BIOCHEMISTRY

Fourth Class-First Couse

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Biochemistry (Metabolism and Others)

Four Class

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Metabolism

The course include:

1- Introduction.

2-Carbohydrate metabolism.

3- Lipid metabolism.

4- Protein metabolism.

5- Nucleic acid metabolism.

6- Replication and transcription of DNA

7- Digestive and absorption.

8- Urine.

9- Blood.

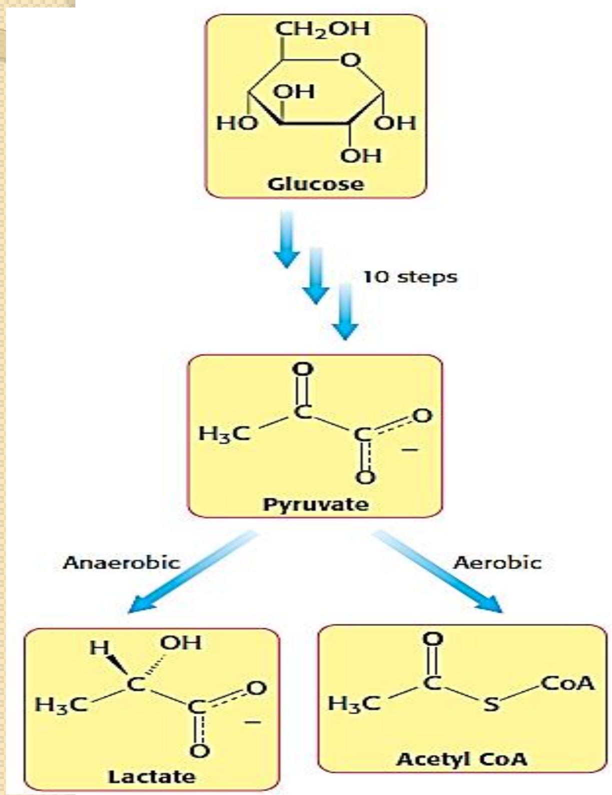
References for biochemistry of four class (Chemistry department/ College of Science Mosul University)

1. Murray R. K., Bender D. A., Botham K. M., Kennelly P. J., Rodwell V. W. (2009)." Harper's Illustrated Biochemistry". 28 ed. The McGraw-Hill Companies. USA.
2. Berg, J. M., Tymoczko, J. L., Stryer, L. (2010). Biochemistry. W. H. Freeman and Company. New York. USA.
3. Harvey, R. A., Ferrier, D. R. (2011). " Lippincott's Illustrated Reviews: Biochemistry "5th ed. Lippincott Williams and Wilkins, a Wolters Kluwer business, China.
4. Nelson, D. L., Cox, M. M., (2008) Lehninger Principles of Biochemistry. 4th Ed., USA

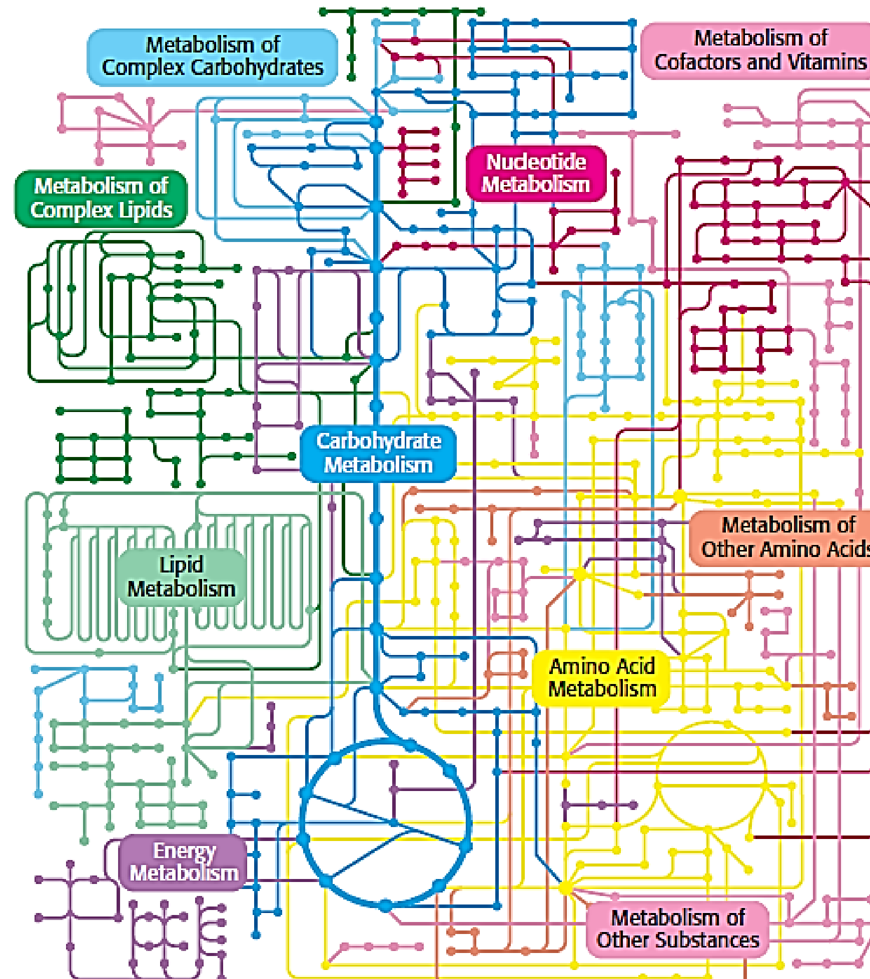
٥- كتاب الكيمياء الحياتية الجزء الثاني ٢٠١٠ ، تأليف د.طارق يونس و د.لؤي عبد علي الهلالي، دار ابن الاثير للطباعة والنشر.

Metabolism

Metabolism is essentially a linked series of chemical reactions that begins with a particular molecule and converts it into some other molecule or molecules in a carefully defined fashion (Figure 1). There are many pathways in the cell (Figure 2), and we will examine a few of them in some detail later.



(Figure 1: Glucose metabolism. Glucose is metabolized to pyruvate in 10 linked reactions. Under anaerobic conditions, pyruvate is metabolized to lactate and, under aerobic conditions, to acetyl CoA. The glucose-derived carbons of acetyl CoA are subsequently oxidized to CO2.



(Figure 2: Metabolic pathways.) [4]

Metabolism

Metabolism is the term used to describe the interconversion of chemical compounds in the body, the pathways taken by individual molecules, their interrelationships, and the mechanisms that regulate the flow of metabolites through the pathways. Metabolic pathways fall into three categories(Figure 3):

(1) **Anabolic pathways, which are those**

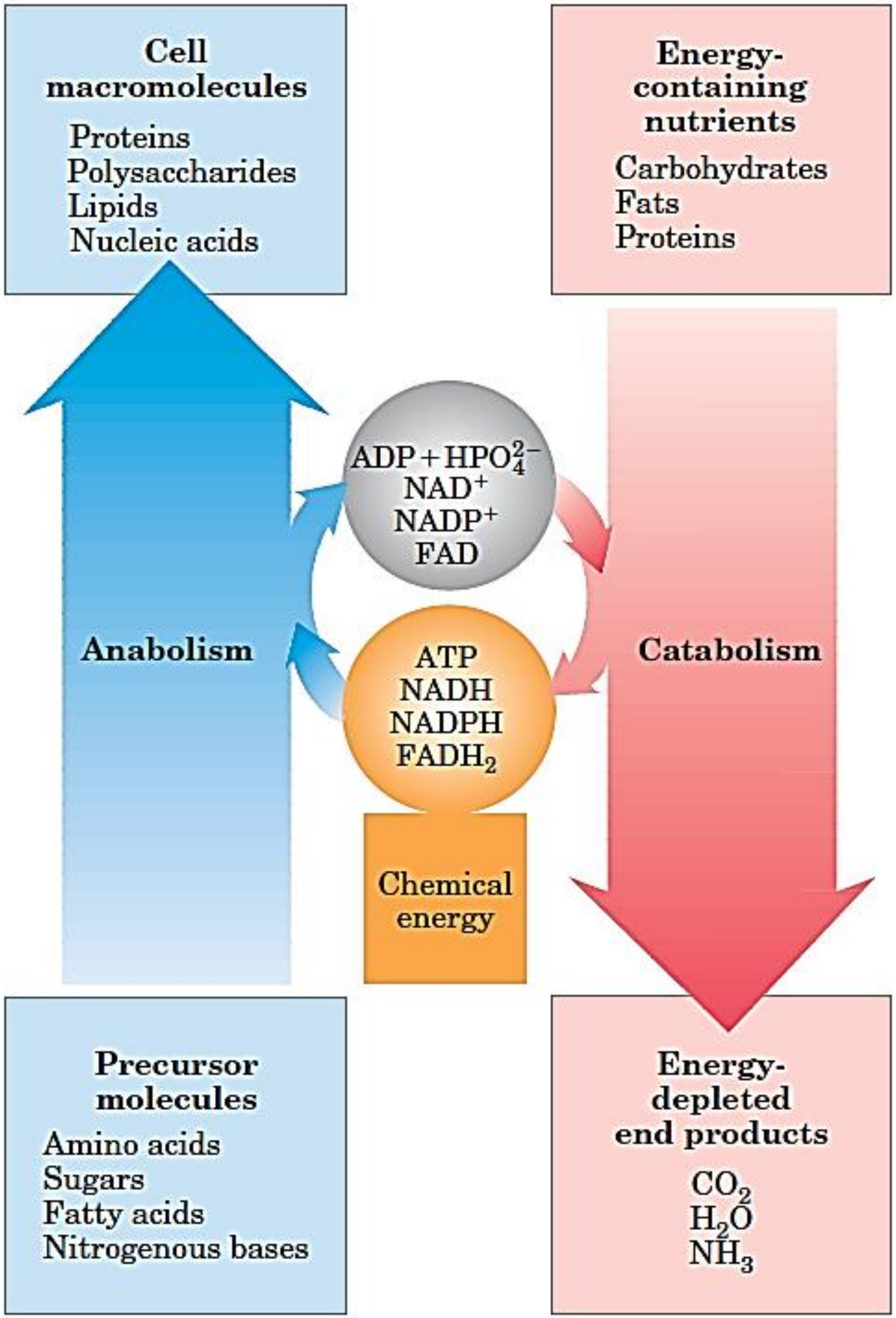
involved in the synthesis of larger and more complex compounds from smaller precursors—eg, the synthesis of protein from amino acids and the synthesis of reserves of triacylglycerol and glycogen.

Anabolic pathways are endothermic.

(2) **Catabolic pathways, which are involved in the breakdown of larger molecules, commonly**

involving oxidative reactions; they are exothermic, producing reducing equivalents, and, mainly via the respiratory chain, ATP.

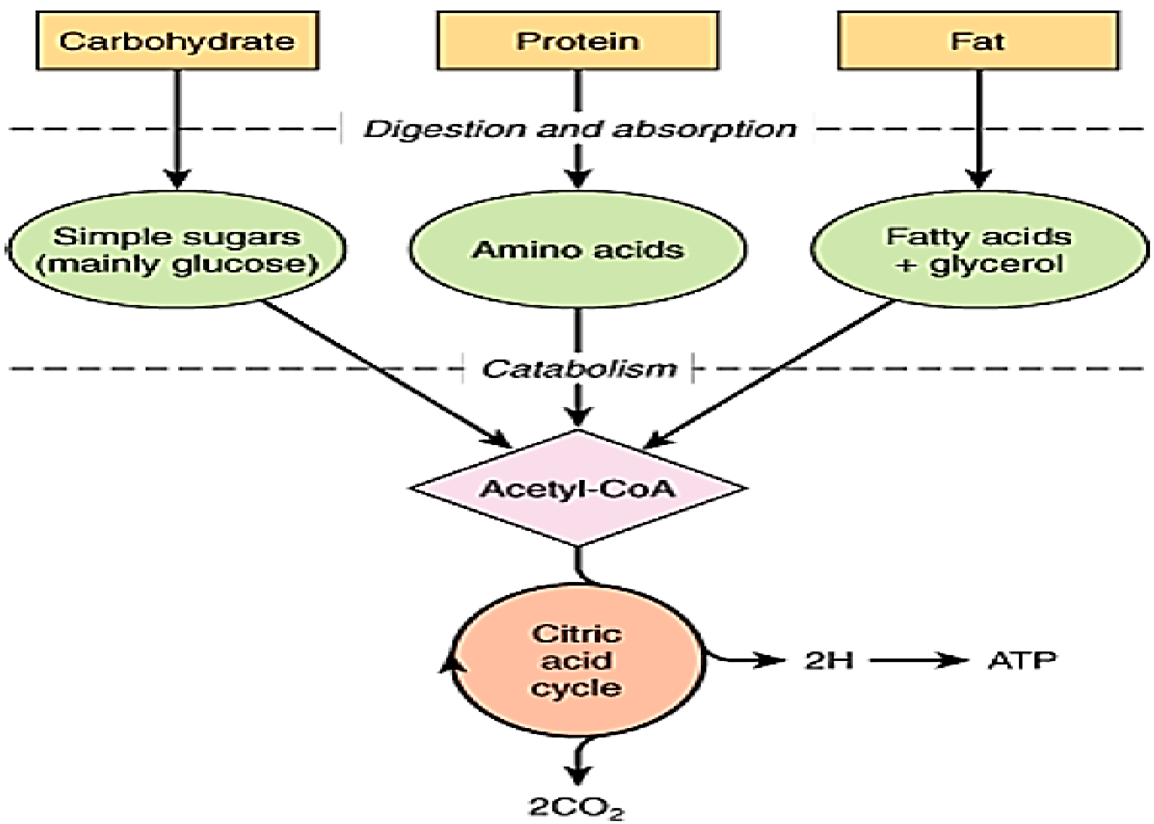
(3) **Amphibolic pathways, which occur at the "crossroads" of metabolism, acting as links between the** anabolic and catabolic pathways, eg, the citric acid cycle.



(FIGURE 3: Energy relationships between catabolic and anabolic pathways. Catabolic pathways deliver chemical energy in the form of ATP, NADH, NADPH, and FADH2. These energy carriers are used in anabolic pathways to convert small precursor molecules into cellular macromolecules.)

PATHWAYS THAT PROCESS THE MAJOR PRODUCTS OF DIGESTION

The nature of the diet sets the basic pattern of metabolism. There is a need to process the products of digestion of dietary carbohydrate, lipid, and protein. These are mainly glucose, fatty acids and glycerol, and amino acids, respectively. In ruminants (and, to a lesser extent, other herbivores), dietary cellulose is fermented by symbiotic microorganisms to short-chain fatty acids (acetic, propionic, butyric), and metabolism in these animals is adapted to use these fatty acids as major substrates. All the products of digestion are metabolized to a **common product, acetyl-CoA, which is then oxidized by the citric acid cycle** (Figure 4).

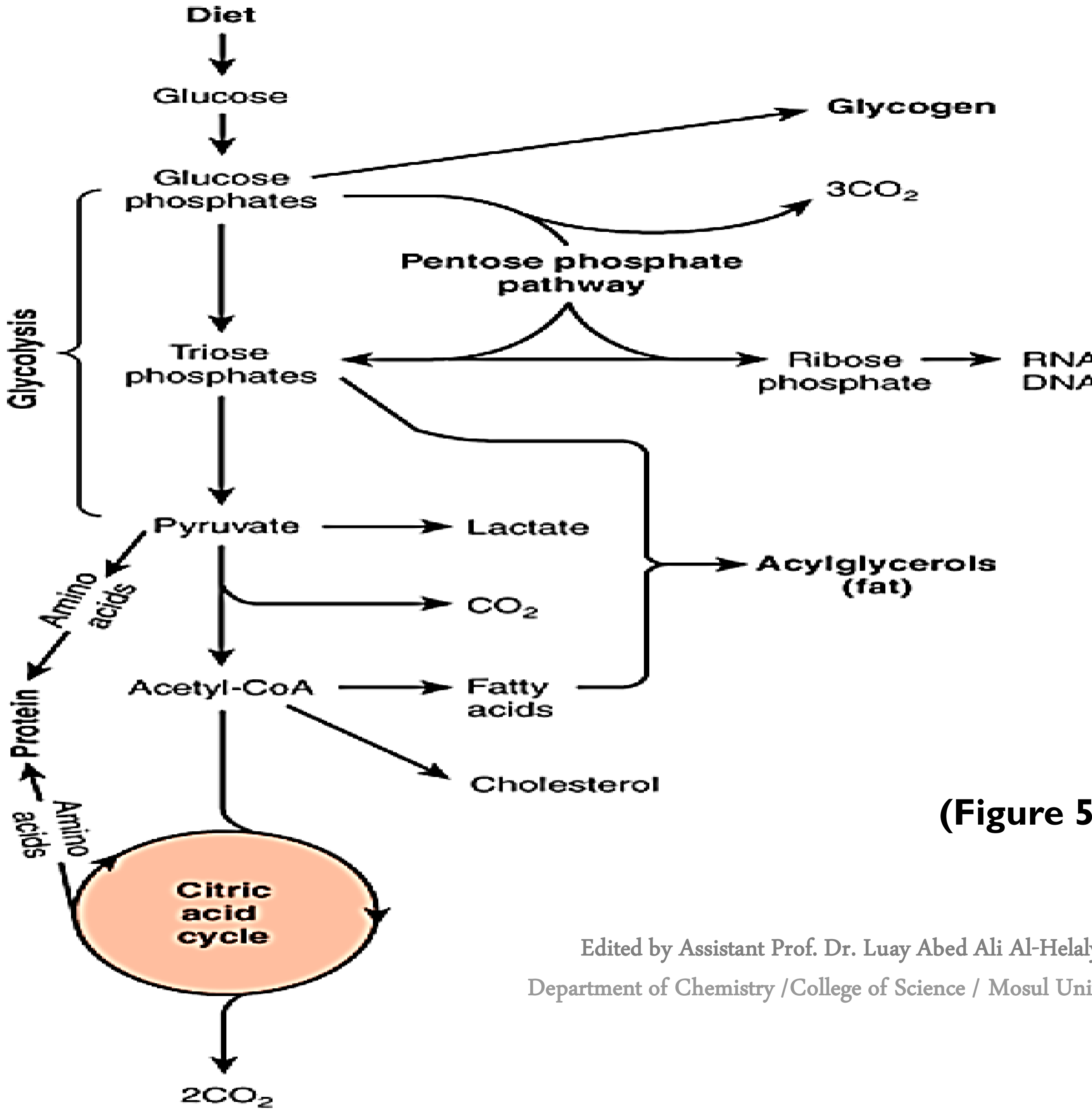


(Figure 4)

[7]

Carbohydrate Metabolism Is Centered on the Provision & Fate of Glucose

Glucose is the major fuel of most tissues (Figure 5). It is metabolized to pyruvate by the pathway of **glycolysis. Aerobic tissues metabolize pyruvate to acetyl-CoA, which can enter the citric acid cycle for complete** oxidation to CO_2 and H_2O, linked to the formation of ATP in the process of **oxidative phosphorylation**. Glycolysis can also occur anaerobically (in the absence of oxygen) when the end product is lactate.



(Figure 5)

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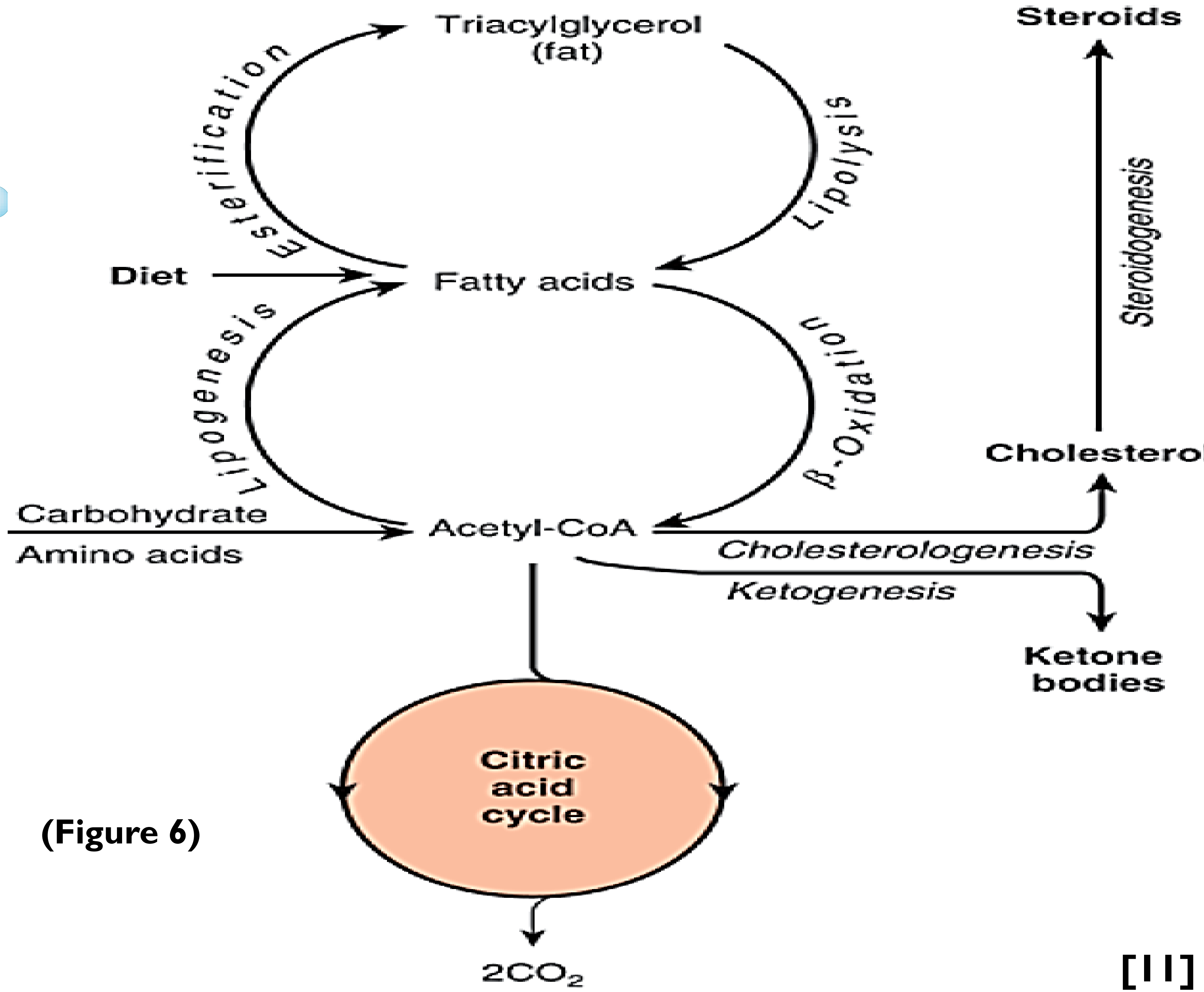
Lipid Metabolism Is Concerned Mainly with Fatty Acids & Cholesterol

The source of long-chain fatty acids is either dietary lipid or de novo synthesis from acetyl-CoA derived from carbohydrate or amino acids. Fatty acids may be oxidized to **acetyl-CoA (β-oxidation) or esterified with glycerol,** forming **triacylglycerol (fat) as the body's main fuel reserve.**

Acetyl-CoA formed by β-oxidation may undergo three fates (Figure 6):

1. As with acetyl-CoA arising from glycolysis, it is **oxidized to CO_2 + H_2O via the citric acid cycle.**
2. It is the precursor for synthesis of **cholesterol and other steroids.**
3. In the liver, it is used to form **ketone bodies (acetoacetate and 3-hydroxybutyrate) that are important fuels** in prolonged fasting.

[10]



Triacylglycerol
(fat)
Steroids
Esterification
Lipolysis
Steroidogenesis
Diet
Fatty acids
Lipogenesis
β-Oxidation
Cholesterol
Carbohydrate
Amino acids
Acetyl-CoA
Cholesterologenesis
Ketogenesis
Ketone
bodies
Citric
acid
cycle
$2CO_2$

(Figure 6)

[11]

Much of Amino Acid Metabolism Involves Transamination

- The amino acids are required for protein synthesis (Figure 7). Some must be supplied in the diet (the **essential amino acids), since they cannot be synthesized in the body. The remainder are nonessential amino acids,**

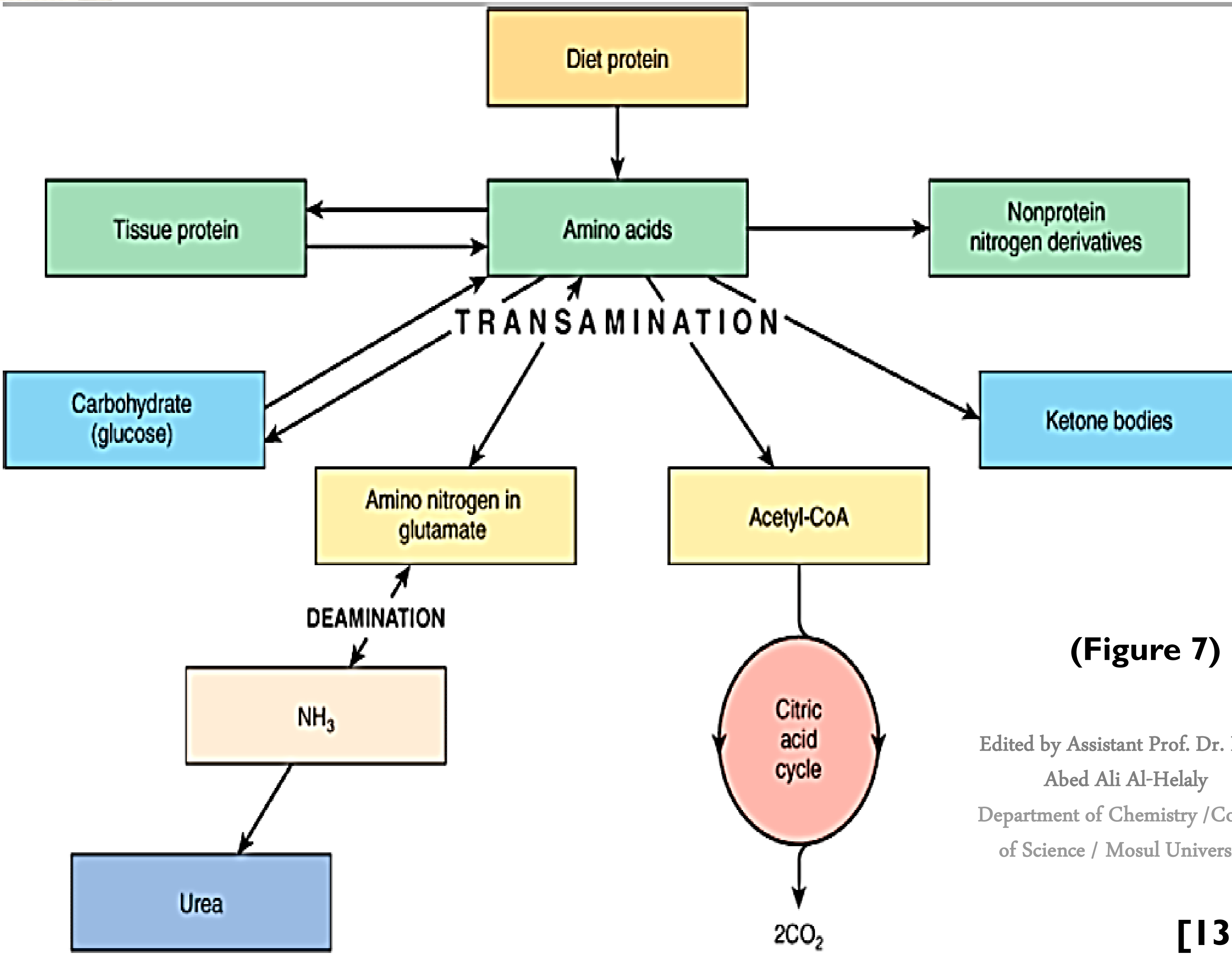
which are supplied in the diet, but can also be formed from metabolic intermediates by **transamination using the** amino nitrogen from other amino acids. After **deamination, amino nitrogen is excreted as urea, and the carbon** skeletons that remain after transamination may:

(1) be oxidized to CO_2 via the citric acid cycle,

(2) be used to synthesize glucose (gluconeogenesis), or

(3) form ketone bodies, which may be oxidized or be used for synthesis of fatty acids.

[12]



(Figure 7)

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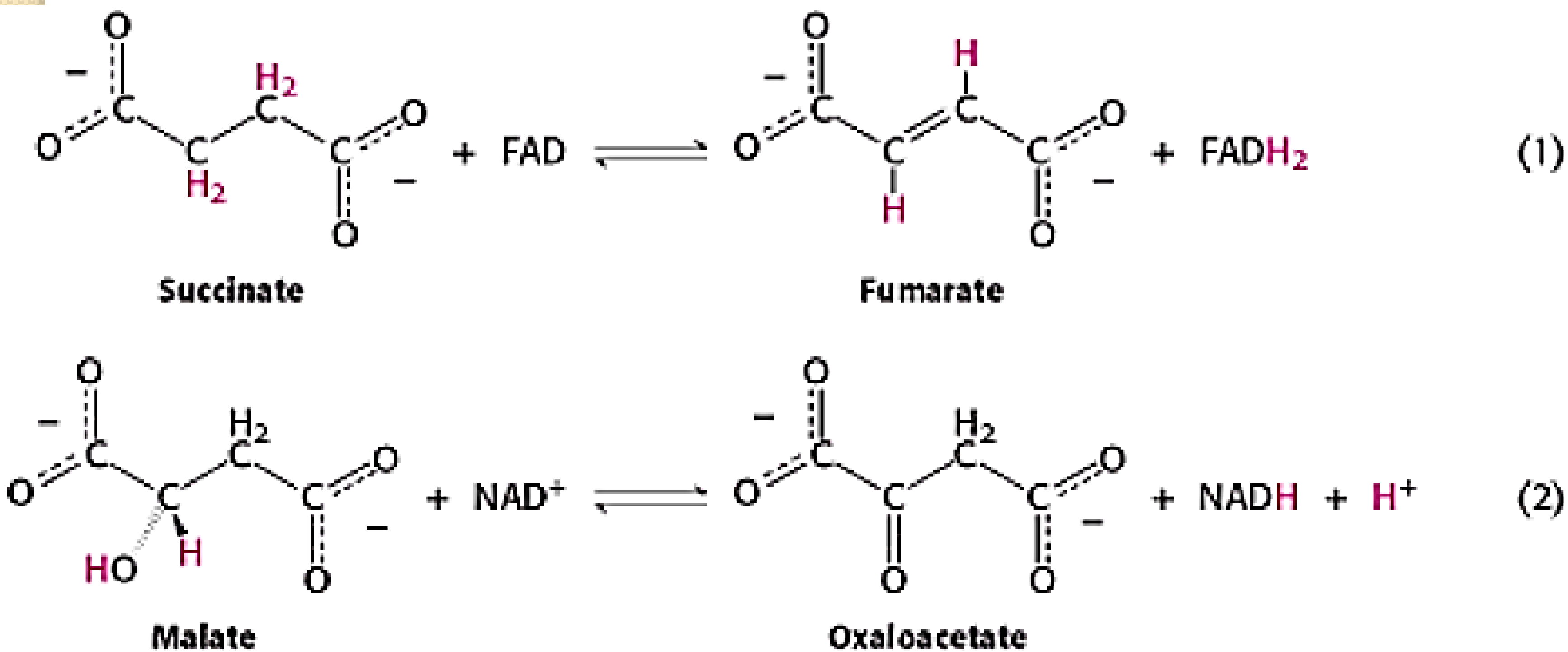
Key Reactions Are Reiterated Throughout Metabolism

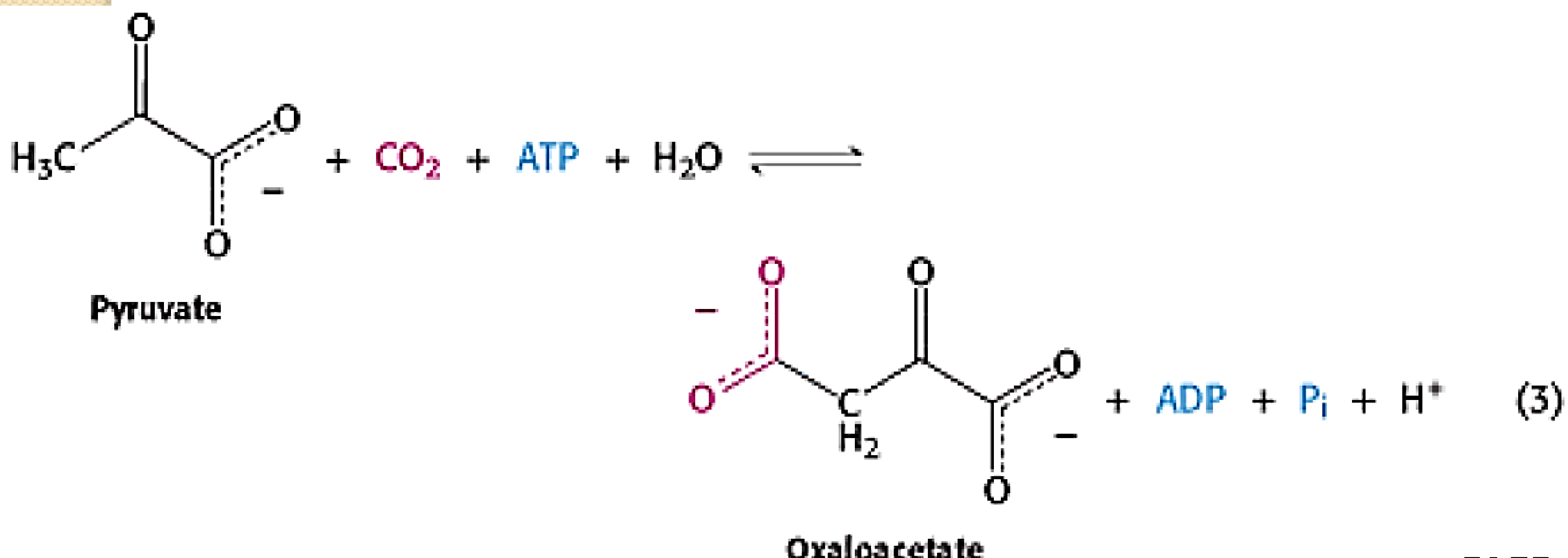
1. ***Oxidation-reduction reactions are essential components of many pathways. Useful energy is often derived from the***

1. oxidation of carbon compounds. Consider the following two reactions:



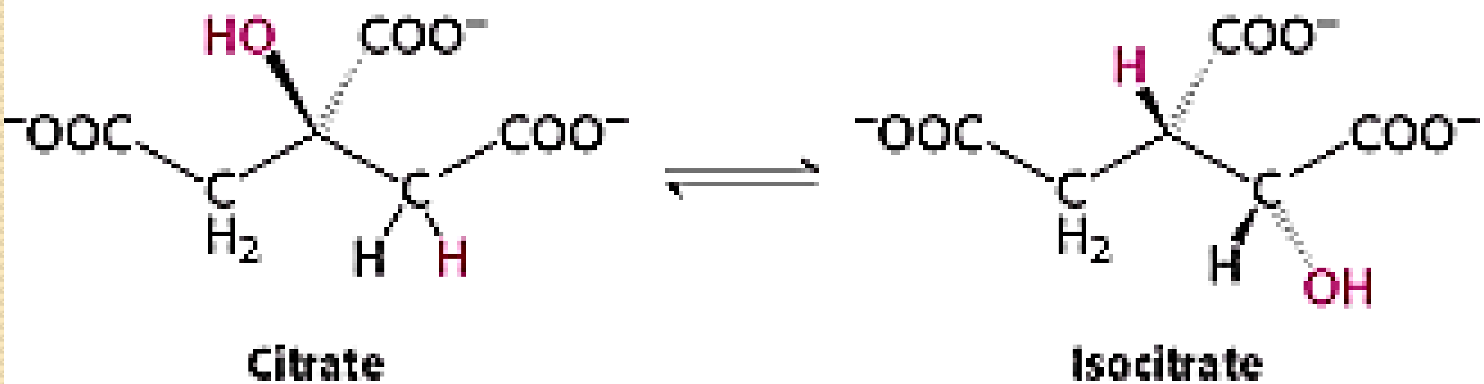
[14]

2. ***Ligation reactions form bonds by using free energy from ATP cleavage. Reaction 3 illustrates the ATP-dependent*** formation of a carbon-carbon bond, necessary to combine smaller molecules to form larger ones. Oxaloacetate is formed from pyruvate and CO_2.



[15]

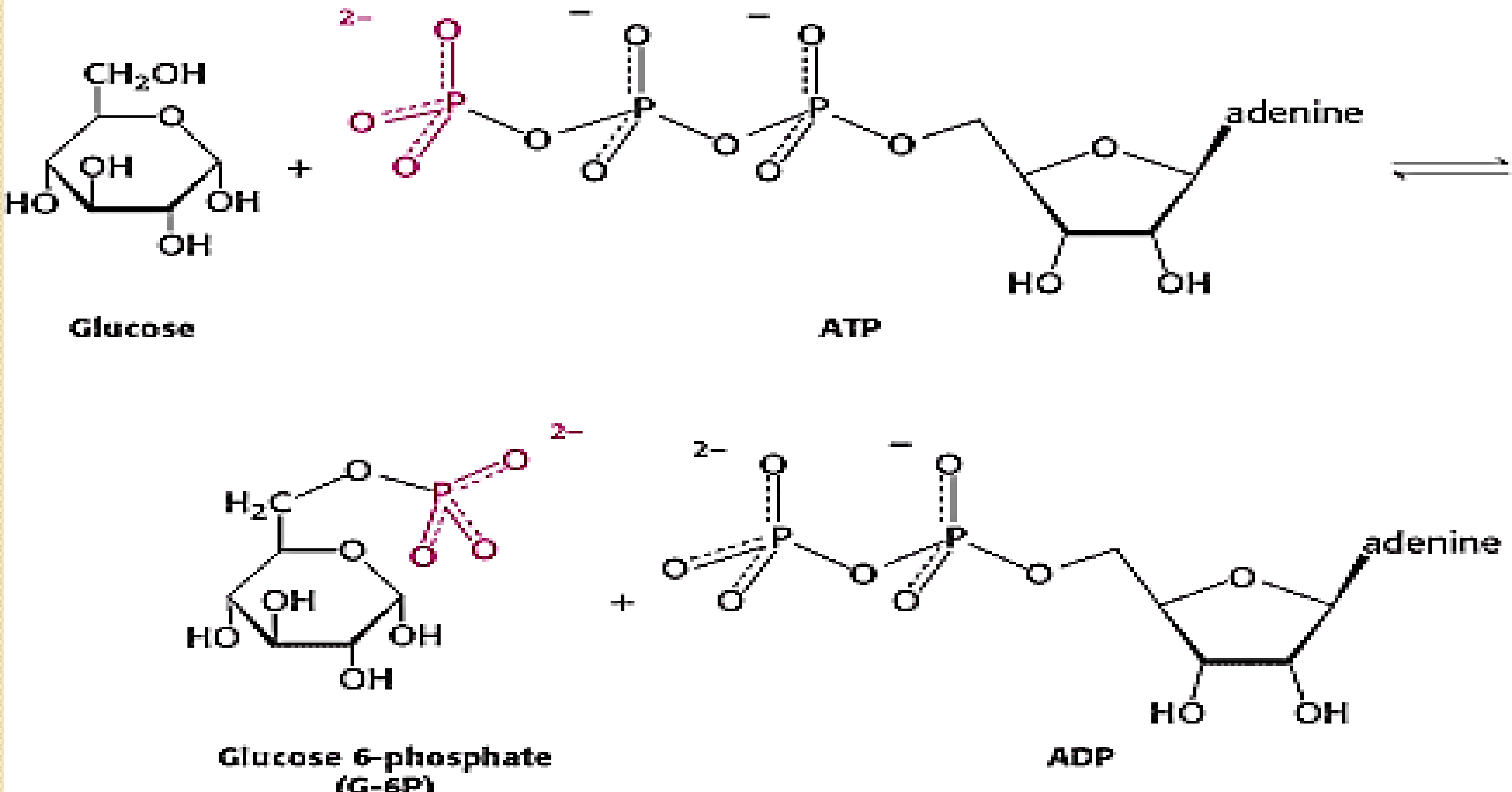
3. ***Isomerization reactions rearrange particular atoms within the molecule. Their role is often to prepare a molecule for*** subsequent reactions such as the oxidation-reduction reactions described in point 1.



(4)

[16]

4. *Group-transfer reactions play a variety of roles. Reaction 5 is representative of such a reaction. A phosphoryl group is* transferred from the activated phosphoryl-group carrier, ATP, to glucose. This reaction traps glucose in the cell so that further catabolism can take place.

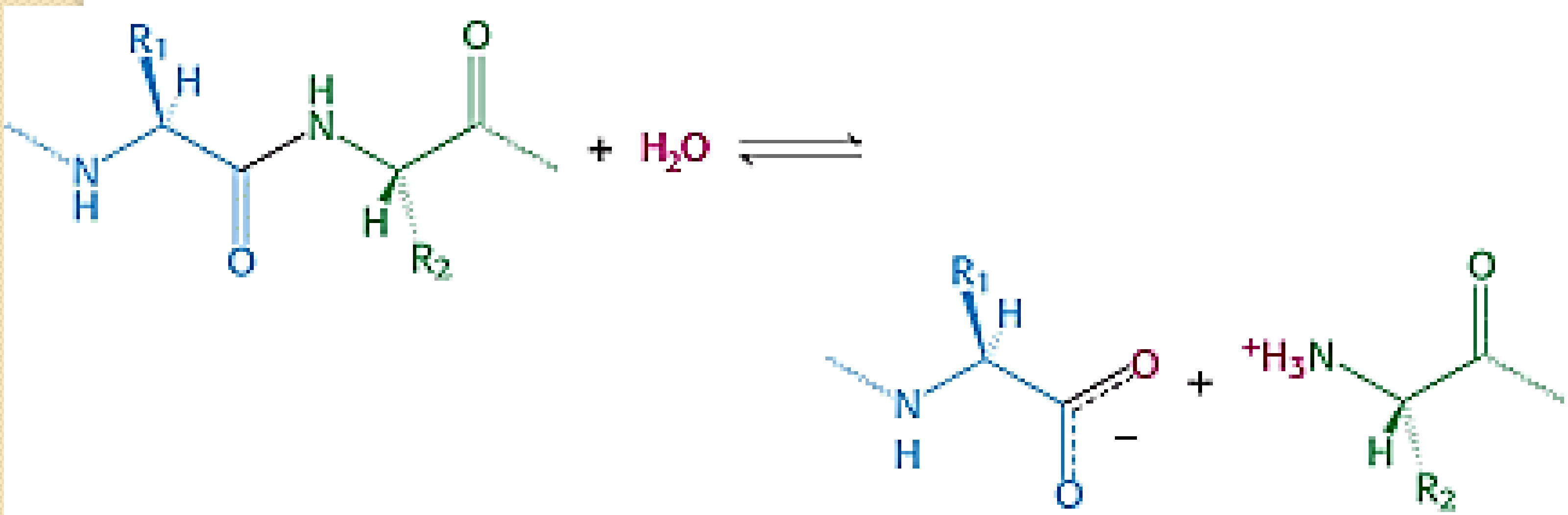


(5)

[17]

5. ***Hydrolytic reactions cleave bonds by the addition of water. Hydrolysis is a common means employed to break down***

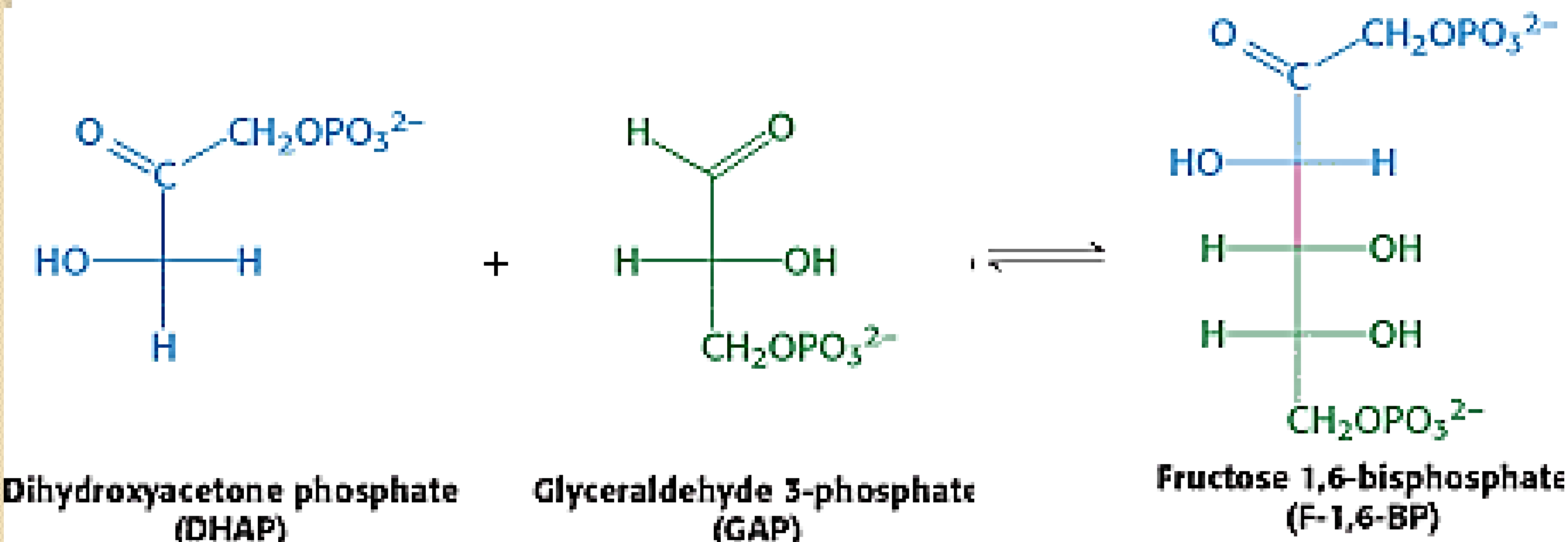
Proteins are digested by hydrolytic cleavage Reaction 6 illustrates the hydrolysis of a peptide to yield two smaller peptides.



(6)

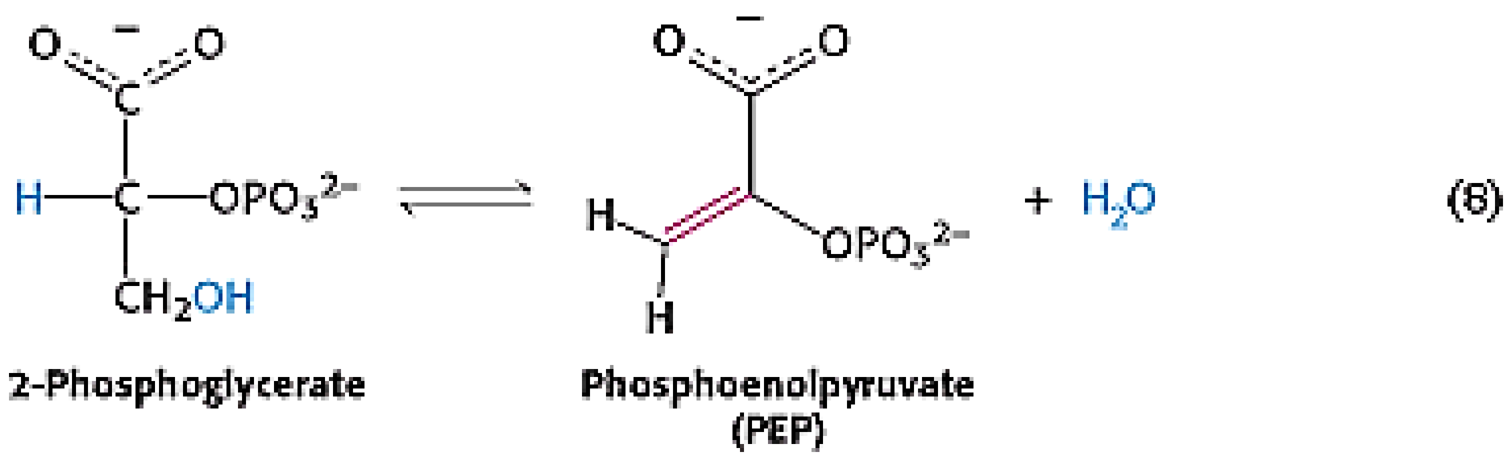
[18]

6. ***The addition of functional groups to double bonds or the removal of groups to form double bonds constitutes the final*** class of reactions. The enzymes that catalyze these types of reaction are classified as lyases . An important example, illustrated in reaction 7, is the conversion of the six-carbon molecule fructose 1,6-bisphosphate (F-1, 6-BP) into 2 three-carbon fragments: dihydroxyacetone phosphate and glyceraldehyde 3-phosphate.



[19]

This reaction is a key step in glycolysis, a key pathway for extracting energy from glucose . Dehydrations to form double bonds, such as the formation of phosphoenolpyruvate from 2-phosphoglycerate (reaction 8), are important reactions of this type.

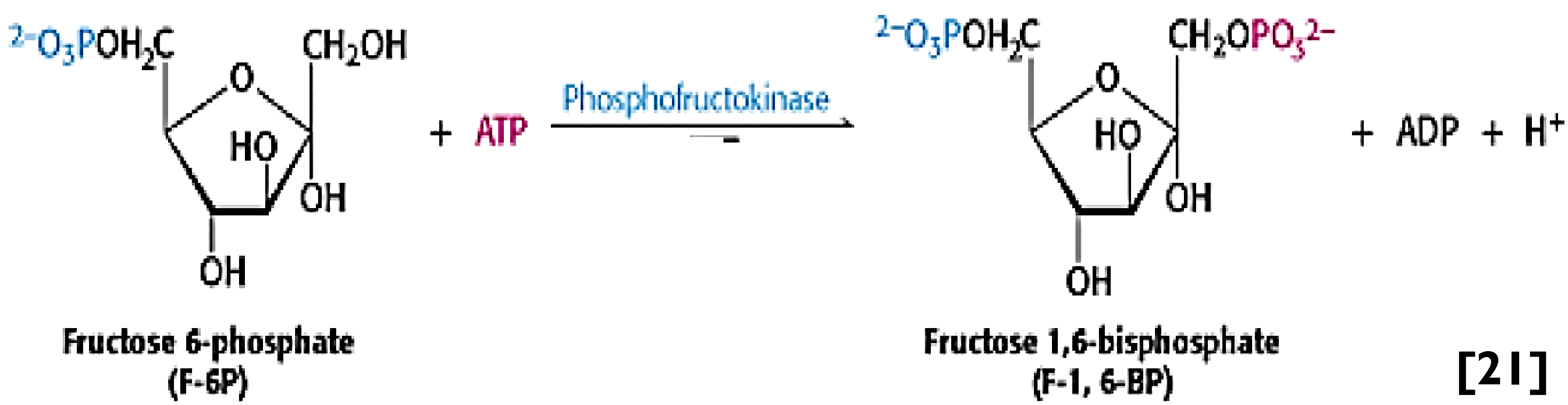


[20]

Recurring Motifs in Metabolic Regulation

Anabolism and catabolism must be precisely coordinated. Metabolic networks sense and respond to information on the status of their component pathways. The information is received and metabolism is controlled in several ways:

1. ***Allosteric interactions.*** The flow of molecules in most metabolic pathways is determined primarily by the activities of certain enzymes rather than by the amount of substrate available. Enzymes that catalyze essentially irreversible reactions are likely control sites, and the first irreversible reaction in a pathway (the committed step) is nearly always tightly controlled. Enzymes catalyzing committed steps are allosterically regulated, as exemplified by phosphofructokinase in glycolysis .



[21]

2. ***Covalent modification.*** Some regulatory enzymes are controlled by covalent modification in addition to allosteric interactions. For example, the catalytic activity of glycogen phosphorylase is enhanced by phosphorylation, whereas that of glycogen synthase is diminished. Specific enzymes catalyze the addition and removal of these modifying groups (Figure 8).

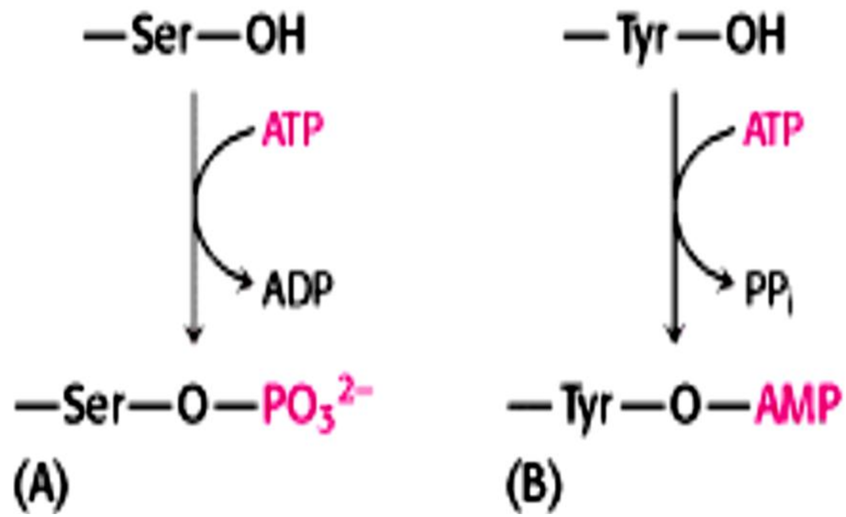


Figure 8: Covalent Modifications. Covalent modifications. Examples of reversible covalent modifications of proteins: (A)phosphorylation, (B) adenylation.

3. ***Enzyme levels.*** The amounts of enzymes, as well as their activities, are controlled. The rates of synthesis and degradation of many regulatory enzymes are altered by hormones. **[22]**

4. *Compartmentation*. The metabolic patterns of eukaryotic cells are markedly affected by the presence of compartments (Figure 9)). The fates of certain molecules depend on whether they are in the cytosol or in mitochondria, and so their flow across the inner mitochondrial membrane is often regulated. For example, fatty acids are transported into mitochondria for degradation only when energy is required, whereas fatty acids in the cytosol are esterified or exported.

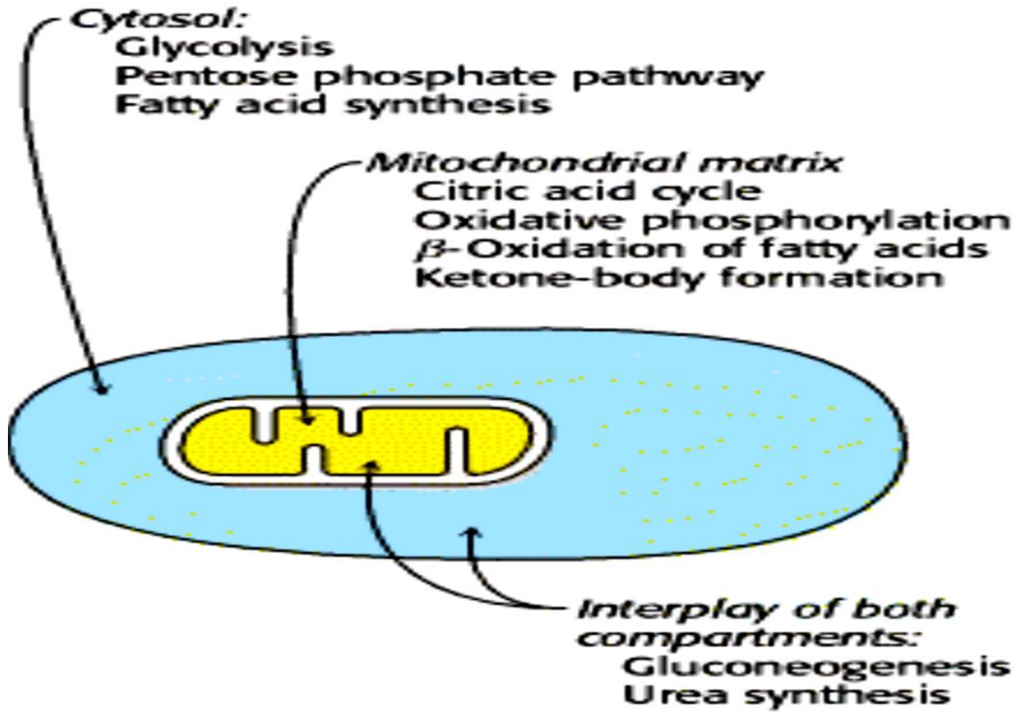


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Figure 9: Compartmentation of the Major Pathways of Metabolism.

5. *Metabolic specializations of organs*. Regulation in higher eukaryotes is enhanced by the existence of organs with different metabolic roles. Metabolic specialization is the result of differential gene expression.