Glucose Oxidation
(I. Glycolysis)

Students Learning Outcomes

❖ By the end of this lecture, the students should be able to:

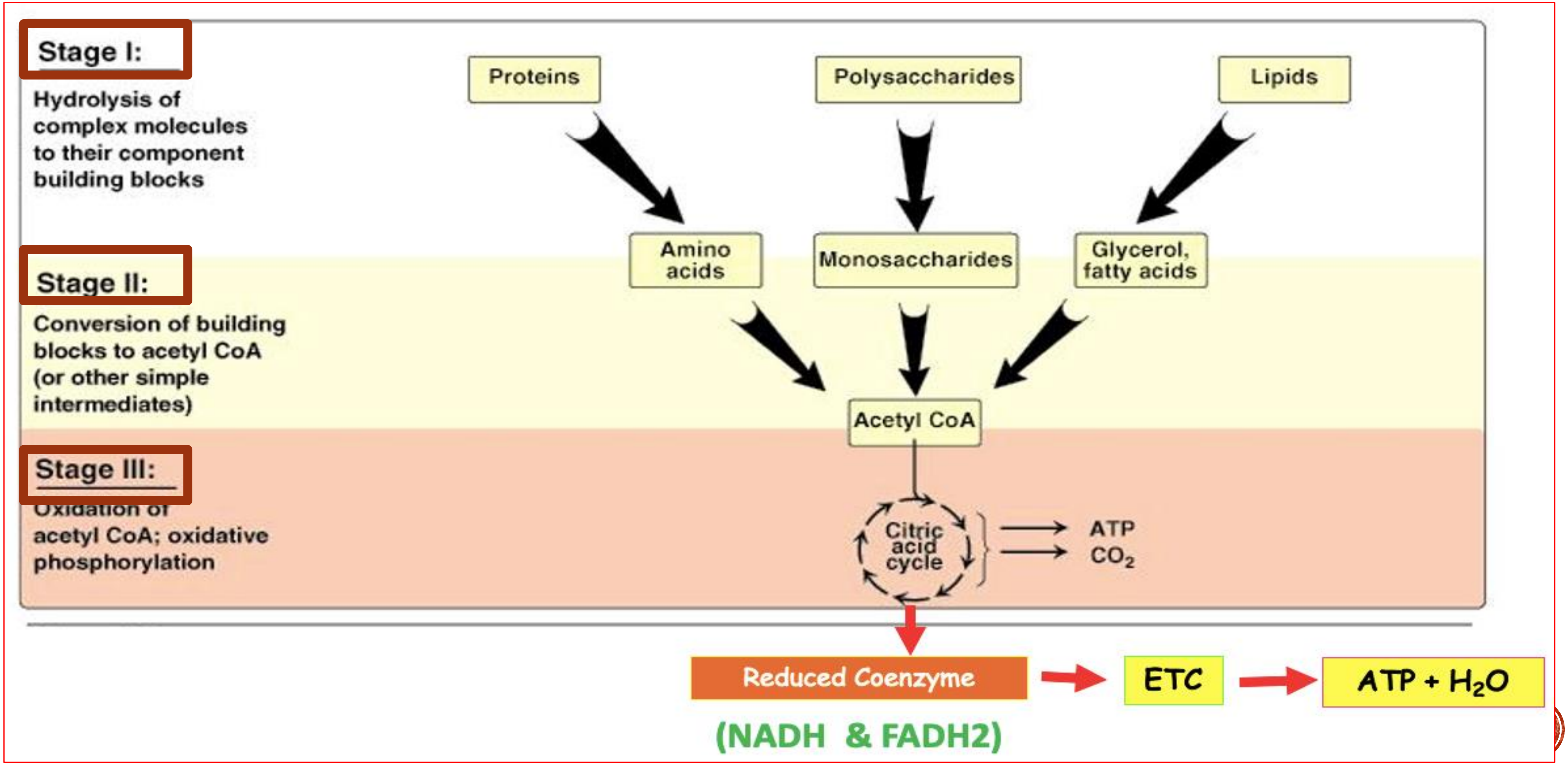
1. Define glycolysis and recognize its site, phases, energy and regulation.
2. Explain oxidative decarboxylation of pyruvic acid.

Content

I. Glycolysis

II. Oxidative decarboxylation of pyruvic acid

Fate of food staff & stages of metabolism



Pathways of glucose oxidation

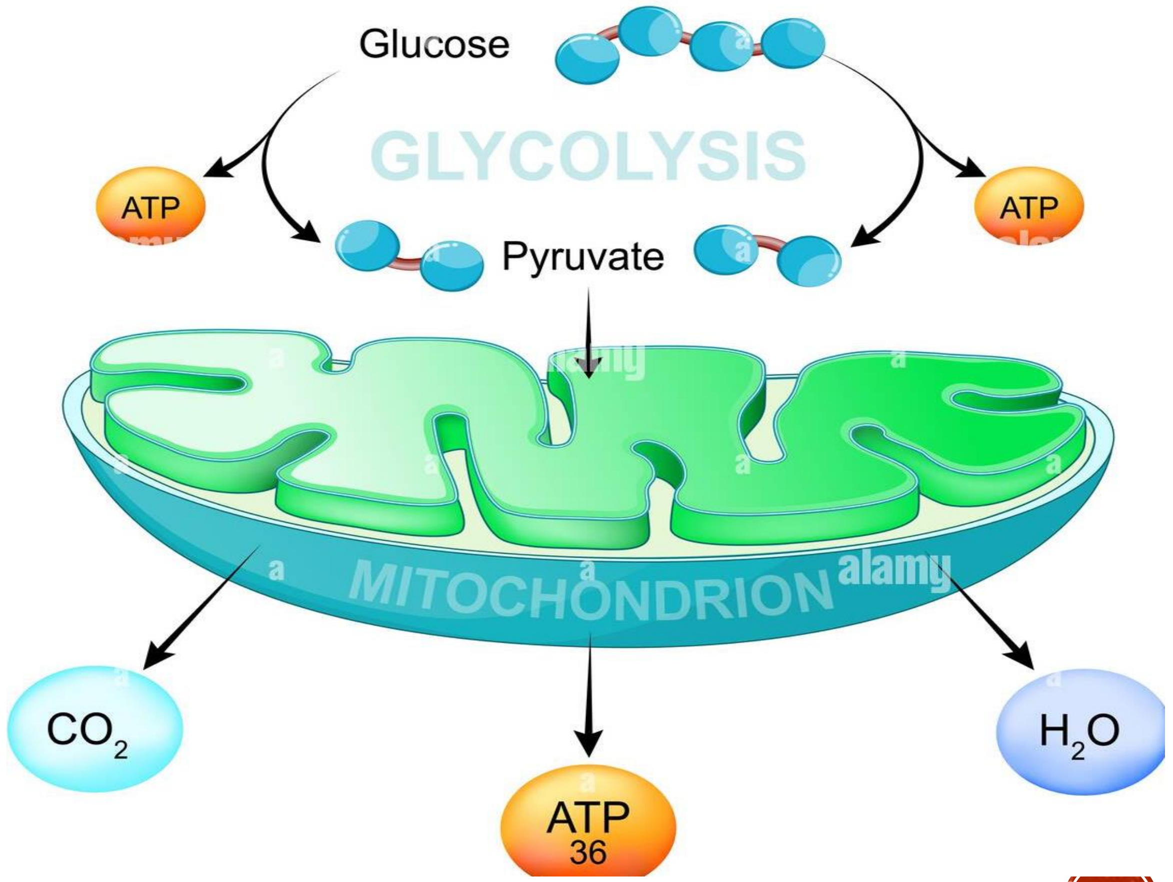
Major pathway	Minor pathway
1. **Glycolysis** 2. **Citric acid cycle (kerbs cycle)**	1. **Pentose shunt**
Mainly for **energy** production	Production of important **derivatives.** ***(not for energy production)***

Glycolysis

1. Definition
2. Site
3. Phases (Steps)
4. Products
5. Regulation
6. Fate of pyruvate

Definition of Glycolysis.
(Glyco / sugar. & lysis / breakdown

- The process by which glucose is broken down in order to begin obtaining some of the energy stored in the glucose molecule for use by the body.

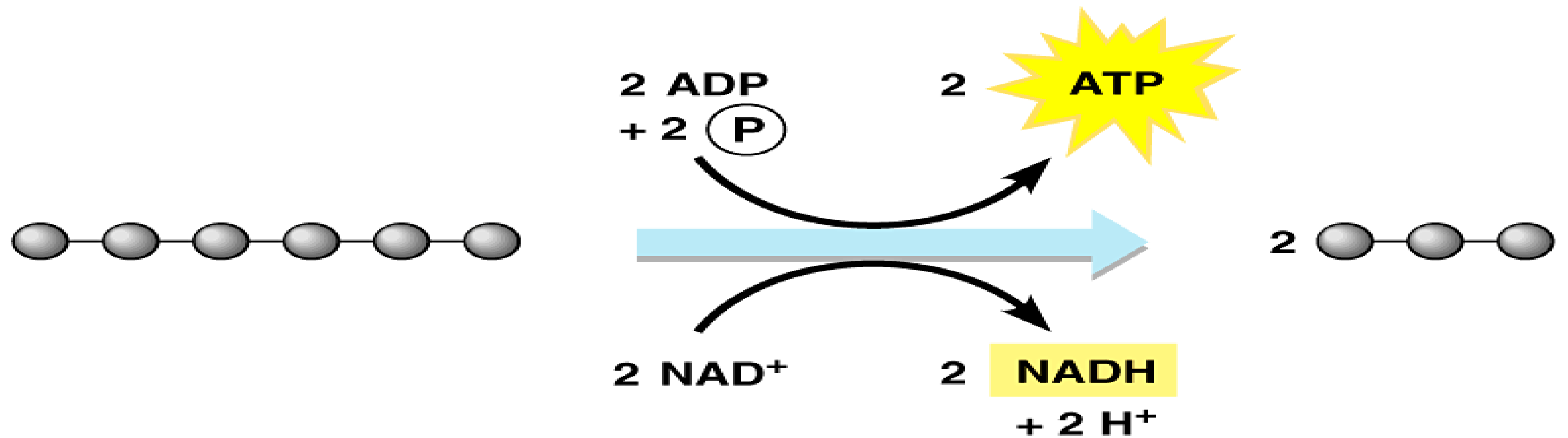


Definition of Glycolysis.
(Glyco / sugar. & lysis / breakdown

❖It is a series of biochemical reactions **involving breakdown of glucose (6C) to :**

- ✓**2 molecules pyruvic acid (3C) (in presence of O_2 "Aerobic") or**
- ✓**2 molecules of lactic acid (3C) (in absence of O_2 "Anerobic") .**

❖ **with a net generation of 2 ATP & 2 NADH**

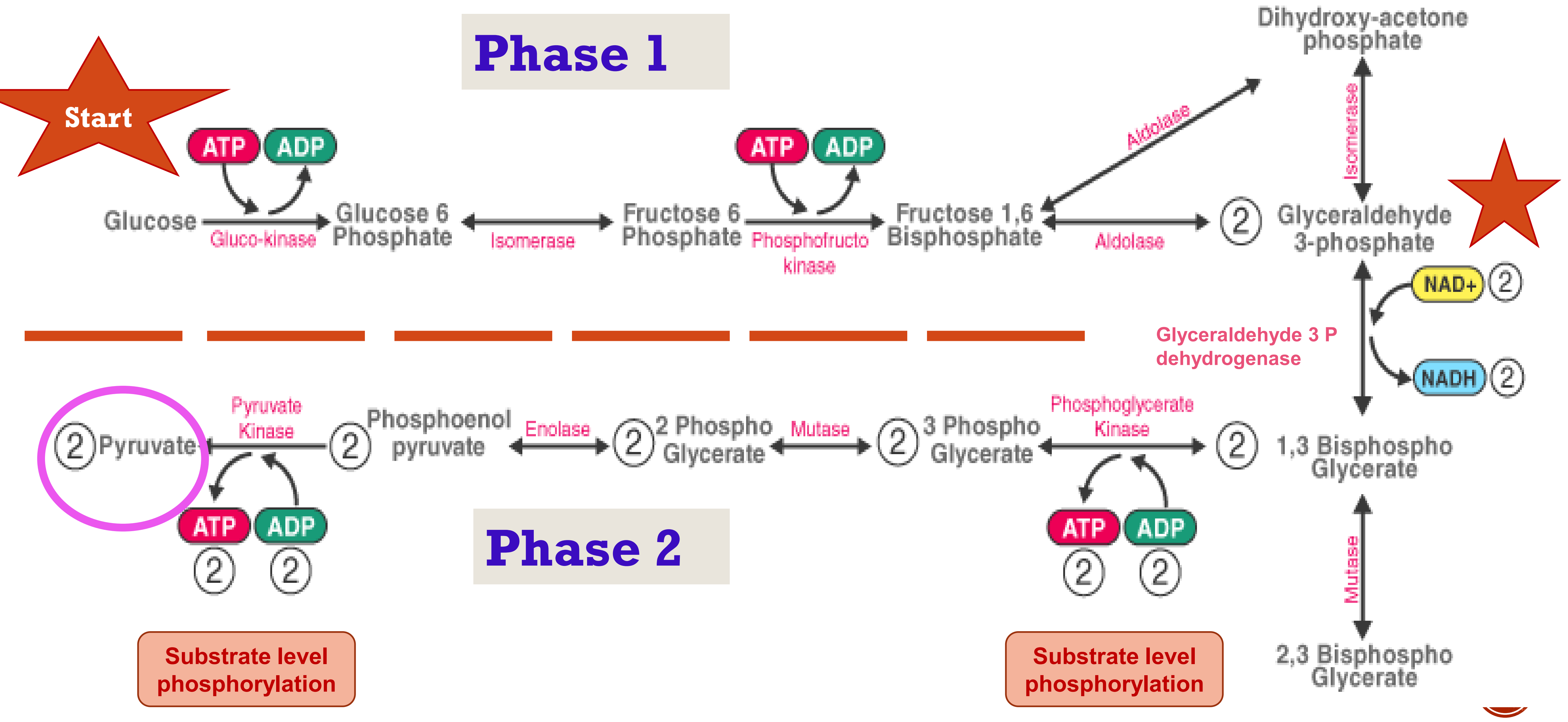


Site of Glycolysis.

Site: In Cytosol of all cells

- ✓ if a cell has mitochondria and oxygen, glycolysis is ***aerobic.***
- ✓ if either mitochondria or oxygen is lacking, glycolysis may occur ***anaerobically***
- ✓ So, glycolysis is important in ***mature RBCs, cornea*** and ***lens*** (due to absence of mitochondria) and in ***muscle*** (due to lack of oxygen during muscular exercise).

2 Phases of glycolysis (10 enzymatic reactions)



Phase 1 Energy requiring	Phase 2 Energy producing
The first 5 reactions	**The last 5 reactions**
Converts glucose → 2 **molecules of Glyceraldehyde 3-P** (G 3 P)	Converts each **Glyceraldehyde 3-P molecule** → **pyruvate**
Consume 2 ATPs for 2 reactions: Glucose —(Hexokinase/glucokinase)→ Glucose 6 P Fructose 6 P —(Phosphofructokinase 1)→ Fructose 1,6 BP	**Produces 2 ATP (X2) =4 ATP** **(by substrate level phosphorylation)** from 2 reactions: 1,3 diphosphoglycerate —(Phosphoglycerate kinase)→ 3 P glycerate Phosphoenolpyruvate —(Pyruvate kinase)→ pyruvate
	Produce also **1 NADH+H (X2)= 2 NADH+H**
	All the products of phase 2 must be multiplied by 2

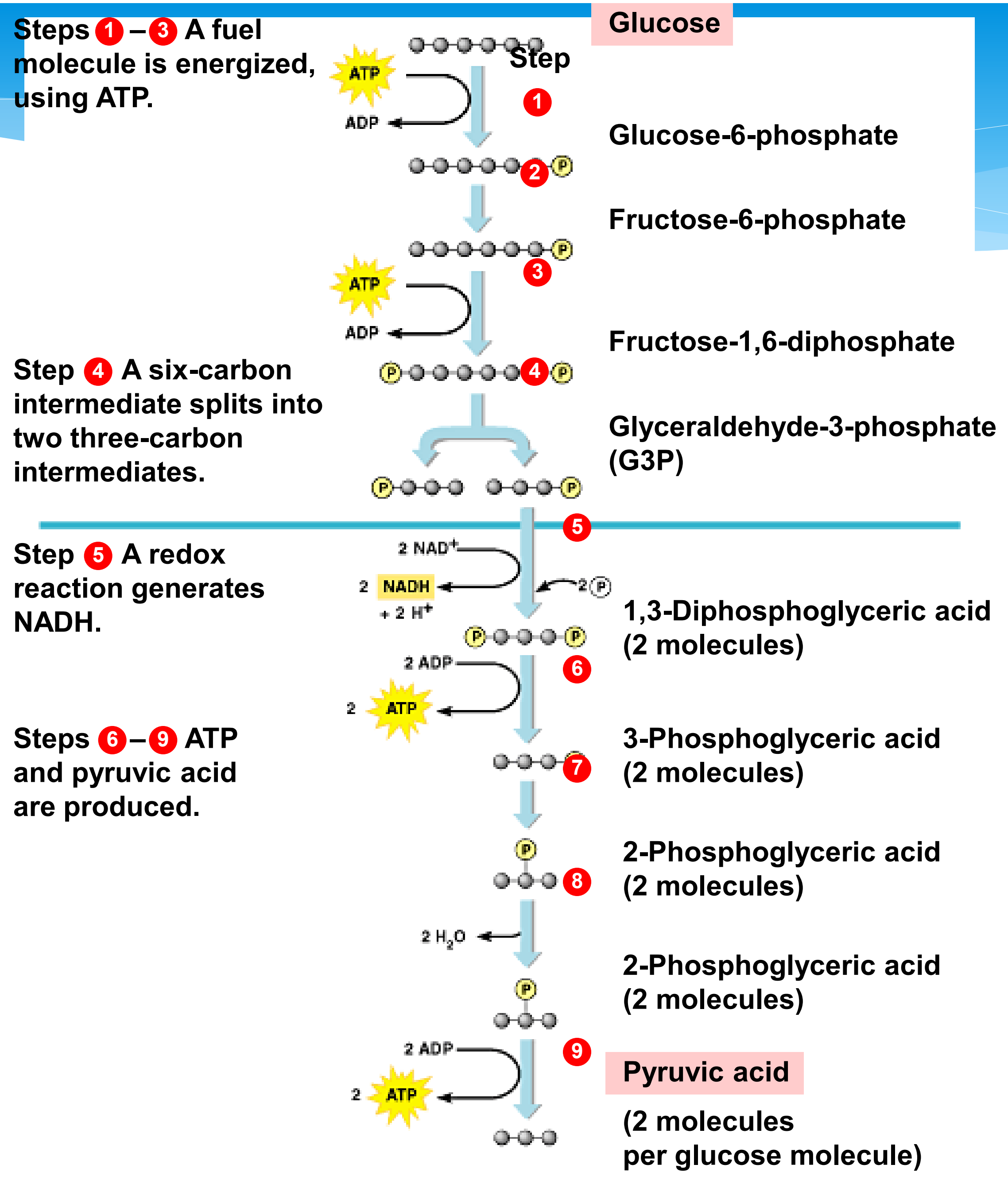
Net gain of energy 2 ATP(+2NADH+H

Glycolysis

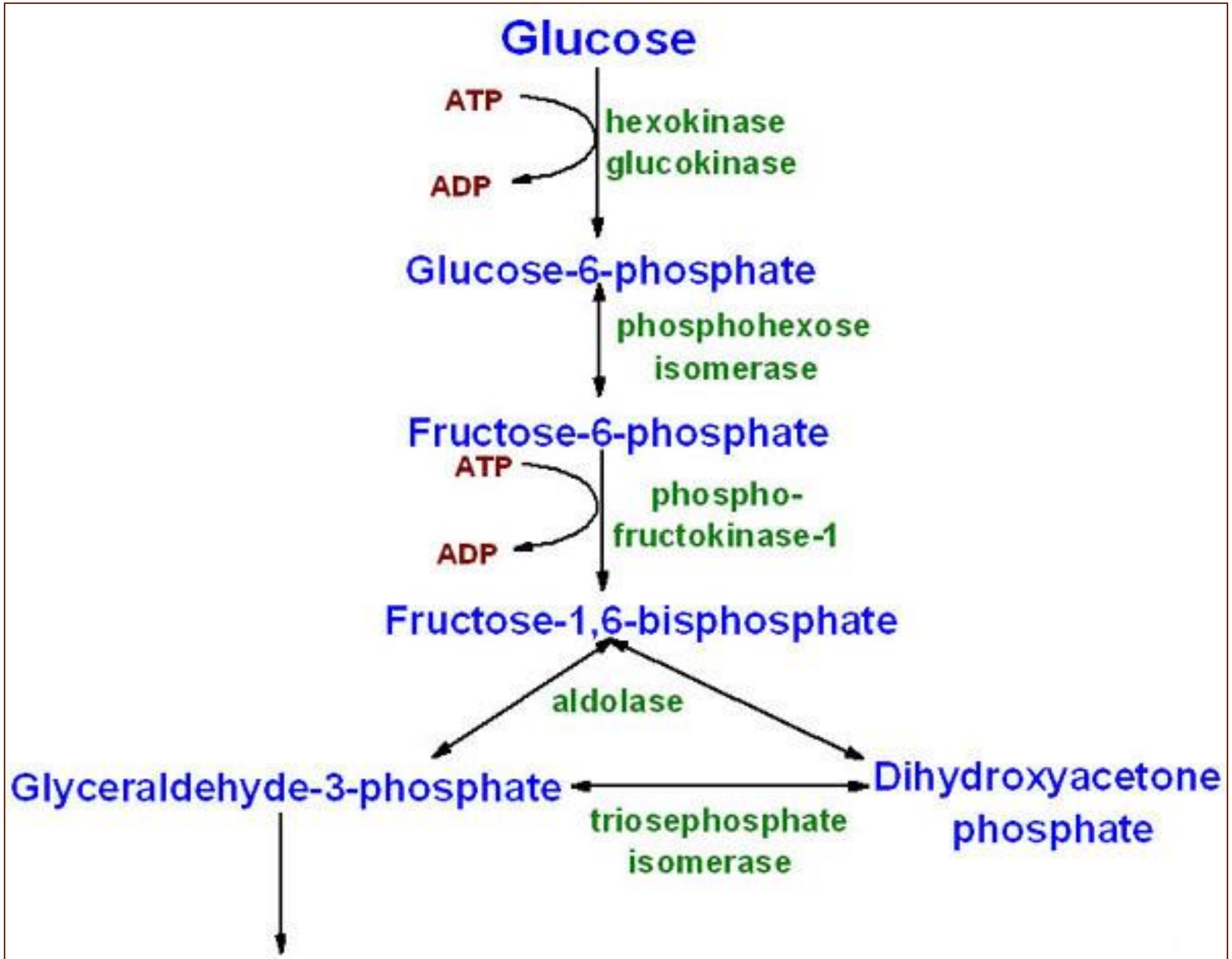
Energy In: 2 ATP

Energy Out: 4 ATP

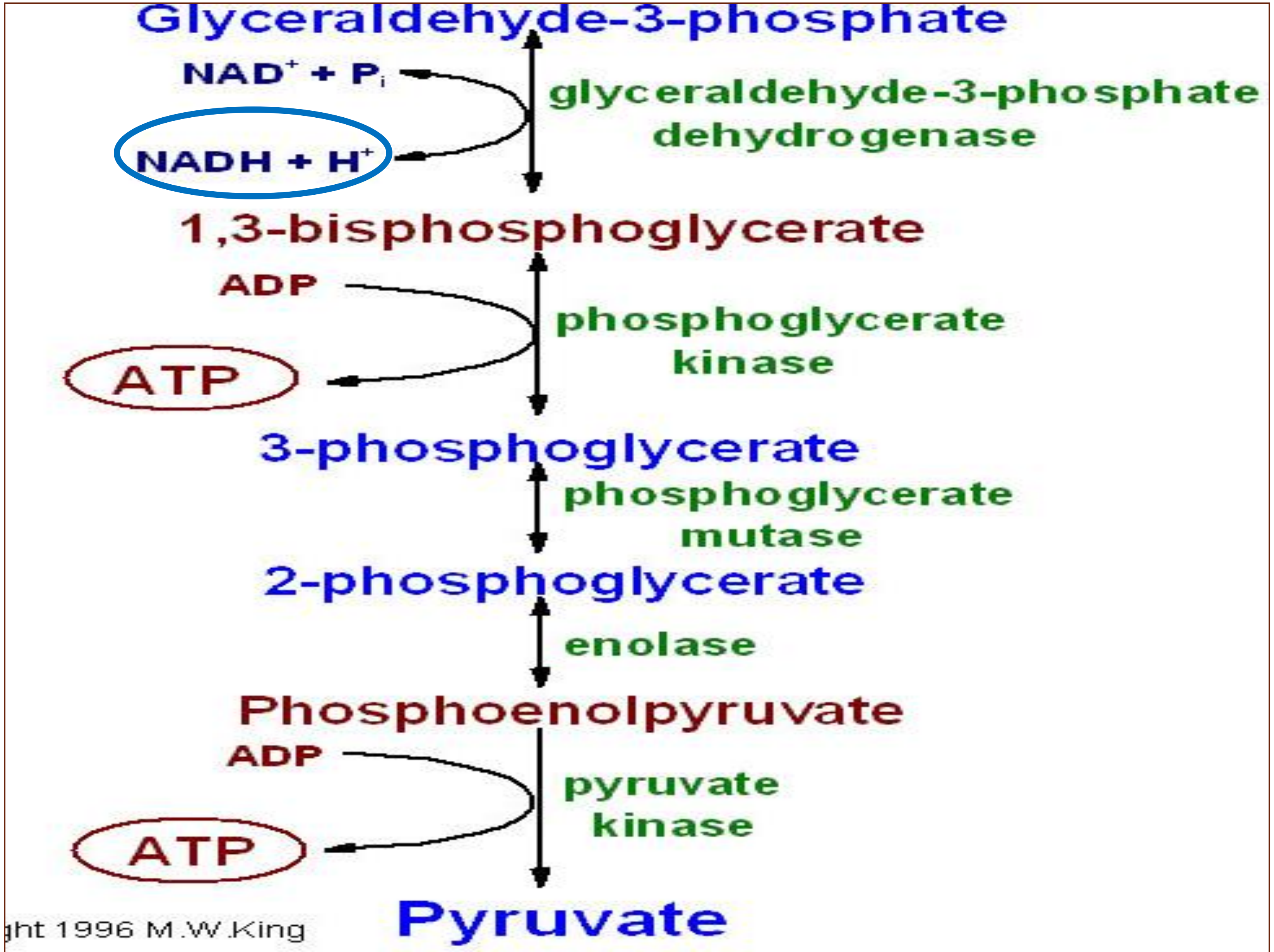
NET 2 ATP



1st stage (Phase 1)



2nd stage (Phase 2)



Glycolysis_ The Reactions

Fate of pyruvate

According to the availability of O_2

I) In aerobic condition (aerobic glycolysis)

(in presence of O_2)

Pyruvate gives → **Acetyl CoA** + CO_2+ NADH+H

(**by oxidative decarboxylation**)

1) Acetyl CoA → enter Krebs cycle for (more energy production).

2) NADH+H → oxidized in the electron transport chain in the mitochondria to produce ATP (more energy production).

Fate of pyruvate

According to the availability of O2:

II) In anerobic condition (anerobic glycolysis) (no O2 or mitochondria)

- ✓As in exercising muscles and RBCs
- ✓Pyruvate gives → **lactic acid.**
- ✓Requires: - Lactate dehydrogenase
  - NADH+ H

- ✓**In muscle**
  - Accumulation of lactic acid causes a decrease in ***muscle cell pH.***
  - Elevated muscle lactate accounts for ***fatigue and pain*** induced by strenuous exercise.

Energy production in glycolysis

	ENERGY	
Phase 1	**2 ATPs** are utilized i.e. (minus 2 ATP) by hexokinase & phosphofructokinase	
Phase 2	1 G3P→ 1 pyruvate producing and ❖ **1 NADH is released**→ gives 3 ATP (in mitochondria) ❖ **2 ATP**s are produced (By substrate level phosphorylation) **(X 2) = 4 ATP + 2 NADH+H**	
For each 1 glucose oxidation by glycolysis	+ 2 Pyruvate - (minus) 2 ATP + 4 ATP +2 (NADH+H) = **2 pyruvate + 2 ATP +2 NADH+H.** **2 NADH+H** —Aerobic condition → ETC→ **6 ATP (in ETC)** **Or** **2 NADH+H** —Anaerobic condition → lactate→ **no ATP (NADH is utilized by lactate dehydrogenase)**	
	Aerobic condition	**Anaerobic condition**
	8 ATPs/ 1 molecule glucose 2 ATP (substrate level phosphorylation) + 6 ATP (from NADH+H)	**2 ATPs / 1 molecule glucose**

	Anaerobic glycolysis	Aerobic Glycolysis
Site	Specially in the Cytoplasm of 1-RBCs (no mitochondria) 2- Contracting skeletal muscles (no O2)	Cytoplasm of all tissue
End products	• **2 lactate** • **2 NAD** • **2 ATP**	• **2 pyruvate** • **2 NADH + H** (Each NADH + H enter ETC and give 3 ATP) • **8 ATP** (2 SLP + 6 from NADH+ H in ETC)
Net ATP	2 ATP (from substrate level phosphorylation)	Net ATP: 8 ATP • 2 ATP from substrate level phosphorylation. (SLP) + • 2 NADH+ H→ 6 ATP in ETC
Lactate dehydrogenase enzyme (LDH)	Used	Not used

Rate limiting enzymes of glycolysis

- ✓ 3 enzymes in this pathway

  1. Glucokinase/hexokinase
  2. Phosphofructokinase 1 (PFK-1)
  3. Pyruvate kinase (PK)

why ?

- ✓ They catalyze the irreversible reactions.

Regulation of glycolysis

By controlling of 3 irreversible enzymes (key enzymes): **Glucokinase (hexokinase), Phosphofructokinase (PFK-1)** and **Pyruvate kinase**

1- Insulin/glucagon ratio: The main hormonal regulator of glucose utilization

	Insulin	Glucagon
Secreted in response to	1- Feeding state 2-High blood glucose level (hyperglycaemia).	1. Carbohydrate deficiency / Fasting 2. Low blood glucose level (hypoglycaemia).
Effect on glycolytic enzymes	Stimulates it	Represses it

2-Regulation according to the energy level in the cell

✓**High ATP, high NADH:** no need for more ATP, so → **down regulation** of glycolytic enzyme

✓**High ADP, & high NAD:** cell need energy, so,→ **upregulation** of glycolytic enzymes

Differences between glucokinase and hexokinase

	Glucokinase	Hexokinase
1. Site	Liver and pancreatic β islet cells	All tissue
2. Affinity to glucose	Low affinity (high km) i.e. it acts only in the presence of high blood glucose concentration.	High affinity (low km) i.e. it acts even in the presence of low blood glucose concentration
3. Substrate	Glucose only	Glucose, galactose and fructose
4. Effect of insulin	Induces synthesis of glucokinase.	No effect
5. Effect of glucose-6-p	No effect	Allosterically inhibits hexokinase

Clinical Relevance of glycolysis

1-Inherited deficiency of Pyruvate Kinase→ hemolytic anemia (RBCs depends on glycolysis for ATP production).

2- Fluoride: inhibits enolase enzyme→ a. in toothpaste: inhibit glycolysis in bacteria→ no lactic acid that causes dental caries (protect from dental caries).

b. Fluoride-containing tubes: are used to reduce glycolysis in blood samples used for estimation of blood glucose.

II) In aerobic condition (aerobic glycolysis) (in presence of O_2)

Pyruvate gives → **Acetyl CoA** + CO_2 + NADH+H (by oxidative decarboxylation)

Oxidative Decarboxylation of Pyruvate

Oxidative decarboxylation of pyruvate

1 NADH = 3 ATP

Under aerobic condition (aerobic glycolysis)

✓**Pyruvate must enter to the mitochondria to undergo oxidative decarboxylation.**

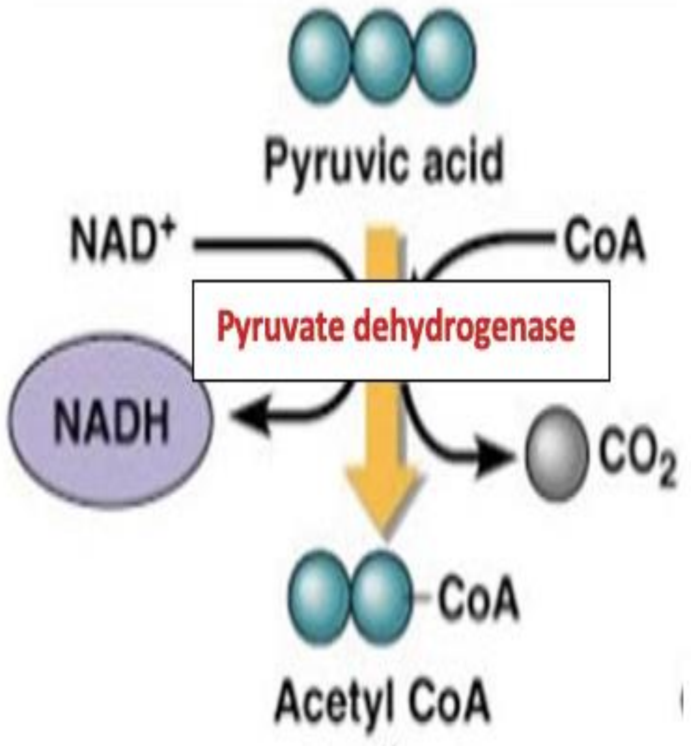
✓**Site : Mitochondria of all cells except RBCs**

✓**Requires: Pyruvate dehydrogenase** enzyme

- Multi-enzyme complex with 5 coenzymes:
- *NAD, FAD, CoA-SH, TPP, and lipoic acid*

✓ **Products**: 1 Pyruvate gives → 1 Acetyl CoA +1 CO_2 +1 NADH+H

- **1 NADH+H** then enter to ETC → 3 ATP
- **Acetyl CoA** then enter **Krebs cycle**.



MCQs

Which one of the following glycolytic enzymes is inhibited by fluoride ?

a) Hexokinase
b) Pyruvate kinase
c) Aldolase
d) Phosphofructokinase-1
e) Enolase

MCQs

What is the major role of glycolysis?

a) Synthesizes glucose
b) Produces FADH2
c) Synthesizes glycogen
d) Generates energy
e) Breakdowns glycogen

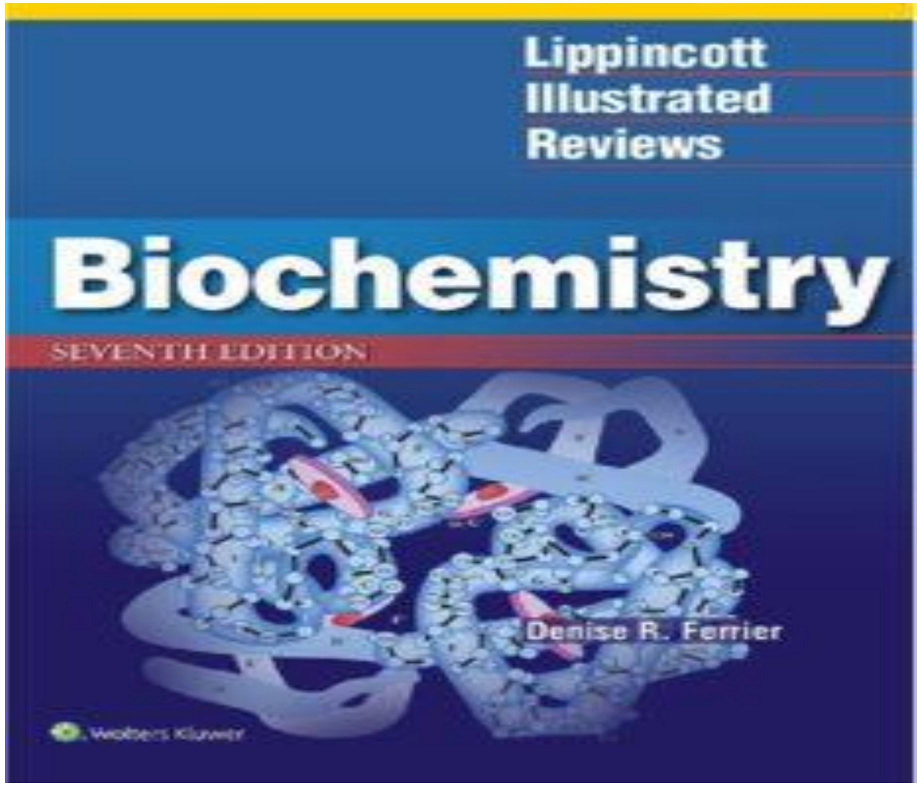
MCQs

The end product of glycolysis (pyruvate) enter TCA as :

a) Acetyl CoA
b) Pyruvate
c) NADH
d) Glucose
e) Oxalacetate


Life
isn't about
finding yourself.
...
Life
is about
creating yourself.

References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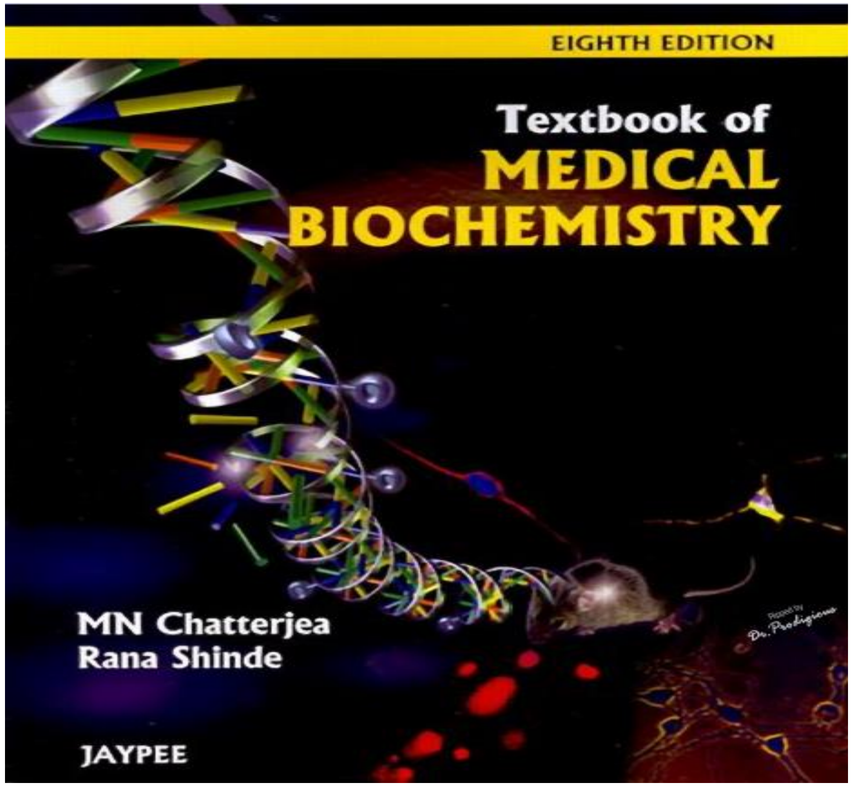
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