Sawa University

Biochemistry I

Carbohydrate Metabolism II

Sawa University | جامعـــــــة ســـــــاوة الاهلية

College of health and medical techniques | كليـــــة التقنيـــات الصحيـة والطبيـة

Department of Medical Laboratories | قسم تقنيات المختبرات الطبية

Stage : 2nd | المرحلـــــــــــــة : الثانية

الجانب النظري محاضرة رقم 7

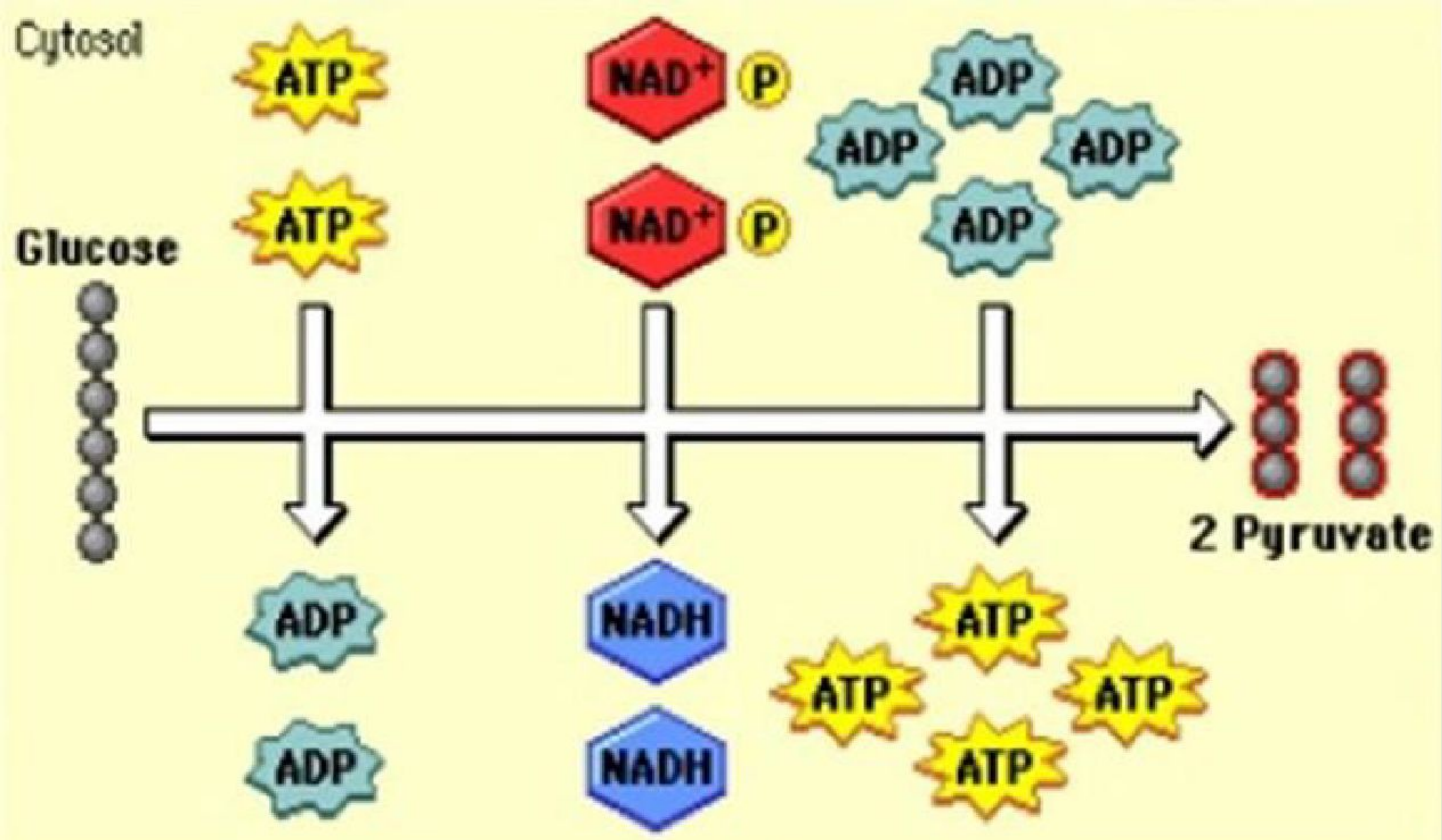
Lecture No. 7 Theoretical

تدريسي المادة : م.د. عبدالرحمن يسر خليفه

Topics

- **Carbohydrate metabolism II:**
  - **Subtopics:**
    - **Glycolysis**
      - **Regulation of Glycolysis**
    - **Pentose Phosphate Pathway**

Glycolysis


Cytosol
ATP
ATP
NAD+
P
NAD+
P
ADP
ADP
ADP
ADP
Glucose
2 Pyruvate
ADP
ADP
NADH
NADH
ATP
ATP
ATP
ATP

- **Basic overview of glycolysis:**
- **Glycolysis** is the stepwise degradation of **glucose** (and other simple sugars).
  - Converts **glucose** to two **C3** units (**pyruvate**).
  - Can function either **aerobically** or **anaerobically**, depending on **the availability of oxygen and the electron transport chain**.
  - **Ten enzymes** catalyze the reactions.
- **Glycolysis consists of two phases**:-

A. **The first phase** (**5 reactions**) in which **glucose** phosphorylated to yield **two molecules of a triose: glyceraldehyde 3-phosphate**.
   - **Two molecules of ATP are consumed**.

A. **The second phase** (**5 reactions**) converts two **glyceraldehyde 3-phosphate** to two **pyruvate**.
   - **Four molecules of ATP are produced.**

- The net result is to produce **two ATP** (**4 - 2 = 2 molecules)** and **two NADH**.
- Occurs in **cytosol.**

A-The First Phase of Glycolysis

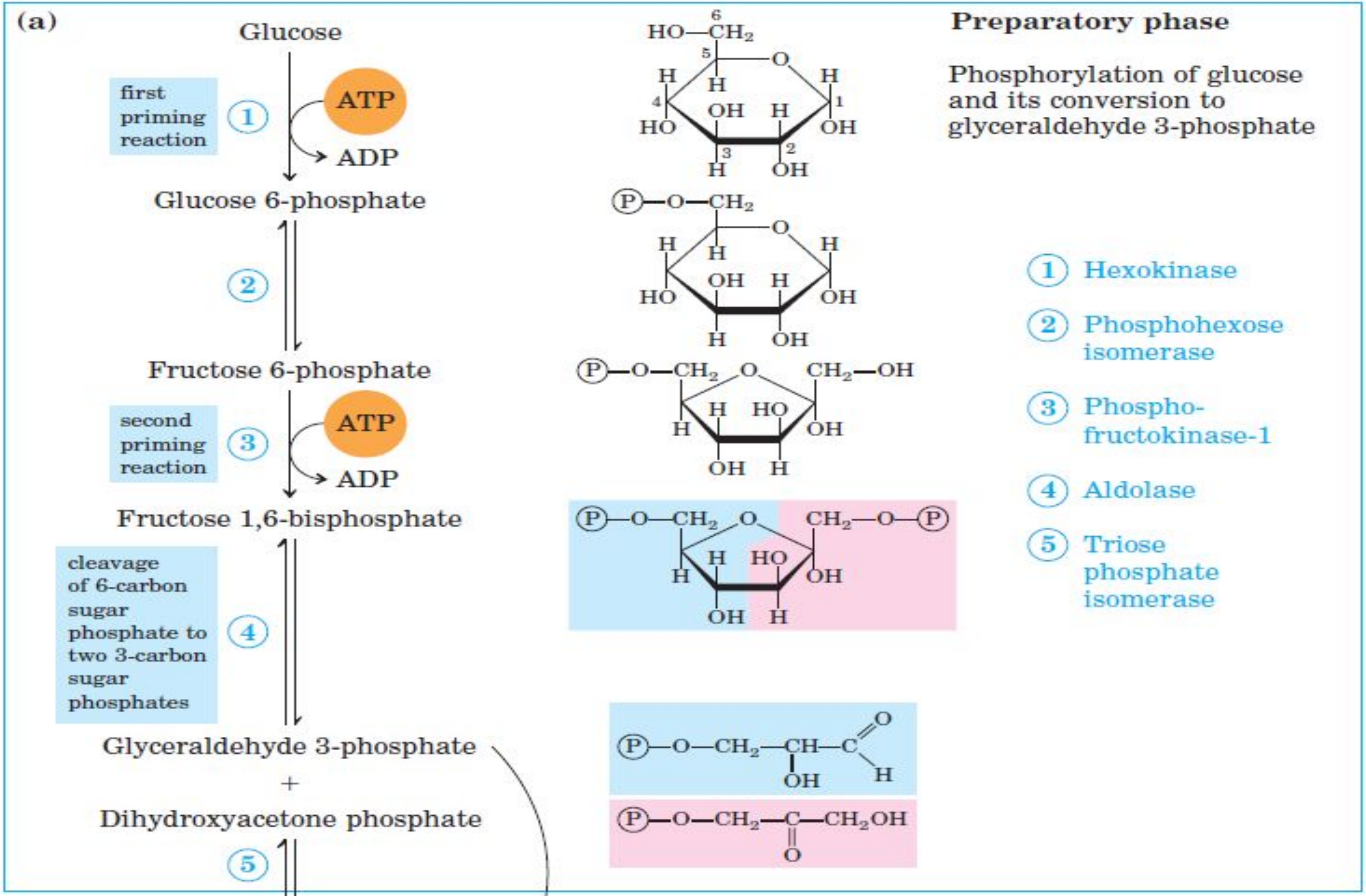
1. **Reaction 1: Phosphorylation of Glucose to Glucose-6-phosphate by Hexokinase or Glucokinase -** using **ATP** as the phosphate donor. **The First Priming Reaction.**

2. **Reaction 2: Isomerization of Glucose-6-Phosphate to Fructose-6-Phosphate. The reaction is catalyzed by phosphohexose isomerase (phosphoglucose isomerase).**

3. **Reaction 3: Phosphorylation of Fructose-6-Phosphate to Fructose 1,6-Bisphosphate by phosphofructokinase-1 (PFK-1).**

4. **Reaction 4: Cleavage of Fructose 1,6-Bisphosphate into two triose phosphates (Dihydroxyacetone phosphate (DHAP) and Glyceraldehyde-3-phosphate) by Fructose 1,6-bisphosphate aldolase.**

5. **Reaction 5: Interconversion of the Triose Phosphates (Dihydroxyacetone phosphate (DHAP) is rapidly and reversibly converted to glyceraldehyde-3-phosphate) by the fifth enzyme of the sequence, triose phosphate isomerase.**


(a)
Glucose
first priming reaction
1
ATP
ADP
Glucose 6-phosphate
2
Fructose 6-phosphate
second priming reaction
3
ATP
ADP
Fructose 1,6-bisphosphate
cleavage of 6-carbon sugar phosphate to two 3-carbon sugar phosphates
4
Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5
Preparatory phase
Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate
1 Hexokinase
2 Phosphohexose isomerase
3 Phospho-fructokinase-1
4 Aldolase
5 Triose phosphate isomerase

B- The Second Phase of Glycolysis

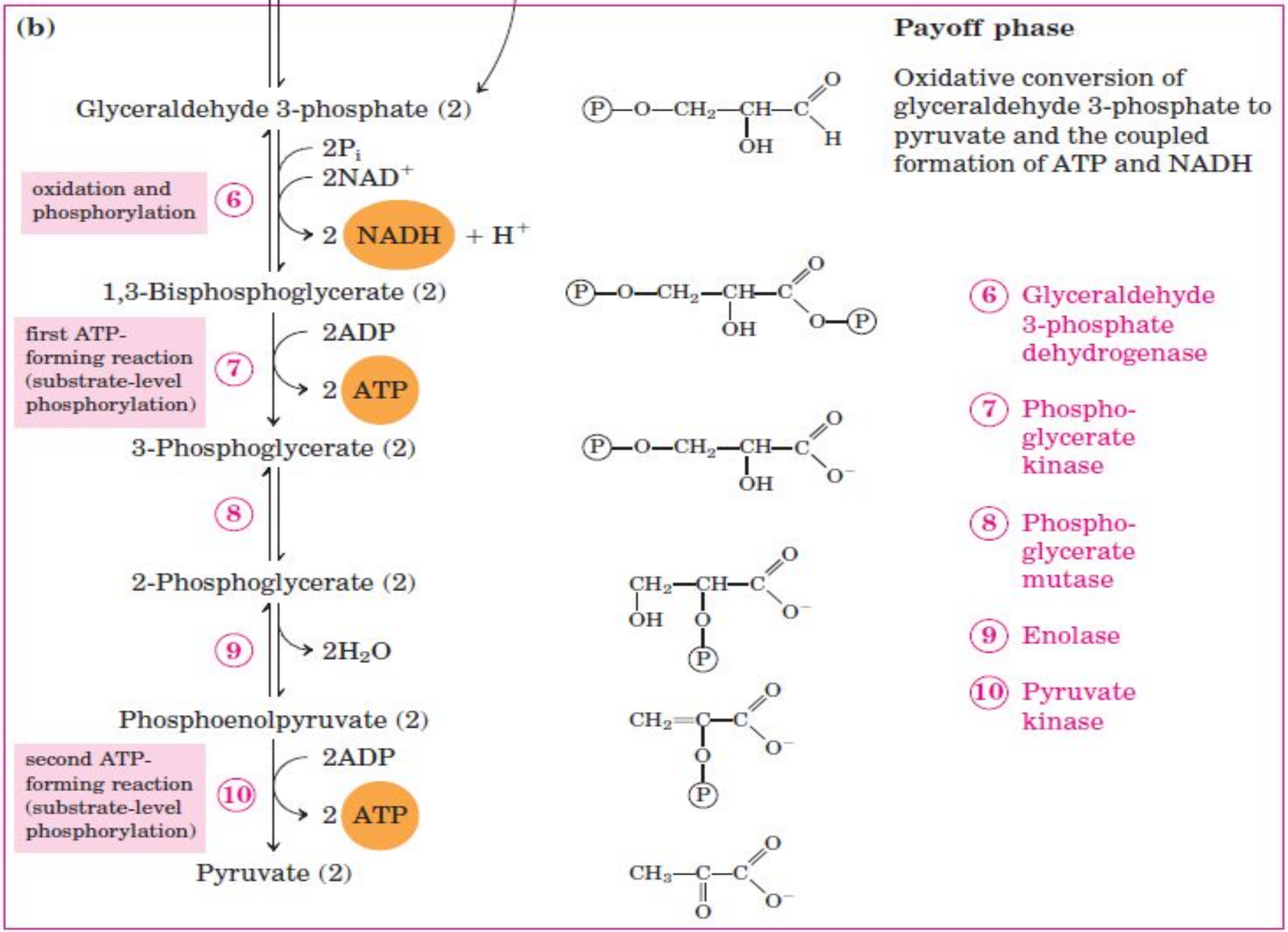
1. **Reaction 6: Oxidation of Glyceraldehyde 3-Phosphate to 1,3 Bisphosphoglycerate by glyceraldehyde-3-phosphate dehydrogenase.**

2. **Reaction 7: Phosphoryl Transfer from 1,3-Bisphosphoglycerate to ADP by phosphoglycerate kinase.**

3. **Reaction 8: Conversion of 3-Phosphoglycerate to 2-Phosphoglycerate by phosphoglycerate mutase.**

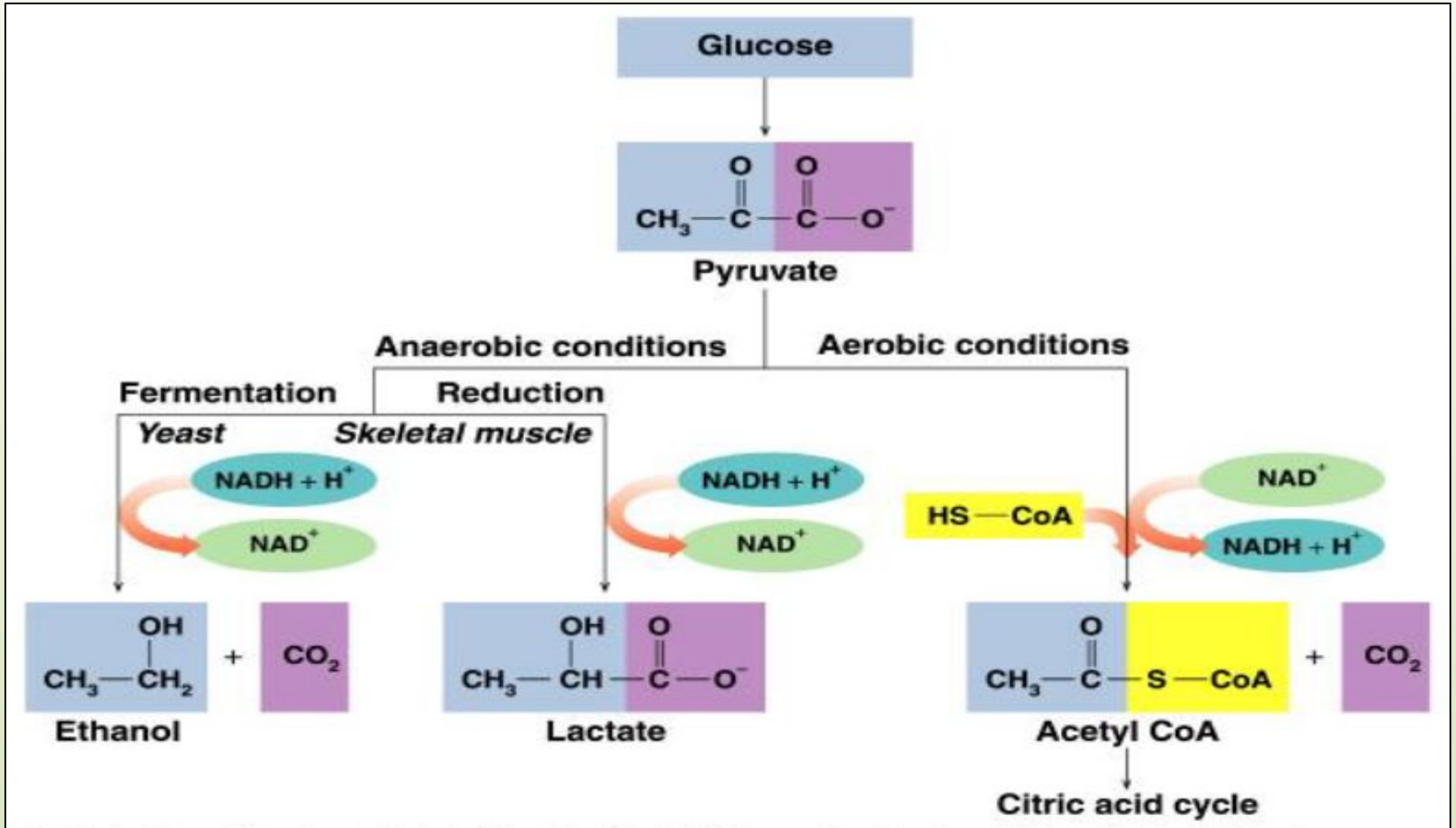
4. **Reaction 9: Dehydration of 2-Phosphoglycerate to Phosphoenolpyruvate (PEP) by enolase.**

5. **Reaction 10: Transfer of the Phosphoryl Group from Phosphoenolpyruvate to ADP by pyruvate kinase.**


(b)
Payoff phase
Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH
Glyceraldehyde 3-phosphate (2)
2P_i
2NAD^+
oxidation and phosphorylation
6
2 NADH + H^+
1,3-Bisphosphoglycerate (2)
first ATP-forming reaction (substrate-level phosphorylation)
2ADP
7
2 ATP
3-Phosphoglycerate (2)
8
2-Phosphoglycerate (2)
9
2H_2O
Phosphoenolpyruvate (2)
second ATP-forming reaction (substrate-level phosphorylation)
2ADP
10
2 ATP
Pyruvate (2)
6 Glyceraldehyde 3-phosphate dehydrogenase
7 Phosphoglycerate kinase
8 Phosphoglycerate mutase
9 Enolase
10 Pyruvate kinase

❖ Pathways for Pyruvate

1. When **oxygen is present in the cell**, (**aerobic conditions**), **pyruvate** from **glycolysis** is **decarboxylated** to produce **acetyl CoA** and **CO_2**.
2. **Lactate Formation**: When **oxygen is not available** (**anaerobic conditions**), **pyruvate** is reduced to **lactate** **by** **lactate dehydrogenase (LDH)**, which replenishes **NAD^+** to continue **glycolysis**.



❖ Regulation of Glycolysis

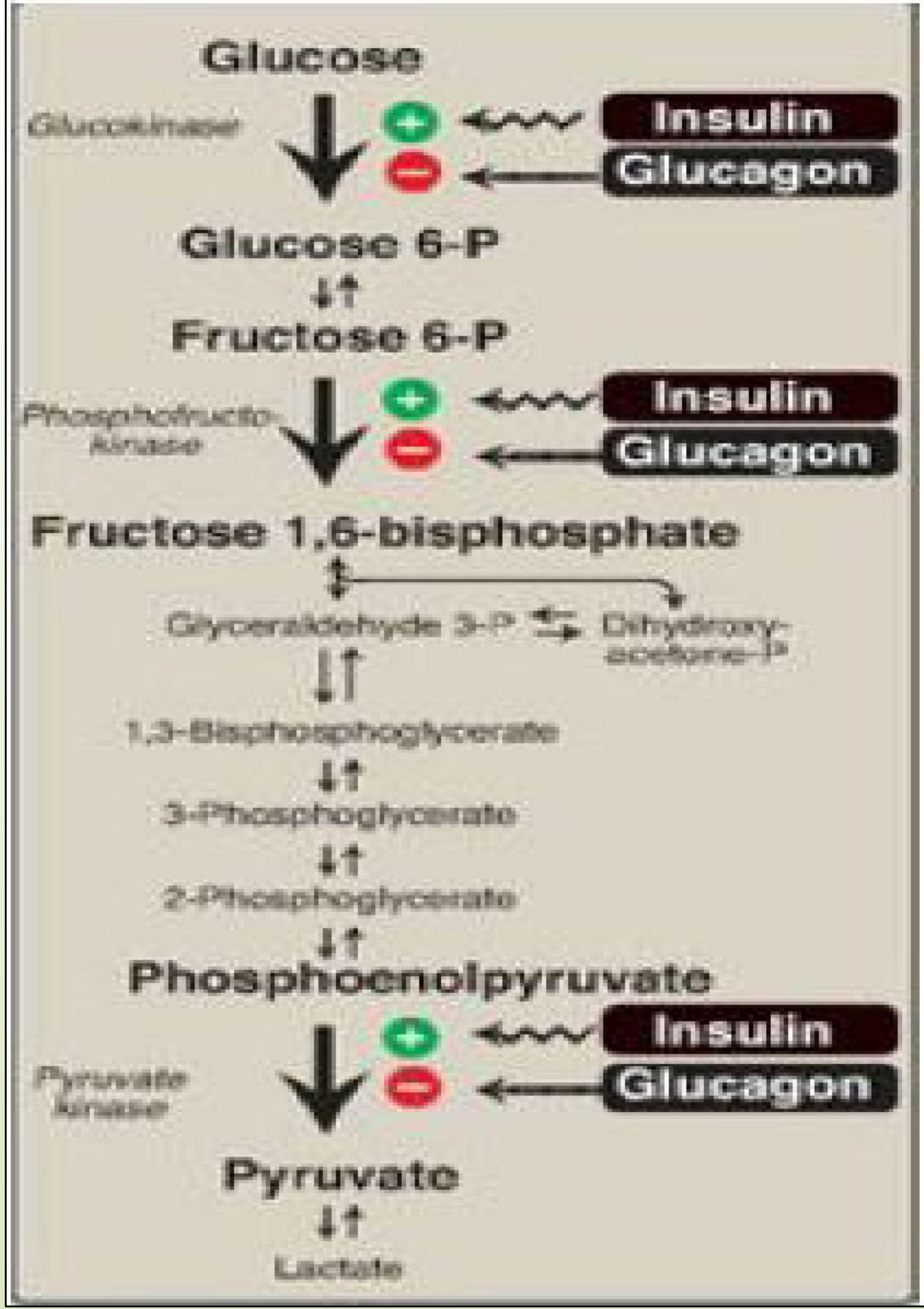
Control Points in Glycolysis

- Three reactions exhibit particularly large decreases in free energy; the enzymes that catalyze these reactions are sites of allosteric control:

1. **Reaction 1 Hexokinase** is **inhibited** by **high levels of glucose-6-phosphate**, which prevents the phosphorylation of glucose.
2. **Reaction 3 Phosphofructokinase**, an allosteric enzyme, is **inhibited** by **high levels of ATP** and **activated** by **high levels of ADP and AMP**.
3. **Reaction 10 Pyruvate kinase**, another allosteric enzyme is **inhibited** by **high levels of ATP** or **acetyl CoA**.

Hormonal Regulation of Glycolysis

- Reciprocal changes occur in the rate-limiting enzymes of **glycolysis** and **gluconeogenesis**.
- Regular intake of **carbohydrate-rich meals** or **insulin administration** increases the levels of **glucokinase, phosphofructokinase,** **and** **pyruvate kinase (PK)** in **the liver**.
- This increase in enzyme levels is due to enhanced gene transcription, resulting in **greater enzyme synthesis**.
- High activity of these three enzymes promotes the conversion of **glucose** to **pyruvate**, typical of the absorptive state.
- Conversely, **gene transcription** and **synthesis of glucokinase**, **phosphofructokinase**, **and pyruvate kinase** decrease when plasma **glucagon** is high and **insulin** is low, as seen in fasting or diabetes.



Pentose Phosphate Pathway

- In most **animal tissues**, **glucose 6-phosphate** is mainly broken down through **glycolysis** to **pyruvate**, leading to **ATP** production via **the citric acid cycle**.
- **Glucose 6-phosphate** can undergo **oxidation** through the **pentose phosphate pathway** (also known as the **phosphogluconate or hexose monophosphate pathway**), producing **pentose phosphates** and **NADPH**.
- Occurs in **the cytoplasm**.

Functions of the Pentose Phosphate Pathway:

- **For Rapidly Dividing Cells**: Produces **pentoses** needed for **RNA**, **DNA**, and essential coenzymes (e.g., **ATP, NADH, $FADH_2$, CoA**).
- **For Tissues Requiring NADPH**: Provides **NADPH**, which is essential for:
  - **Reductive biosynthesis** (e.g., **fatty acid synthesis in liver**, **adipose tissue**, and **lactating mammary gland**).
  - **Cholesterol and steroid hormone synthesis** (e.g., in **liver**, **adrenal gland,** and **gonads**).
  - **Countering oxidative stress**, particularly in cells exposed to oxygen (e.g., **erythrocytes**, **lens**, and **cornea cells**).

Summary of the steps in the pentose phosphate pathway:

1. **Oxidation of Glucose 6-Phosphate**: **Glucose 6-phosphate** is oxidized by the enzyme **glucose 6-phosphate dehydrogenase** (**G6PD**), producing **6-phosphoglucono-δ-lactone** and **NADPH**.

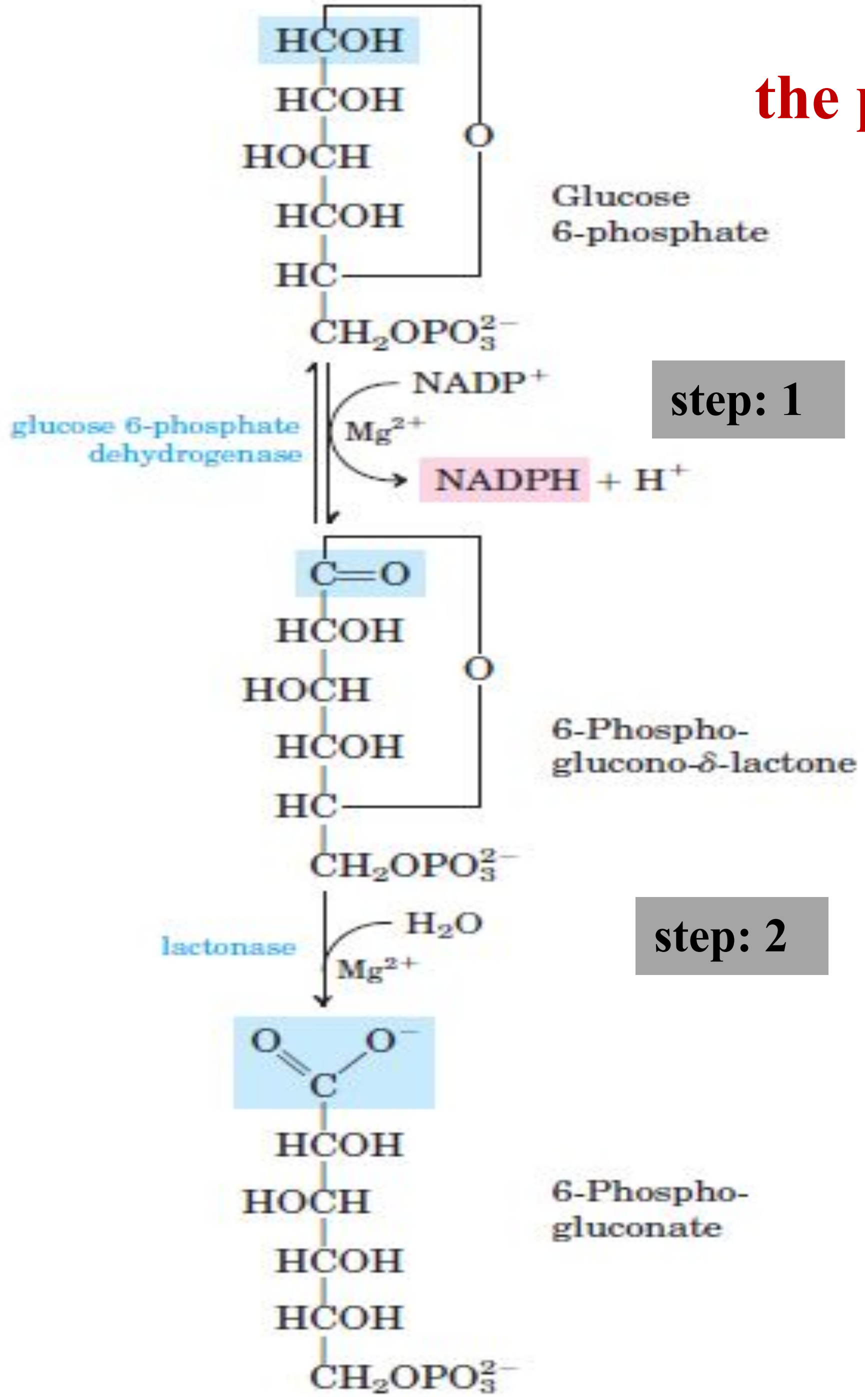
2. **Hydrolysis of 6-Phosphoglucono-δ-Lactone**: The **lactone** is hydrolyzed by **lactonase**, forming **6-phosphogluconate**.

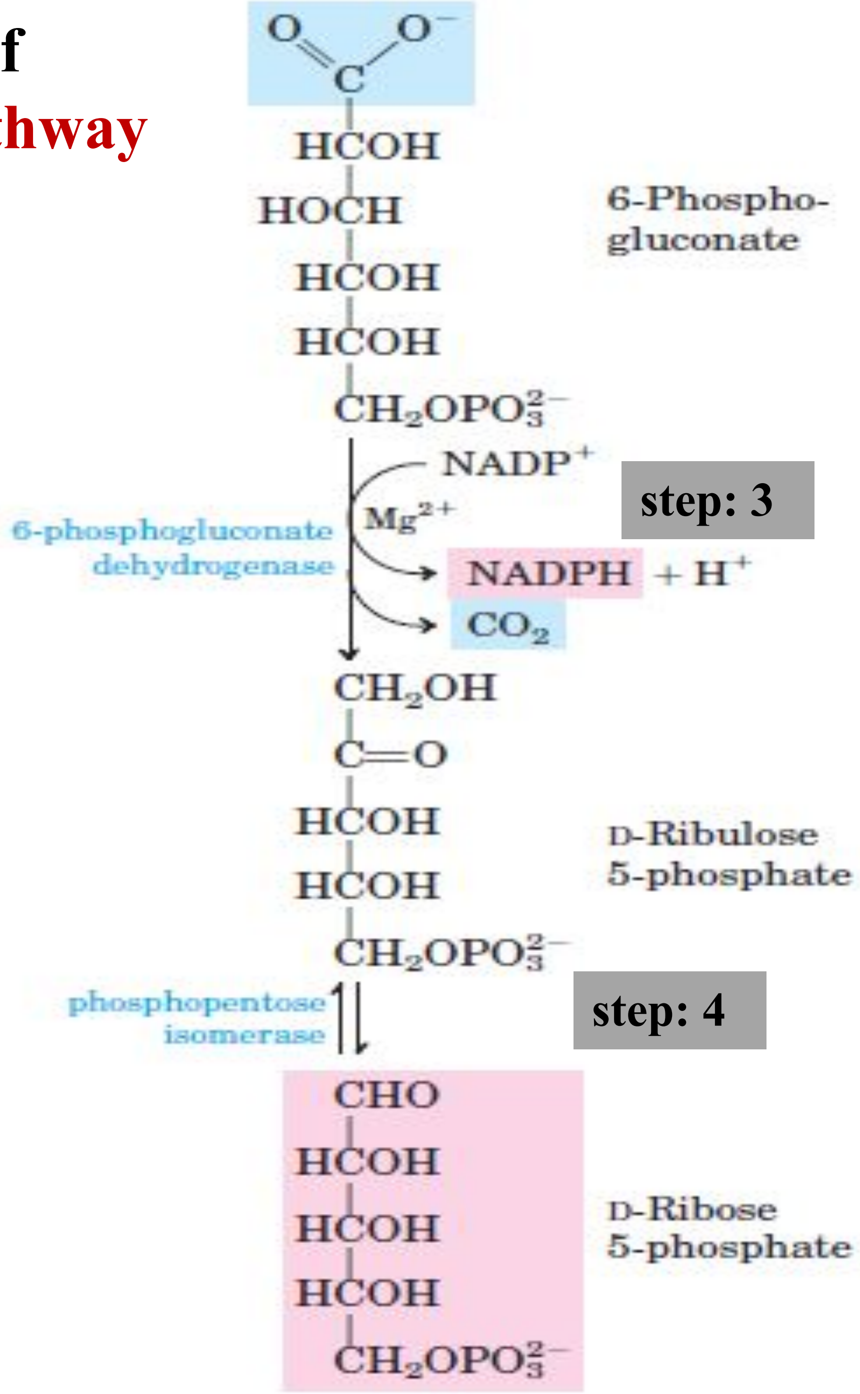
3. **Oxidation and Decarboxylation of 6-Phosphogluconate**: **6-phosphogluconate** is further oxidized and decarboxylated by **6-phosphogluconate dehydrogenase** to produce **ribulose 5-phosphate** and a second molecule of **NADPH**.

4. **Conversion to Ribose 5-Phosphate**: **Phosphopentose isomerase** converts **ribulose 5-phosphate into ribose 5-phosphate**, which can be used for **nucleotide synthesis**.

Note: The net products are **NADPH** (for **biosynthetic reactions**) and **ribose 5-phosphate** (for **nucleotide synthesis**).

Oxidative reactions of the pentose phosphate pathway





Any questions?

Thank You