SHREE H. N. SHUKLA INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH

B.PHRAM

(SEMESTER –III)

SUBJECT NAME: BIOCHEMISTRY

CHAPTER 2: METABOLISM OF CARBOHYSRATES

SUBJECT CODE: BP303TP

Carbohydrate Metabolism

- **Carbohydrate metabolism** denotes the various biochemical processes responsible for the formation, breakdown and interconversion of carbohydrates in living organisms.
- The most important carbohydrate is glucose, a simple sugar (monosaccharide) that is metabolized by nearly all known organisms.
- Glucose and other carbohydrates are part of a wide variety of metabolic pathways across species: plants synthesize carbohydrates from carbon dioxide and water by photosynthesis, storing the absorbed energy internally, often in the form of starch or lipids.
- Plant components are consumed by animals and fungi, and used as fuel for cellular respiration. Oxidation of one gram of carbohydrate yields approximately 4 kcal of energy, while the oxidation of one gram of lipids yields about 9 kcal. Energy obtained from metabolism (e.g., oxidation of glucose) is usually stored temporarily within cells in the form of ATP. Organisms capable of aerobic respiration metabolize glucose and oxygen to release energy with carbon dioxide and water as byproducts.

Metabolic pathways

- Carbon fixation, or photosynthesis, in which CO_2 is reduced to carbohydrate.
- Glycolysis - the oxidation metabolism of glucose molecules to obtain ATP and pyruvate
- Pyruvate from glycolysis enters the Krebs cycle, also known as the citric acid cycle, in aerobic organisms after moving through pyruvate dehydrogenase complex.

- The pentose phosphate pathway, which acts in the conversion of hexoses into pentoses and in NADPH regeneration.
- NADPH is an essential antioxidant in cells which prevents oxidative damage and acts as precursor for production of many biomolecules.
- Glycogenesis - the conversion of excess glucose into glycogen as a cellular storage mechanism; this prevents excessive osmotic pressure buildup inside the cell
- Glycogenolysis - the breakdown of glycogen into glucose, which provides glucose supply for glucose-dependent tissues.
- Gluconeogenesis - *de novo* synthesis of glucose molecules from simple organic compounds. An example in humans is the conversion of a few amino acids in cellular protein to glucose.

Glycolysis

Glycolysis (from *glycose*, an older term[1] for glucose + *-lysis* degradation) is the metabolic pathway that converts glucose $C_6H_{12}O_6$, into pyruvate, $CH_3COCOO^- + H^+$. The free energy released in this process is used to form the high-energy molecules ATP (adenosine triphosphate) and NADH (reduced nicotinamide adenine dinucleotide).

Glycolysis is a determined sequence of ten enzyme-catalyzed reactions. The intermediates provide entry points to glycolysis converted to one of these intermediates. The intermediates may also be directly useful. For example, the intermediate dihydroxyacetone phosphate (DHAP) is a source of the glycerol that combines with fatty acids to form fat.

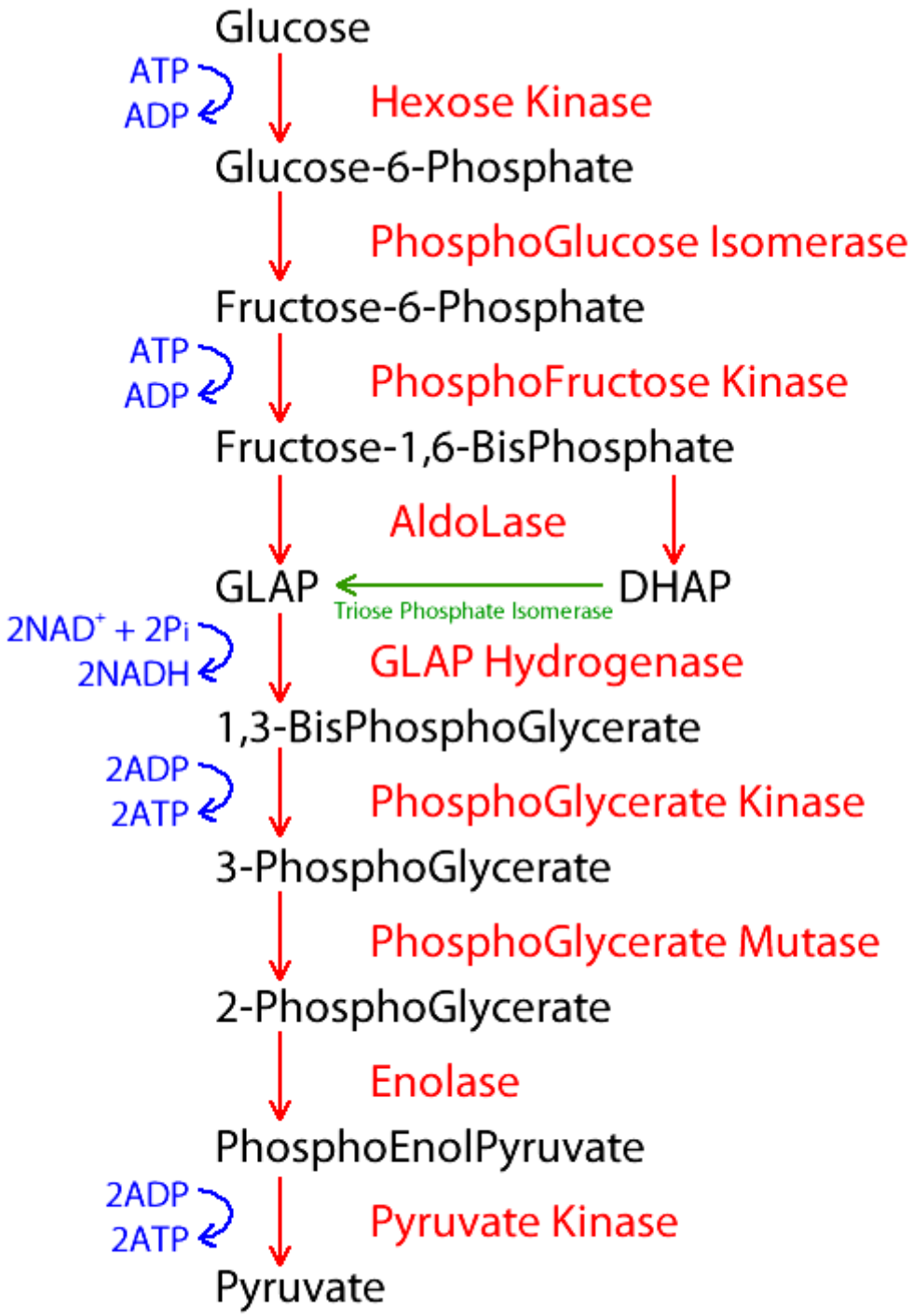
For example, most monosaccharides, such as fructose and galactose, can be Glycolysis is an oxygen independent metabolic pathway, meaning that it does not use molecular oxygen (i.e. atmospheric oxygen) for any of its reactions.

However the products of glycolysis (pyruvate and NADH + H^+) are sometimes metabolized using atmospheric oxygen.

When molecular oxygen is used for the metabolism of the products of glycolysis the process is usually referred to as aerobic, whereas if no oxygen is used the process is said to be anaerobic.

One word questions answers

Sr. No.	Question	Answer
1.	Various biochemical processes responsible for the formation, breakdown and interconversion of carbohydrates in living organisms.	Carbohydrate metabolism
2.	The most important carbohydrate is…	Glucose
3.	The pentose phosphate pathway, which acts in the conversion of hexoses into…	Pentoses and in NADPH regeneration.
4.	No oxygen is used the process is …	anaerobic
5.	Molecular oxygen is used for the metabolism of the products of glycolysis the process is	aerobic
6.	Plants synthesize carbohydrates	carbon dioxide
7.	*De novo* synthesis of glucose molecules from simple organic compounds.	Gluconeogenesis
8.	The products of glycolysis	Pyruvate and NADH + H^+



Simplified Glycolysis diagram. Molecule names contain extra capitals to illustrate components. 21/02/2010 followchemistry.wordpress.com

Thus, glycolysis occurs, with variations, in nearly all organisms, both aerobic and anaerobic. The wide occurrence of glycolysis indicates that it is one of the most ancient metabolic pathways.

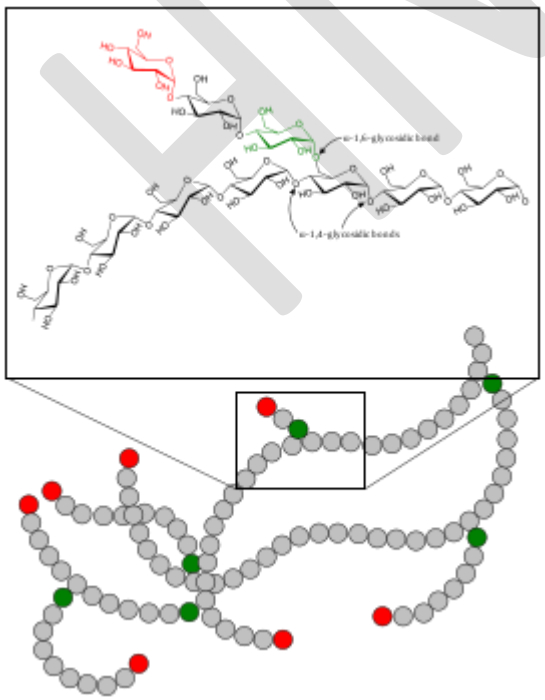
Indeed, the reactions that constitute glycolysis and its parallel pathway, the pentose phosphate pathway, occur metal-catalyzed under the oxygen-free conditions of the Archean oceans, also in the absence of enzymes.[7] Glycolysis could thus have originated from chemical constraints of the prebiotic world.

Glycolysis occurs in most organisms in the cytosol of the cell. The most common type of glycolysis is the *Embden–Meyerhof–Parnas (EMP pathway)*, which was discovered by Gustav Embden, Otto Meyerhof, and Jakub Karol Parnas.

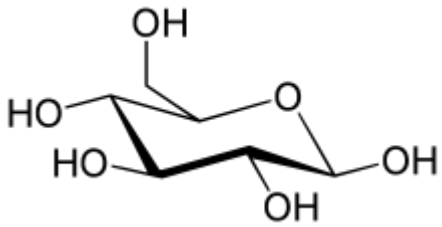
Glycolysis also refers to other pathways, such as the *Entner–Doudoroff pathway* and various heterofermentative and homofermentative pathways. However, the discussion here will be limited to the Embden–Meyerhof–Parnas pathway.

Glycogenolysis

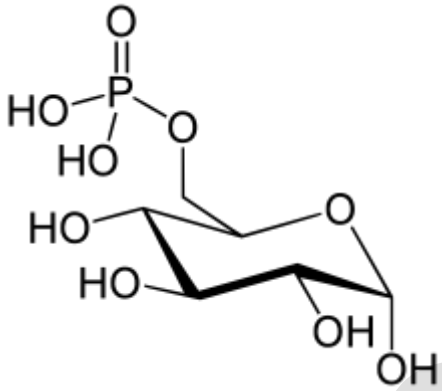
Not to be confused with Glycolysis, Glycogenesis, or Gluconeogenesis.



Glycogen



Glucose



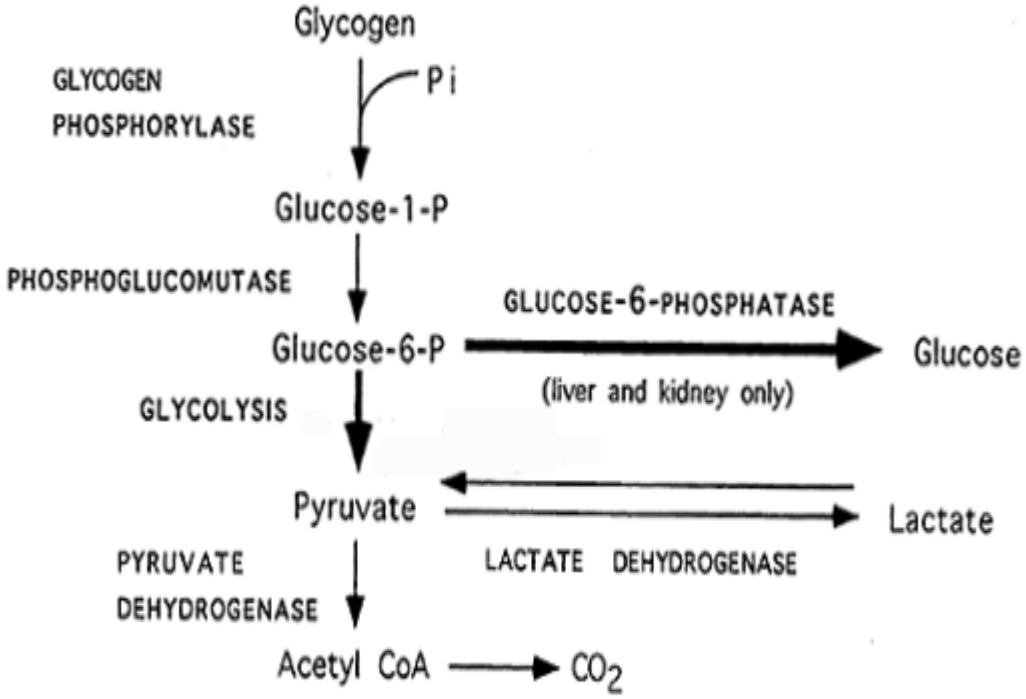
Glucose-6-phosphate

One word questions answers

Sr. No.	Question	Answer
1.	What carbohydrates are reactants in glycolysis?	Glucose
2.	In liver, the accumulation of which of the following metabolite attenuates the inhibitory of ATP on phosphofructokinase	Fructose-1,6-Bisphosphate
3.	Cancer cells have high energy demands for replication and division. Increased flux of glucose into glycolysis replenishes the energy demand. Which of the following enzyme plays an important role in tumor metabolism	Pyruvate Kinase M
4.	Which glucose transporter (GLUT) is important in insulin-dependent glucose uptake	GLUT 2
5.	Which glucose transporter (GLUT) is important in	GLU 5

	fructose transport in the intestine	
6.	Which metabolite negatively regulates pyruvate kinase?	Alanin
7.	During prolong starvation, which of the following hormone is responsible for increasing gluconeogenesis in live	Glucagon
8.	During gluconeogenesis, the three irreversible steps of glycolysis have to be bypassed. The final step is the conversion of glucose-6-P to glucose that is catalyzed by glucose-6-phosphatase. Which of the following statement is true about the reaction step?	Defect in glucose-6-phosphatase leads to abnormal accumulation of glycogen in liver

Glycogenolysis is the breakdown of glycogen (n) to glucose-6-phosphate and glycogen (n-1). Glycogen branches are catabolized by the sequential removal of glucose monomers via phosphorolysis, by the enzyme glycogen phosphorylase.[1]



Mechanism

The overall reaction for the breakdown of glycogen to glucose-1-phosphate is:$glycogen_{(n\ residues)} + P_i \rightleftharpoons glycogen_{(n-1\ residues)}$ + glucose-1-phosphate.

Here, glycogen phosphorylase cleaves the bond linking a terminal glucose residue to a glycogen branch by substitution of a phosphoryl group for the α[1→4] linkage.

Glucose-1-phosphate is converted to glucose-6-phosphate by the enzyme phosphoglucomutase. Glucose residues are phosphorolysed from branches of glycogen until four residues before a glucose that is branched with a α[1→6] linkage. Glycogen debranching enzyme then transfers three of the remaining four glucose units to the end of another glycogen branch. This exposes the α[1→6] branching point, which is

hydrolysed by α[1→6] glucosidase, removing the final glucose residue of the branch as a molecule of glucose and eliminating the branch.

This is the only case in which a glycogen metabolite is not glucose-1-phosphate. The glucose is subsequently phosphorylated to glucose-6-phosphate by hexokinase.

Function

Glycogenolysis takes place in the cells of the muscle and liver tissues in response to hormonal and neural signals. In particular, glycogenolysis plays an important role in the fight-or-flight response and the regulation of glucose levels in the blood.

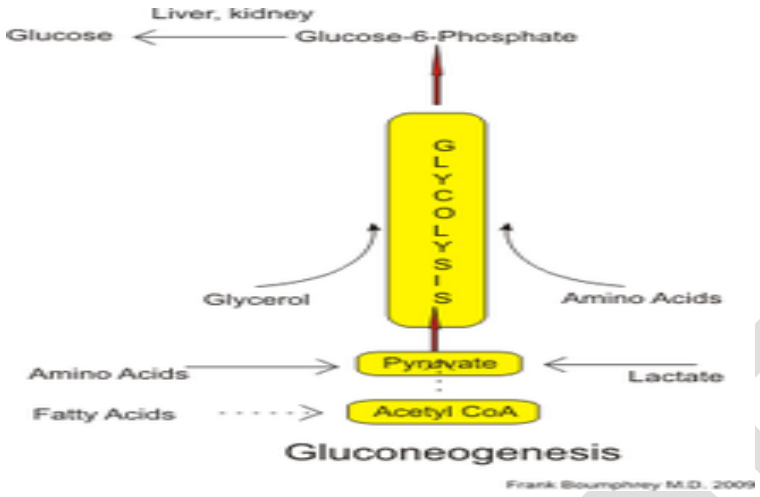
In myocytes (muscle cells), glycogen degradation serves to provide an immediate source of glucose-6-phosphate for glycolysis, to provide energy for muscle contraction.

In hepatocytes (liver cells), the main purpose of the breakdown of glycogen is for the release of glucose into the bloodstream for uptake by other cells.

The phosphate group of glucose-6-phosphate is removed by the enzyme glucose-6-phosphatase, which is not present in myocytes, and the free glucose exits the cell via GLUT2 facilitated diffusion channels in the hepatocyte cell membrane.

Gluconeogenesis

Not to be confused with Glycogenesis or Glyceroneogenesis



Simplified Gluconeogenesis Pathway

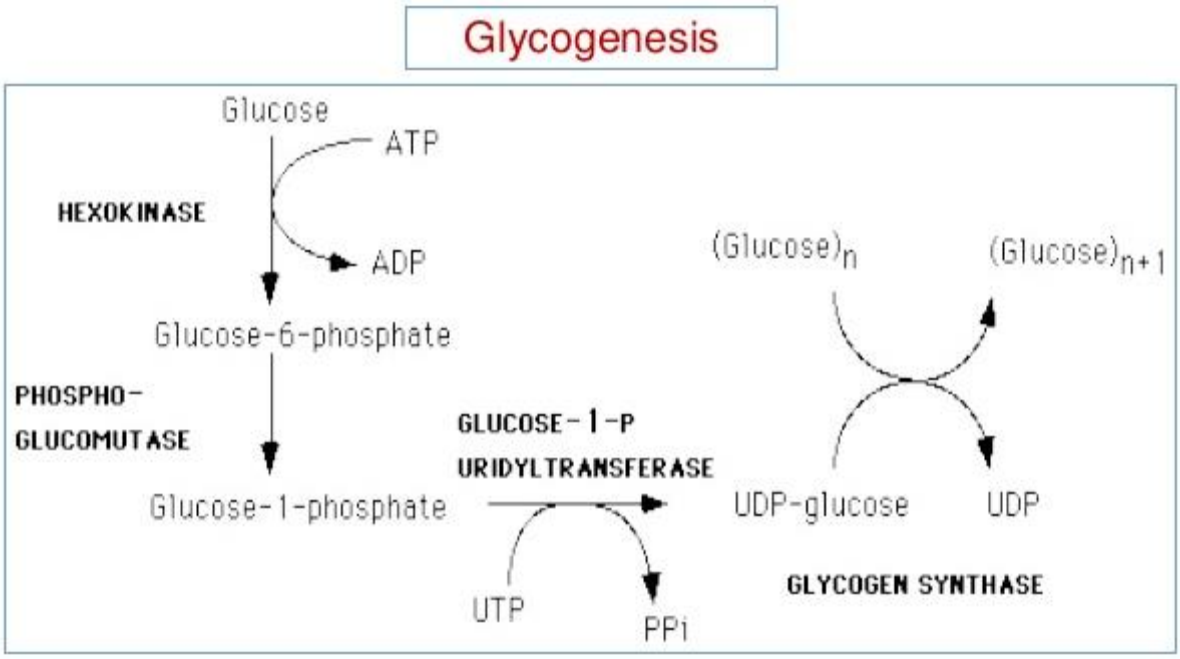
One word questions answers

Sr. No.	Question	Answer
1.	During vigorous exercise, pyruvate produced by glycolysis is converted	Lactate
2.	What stimulates gluconeogenesis and inhibits glycolysis	Ephedrine
3.	Name the enzyme which is responsible for the conversion of pyruvate to phosphoenolpyruvate (PEP)?	Pyruvate carboxykinase
4.	Which hormone maintains blood glucose level by activation of gluconeogenesis?	Glucagon
5.	Name the hormone which is secreted in an emergency or in stress condition?	Epinephrine
6.	Name the pathway for glucose synthesis by non-carbohydrate precursors?	Gluconeogenesis

7.	Glycolysis is a pathway that is Independent of oxygen?	True
8.	Where does glycolysis take place?	Cytosol
9.	Gluconeogenesis is an anabolic pathway that makes glucose from pyruvate.	True
10.	Which of the following enzyme is defective in galactosemia- a fatal genetic disorder in infants	Galactose-1-Phosphate Uridyltransferas

Gluconeogenesis (**GNG**) is a metabolic pathway that results in the generation of glucose from certain non-carbohydrate carbon substrates.

From breakdown of proteins, these substrates include glucogenic amino acids (although not ketogenic amino acids); from breakdown of lipids (such as triglycerides), they include glycerol (although not fatty acids); and from other steps in metabolism they include pyruvate and lactate.



Gluconeogenesis is one of several main mechanisms used by humans and many other animals to maintain blood glucose levels, avoiding low levels (hypoglycemia).

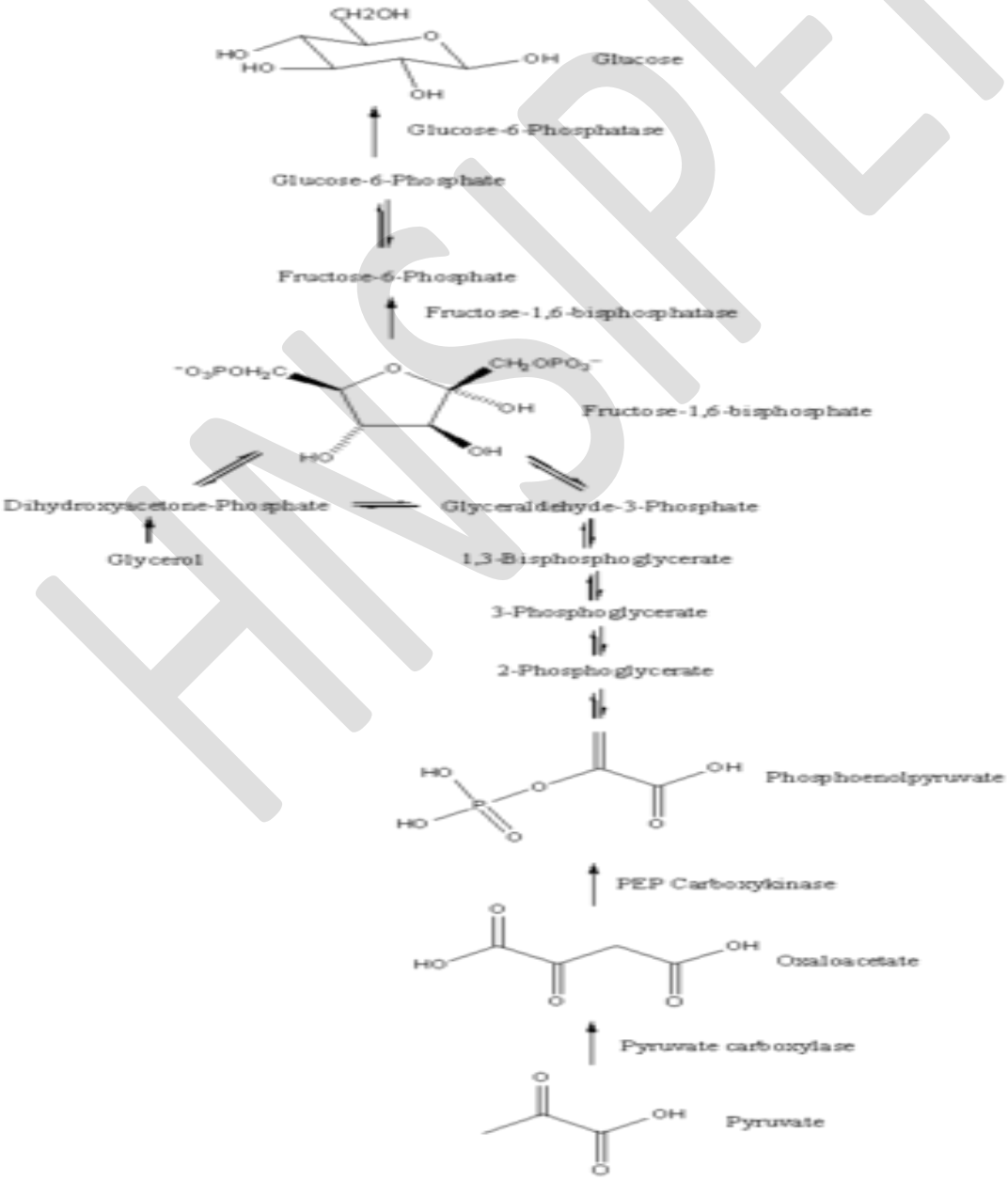
Other means include the degradation of glycogen (glycogenolysis)[1] and fatty acid catabolism.

Gluconeogenesis is a ubiquitous process, present in plants, animals, fungi, bacteria, and other microorganisms. In vertebrates, gluconeogenesis takes place mainly in the liver and, to a lesser extent, in the cortex of the kidneys. In ruminants, this tends to be a continuous process. In many other animals, the process occurs during periods of fasting, starvation, low-carbohydrate diets, or intense exercise. The process is highly endergonic until it is coupled to the hydrolysis of ATP or GTP, effectively making the process exergonic.

For example, the pathway leading from pyruvate to glucose-6-phosphate requires 4 molecules of ATP and 2 molecules of GTP to proceed spontaneously.

Gluconeogenesis is often associated with ketosis. Gluconeogenesis is also a target of therapy for type 2 diabetes, such as the antidiabetic drug, metformin, which inhibits glucose formation and stimulates glucose uptake by cells.

In ruminants, because dietary carbohydrates tend to be metabolized by rumen organisms, gluconeogenesis occurs regardless of fasting, low-carbohydrate diets, exercise, etc.



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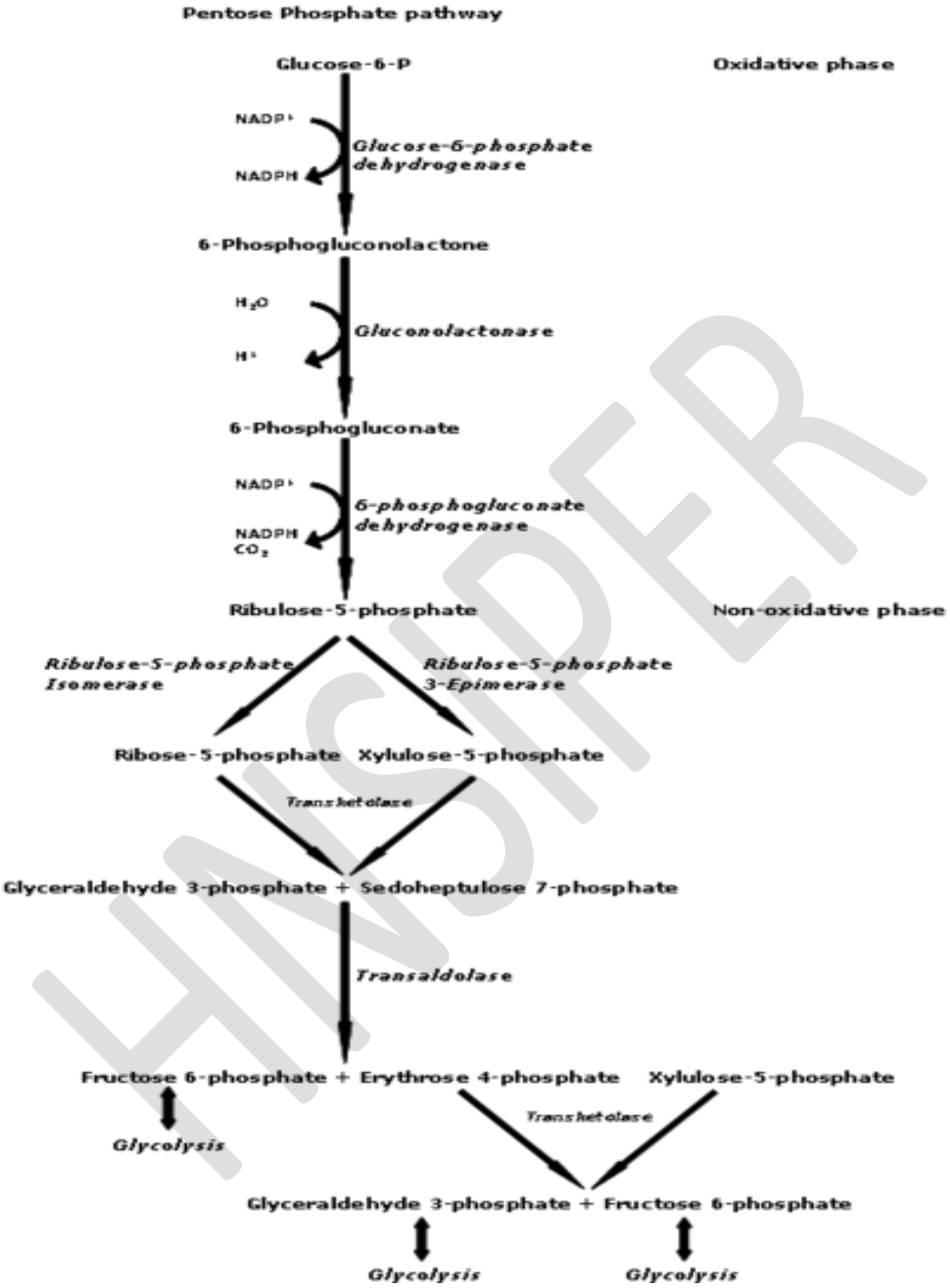
Pentose phosphate pathway

The **pentose phosphate pathway** (also called the **phosphogluconate pathway** and the **hexose monophosphate shunt**) is a metabolic pathway parallel to glycolysis.

It generates NADPH and pentoses (5-carbonsugars) as well as ribose 5-phosphate, the last one a precursor for the synthesis of nucleotides. While it does involve oxidation of glucose, its primary role is anabolic rather than catabolic.

There are two distinct phases in the pathway. The first is the oxidative phase, in which NADPH is generated, and the second is the non-oxidative synthesis of 5-carbon sugars. For most organisms, the pentose phosphate pathway takes place in the cytosol; in plants, most steps take place in plastids.

Similar to glycolysis, the pentose phosphate pathway appears to have a very ancient evolutionary origin. The reactions of this pathway are mostly enzyme-catalyzed in modern cells, however, they also occur non-enzymatically under conditions that replicate those of the Archean ocean, and are catalyzed by metal ions, particularly ferrous ions (Fe(II)).This suggests that the origins of the pathway could date back to the prebiotic world.


Pentose Phosphate pathway
Glucose-6-P
Oxidative phase
NADP+
NADPH
Glucose-6-phosphate dehydrogenase
6-Phosphogluconolactone
H2O
H+
Gluconolactonase
6-Phosphogluconate
NADP+
NADPH
CO2
6-phosphogluconate dehydrogenase
Ribulose-5-phosphate
Non-oxidative phase
Ribulose-5-phosphate Isomerase
Ribulose-5-phosphate 3-Epimerase
Ribose-5-phosphate
Xylulose-5-phosphate
Transketolase
Glyceraldehyde 3-phosphate + Sedoheptulose 7-phosphate
Transaldolase
Fructose 6-phosphate + Erythrose 4-phosphate
Xylulose-5-phosphate
Transketolase
Glycolysis
Glyceraldehyde 3-phosphate + Fructose 6-phosphate
Glycolysis
Glycolysis

One word questions answers

Sr.No.	Questions	Answers
1	The pentose phosphate pathway is also called as.	Hexose monophosphate shunt
2	The primary role of pentose phosphate pathway is anabolic or catabolic?	Anabolic
3	The reaction of pentose phosphate pathway is catalyzed by mostly which metal ions…	Ferrous metal ion
4	For most organisms, the pentose phosphate pathway takes place in…	Cytosol
5	The pentose phosphate pathway has two distinct phase in which first one is.	Oxidative phase
6	The pentose phosphate pathway, first oxidative phase in which what is generated?	NADPH
7	The pentose phosphate pathway has two distinct phase in which second one is.	Non oxidative phase
8	The pentose phosphate pathway, non oxidative phase in which what is synthesized?	5-carbon sugars