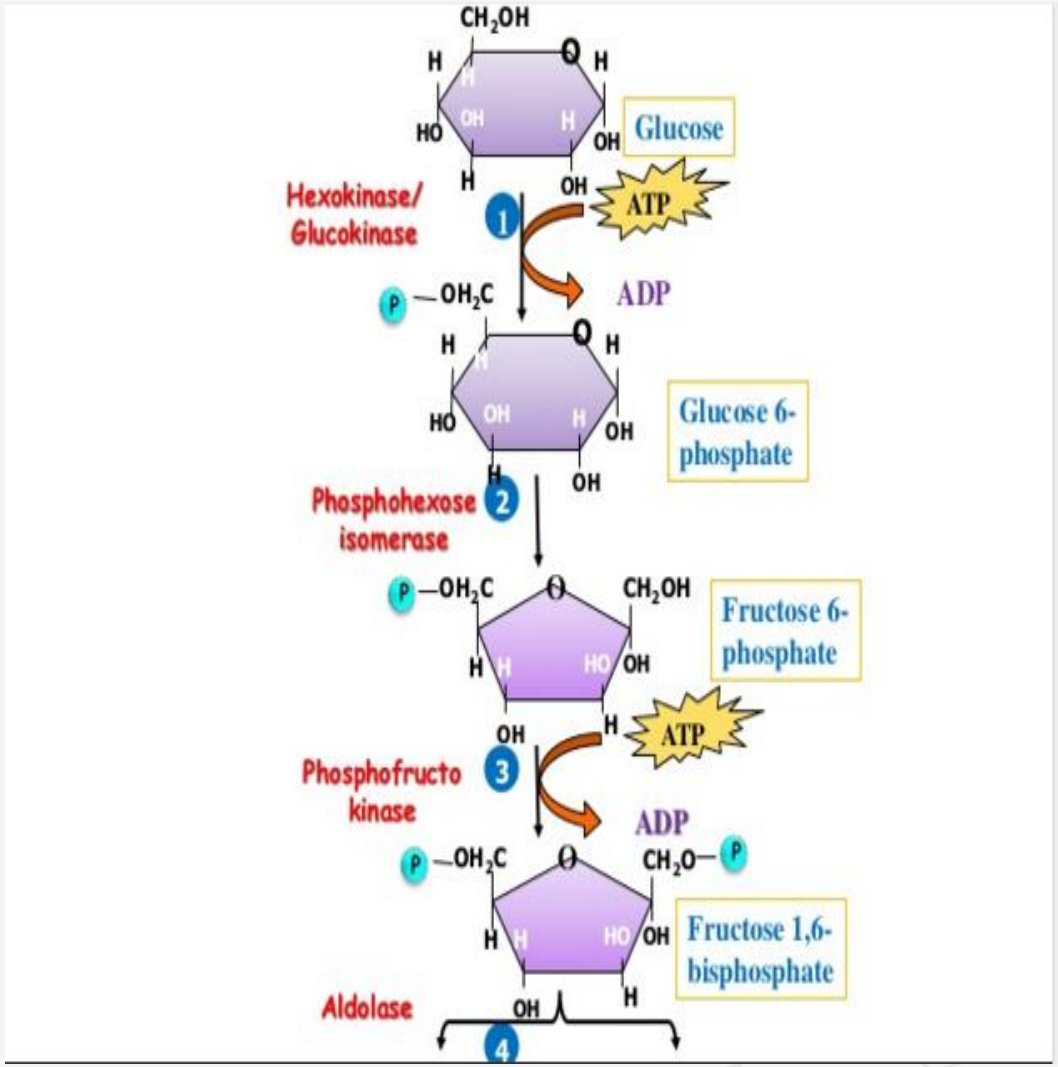
1 Aerobic Phase

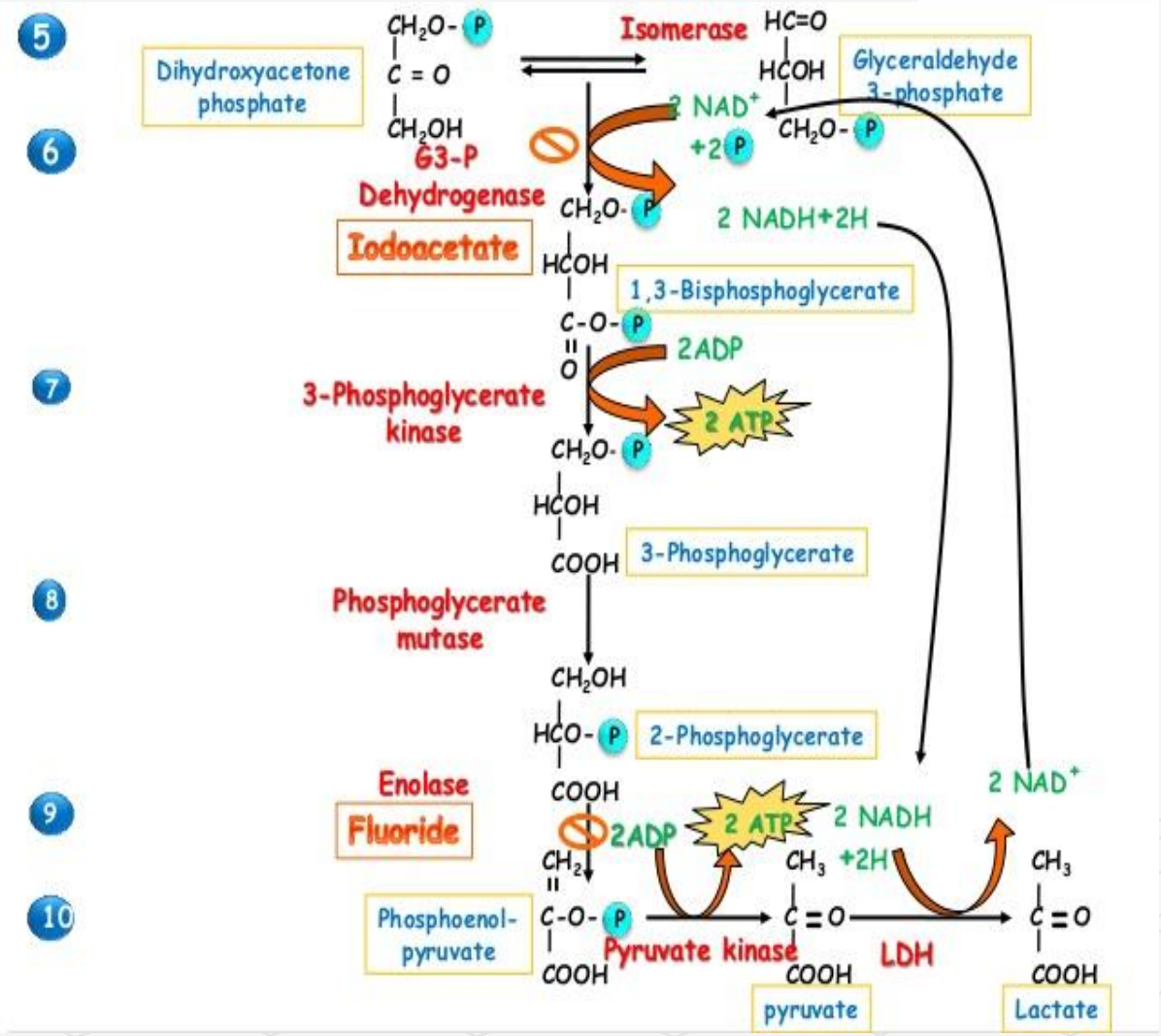
Aerobic phase includes the conversion of glucose to pyruvate. Oxidation is carried out by dehydrogenation and reducing equivalent is transferred to NAD. NADH + H+ in presence of O2 is oxidized in electron- transport chain producing ATP.

2 Anaerobic Phase

This phase includes the conversion of Glucose to lactate. NADH cannot be oxidized, so no ATP is produced in electron transport chain. But the NADH is oxidized to NAD+ by conversion of pyruvate to Lactate, without producing ATP.

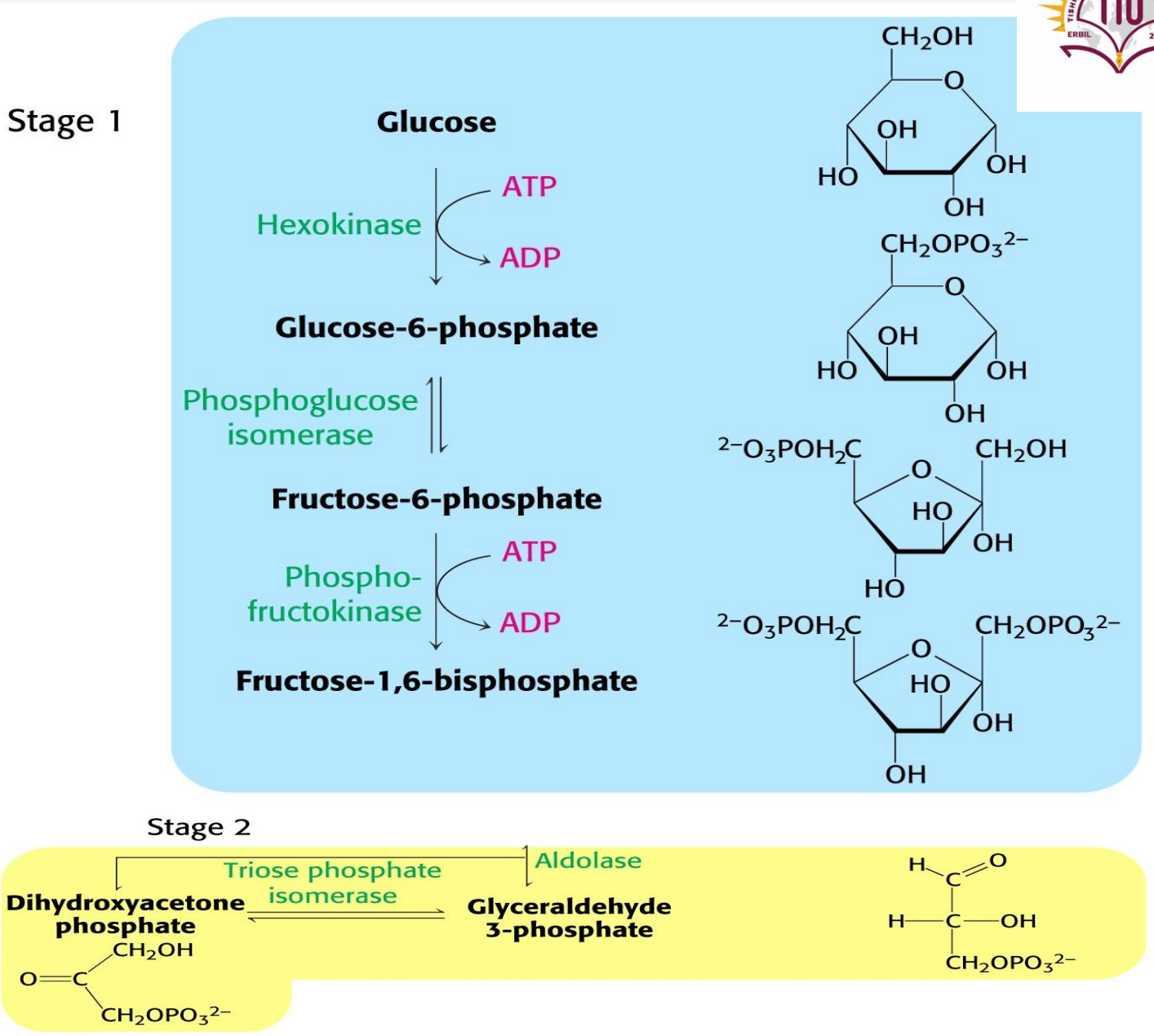
Glycolysis reactions





Stages of Glycolysis

- Investment of 2 ATP
- Production of 2 Glyceraldehyde-3-P (GAP)
- The two highly regulated steps are hexokinase and phosphofructokinase 1 (both respond directly or indirectly to energy charge).



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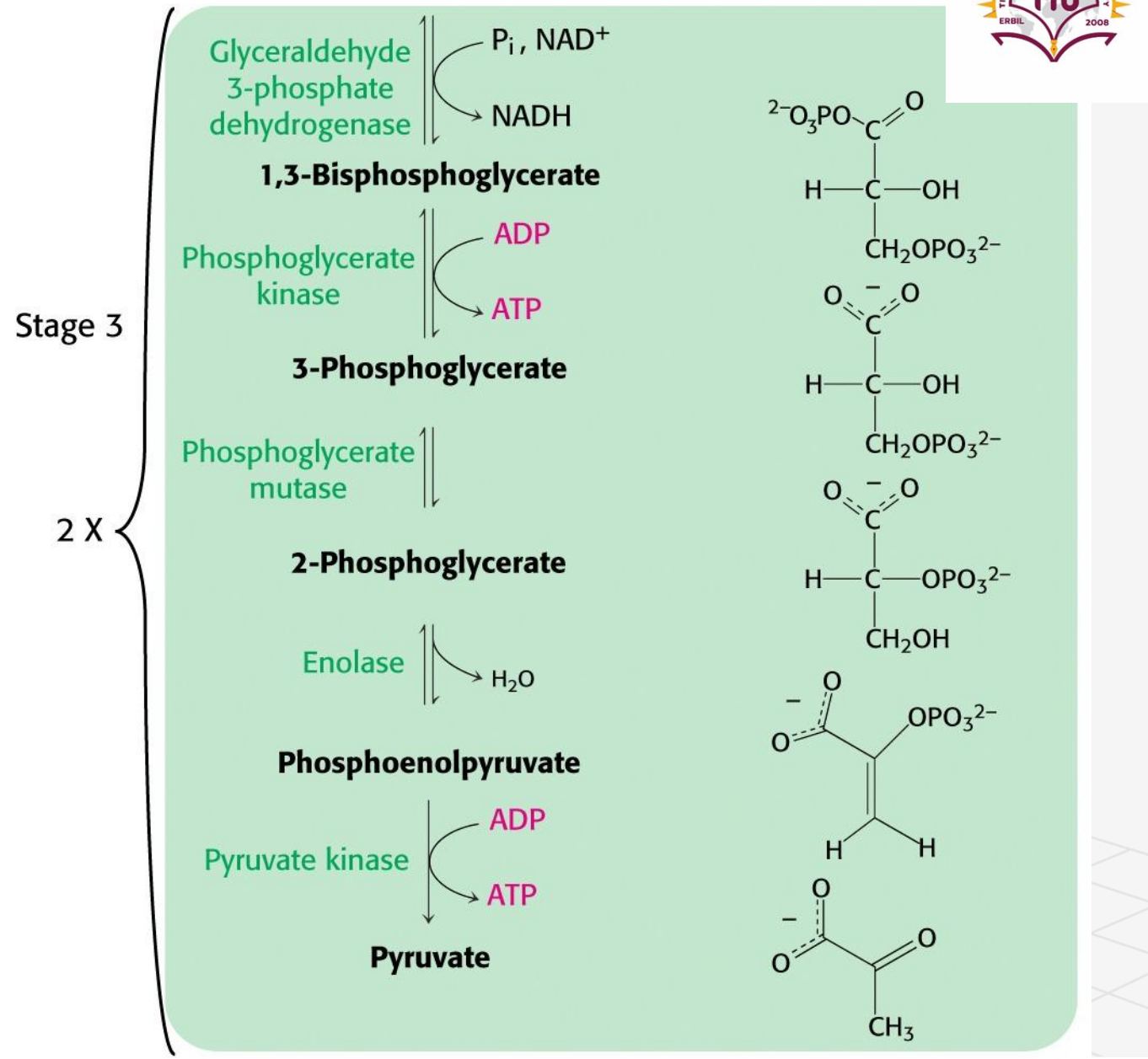
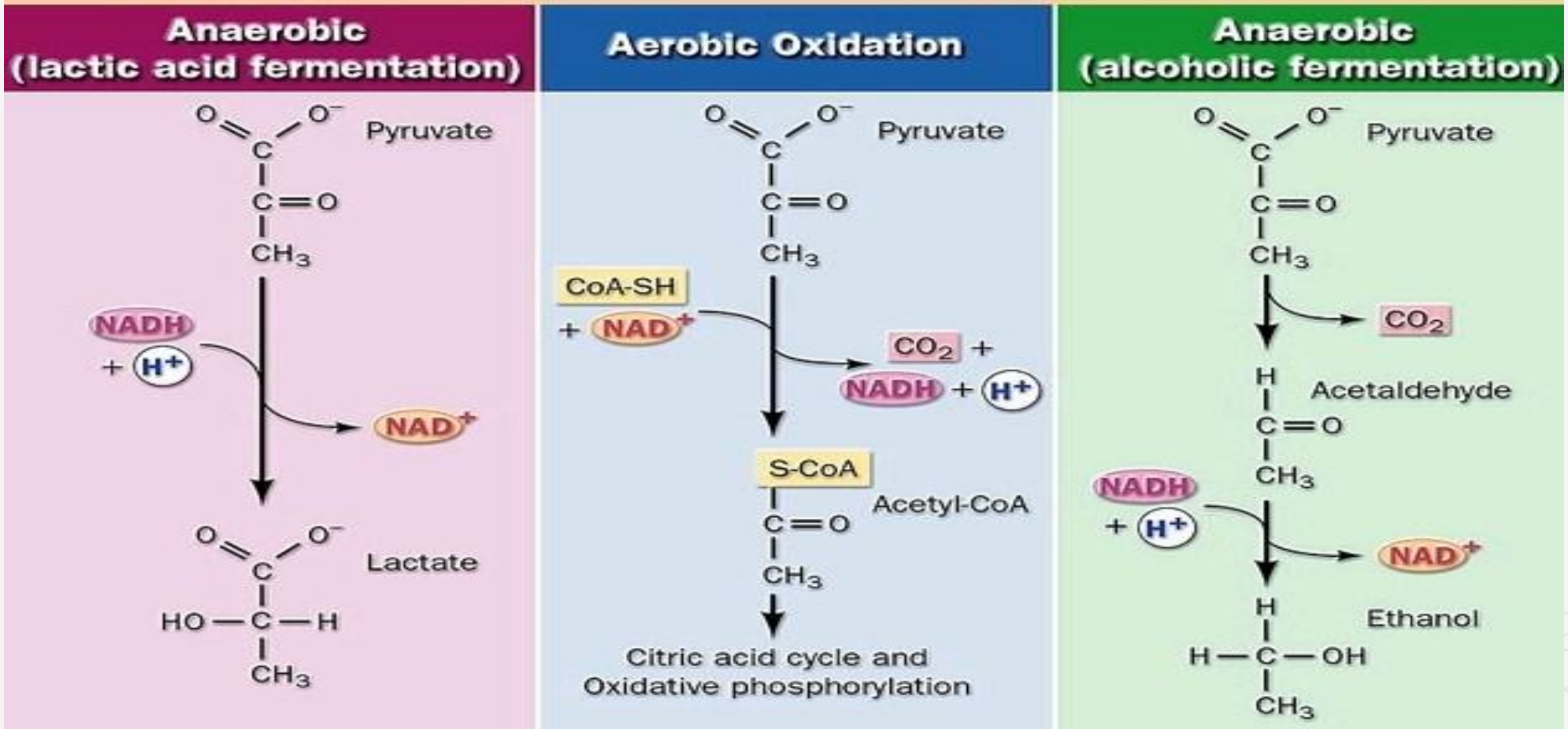
- Reducing power is captured in the form of NADH; this is a critical step.
- Phosphoglycerate kinase and pyruvate kinase catalyze a substrate level phosphorylation reaction yielding 4 ATP (2 net ATP).
- The two pyruvate molecules are further metabolized.

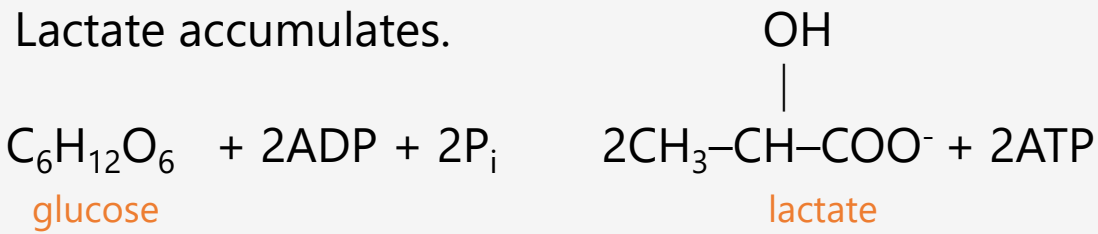


Three fates of pyruvate produced by glycolysis



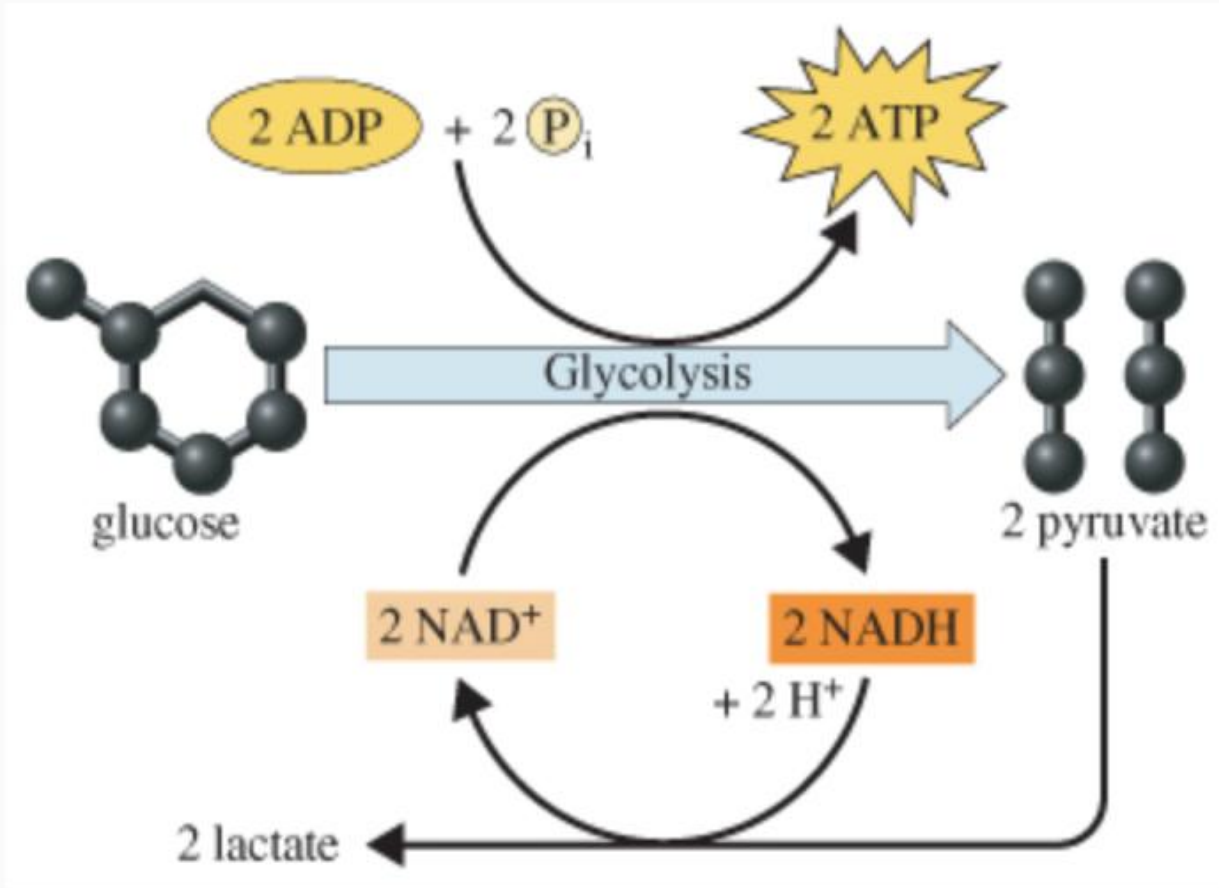
During strenuous exercise,

- Oxygen in the muscles is depleted.
- Anaerobic conditions are produced.
- Lactate accumulates.



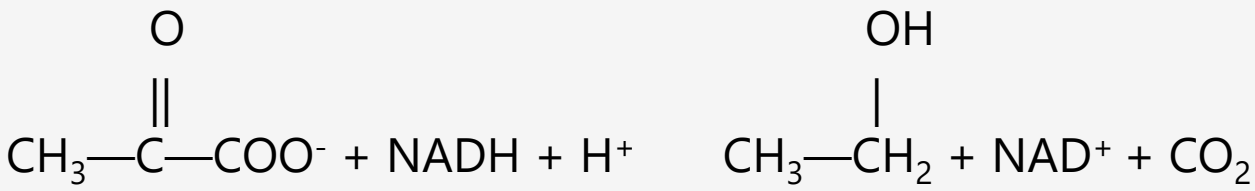
- Muscles tire and become painful.
- After exercise, a person breathes heavily to repay the oxygen debt and reform pyruvate in the liver.

Under anaerobic conditions (a lack of oxygen), glycolysis continues in most cells despite the fact that oxidative phosphorylation stops, and its production of NAD^+ (which is needed as an input to glycolysis) also stops. The diagram illustrates the process of fermentation, which is used by many cells in the absence of oxygen. In fermentation, the NADH produced by glycolysis is used to reduce the pyruvate produced by glycolysis to either lactate or ethanol. Fermentation results in a net production of 2 ATP per glucose molecule.



Fermentation

- Occurs in anaerobic microorganisms such as yeast.
- De-carboxylates pyruvate to acetaldehyde, which is reduced to ethanol.
- Regenerates NAD^+ to continue glycolysis.



pyruvate

ethanol

Disorders of Glycolysis

1) Pyruvate Kinase Deficiency

- Genetic deficiency of **PK** in RBCs leads to hemolytic anemia.

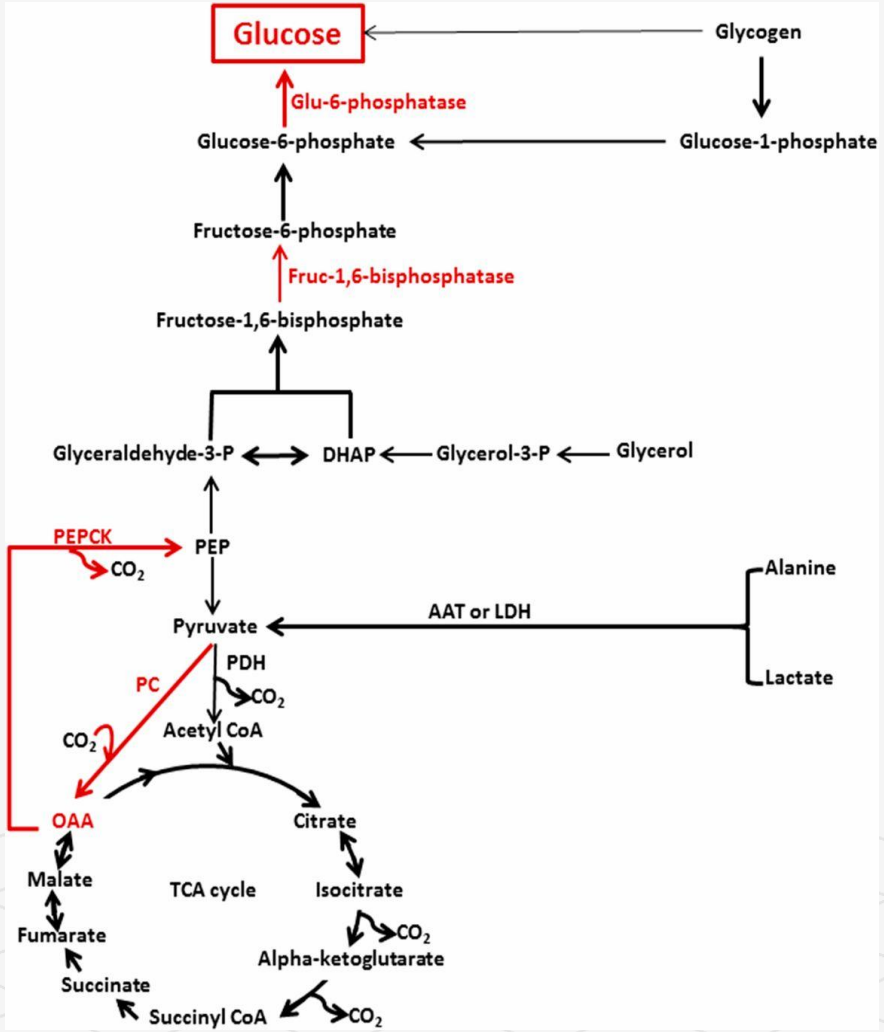
2) Hexokinase Deficiency

3) Lactic Acidosis

- It's the accumulation of lactic acid in the blood.

Gluconeogenesis

- Net synthesis or formation of glucose from non-carbohydrate substrates is termed gluconeogenesis.
- Various amino acids, lactate, pyruvate, propionate and glycerol are sources of carbon for the pathway.
- Gluconeogenesis meets the needs of the body for glucose when sufficient carbohydrate is not available from the diet or glycogen reserves.
- A supply of glucose is necessary especially for the nervous system and erythrocytes.
- Failure of gluconeogenesis is usually fatal.



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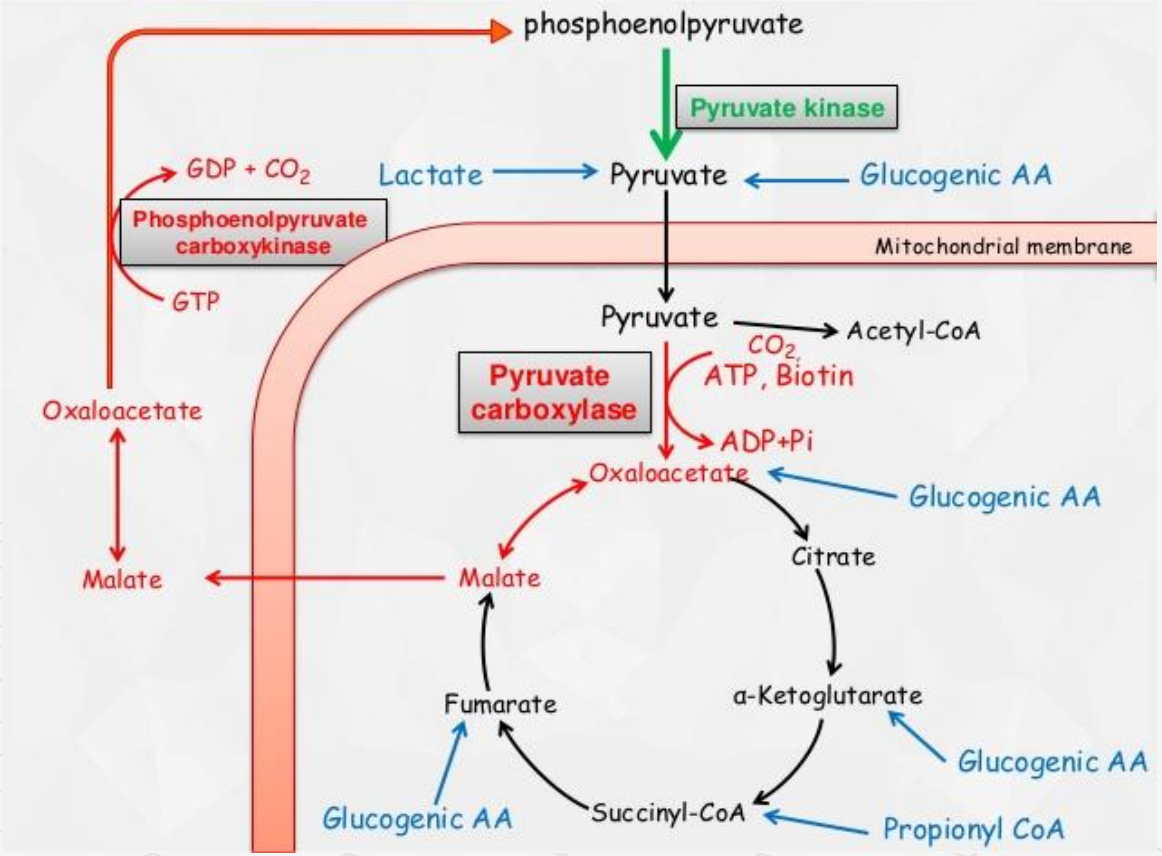
- Gluconeogenesis occurs mainly in liver.
- GNG occurs to a more limited extent in kidney & small intestine under some conditions.

General Features:

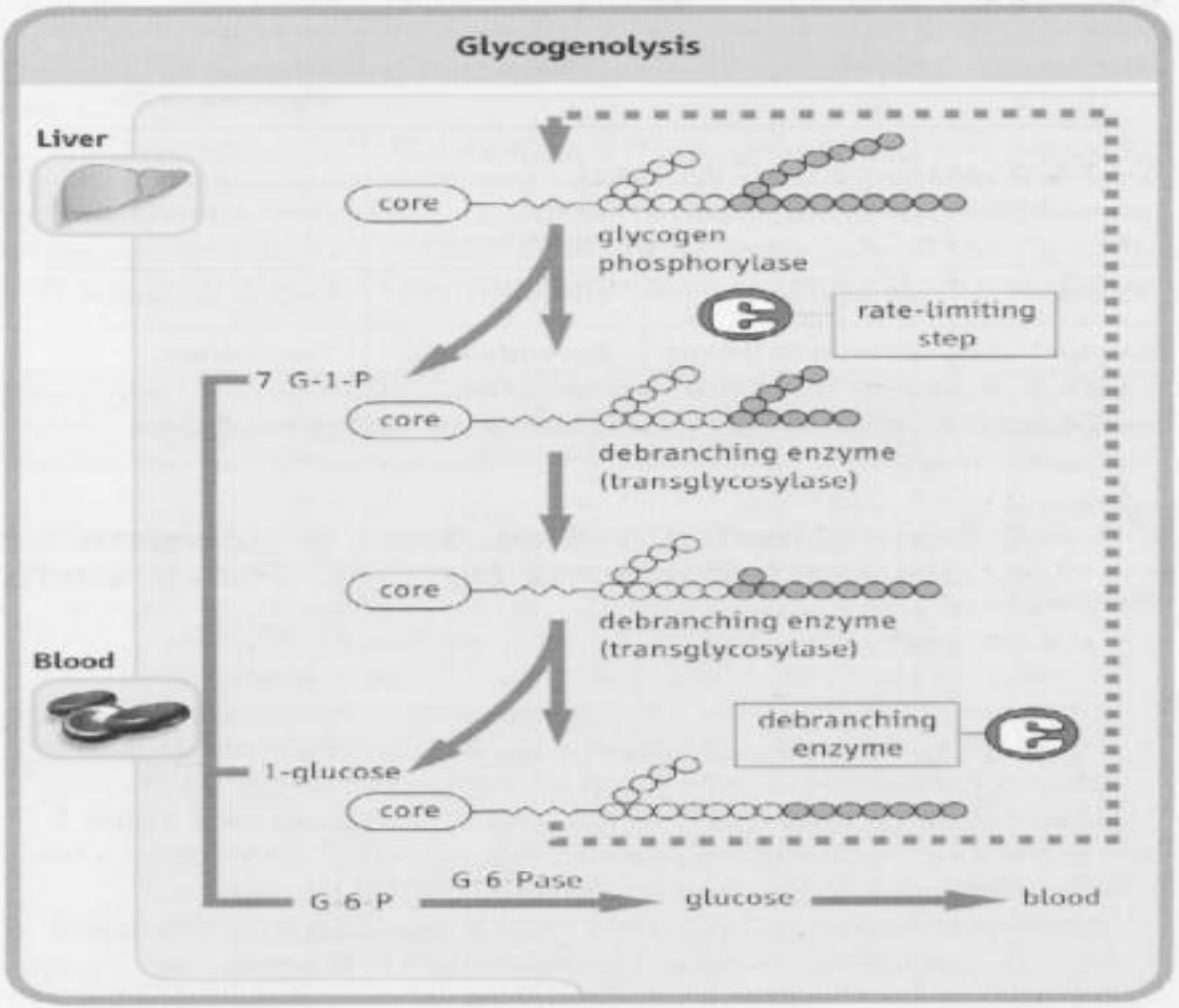
- Tissues:
  - ✓ Liver (80%)
  - ✓ Kidneys (20 %)
- Subcellular location of enzymes:
  - ✓ Pyruvate carboxylase: mitochondrial
  - ✓ Glucoe – 6- phosphatase : ER
  - ✓ All other enzymes : Cytoplasmic



Glycogen Metabolism: **Glycogen is the major storage form of carbohydrate in animals .It is mainly stored in liver and muscles and is mobilized as glucose whenever body tissues require.**

Degradation of Glycogen (glycogenolysis)

1. *Shortening of chains*
2. *Removal of Branches*
3. *Lysosomal Degradation of Glycogen*



Step 1: Action of Glycogen Phosphorylase:

Step 2: Action of Debranching Enzyme:

Step 3: Formation of Glucose-6-Phosphate and Glucose:

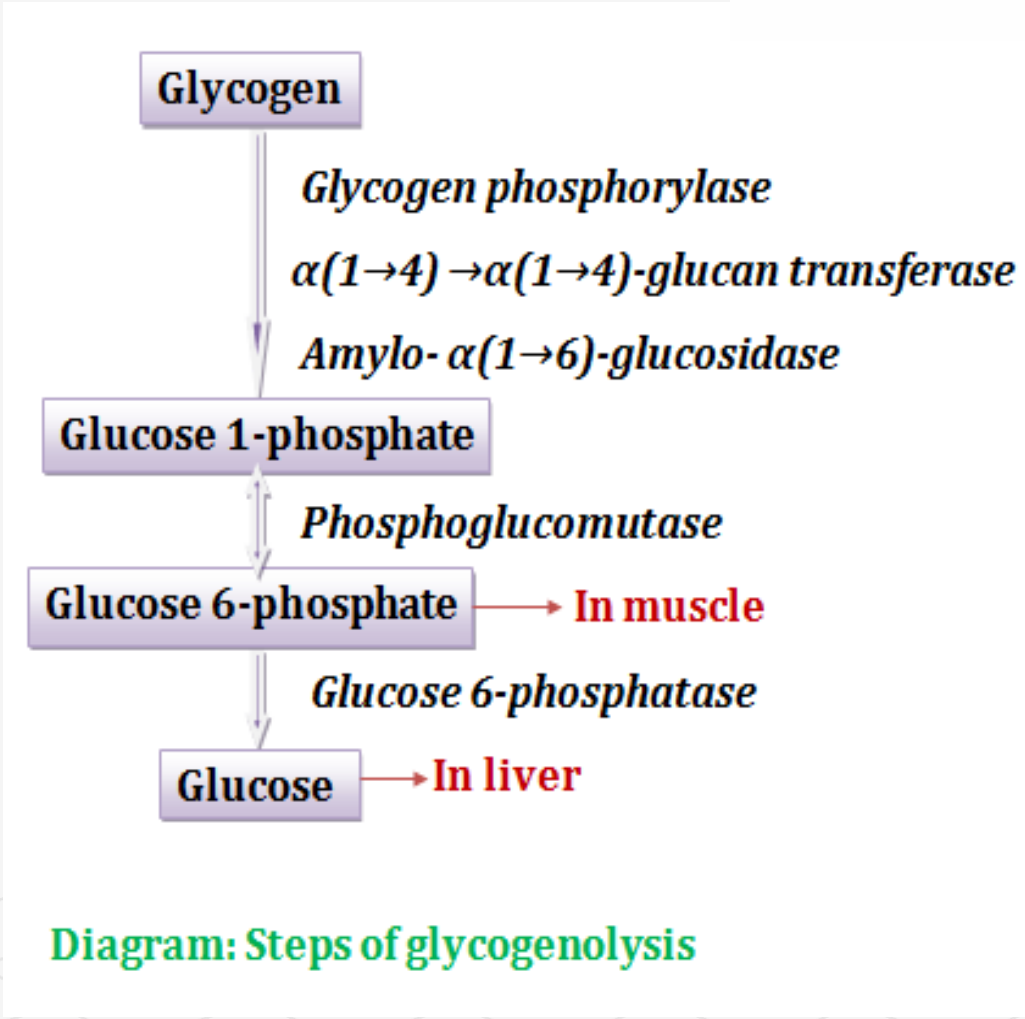


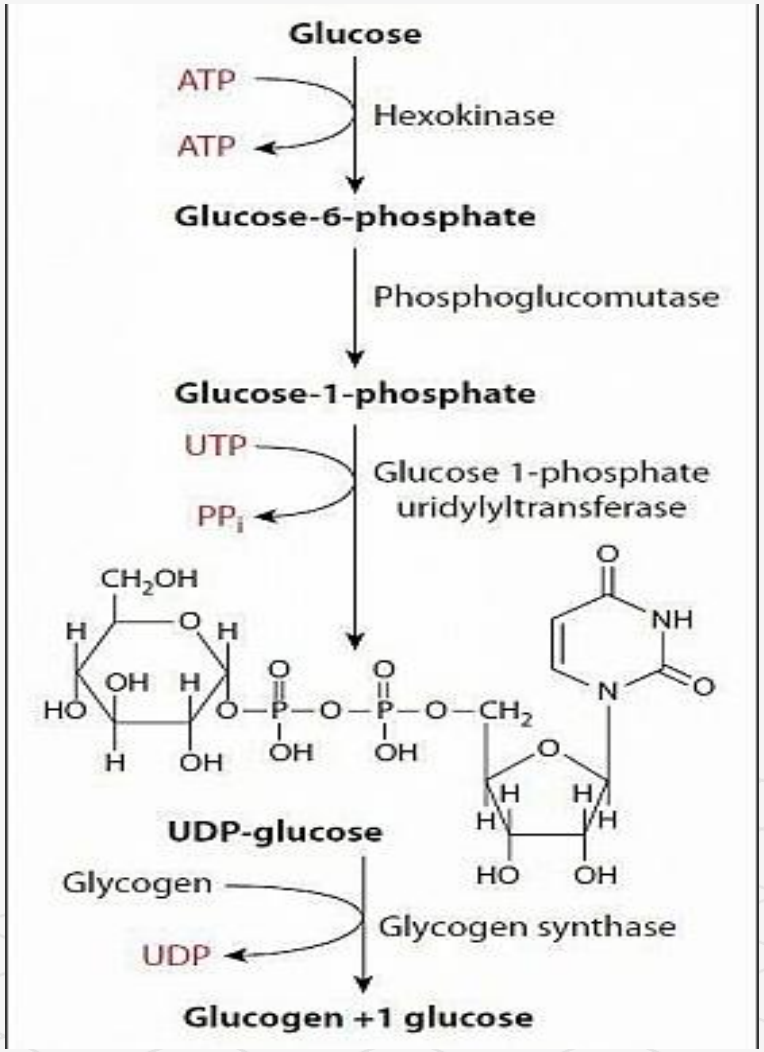
Diagram: Steps of glycogenolysis

Synthesis of Glycogen (Glycogenesis)

- ✓ The storage form of glucose, occurs after a meal.
- ✓ Requires a set of three reactions (1st and 2nd are preparatory and in 3rd there is chain elongation):

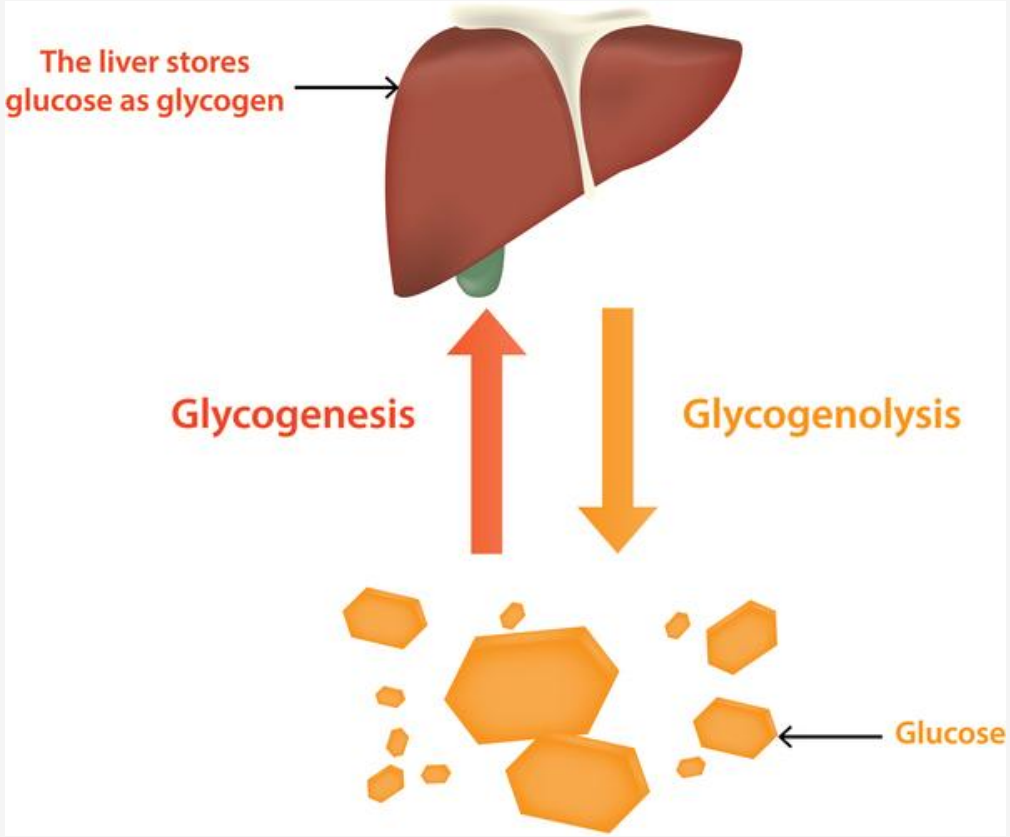
1. Synthesis of glucose-1-phosphate (G1P) from glucose-6-phosphate by *phosphoglucomutase.*
2. Synthesis of UDP-glucose from G1P by UDP-glucose *phosphorylase.*

2. Synthesis of Glycogen from UDP-glucose. Requires *Glycogen synthase* to grow the chain



Glycogen storage diseases

- These are a group of genetic diseases that result from a defect in an enzyme required for either glycogen synthesis or degradation.
- They result in either formation of glycogen that has an abnormal structure or the accumulation of excessive amounts of normal glycogen in specific tissues,
- A particular enzyme may be defective in a single tissue such as the liver or the defect may be more generalized, affecting muscle, kidney, intestine and myocardium.



- The severity of the diseases may range from fatal in infancy to mild disorders that are not life threatening some of the more prevalent glycogen storage diseases are the following.

Table of Glycogen Storage Diseases

	Type: Name	Enzyme affected	Primary organ	Manifestations
1	Type 0	glycogen synthase	Liver	Hypoglycemia and early death
2	Type Ia: von Gierke's	Glucose-6-phosphatase	Liver	hepatomegaly, kidney failure,fatty liver, hyperlacticacidimia and severe hypoglycemia
3	Type II: Pompe's	Lysosomal a-1,4-glucosidase, lysosomal acid a-glucosidase acid maltase	Skeletal and cardiac muscle	Muscular dystrophy, severe cardiomegaly, early death.
4	Type V: McArdle's	Muscle phosphorylase	Skeletal muscle	Muscle excersize-induced cramps and pain, myoglobinuria

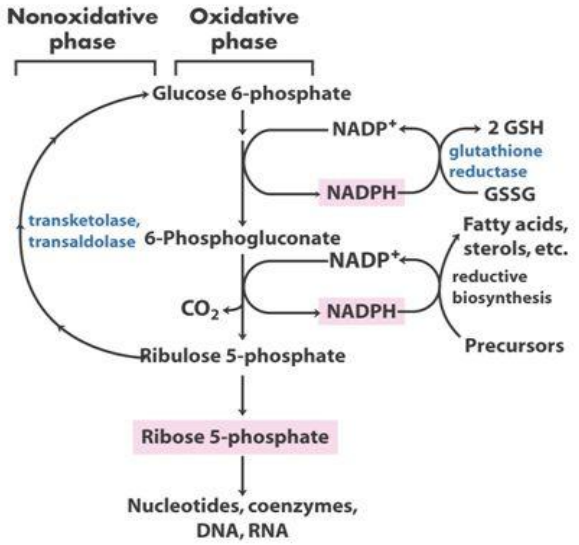
Pentose phosphate pathway

Is primarily an anabolic pathway that utilizes the 6 carbons of glucose to generate 5 carbon sugars and reducing equivalents.

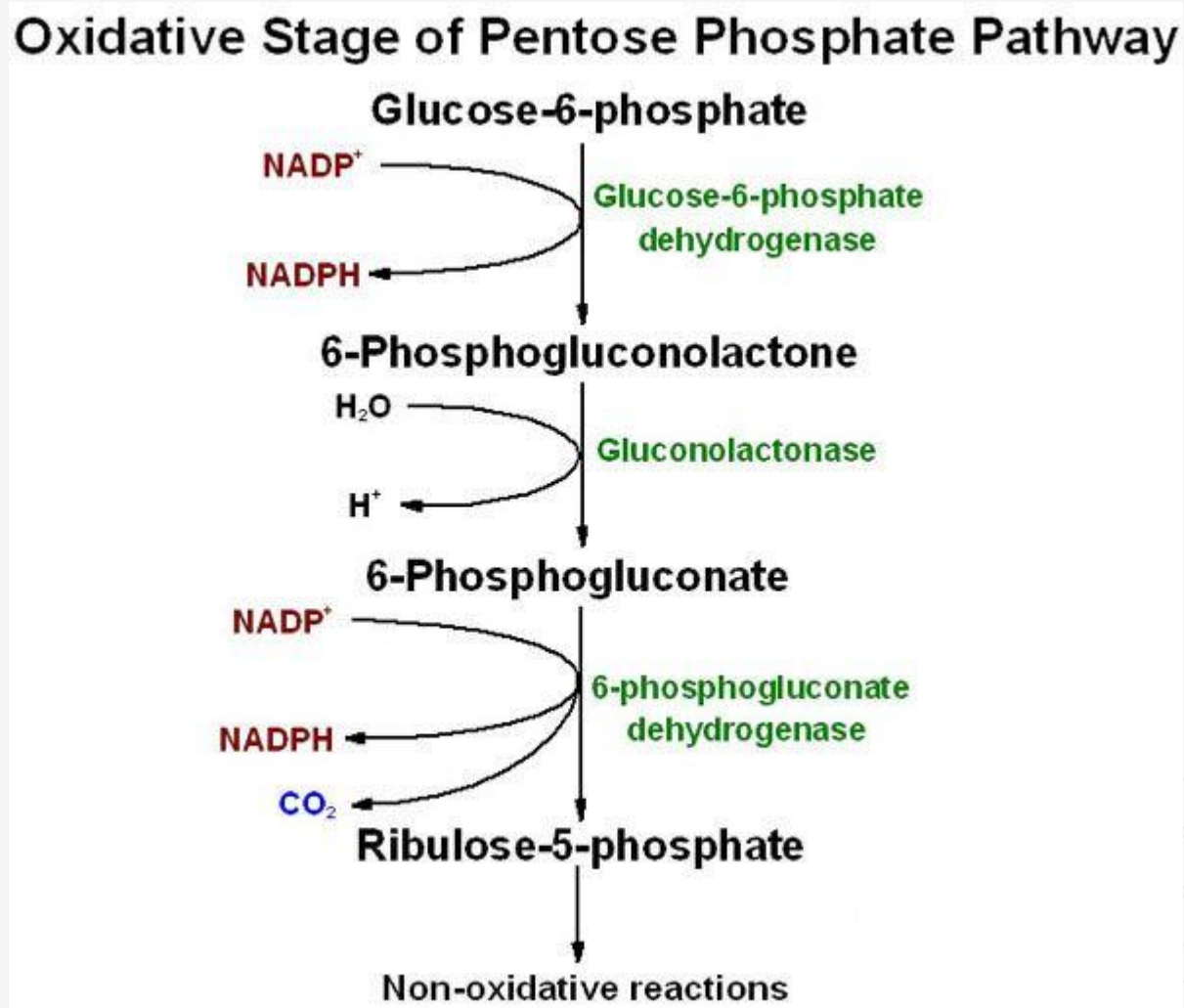
The primary functions of this pathway are:

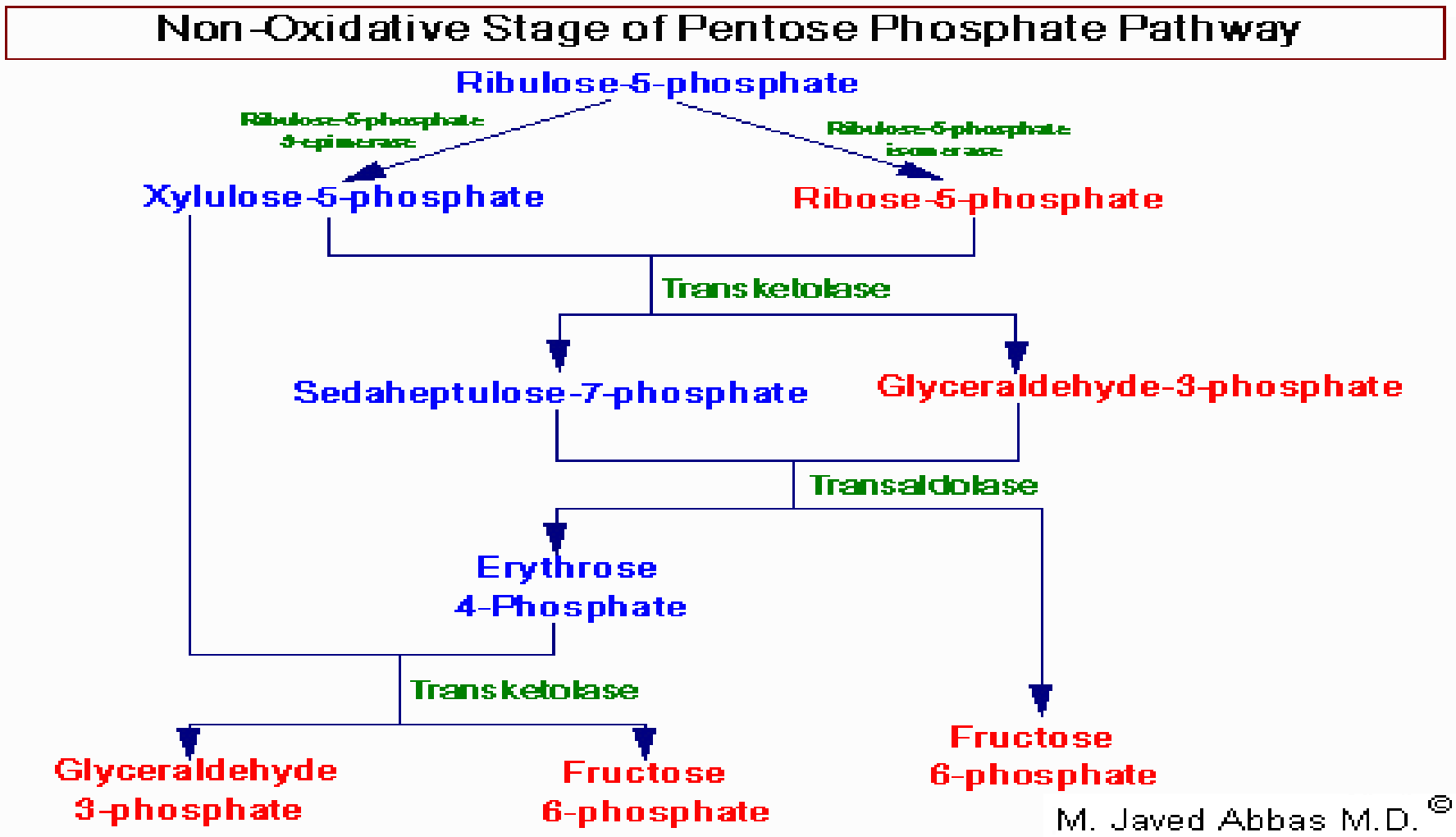
1. To generate reducing equivalents, in the form of NADPH, for reductive biosynthesis reactions within cells.
2. To provide the cell with ribose-5-phosphate(R5P) for the synthesis of the nucleotides and nucleic acids.
3. It can also operate to metabolize dietary pentose sugars derived from the digestion of nucleic acids as well as to rearrange the carbon skeletons of dietary carbohydrates into glycolytic/gluconeogenic intermediates.

The main product of PPP is ribose 5-phosphate and NADPH



- **PPP oxidizes glucose 6-phosphate, producing ribose 5-phosphate (precursor for nucleotides) and NADPH (reducing agent for lipid biosynthesis).**

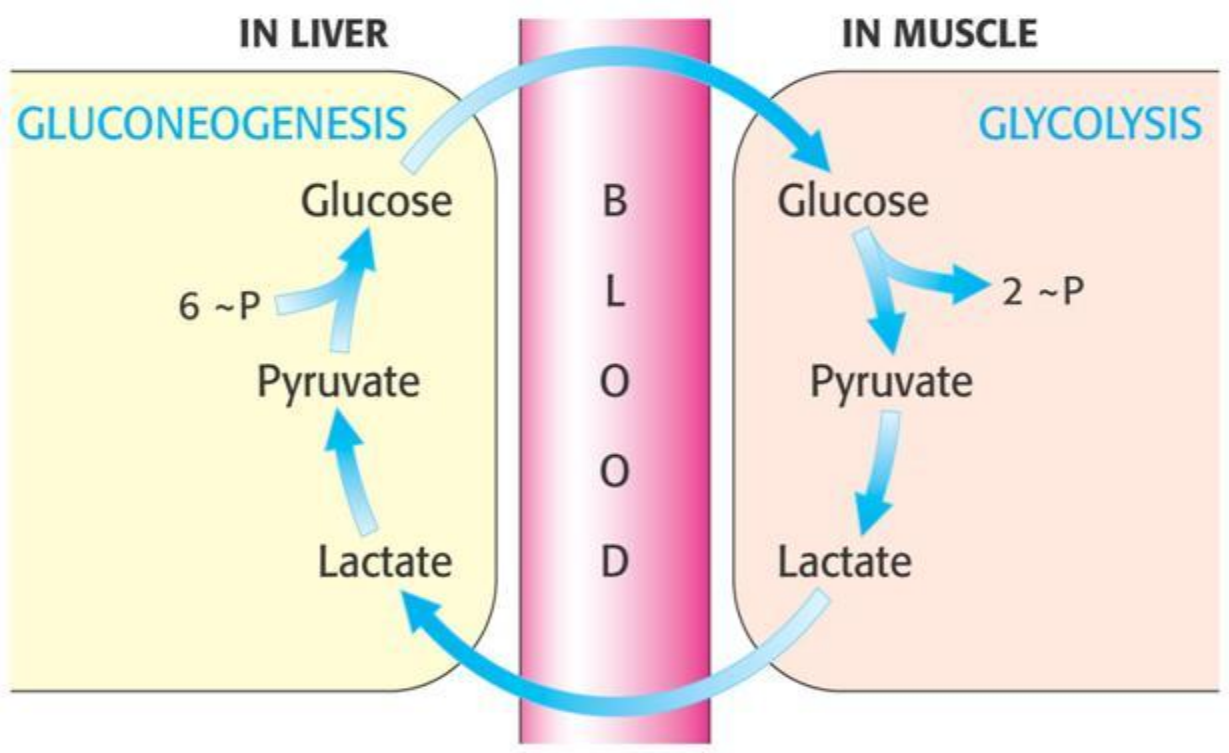

Oxidative Stage of Pentose Phosphate Pathway
Glucose-6-phosphate
NADP+
NADPH
Glucose-6-phosphate dehydrogenase
6-Phosphogluconolactone
H2O
H+
Gluconolactonase
6-Phosphogluconate
NADP+
NADPH
CO2
6-phosphogluconate dehydrogenase
Ribulose-5-phosphate
Non-oxidative reactions


Non-Oxidative Stage of Pentose Phosphate Pathway
Ribulose-5-phosphate
Ribulose-5-phosphate 3-epimerase
Ribulose-5-phosphate isomerase
Xylulose-5-phosphate
Ribose-5-phosphate
Transketolase
Sedaheptulose-7-phosphate
Glyceraldehyde-3-phosphate
Transaldolase
Erythrose 4-Phosphate
Transketolase
Glyceraldehyde 3-phosphate
Fructose 6-phosphate
Fructose 6-phosphate
M. Javed Abbas M.D. ©

The Cori - cycle

The cori cycle refers to the metabolic pathway in which lactate produced by anaerobic glycolysis in the muscles move via the blood stream to the liver where it is converted into blood glucose and glycogen.

1. It is a cycle in which … glycogen in the muscle is degraded to produce lactic acid → blood→ liver → where it is changed back into glycogen.
2. When needed the glycogen is broken down into glucose and the blood carries the glucose to the muscle.
3. During the muscle activity require moderate amount of glucose, which can be supplied by the blood glucose or breakdown of glycogen reservoir present in the muscle tissue.



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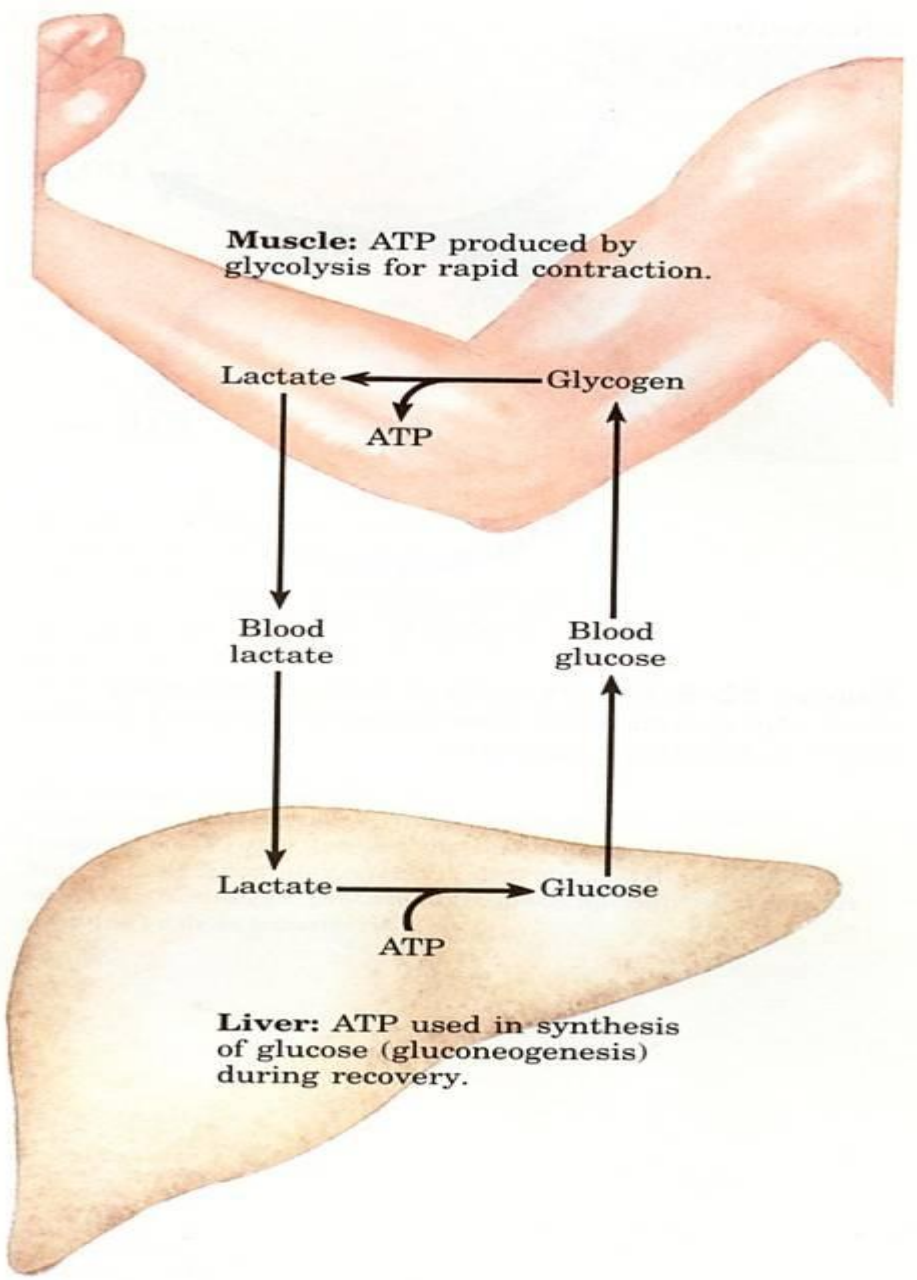
In an actively contracting muscle, only about 8% of the pyruvate is utilized by the citric acid cycle and the remaining is, therefore, reduced to lactate. The lactic acid thus generated should not be allowed to accumulate in the muscle tissues. The muscle cramps, often associated with strenuous muscular exercise are thought to be due to lactate accumulation. This lactate diffuses into the blood. During exercise, blood lactate level increases considerably. Lactate then reaches liver where it is oxidized to pyruvate. It is then taken up through gluconeogenesis pathway and becomes glucose, which can enter into blood and then taken to muscle. This cycle is called cori's cycle, by which the lactate is efficiently reutilized by the body.



Next Lecture

Quiz

Metabolic Pathways

and

Biological Oxidation