BIOCHEMISTRY

Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway

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LEHNINGER
PRINCIPLES OF BIOCHEMISTRY

Fifth Edition

CHAPTER 14
Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway

MAJOR PATHWAYS OF GLUCOSE UTILIZATION

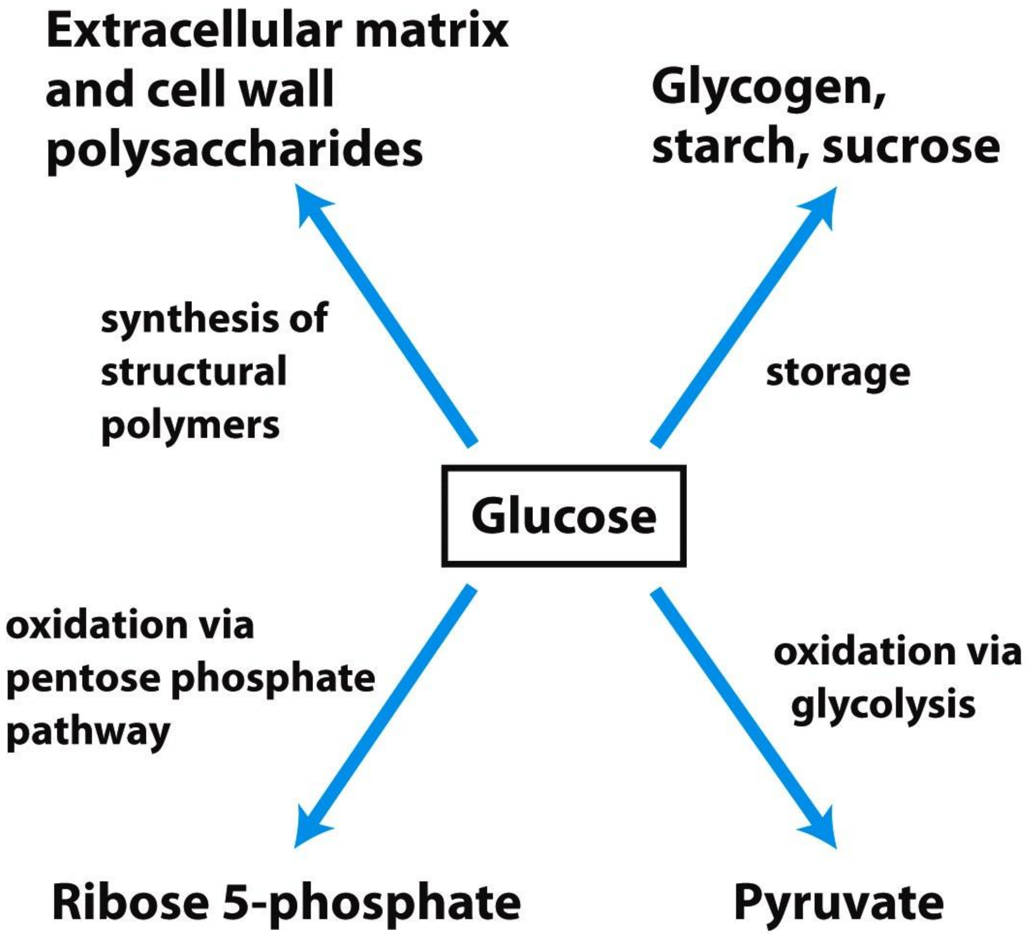

Figure 14-1
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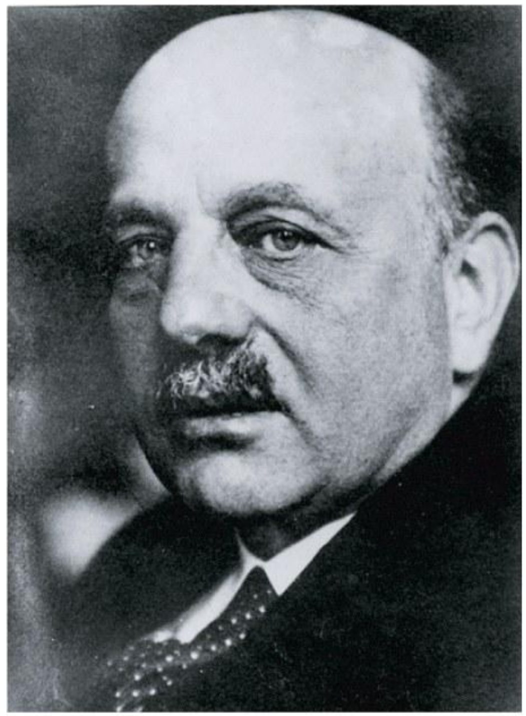
Although not the only possible fates for glucose, these four pathways are the most significant in terms of the amount of glucose that flows through them in most cells

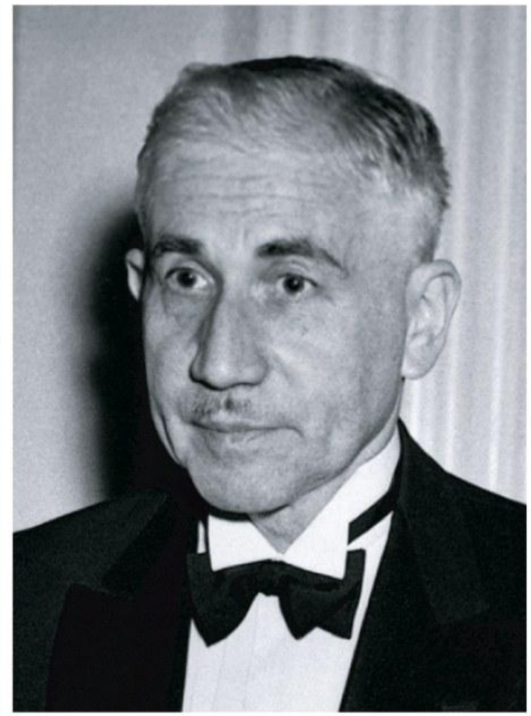
GLYCOLYSIS

In glycolysis (from the Greek glykys, "sweet" or "sugar," and lysis, "splitting"), a molecule of glucose is degraded in a series of enzyme-catalyzed reactions to yield two molecules of the three-carbon compound pyruvate.

Hans von Euler-Chelpin
1873–1964



Gustav Embden
1874–1933



Otto Meyerhof
1884–1951

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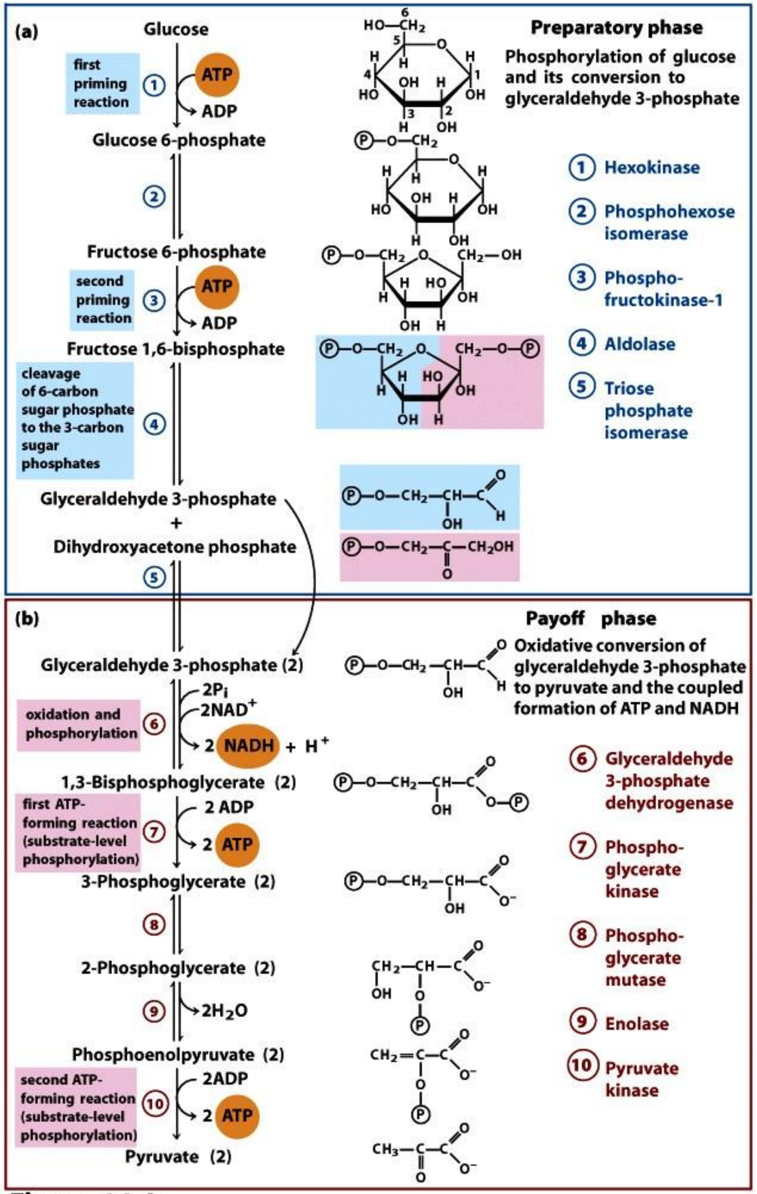

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Glycolysis Has Two Phases

For each molecule of glucose that passes through the preparatory phase (a), two molecules of glyceraldehyde 3-phosphate are formed; both pass through the payoffphase (b). Pyruvate is the end product of the second phase of glycolysis. For each glucose molecule, two ATP are consumed in the preparatory phase and four ATP are produced in the payoff phase, giving a net yield of two ATP per molecule of glucose converted to pyruvate.

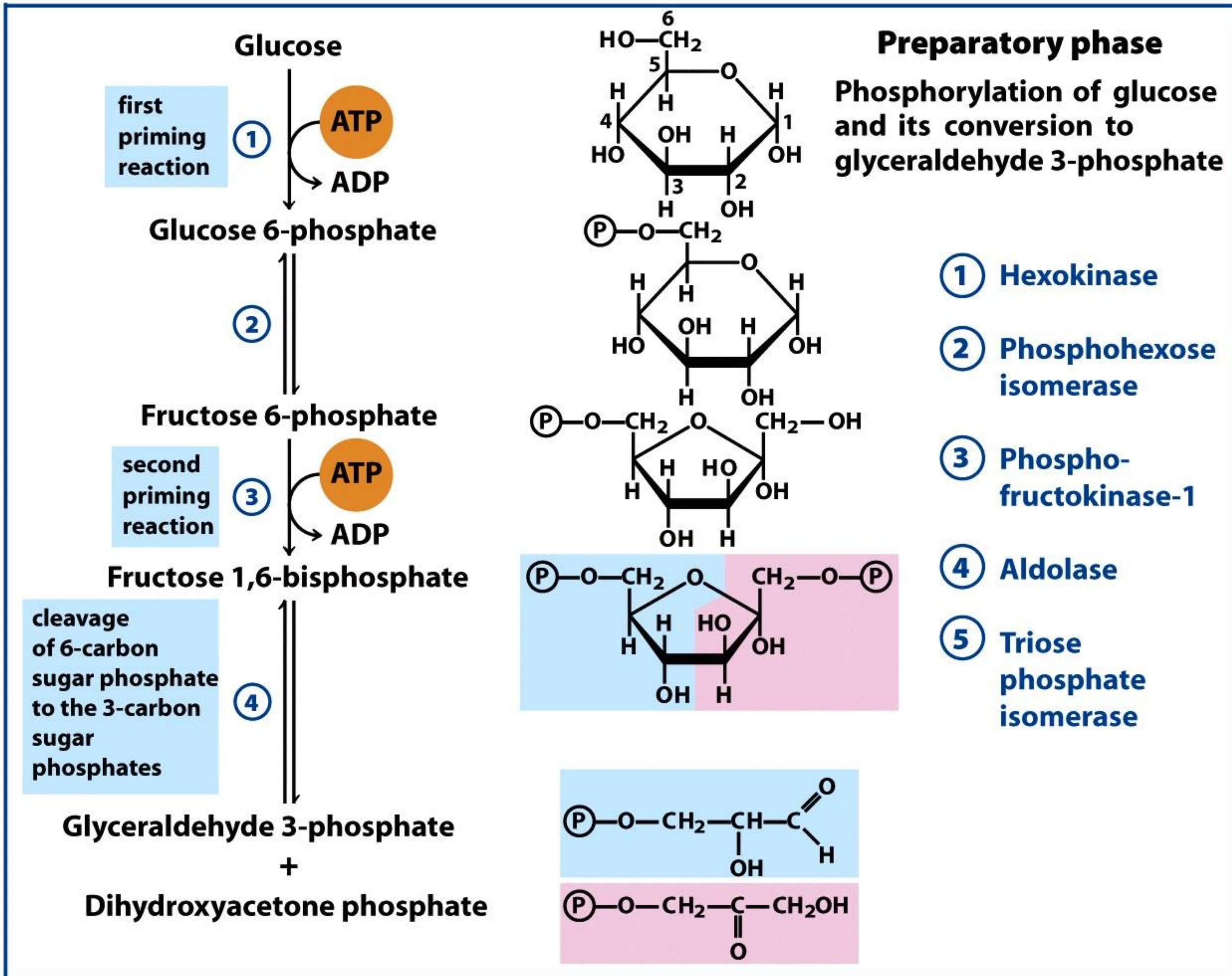

Figure 14-2a

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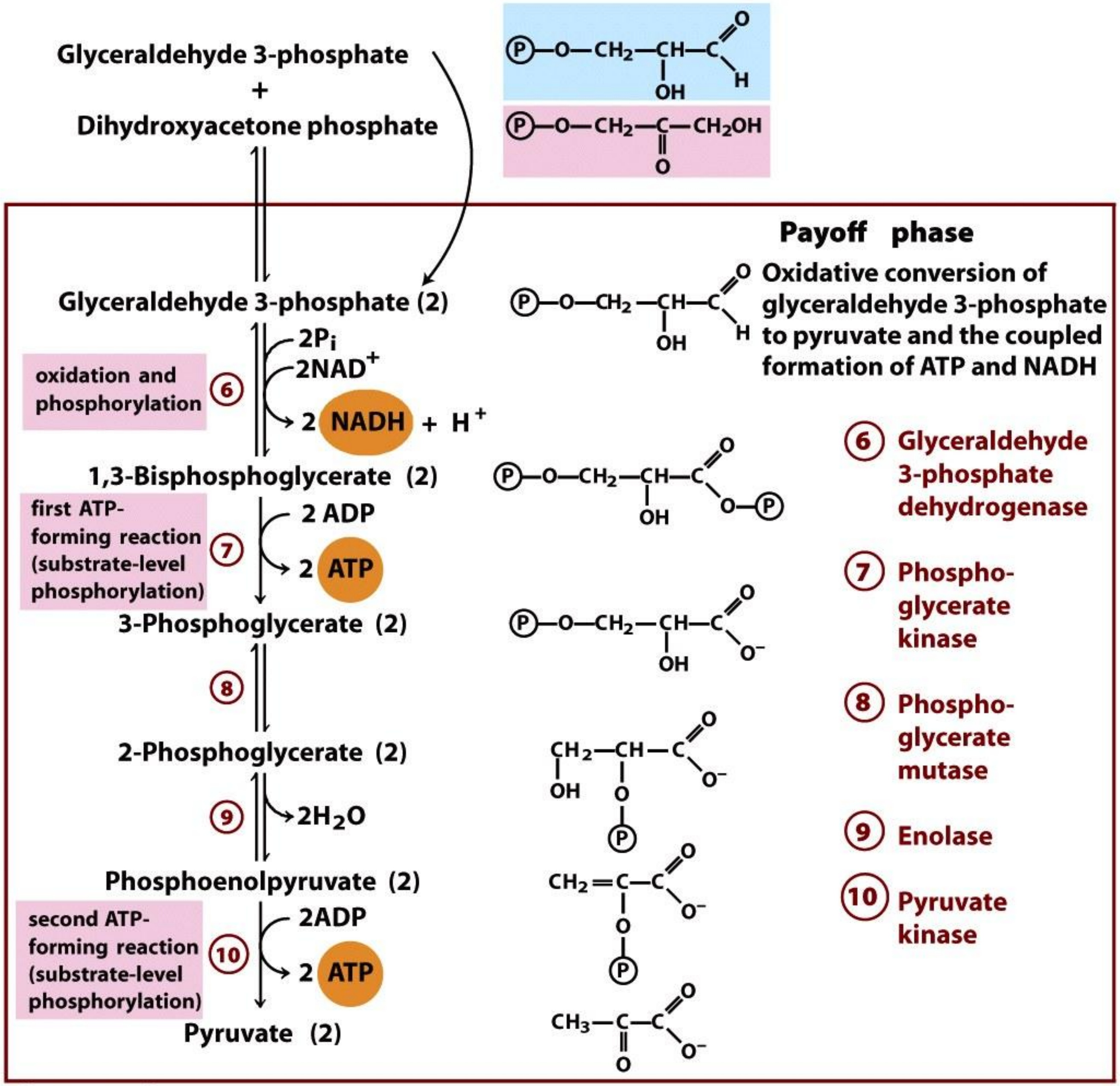

Figure 14-2b

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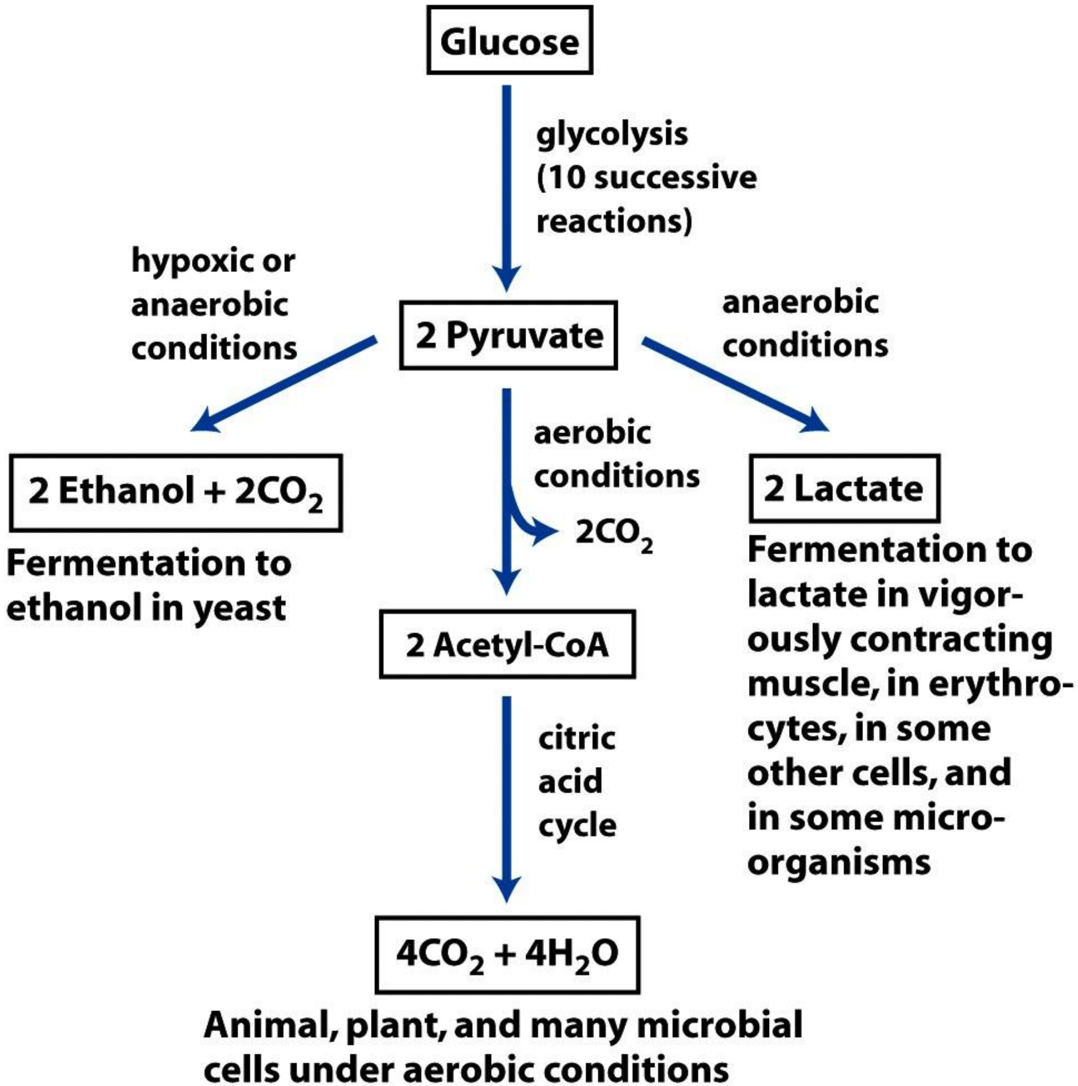
THREE POSSIBLE CATABOLIC FATES OF THE PYRUVATE FORMED IN GLYCOLYSIS



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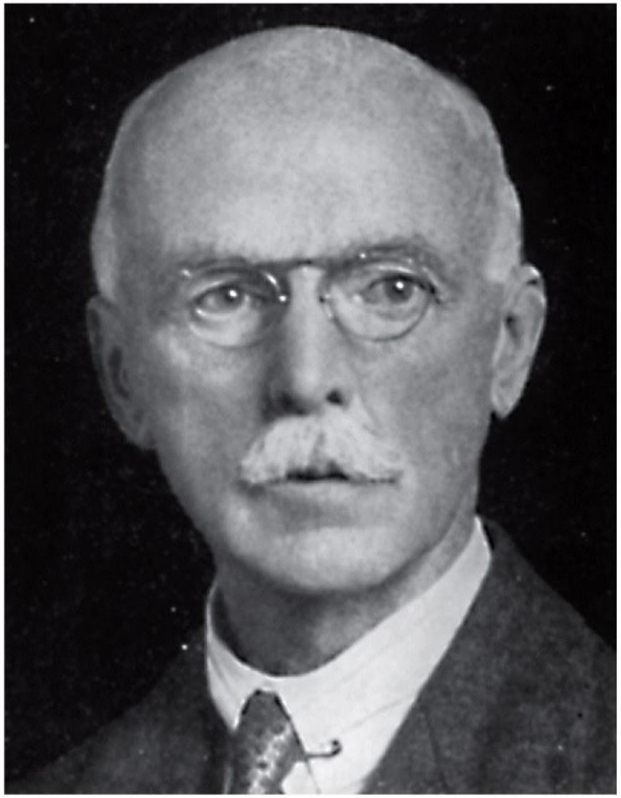
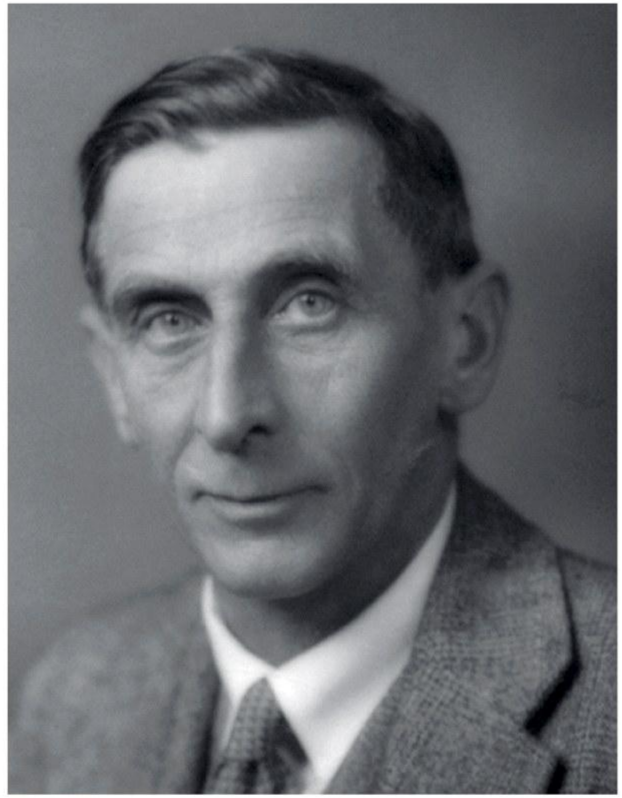
THE PREPARATORY PHASE OF GLYCOLYSIS REQUIRES ATP



Arthur Harden
1865–1940



William Young
1878–1942

In 1906, Arthur Harden and William Young tested their hypothesis that inhibitors of proteolytic enzymes would stabilize the glucose-fermenting enzymes in yeast extract to predicted stimulation of glucose metabolism.

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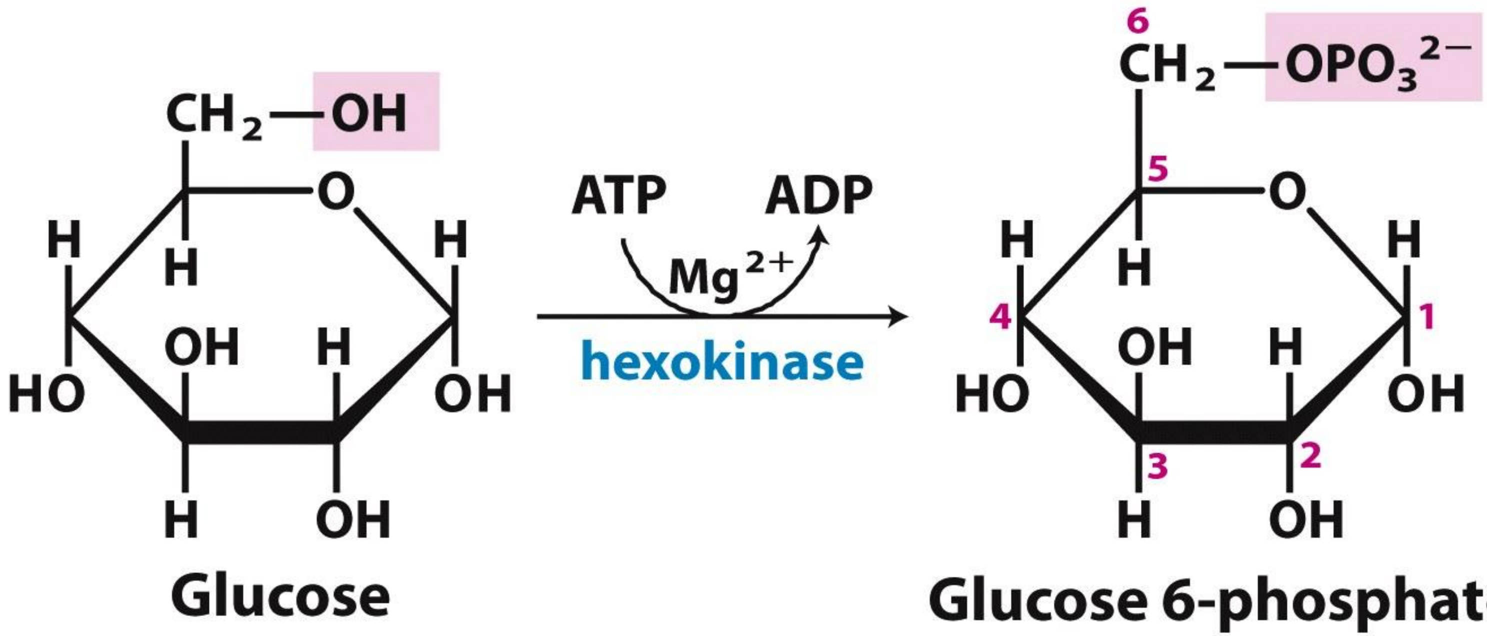
1. PHOSPHORYLATION OF GLUCOSE

In the first step of glycolysis, glucose is activated for subsequent reactions by its phosphorylation at C-6 to yield glucose 6-phosphate, with ATP as the phosphoryl donor



$$\Delta G'^{\circ} = -16.7 \text{ kJ/mol}$$

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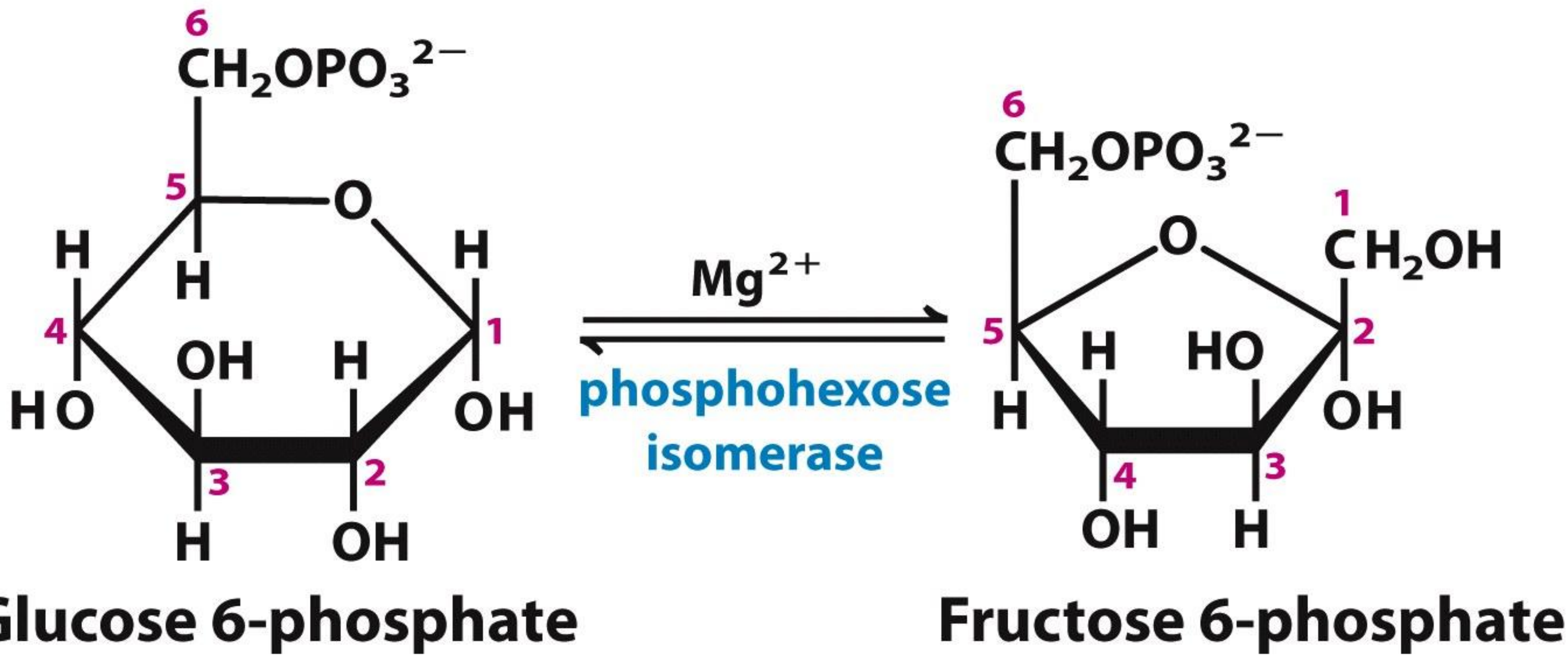
2. CONVERSION OF GLUCOSE 6-PHOSPHATE TO FRUCTOSE 6-PHOSPHATE



$\Delta G'^{\circ} = 1.7$ kJ/mol

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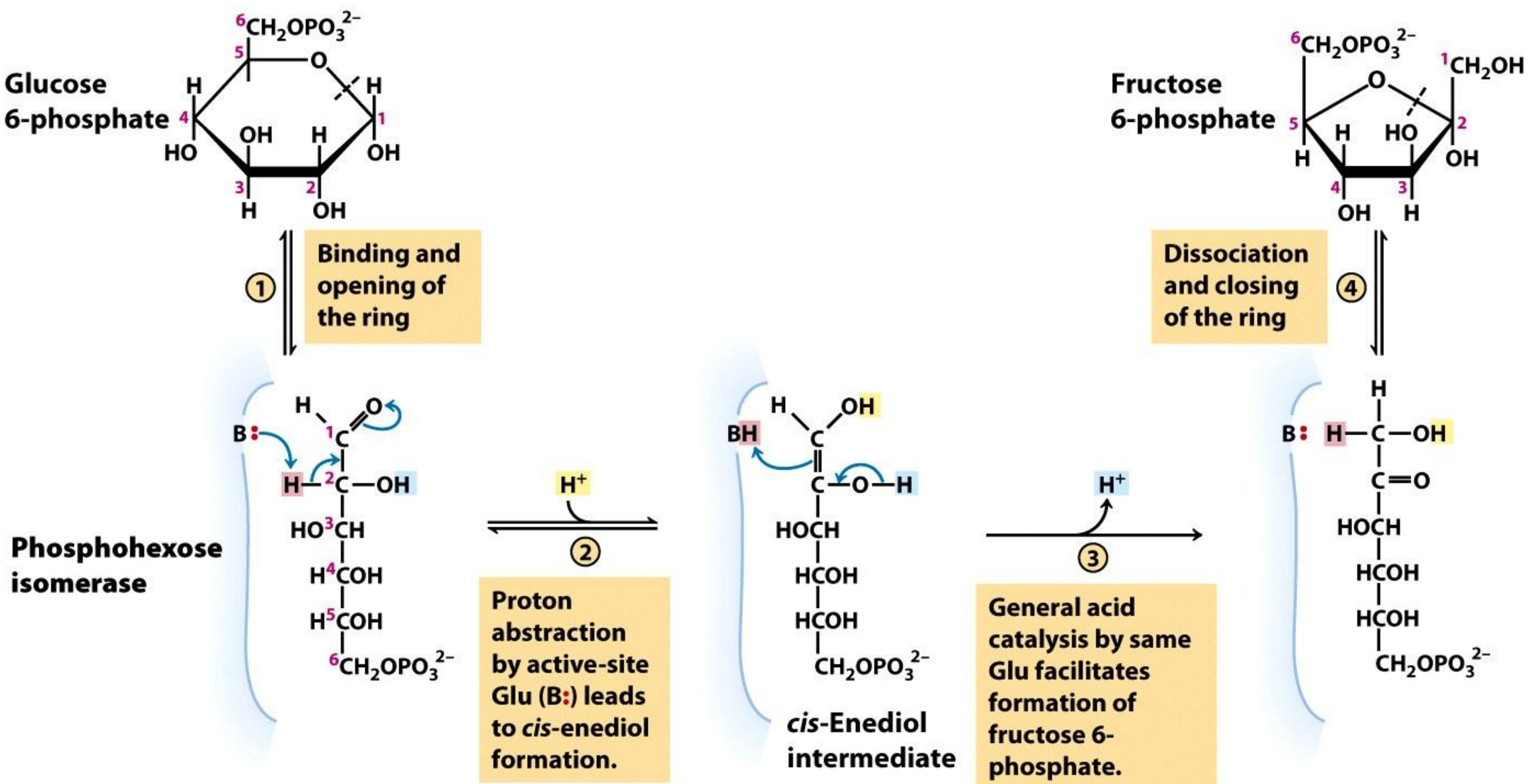
THE PHOSPHOHEXOSE ISOMERASE REACTION



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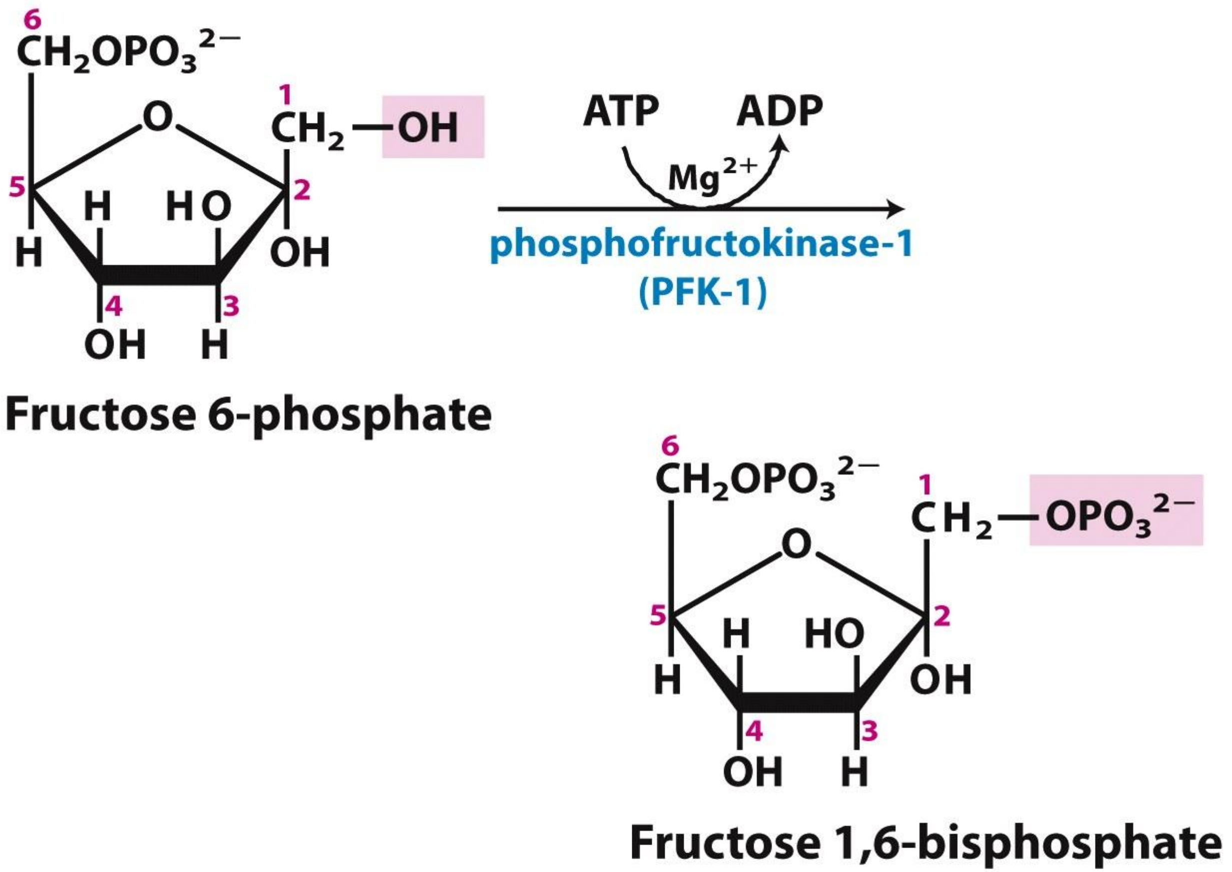
3. PHOSPHORYLATION OF FRUCTOSE 6-PHOSPHATE TO FRUCTOSE 1,6-BISPHOSPHATE



$$\Delta G'^{\circ} = -14.2 \text{ kJ/mol}$$

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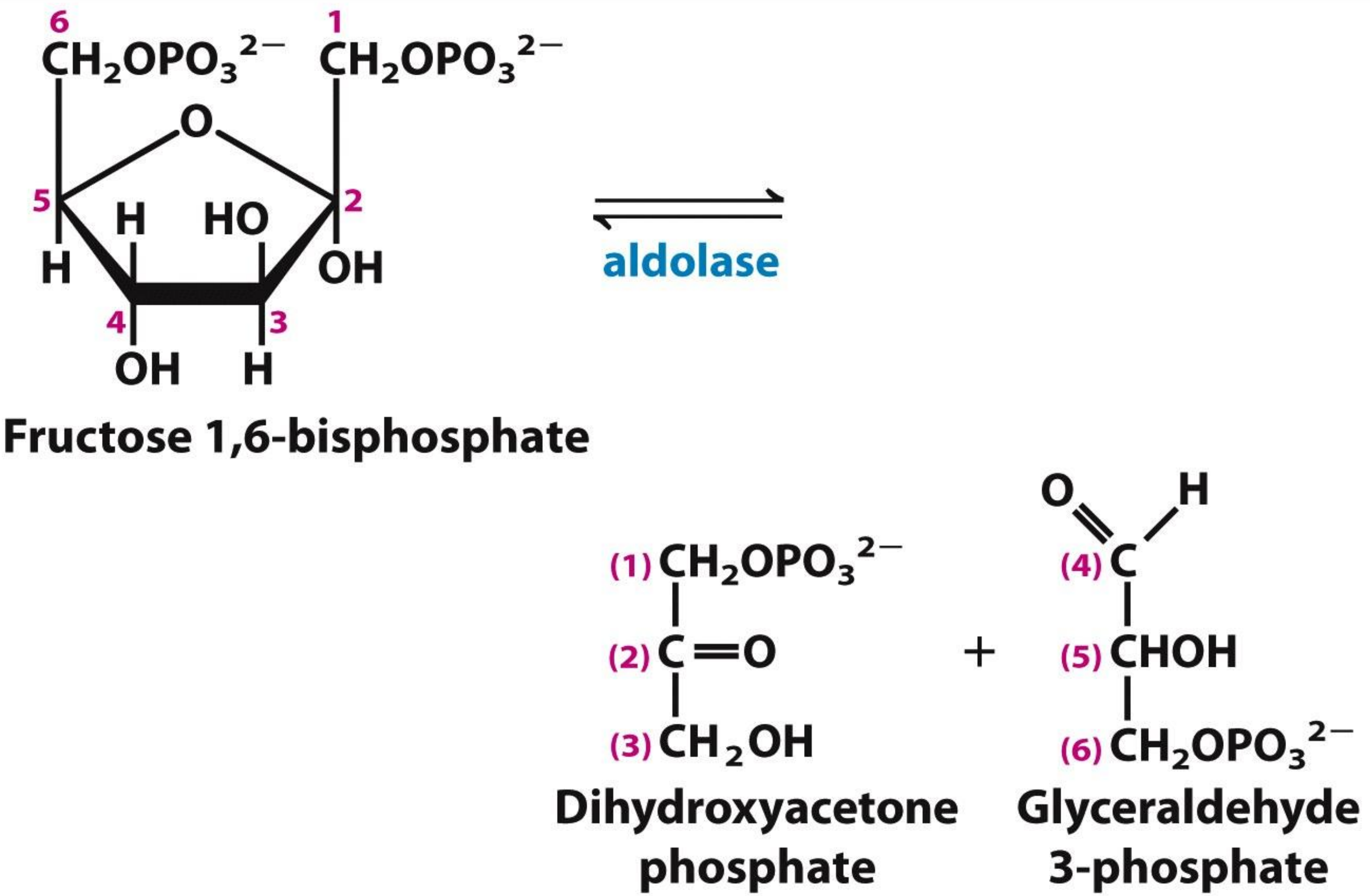
4. CLEAVAGE OF FRUCTOSE 1,6-BISPHOSPHATE



$$\Delta G'^{\circ} = 23.8\ \text{kJ/mol}$$

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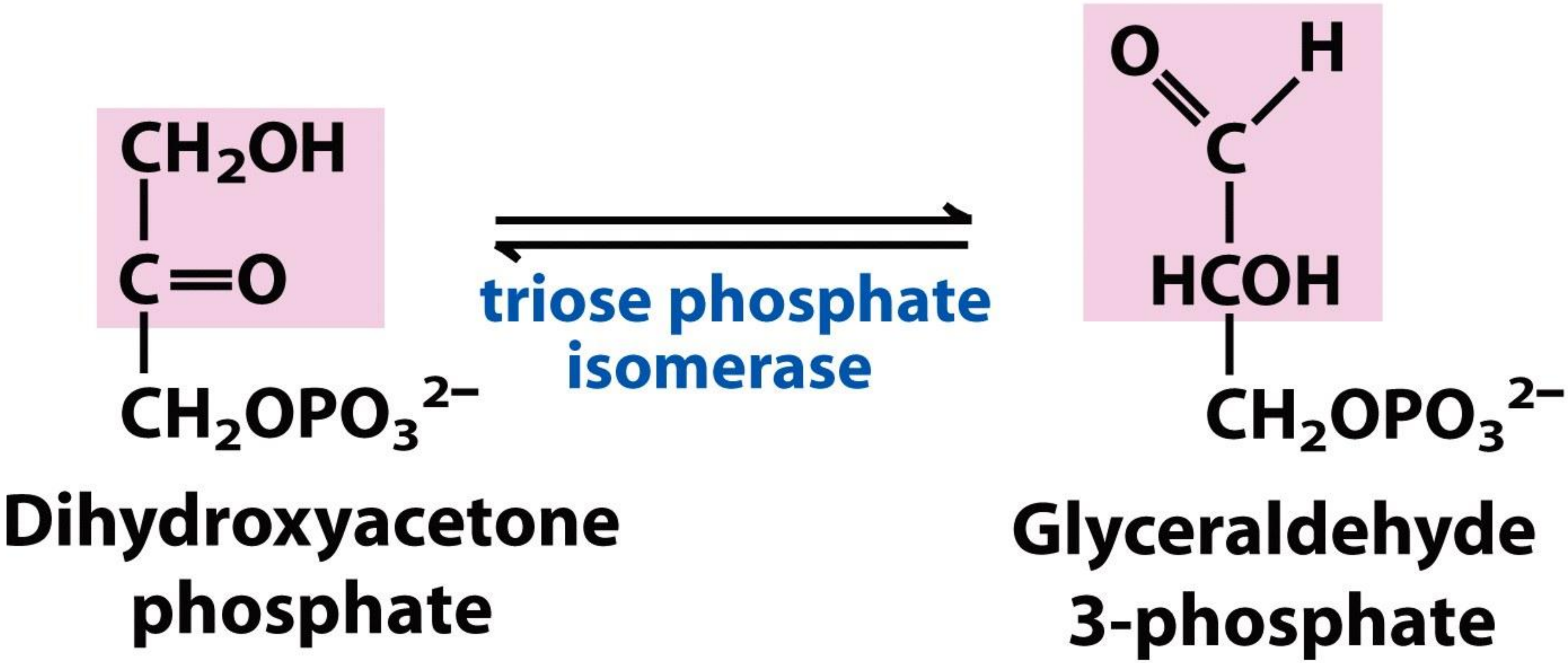
5. INTERCONVERSION OF THE TRIOSE PHOSPHATES



$\Delta G'^{\circ} = 7.5\ \text{kJ/mol}$

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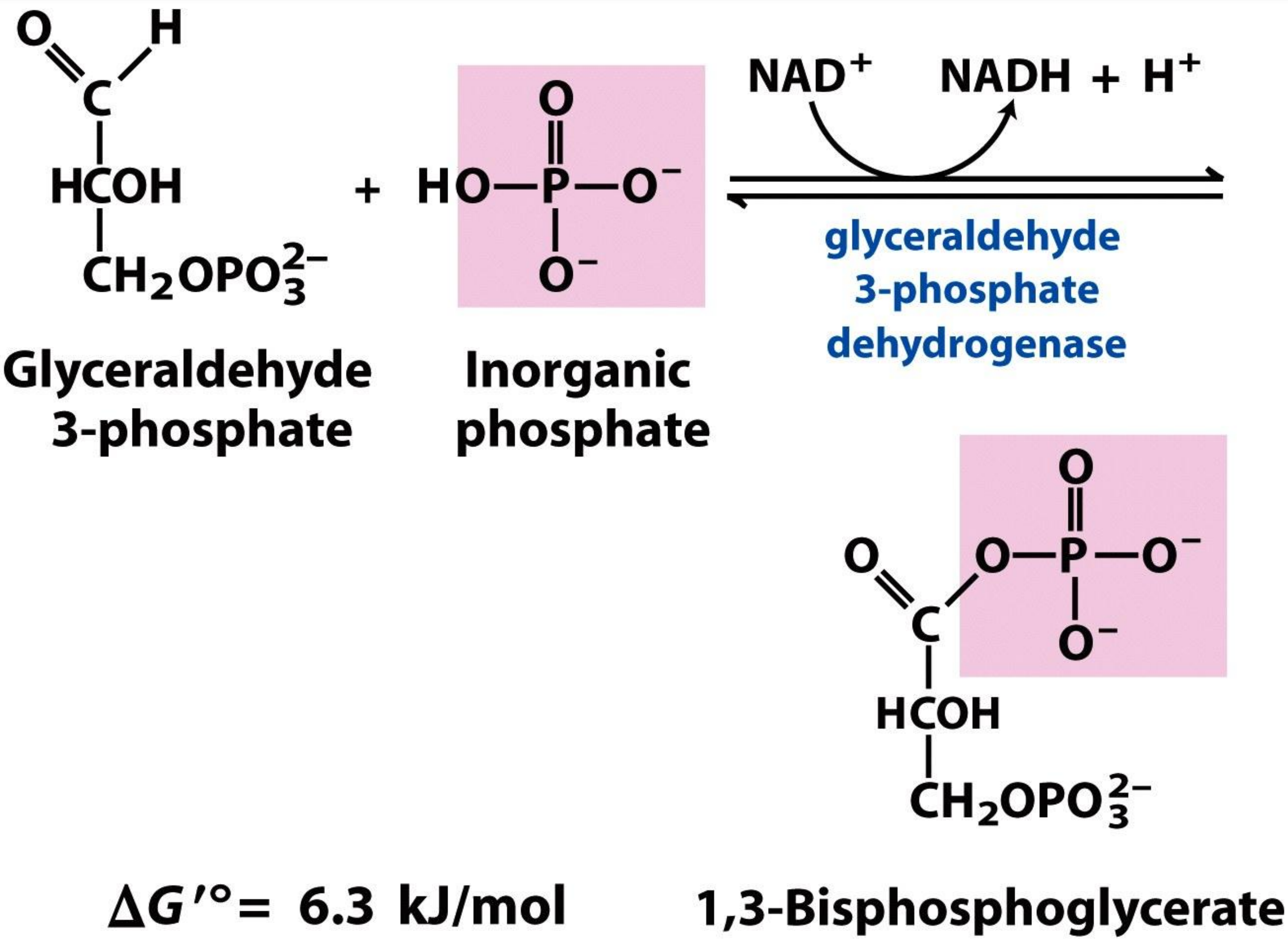
6. OXIDATION OF GLYCERALDEHYDE 3-PHOSPHATE TO 1,3-BISPHOSPHOGLYCERATE



$\Delta G'° = 6.3$ kJ/mol

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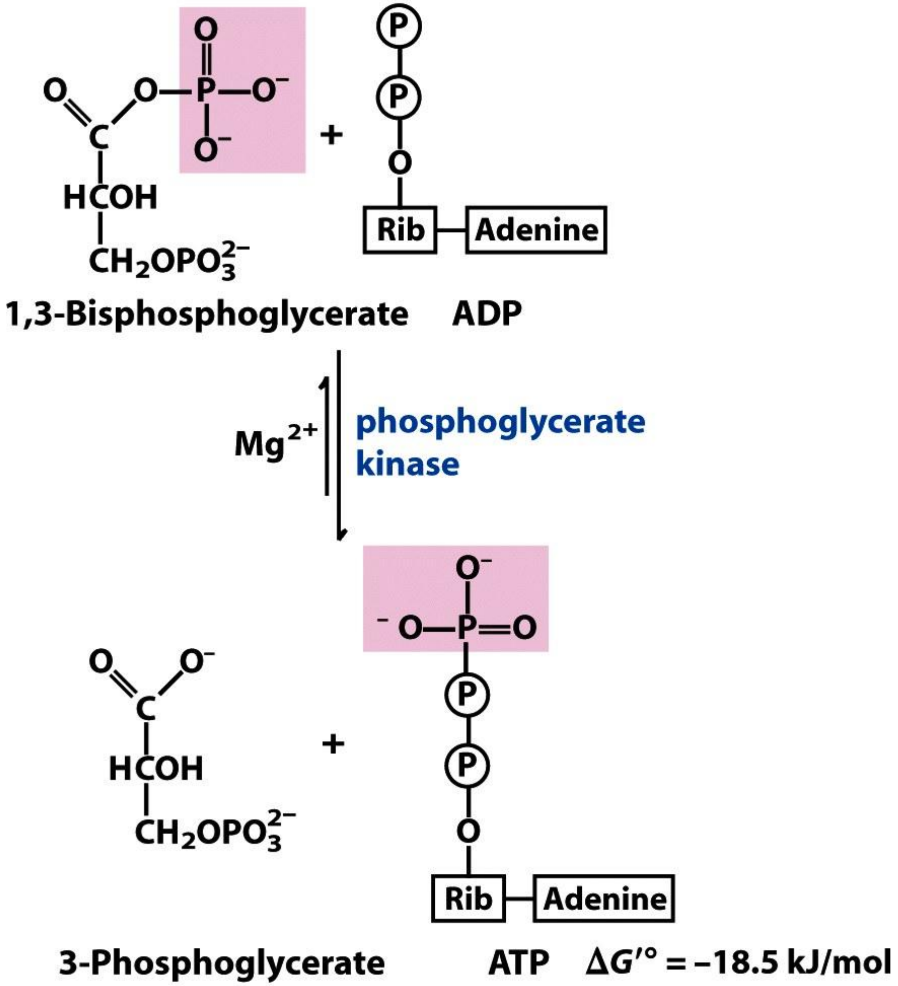
7. PHOSPHORYL TRANSFER FROM 1,3-BISPHOSPHOGLYCERATE TO ADP



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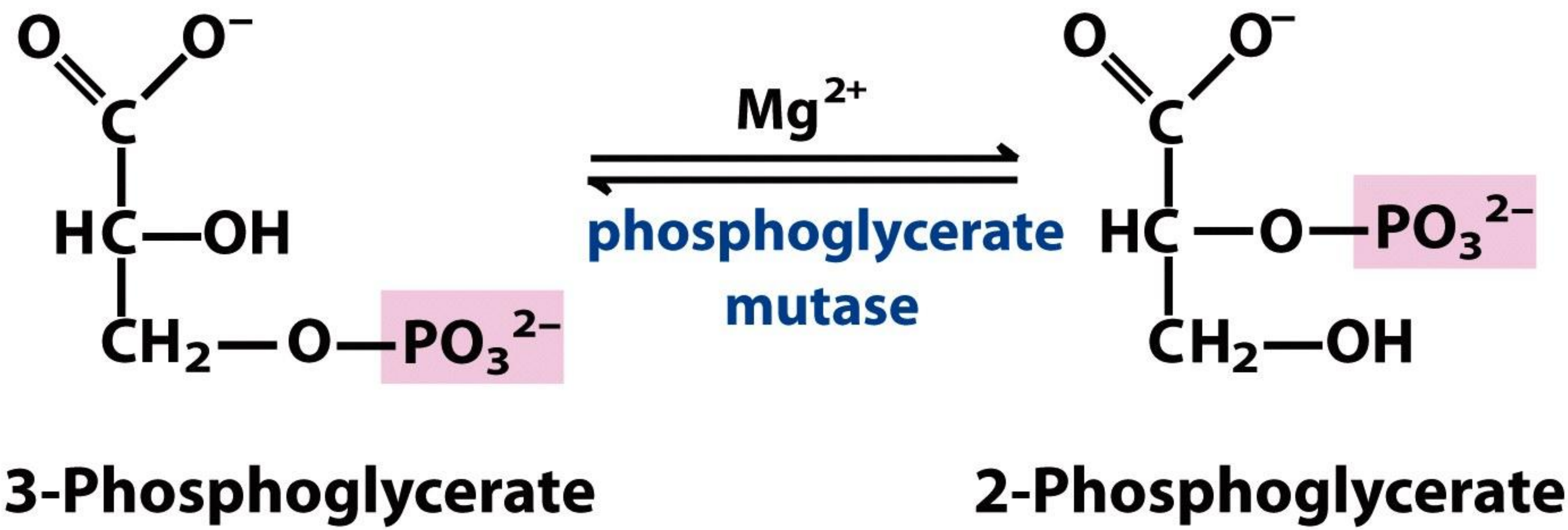
8. CONVERSION OF 3-PHOSPHOGLYCERATE TO 2-PHOSPHOGLYCERATE



$\Delta G'^{\circ} = 4.4$ kJ/mol

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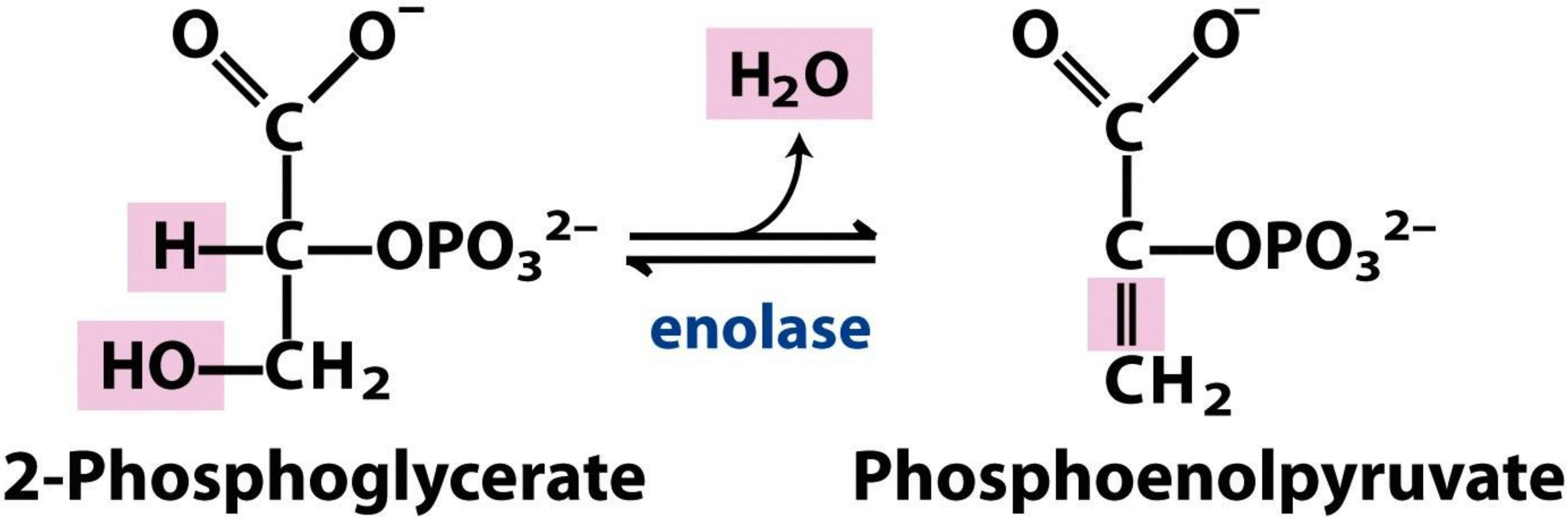
9. DEHYDRATION OF 2-PHOSPHOGLYCERATE TO PHOSPHOENOLPYRUVATE



$\Delta G'^{\circ} = 7.5$ kJ/mol

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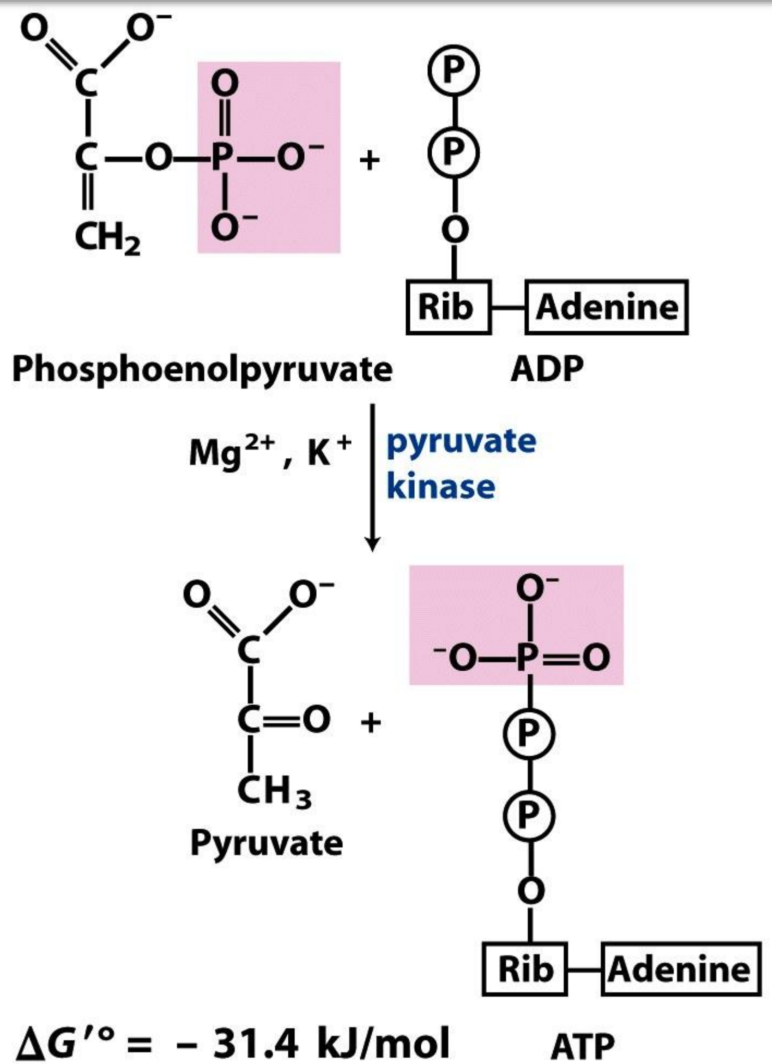
10. TRANSFER OF THE PHOSPHORYL GROUP FROM PHOSPHOENOLPYRUVATE TO ADP



$\Delta G'^{\circ} = -31.4$ kJ/mol

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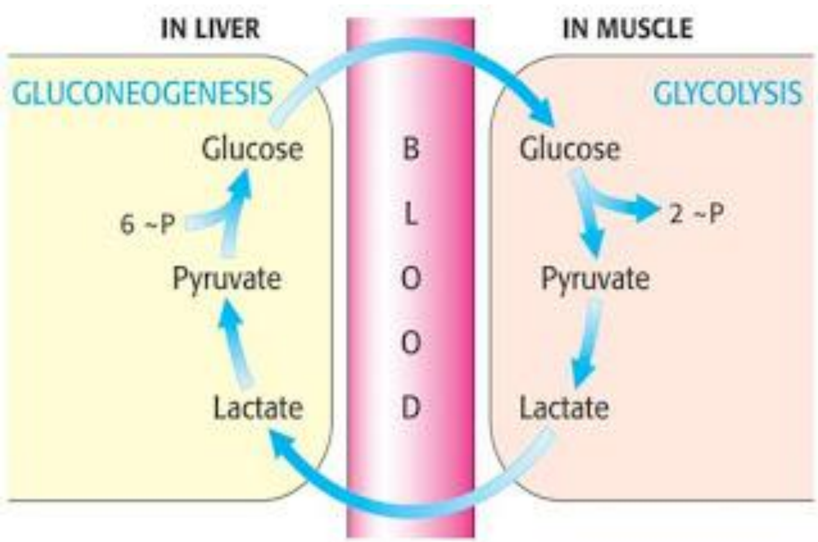
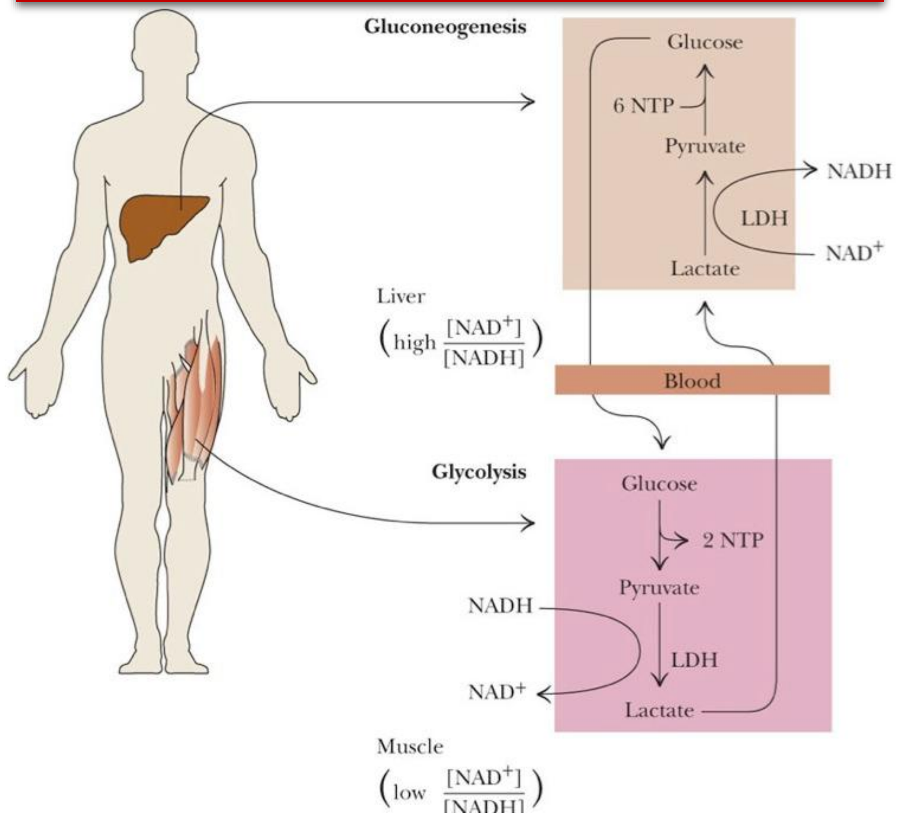
TABLE 14–2	Free-Energy Changes of Glycolytic Reactions in Erythrocytes	
Glycolytic reaction step	**$\Delta G'^{\circ}$ (kJ/mol)**	**ΔG (kJ/mol)**
(1) Glucose + ATP ⟶ glucose 6-phosphate + ADP	−16.7	−33.4
(2) Glucose 6-phosphate ⇌ fructose 6-phosphate	1.7	0 to 25
(3) Fructose 6-phosphate + ATP ⟶ fructose 1,6-bisphosphate + ADP	−14.2	−22.2
(4) Fructose 1,6-bisphosphate ⇌ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate	23.8	−6 to 0
(5) Dihydroxyacetone phosphate ⇌ glyceraldehyde 3-phosphate	7.5	0 to 4
(6) Glyceraldehyde 3-phosphate + P_i + NAD^+ ⇌ 1,3-bisphosphoglycerate + NADH + H^+	6.3	−2 to 2
(7) 1,3-Bisphosphoglycerate + ADP ⇌ 3-phosphoglycerate + ATP	−18.8	0 to 2
(8) 3-Phosphoglycerate ⇌ 2-phosphoglycerate	4.4	0 to 0.8
(9) 2-Phosphoglycerate ⇌ phosphoenolpyruvate + H_2O	7.5	0 to 3.3
(10) Phosphoenolpyruvate + ADP ⟶ pyruvate + ATP	−31.4	−16.7

ΔG is the standard free-energy change, as defined in Chapter 13 (pp. 491–492). ΔG is the free-energy change calculated from the actual concentrations of glycolytic intermediates present under physiological conditions in erythrocytes, at pH 7. The glycolytic reactions bypassed in gluconeogenesis are shown in red.

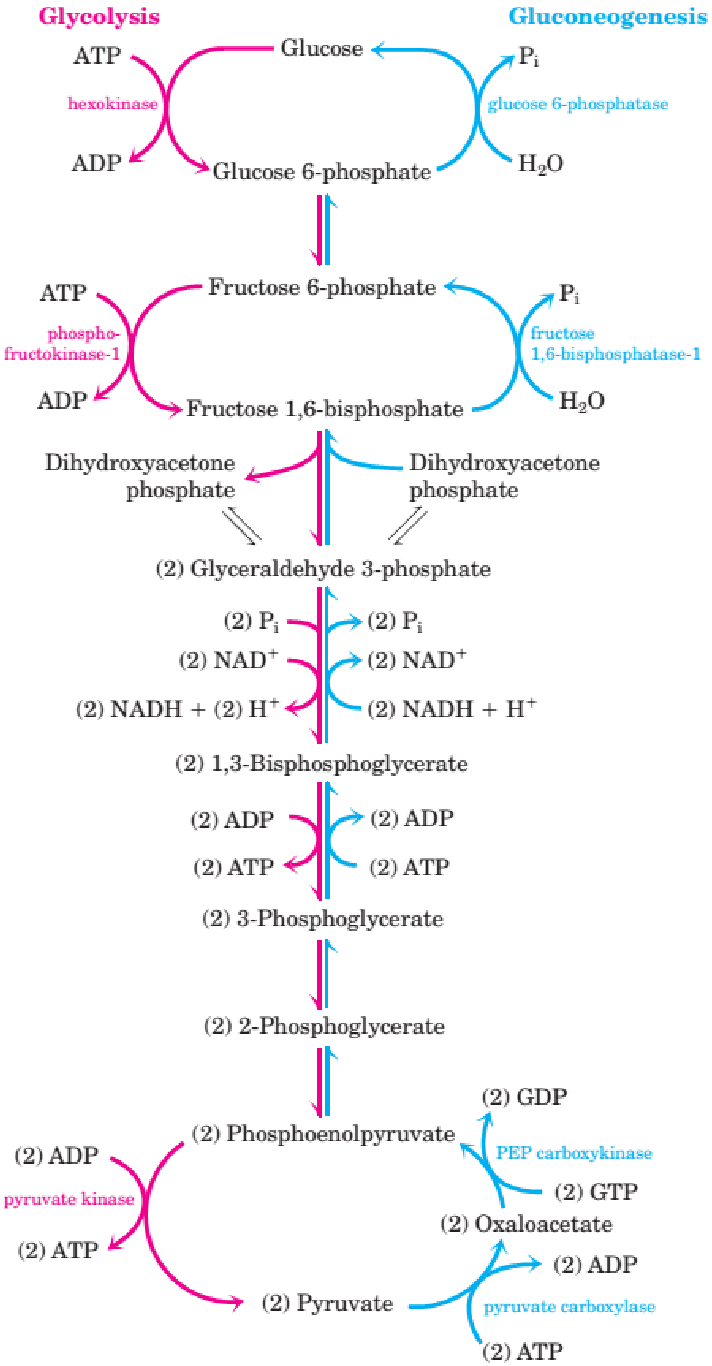
GLUCONEOGENESIS





For these times, organisms need a method for synthesizing glucose from noncarbohydrate precursors. This is accomplished by a pathway called **gluconeogenesis** "new formation of sugar", which converts pyruvate and related three- and four-carbon compounds to glucose.

OPPOSING PATHWAYS OF GLYCOLYSIS AND GLUCONEOGENESIS IN RAT LIVER



The reactions of glycolysis are on the left side, in red; the opposing pathway of gluconeogenesis is on the right, in blue.

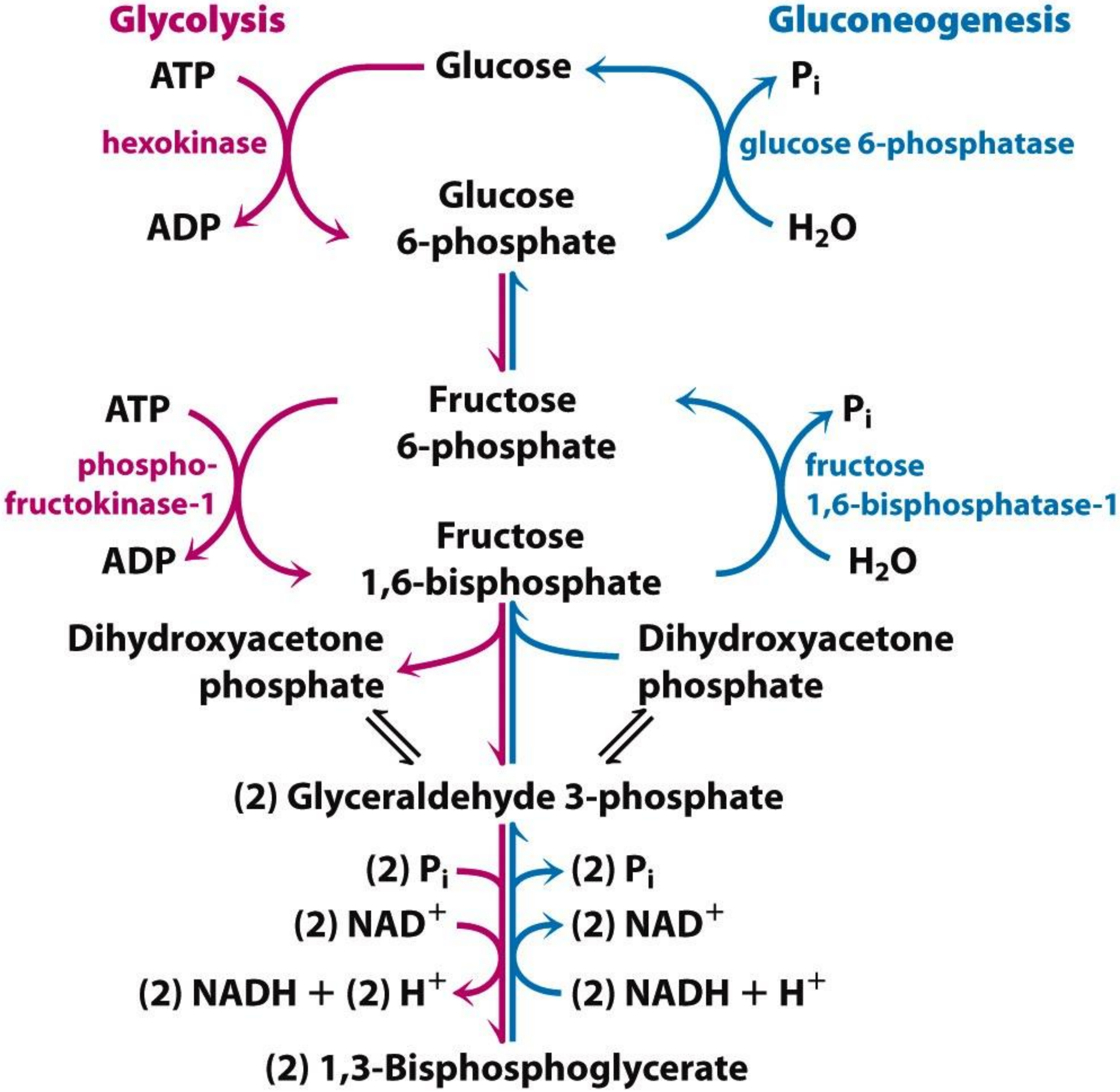


Figure 14-16 part 1

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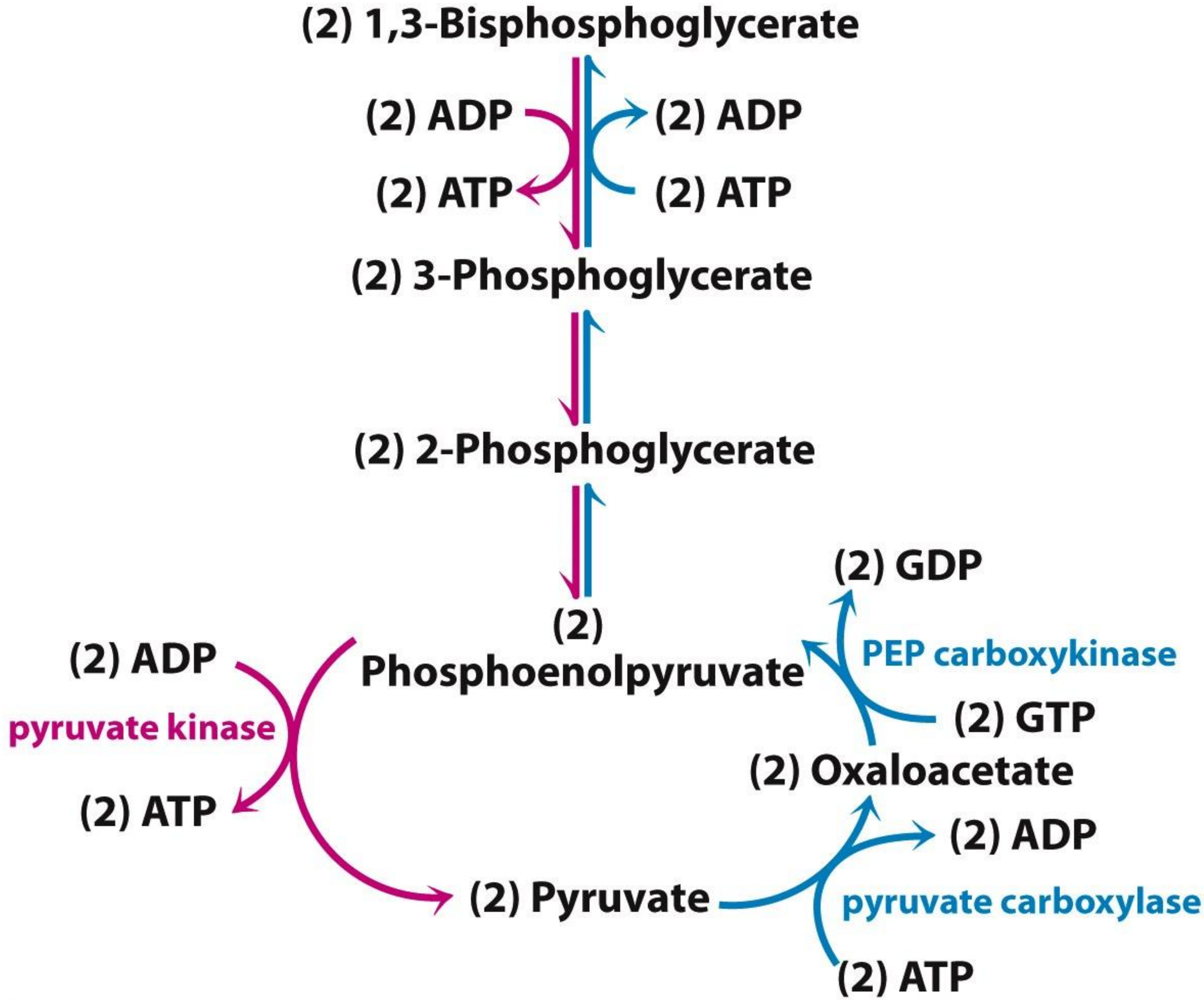

Figure 14-16 part 2
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GENERAL SCHEME OF THE PENTOSE PHOSPHATE PATHWAY

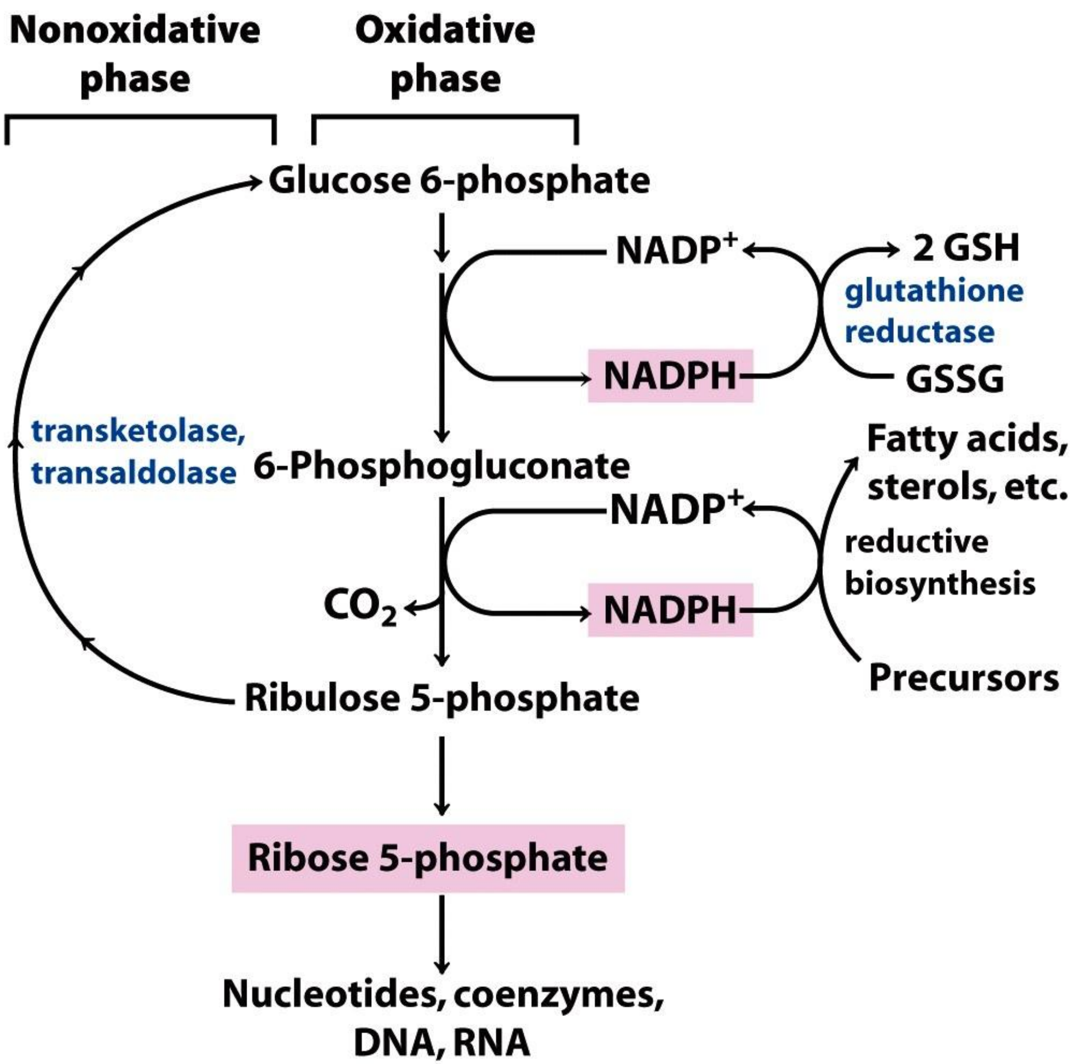

Figure 14-20
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- ❑ NADPH formed in the oxidative phase is used to reduce glutathione, GSSG and to support reductive biosynthesis.

- ❑ The other product of the oxidative phase is ribose 5-phosphate, which serves as a precursor for nucleotides, coenzymes, and nucleic acids.

THANK YOU

YUSRON SUGIARTO