CARBOHYDRATE METABOLISM
Glycolysis

- D-glucose - a major fuel, occupies a central position in metabolism, relatively rich in potential energy

(complete oxidation to carbon dioxide and water proceeds with a standard free energy of –2,840 kJ/mol)

- When the cell's energy demands suddenly increase, glucose can be released quickly from intracellular storage polymers

- Glucose - a precursor, provides metabolic intermediates, the necessary starting material for biosynthetic reactions

- E. Coli can obtain from glucose the carbon skeletons for amino acids, nucleotides, coenzymes, fatty acids

In higher plants and animals, glucose has four major fates

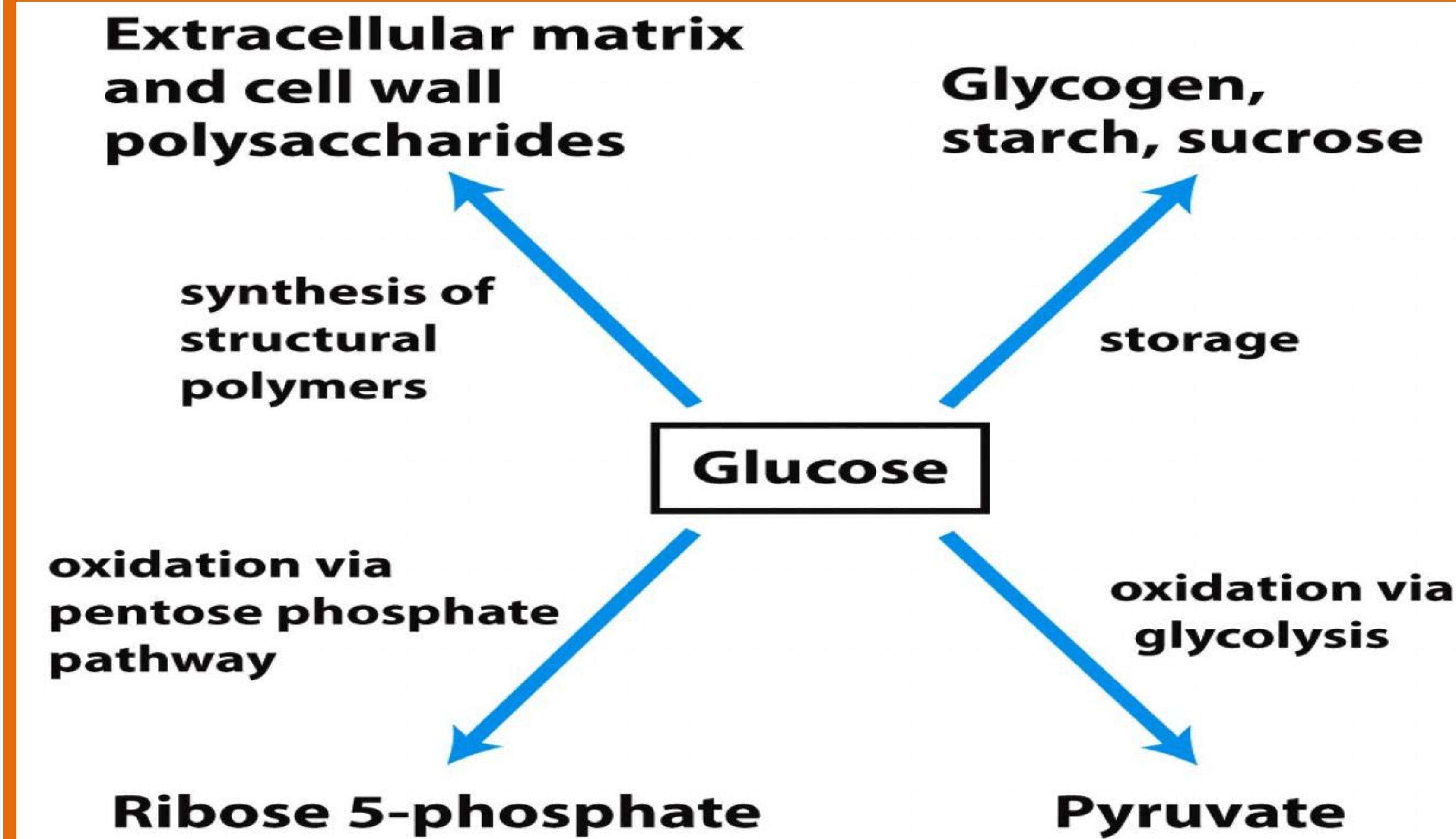

Figure 14-1
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- **Glycolysis** (from the Greek *glykys*, meaning "sweet" and *lysis*, meaning "splitting")

- Glycolysis - the first metabolic pathway to be elucidated and is probably the best understood

- Described by Gustav Embden, Otto Meyerhof and Jacob Parnas

- Known as **Embden-Meyerhof-Parnas** pathway (**EMP**)

- Almost universal catabolic pathway of glucose catabolism

- Reactions of Glycolysis take place in the **cytosol of cells**
- **Unique**; it can utilize O_2 if available and can also work in the absence of O_2

- Glycolytic sequence of reactions **differ** from one specie to another only in:

1. how the rate is regulated
2. subsequent metabolic fate of pyruvate formed

- Breakdown of the (6C) 1 glucose into 2 molecules of the (3C) pyruvate occurs in **10 steps** (reactions)

- **First 5 reactions – Phase 1** (**Preparatory phase/energy investment phase)**

- **Last 5 reactions – Phase 2** (**Payoff Phase/energy production phase/oxidative phase)**

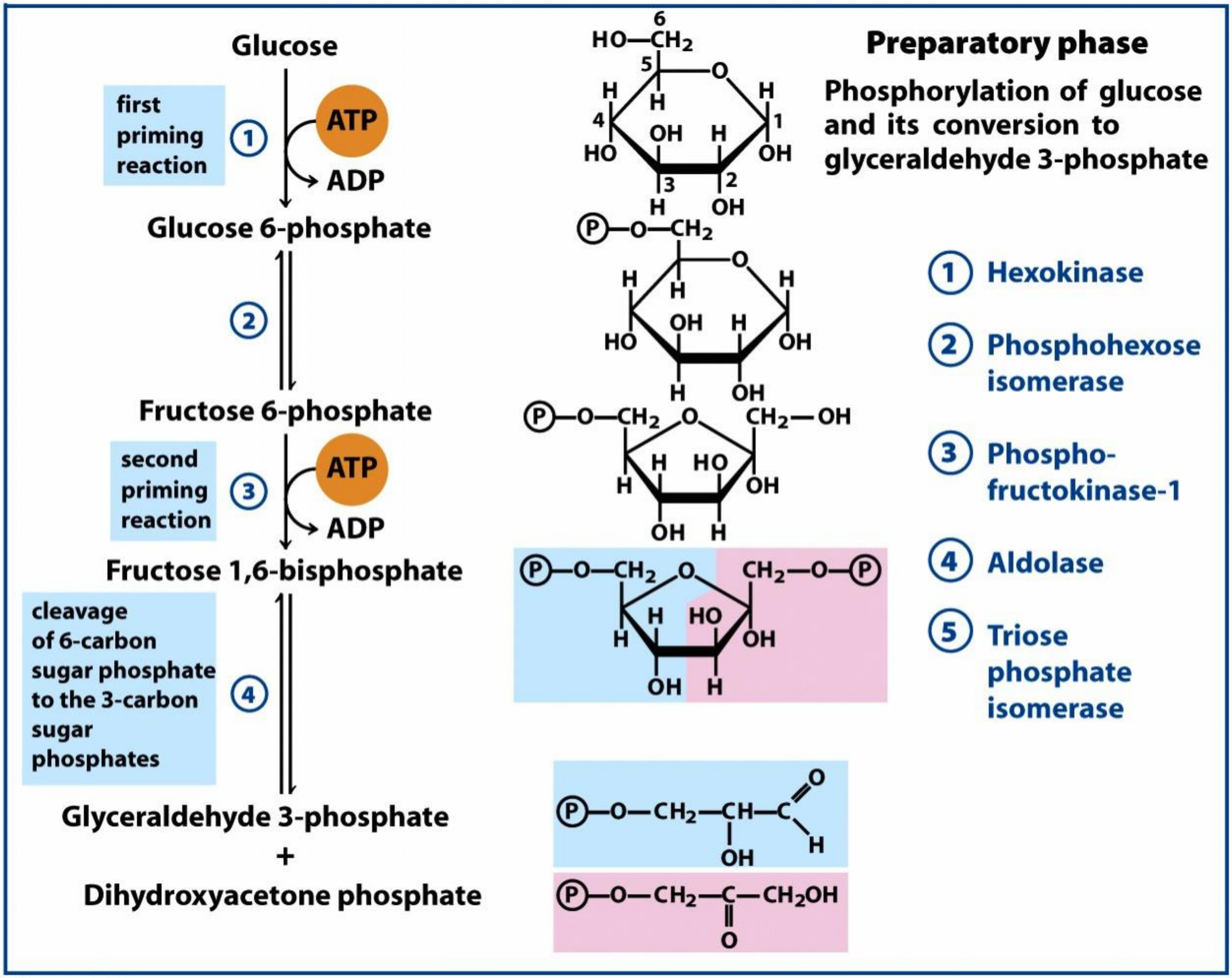

Figure 14-2a

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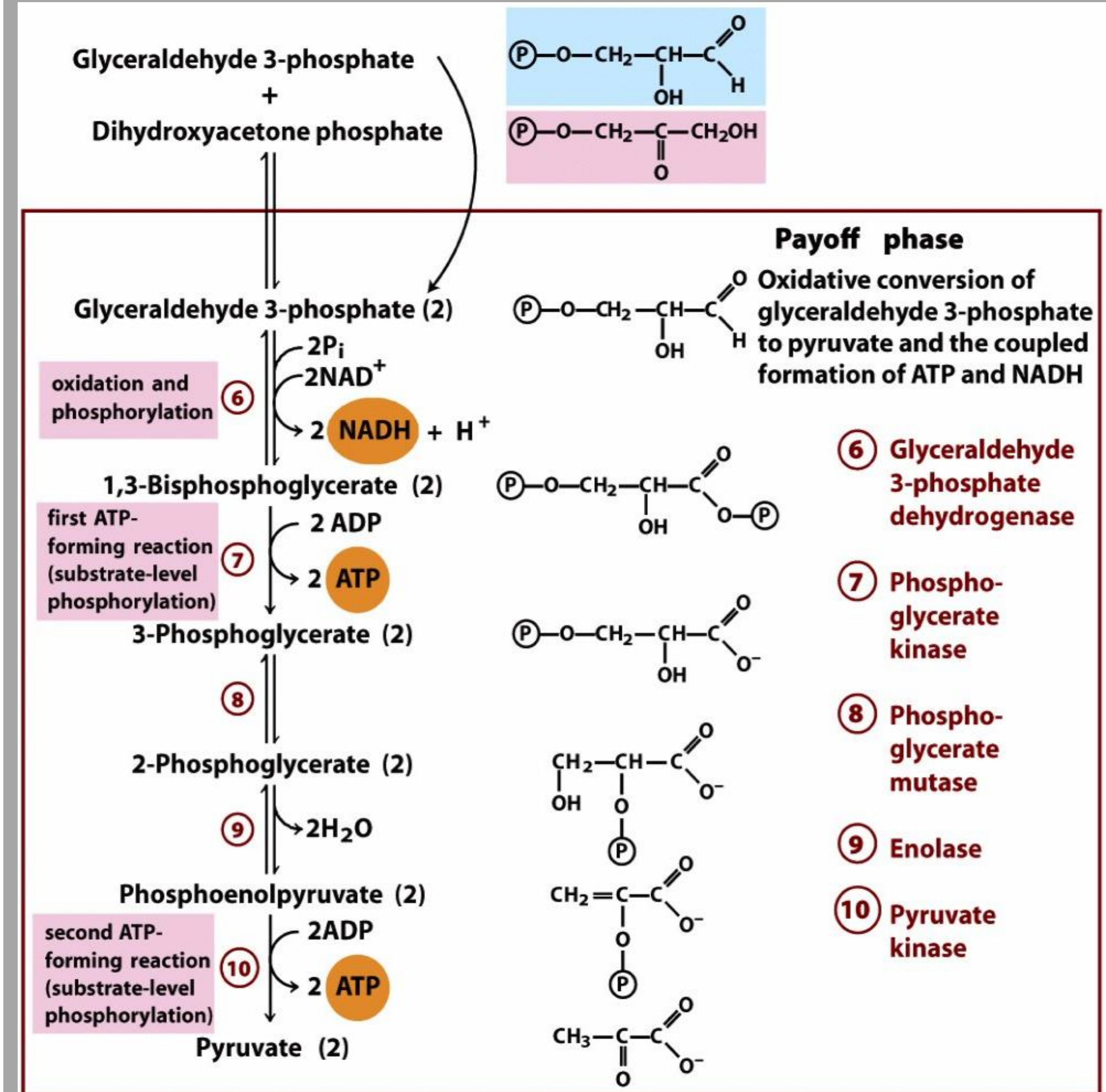

Figure 14-2b

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For each molecule of glucose that passes through preparatory phase, 2 molecules of glyceraldehyde-3-phosphate are formed; both pass through the payoff phase.

Pyruvate is the end product of second phase of glycolysis.

For each glucose molecule, 2 ATP are consumed in the preparatory phase & 4 ATP are produced in the payoff phase, giving a net yield of 2 ATP per molecule of glucose converted to pyruvate.

3 Important Chemical Transformations

1. Degradation of C skeleton of glucose to yield pyruvate
2. Phosphorylation of ADP to ATP
3. Transfer of H atoms or e to NAD+, forming NADH

Overall Equation for Glycolysis

$$\text{Glucose} + 2\text{NAD}^+ + 2\text{ADP} + 2\text{P}_i \longrightarrow 2\text{ pyruvate} + 2\text{NADH} + 2\text{H}^+ + 2\text{ATP} + 2\text{H}_2\text{O}$$

Energetics

Phase 1:

Reaction 1=1 ATP used

Reaction 3=1 ATP used

- 2 ATPs

Phase 2:

Reaction 7=**2** ATPs produced

Reaction 10=**2** ATPs produced

Reaction 6=2 NADH+2H$^+$produced= **5*** ATPs produced

+ 9 ATPs

NET= +9-2= 7ATPs, when 1 glucose is oxidized up to pyruvate

*this is calculated as 2.5ATP per NADH

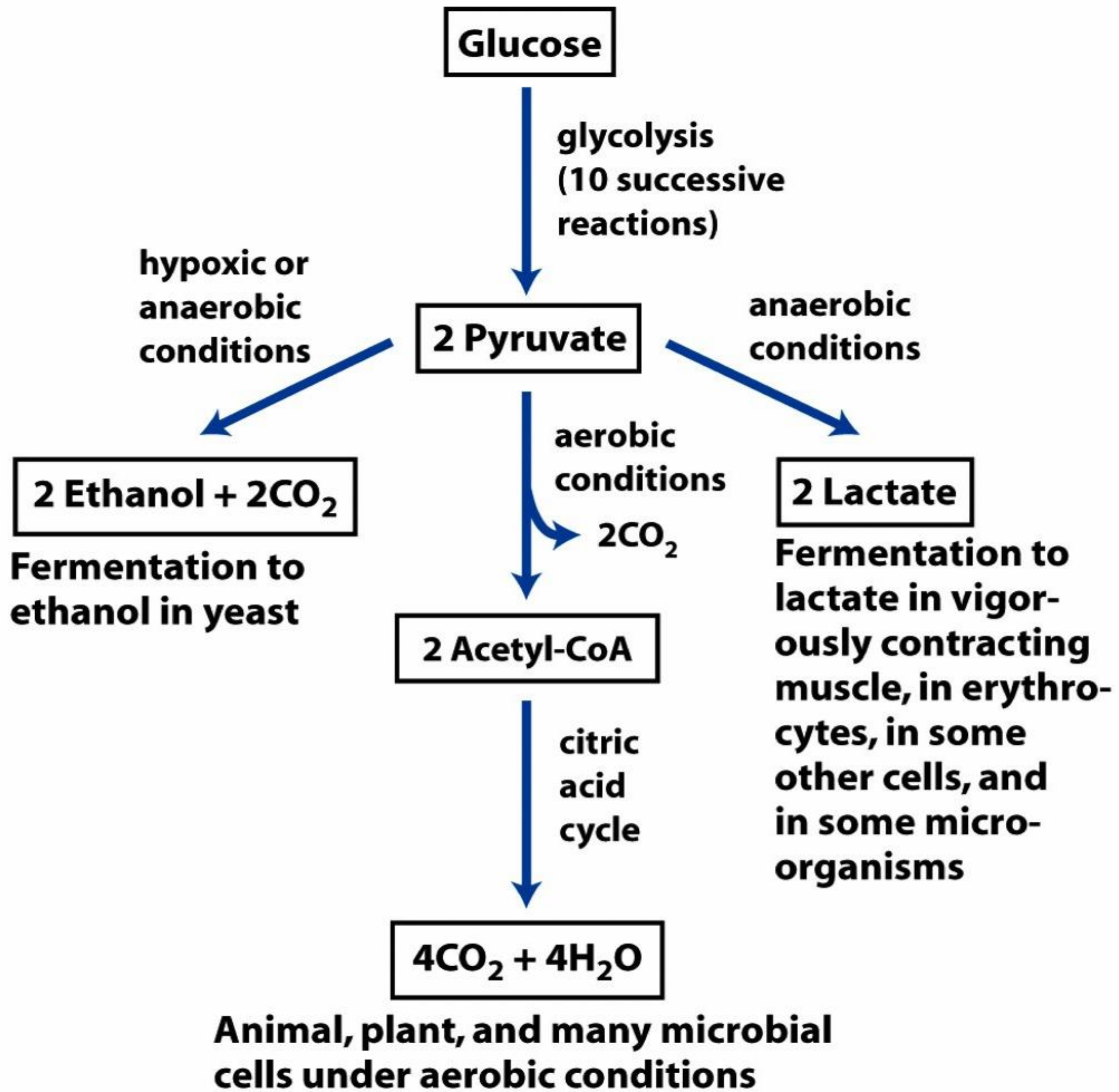

Figure 14-3
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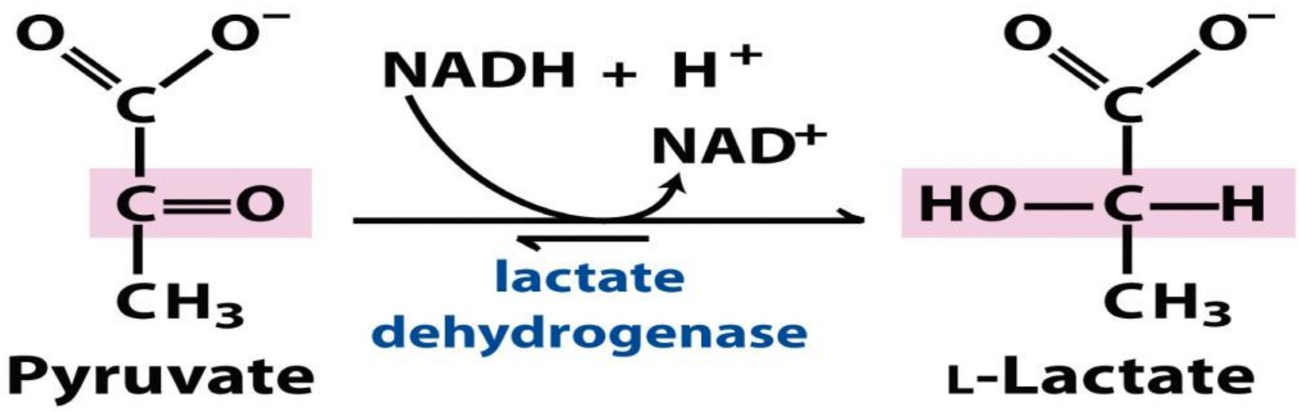
Three possible catabolic fates of pyruvate formed in glycolysis

Lactic acid fermentation

- Vigorously contracting skeletal muscle - function anaerobically, the pyruvate cannot be oxidized further due to lack of oxygen
- So, pyruvate is reduced to lactate
- Certain tissues & cells (retina, brain, RBCs) convert glucose to lactate even under aerobic conditions (as these don't have mitochondria)
- Lactate (the dissociated form of lactic acid) is also the product of glycolysis under anaerobic conditions in microorganisms that carry out the lactic acid fermentation



$$\Delta G'^{\circ} = -\ 25.1\ \text{kJ/mol}$$

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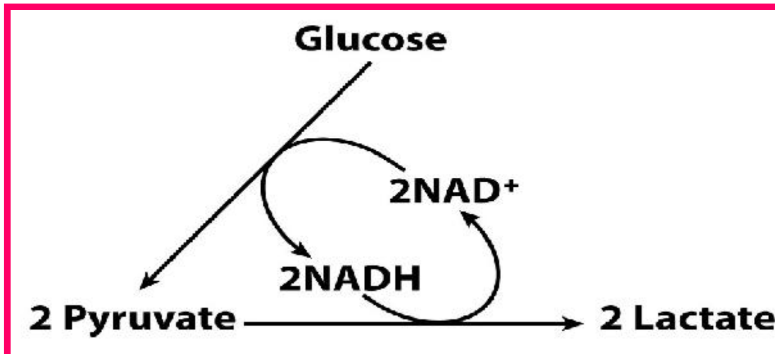

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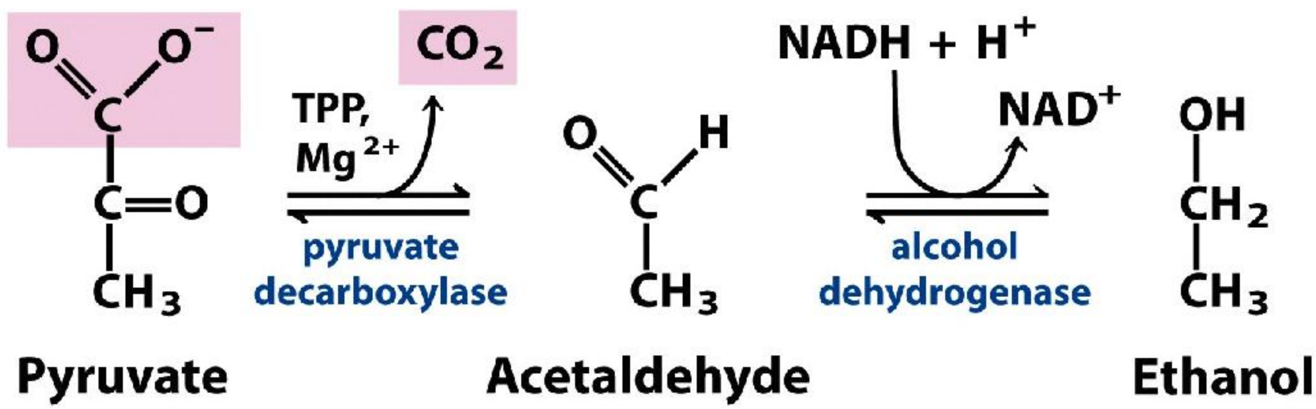
Ethanol or Alcohol fermentation

In some plant tissues & in certain invertebrates, protests & microorganisms such as brewer's yeast, pyruvate is converted anaerobically into ethanol & CO_2



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Overall Equation

Lactic acid Fermentation

Glucose + 2 ADP + 2 P_i → 2 lactate + 2 ATP + 2H2O

Ethanol Fermentation

Glucose + 2 ADP + 2 P_i → 2ethanol + 2 ATP + 2H2O

David L. Nelson and Michael M. Cox

- ***LEHNINGER***
- ***PRINCIPLES OF BIOCHEMISTRY***
- ***Fifth Edition***

Hans Krebs, 1900–1981

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CHAPTER 16
The Citric Acid Cycle

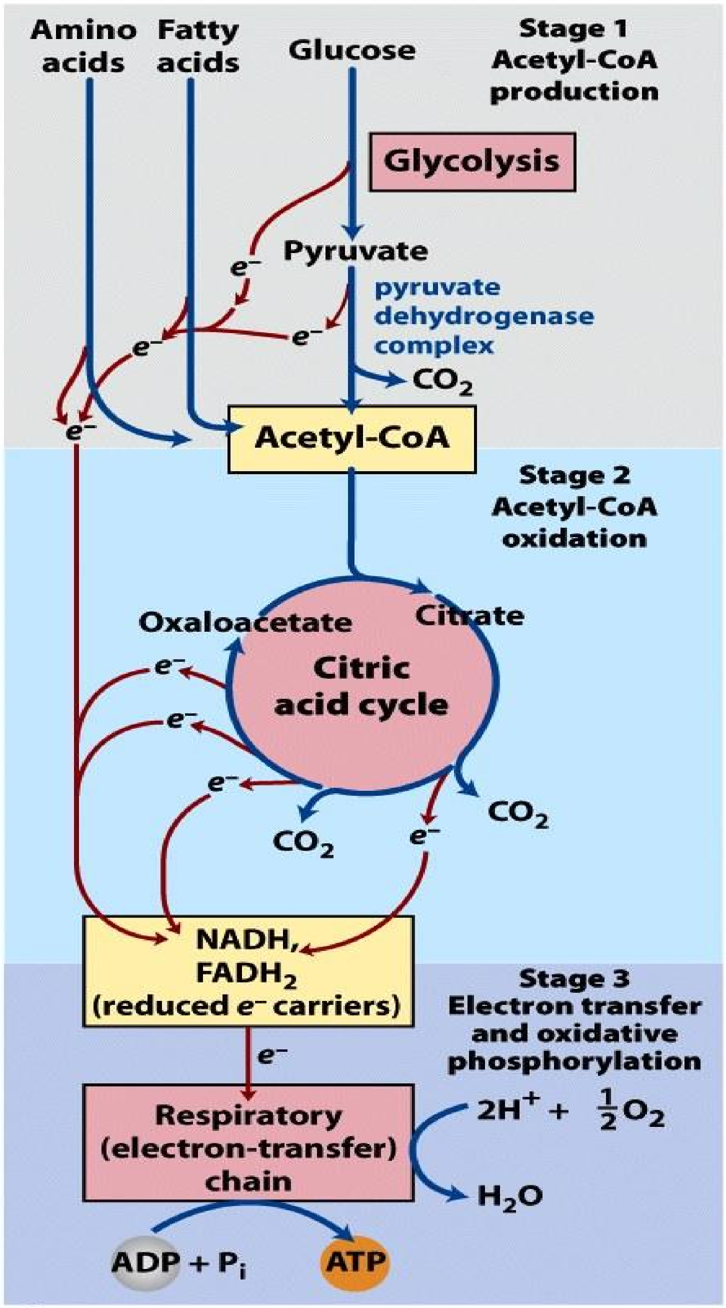

Figure 16-1
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Catabolism of proteins, fats, carbohydrates in 3 stages of cellular respiration

Stage 1: oxidation of fatty acids, glucose, and some amino acids yields acetyl-CoA.

Stage 2: oxidation of acetyl groups in the citric acid cycle includes four steps in which electrons are abstracted.

Stage 3: electrons carried by NADH and $FADH_2$ are funneled into a chain of mitochondrial (or, in bacteria, plasma membrane-bound) electron carriers—the respiratory chain—ultimately reducing O_2 to H_2O.This electron flow drives the production of ATP.

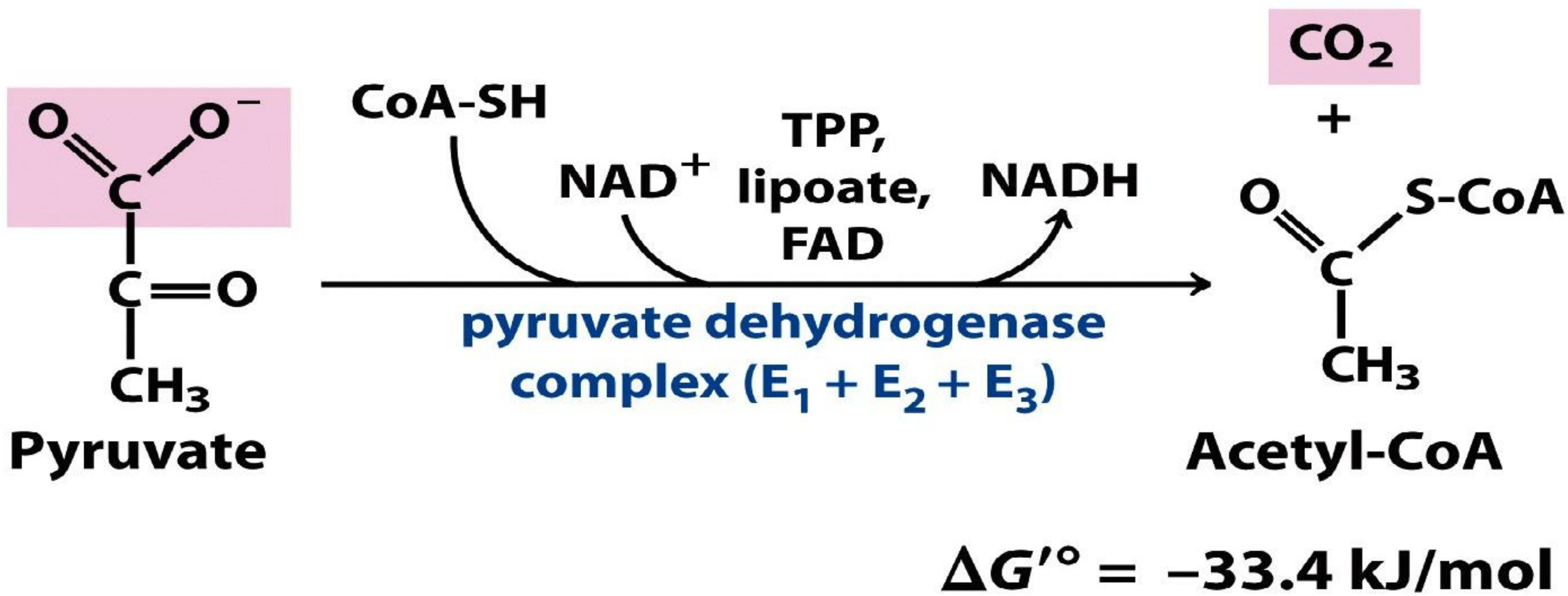

Figure 16-2
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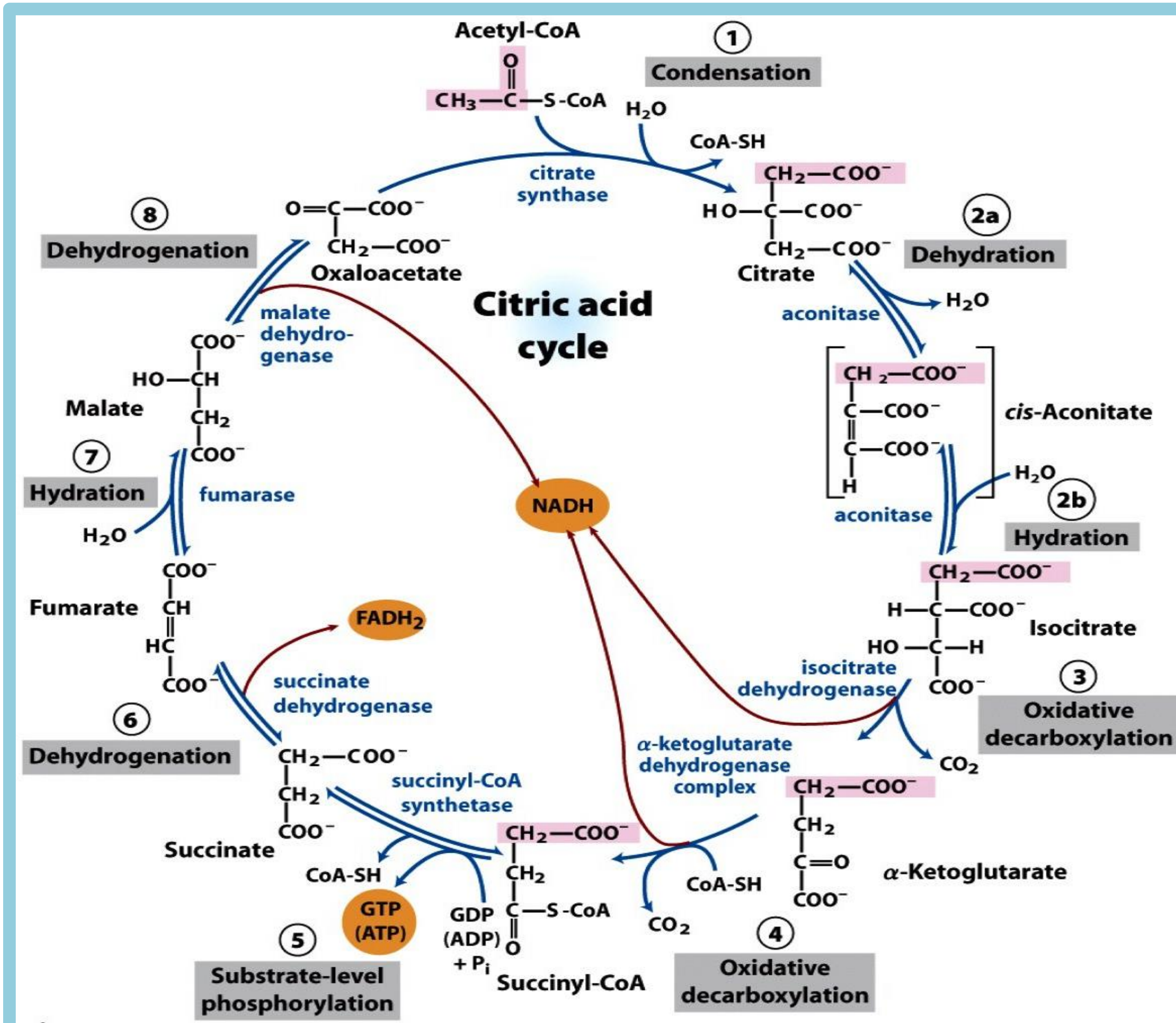

Figure 16-7

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- 2 C atoms enter the cycle as acetyl CoA & leave as CO_2

Energy produced

3 NAD+ reduced to 3NADH=+7.5 * ATPs

1 FAD reduced to 1FADH2 =+1.5 * ATPs

1 GDP converted to GTP =+1 ATP

Net = 10 ATPs for 1 acetyl-CoA

FOR 2 acetyl-CoA=20 ATPs

***this is calculated as 2.5ATP per NADH and 1.5ATP per $FADH_2$**

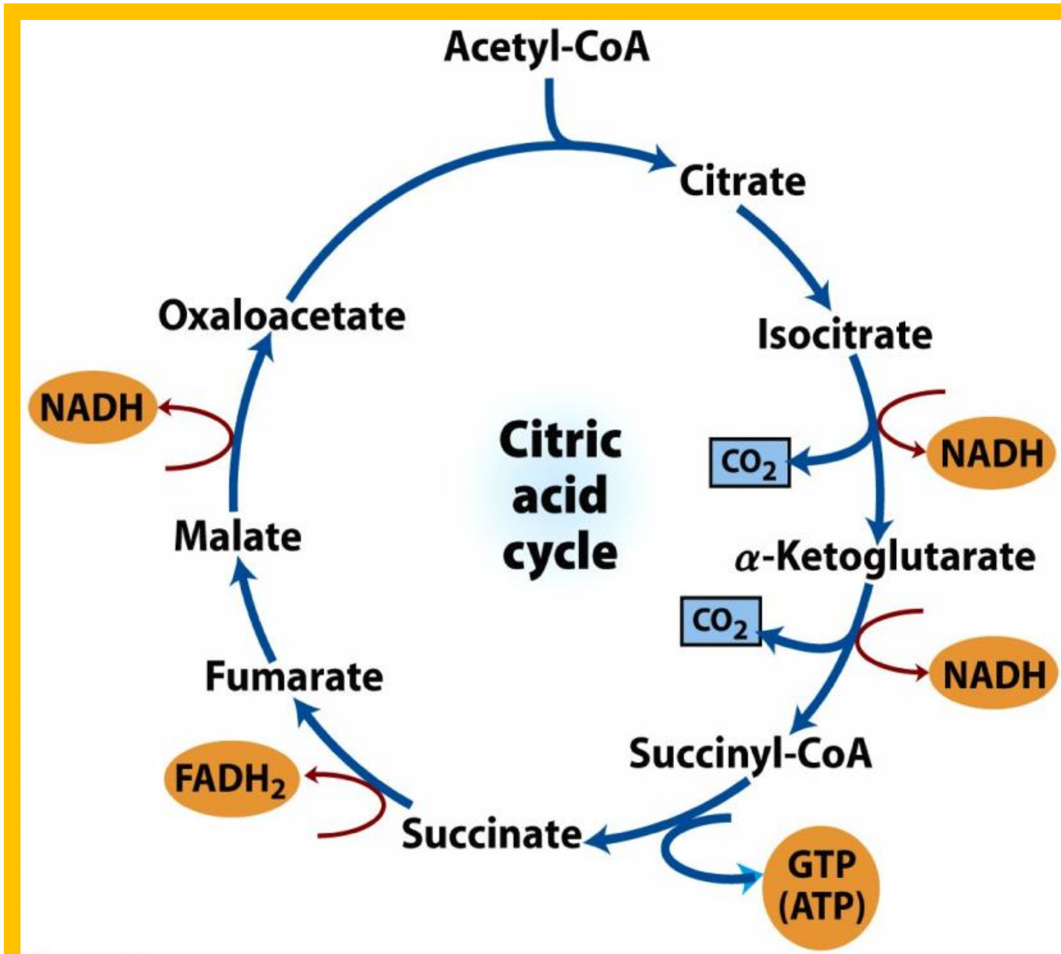

Figure 16-13
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Products of one turn of the citric acid cycle

At each turn of the cycle, 3NADH, 1 $FADH_2$, 1 GTP (or ATP), and 2 CO_2 are released in oxidative decarboxylation reactions.

Here all cycle reactions are shown as proceeding in one direction only, but keep in mind that most of the reactions are reversible

TABLE 16–1	Stoichiometry of Coenzyme Reduction and ATP Formation in the Aerobic Oxidation of Glucose via Glycolysis, the Pyruvate Dehydrogenase Complex Reaction, the Citric Acid Cycle, and Oxidative Phosphorylation

Reaction	Number of ATP or reduced coenzyme directly formed	Number of ATP ultimately formed*
Glucose $\longrightarrow$ glucose 6-phosphate	−1 ATP	−1
Fructose 6-phosphate $\longrightarrow$ fructose 1,6-bisphosphate	−1 ATP	−1
2 Glyceraldehyde 3-phosphate $\longrightarrow$ 2 1,3-bisphosphoglycerate	2 NADH	3 or 5†
2 1,3-Bisphosphoglycerate $\longrightarrow$ 2 3-phosphoglycerate	2 ATP	2
2 Phosphoenolpyruvate $\longrightarrow$ 2 pyruvate	2 ATP	2
2 Pyruvate $\longrightarrow$ 2 acetyl-CoA	2 NADH	5
2 Isocitrate $\longrightarrow$ 2 α-ketoglutarate	2 NADH	5
2 α-Ketoglutarate $\longrightarrow$ 2 succinyl-CoA	2 NADH	5
2 Succinyl-CoA $\longrightarrow$ 2 succinate	2 ATP (or 2 GTP)	2
2 Succinate $\longrightarrow$ 2 fumarate	2 $FADH_2$	3
2 Malate $\longrightarrow$ 2 oxaloacetate	2 NADH	5
Total		30–32

*This is calculated as 2.5 ATP per NADH and 1.5 ATP per $FADH_2$. A negative value indicates consumption.

†This number is either 3 or 5, depending on the mechanism used to shuttle NADH equivalents from the cytosol to the mitochondrial matrix; see Figures 19–30 and 19–31.

Table 16-1

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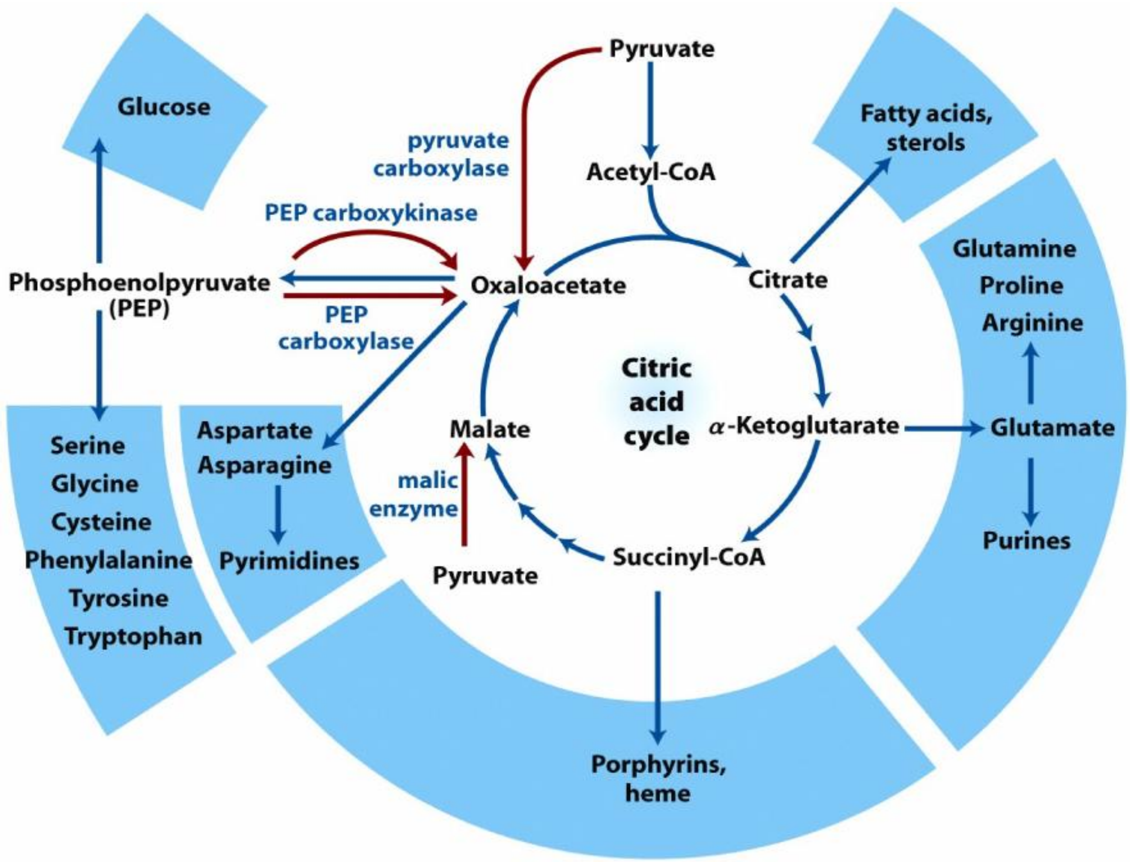

Figure 16-15
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Role of the citric acid cycle (CAC) in Anabolism

Intermediates of CAC are drawn off as precursors in many biosynthetic pathways.

Shown in **red** are 4 ***Anaplerotic reactions*** that replenish depleted cycle intermediates

TABLE 16–2 Anaplerotic Reactions

Reaction	Tissue(s)/organism(s)
Pyruvate + HCO_3^- + ATP $\xrightleftharpoons{\text{pyruvate carboxylase}}$ oxaloacetate + ADP + P_i	Liver, kidney
Phosphoenolpyruvate + CO_2 + GDP $\xrightleftharpoons{\text{PEP carboxykinase}}$ oxaloacetate + GTP	Heart, skeletal muscle
Phosphoenolpyruvate + HCO_3^- $\xrightleftharpoons{\text{PEP carboxylase}}$ oxaloacetate + P_i	Higher plants, yeast, bacteria
Pyruvate + HCO_3^- + NAD(P)H $\xrightleftharpoons{\text{malic enzyme}}$ malate + $NAD(P)^+$	Widely distributed in eukaryotes and bacteria

Table 16-2
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