Carbohydrate Metabolism (1)

Intermediary Metabolism

Intermediary metabolism: the intracellular process by which nutritive material is converted into cellular components.

Metabolism: is the entire network of chemical reactions carried out by living cells. It is also refer to the intermediate steps within the cells in which the nutrient molecules or foodstuffs are metabolized and converted into cellular components **catalysed by enzymes**.

The fate of dietary components after digestion and absorption constitutes **metabolism** the metabolic pathways taken by individual molecules, their interrelationships and the mechanisms that regulate the flow of metabolites through the pathways.

However, **in cells**, these reactions rarely occur in isolation, but rather **are organized into multistep sequences** called ***pathways***, where **the product of one reaction becomes the substrate for the next reaction, such as glycolysis.** Different pathways can also **intersect**, forming an integrated and purposeful network of chemical reactions. These are collectively called ***metabolism***, which is **the sum of all the chemical changes occurring in a cell, a tissue, or the body.** Most pathways can be classified as either **catabolic (degradative)** or **anabolic (synthetic).**

- **Catabolic pathways**: involve reactions that breakdown complex molecules, such as proteins, polysaccharides, and lipids, to a few simple molecules, like,

CO_2, NH_3 (ammonia) and water. **Catabolic reactions serve to capture chemical energy in the form of ATP from the degradation of energy – rich fuel molecules.** Catabolism also allows molecules in the diet (or nutrient molecules stored in cells) to be converted into building blocks needed for the synthesis of molecules energy generation by **degradation of complex molecules occurs in three stages :**

1- Hydrolysis of complex molecules.

2- Conversion of building blocks to simple intermediates.

3- Oxidation of acetyl CoA.

- ***Anabolic pathways***: form complex end products from simple precursors, like synthesis of glycogen, polysaccharides from glucose. **Anabolic reaction required energy,** which is generally provided by the breakdown of ATP to ADP and Pi. Also anabolic reactions involve chemical reductions in which the reducing power is most frequently provided by the electron donor NADPH.

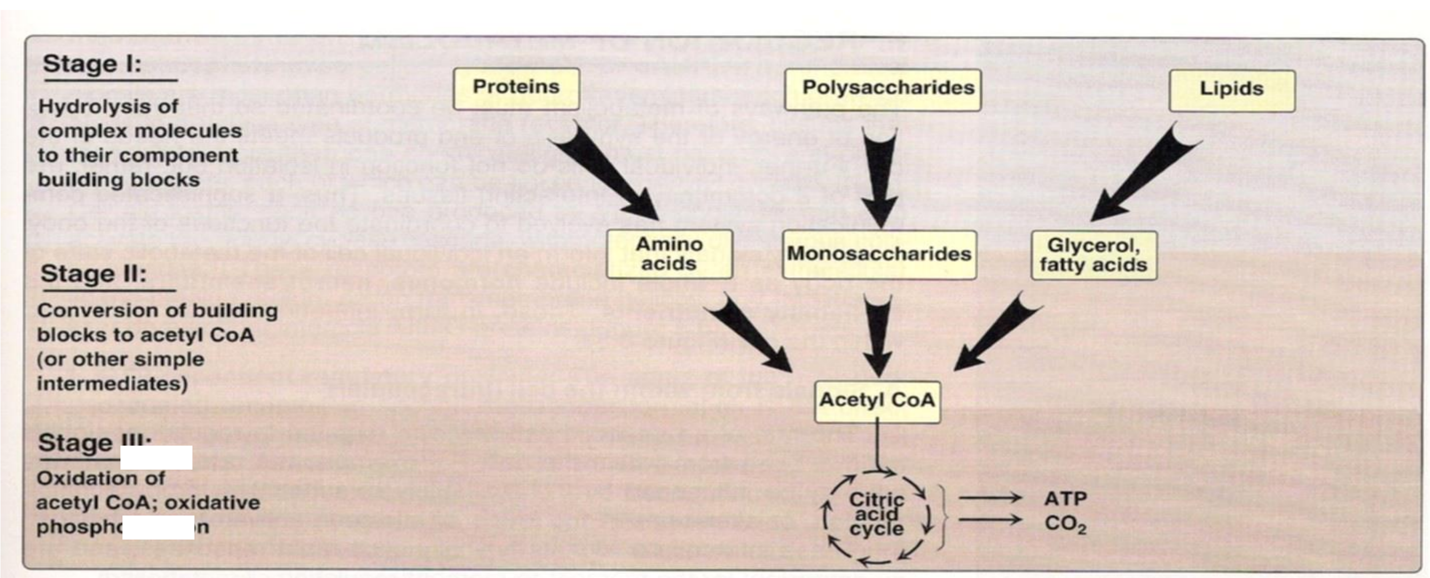

Figure 8.3
Three stages of catabolism.

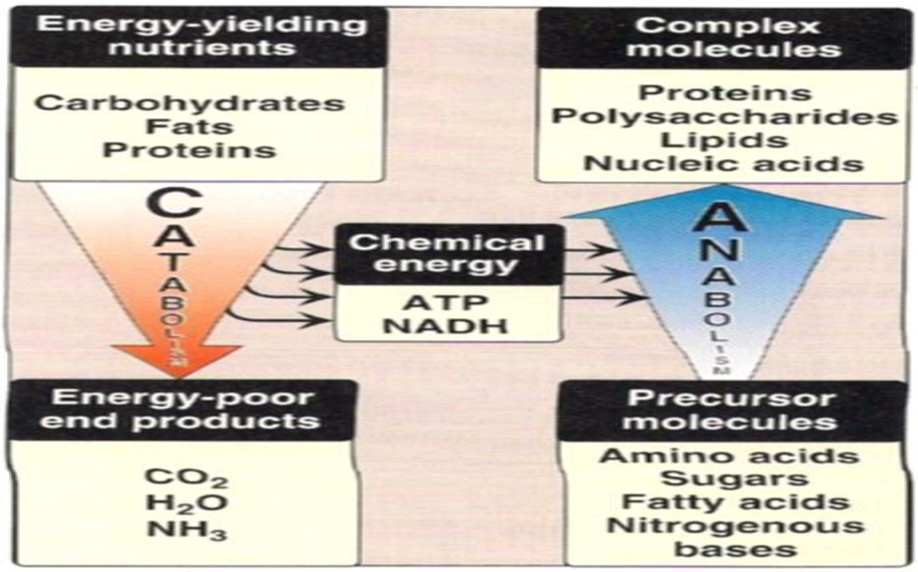

Figure 8.4
Comparison of catabolic and anabolic pathways.

- Metabolic pathways may have a third category called **Amphibolic pathway occur at the "crossroads" of metabolism, acting as links between the anabolic and catabolic pathways, e.g., citric acid cycle.**

Cellular Regulation of Metabolic Pathways:

The regulation of metabolic pathways may occur at several levels.

1- The reaction rate is a function of pH, intracellular concentration of substrates, products and cofactors.

2- Control of metabolic sequence through the action of regulatory enzymes.

3- Regulation through the genetic control of the rate of enzyme synthesis.

4- Regulatory signals that inform an individual cell of the metabolic state of the body as a whole include hormones, neurotransmitters and the availability of nutrients.

Digestion of carbohydrates:

- The major dietary carbohydrates are **starch, sucrose, and lactose.**
- Human can digest **only** polysaccharides consisting of **α(1→ 4) glycosidic** linkage or **α(1→ 4)** linkage with **α(1→ 6) branch points**.
- Liquid food materials like milk, soup, fruit juice escape digestion in the mouth as they swallowed, but solid foodstuffs are masticated thoroughly before they swallowed.
- **Digestion in Mouth**: **Salivary α - amylase (ptyalin)** (which requires **Cl^-** ion for activation, **pH about 6.7**) will **hydrolyzes α-(1→ 4) glycosidic linkage**, molecules like **starch, glycogen,** and **dextrin** will produce smaller molecules: **maltose, glucose and maltotriose.**
- **There is no digestion for carbohydrates in stomach**, but some dietary **sucrose** may be hydrolyzed to glucose and fructose by HCl.

- **Digestion in the intestine**: food bolus reaches the duodenum from stomach where it meets the **pancreatic juice**. Pancreatic juice contain **bicarbonate (HCO_3^-) neutralizes the stomach acid, raising the pH** into the optimal range for the action of the **intestinal enzymes**.

1) Digestion of pancreatic enzymes:

a- The pancreas secretes an **α - amylase** also called **amylopsin**, it is similar to salivary amylase, the enzyme **hydrolyze α - (1→ 4) glycosidic linkages** between glucose residues.

b- The products of pancreatic α - **amylase** are the disaccharides **maltose, maltotriose, and small oligosaccharides containing α - (1→ 4) and α - (1→ 6) linkages**.

2) Digestion by enzymes of intestinal cells:

Action of intestinal juice:

a- intestinal amylase: This hydrolyzes **terminal α - (1→ 4) glycosidic linkage** in polysaccharides and oligosaccharide molecules liberating **free glucose molecule.**

b- Isomaltase: It catalyze the hydrolysis of **α-(1→ 6) glycosidic linkage**, producing **maltose & glucose**.

c- Maltase: hydrolyze the **α - (1→ 4) glycosidic linkage**, producing **two glucose molecules.**

d- Lactase: It is a β - galactosidase. Lactose is hydrolyzed to **glucose and galactose.**

e- Sucrase: This enzyme converts sucrose to **glucose and fructose.**

- ***Carbohydrates that cannot be digested***: indigestible polysaccharides are part of **dietary fiber** that passes through the intestine into the feces.
  For example, because enzymes produced by **human cells cannot cleave the (β-1, 4) bonds** of carbohydrates, these polysaccharides (like **cellulose**) are **indigestible.**

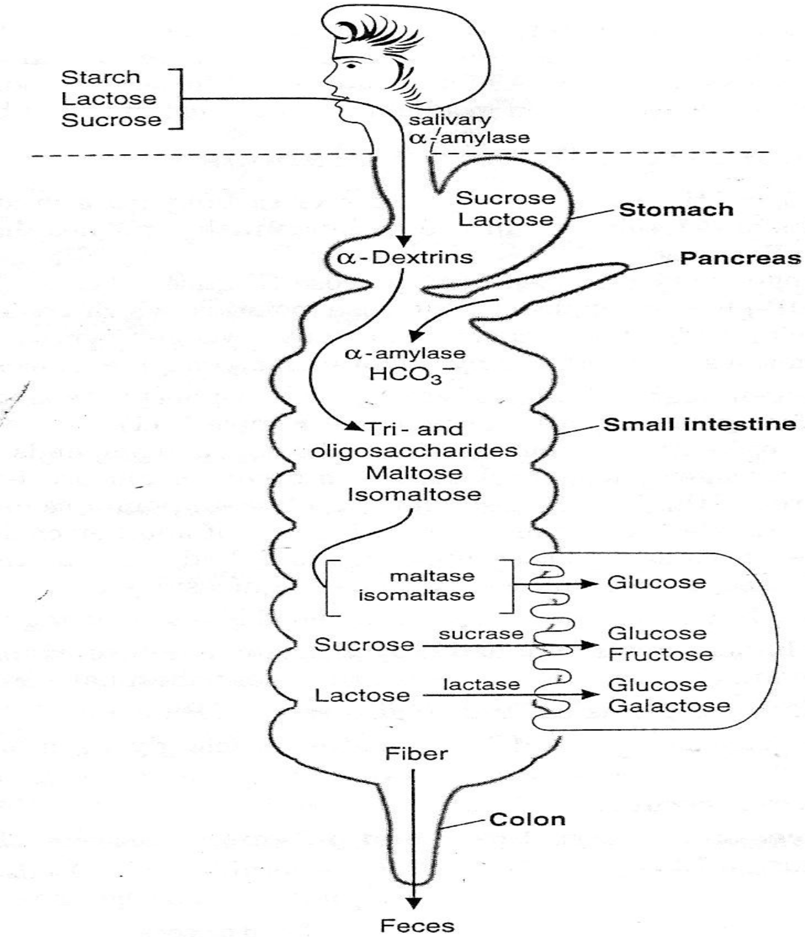

Figure 5-10. Digestion of carbohydrates. Starch is digested by salivary and pancreatic α-amylases and intestinal cell maltase and isomaltase. Sucrose and lactose are digested by intestinal enzymes.

Absorption of glucose, fructose and galactose:

Mechanisms of absorption:

1-Simple Diffusion: This is dependent on sugar concentration gradients between **the intestinal lumen, mucosal cells** and **blood plasma**. All the monosaccharaides are probably absorbed to some extent by **simple "passive" diffusion**.

2- Active Transport Mechanisms:

- **Glucose, fructose and Galactose**, the final products generated by digestion of dietary carbohydrates, are absorbed by intestinal epithelial cells.
- **Galactose and glucose** are absorbed **very fast**, **fructose and mannose intermediate rate** and the **pentoses** are absorbed **slowly**. **Galactose** is absorbed **more rapidly** than **glucose.**
- They are transported into the cells on transport proteins**, moving down a concentration gradient.**
- **The carrier protein has two binding sites one for Na and** another for the **glucose.** The carrier protein is **specific for sugar** and it is **mobile**.

<u>Glucose Transporters (GluT)</u>

- Glucose also moves into cells on transport protein **called glucose transporters (GluT)** that carries sodium ions in addition to the monosaccharide.
- Glucose Transporters(Glu-T) are several **(Glu-T-1 to** 7 **).**The most important are **GluT-2** and **GluT-4**
- **GluT-2**: Operates in **intestinal epithelial cells**; **<u>it is not Na dependent.</u>**
- **GluT-4**: Operates principally in **muscles** and **adipose tissue**.

The **<u>GluT-4 is under control of insulin</u>** and moves between cytoplasm and membrane.

((Note: Other "GluT" molecules are not under control of insulin)).

- **GluT-1** : is present mainly in **RB cells** and **brain**. Also present in **retina, colon** and **placenta.**

Absorption of other sugars:

- Sugars like **D-fructose** and **D-mannose** are probably absorbed by **"facilitated transport"** which requires the presence of carrier protein **but does not require energy**.
- Other sugars like pentoses and L-isomers of glucose and galactose are **absorbed passively by simple diffusion.**

Factors influencing rate of absorption:

1- **State of mucous membrane and length of time of contact.**

2- **Hormones**: **thyroid hormones increase** hexoses absorption, while **adrenal cortex hormones deficiency decrease** the hexoses absorption due to decreased **Na** concentration in body fluids. **Insulin** has no effect on absorption of glucose.

3- **Vitamins:** deficiency of **B-vitamins** decreased hexoses absorption.

4- **Inherited enzyme deficiencies** like **sucrase** and **lactase** can interfere with hydrolysis of corresponding disaccharides and their absorption

The anaerobic phase of glucose metabolism occurs whether O_2 is present or not.

B. Reactions of glycolysis (Figure 5-17)

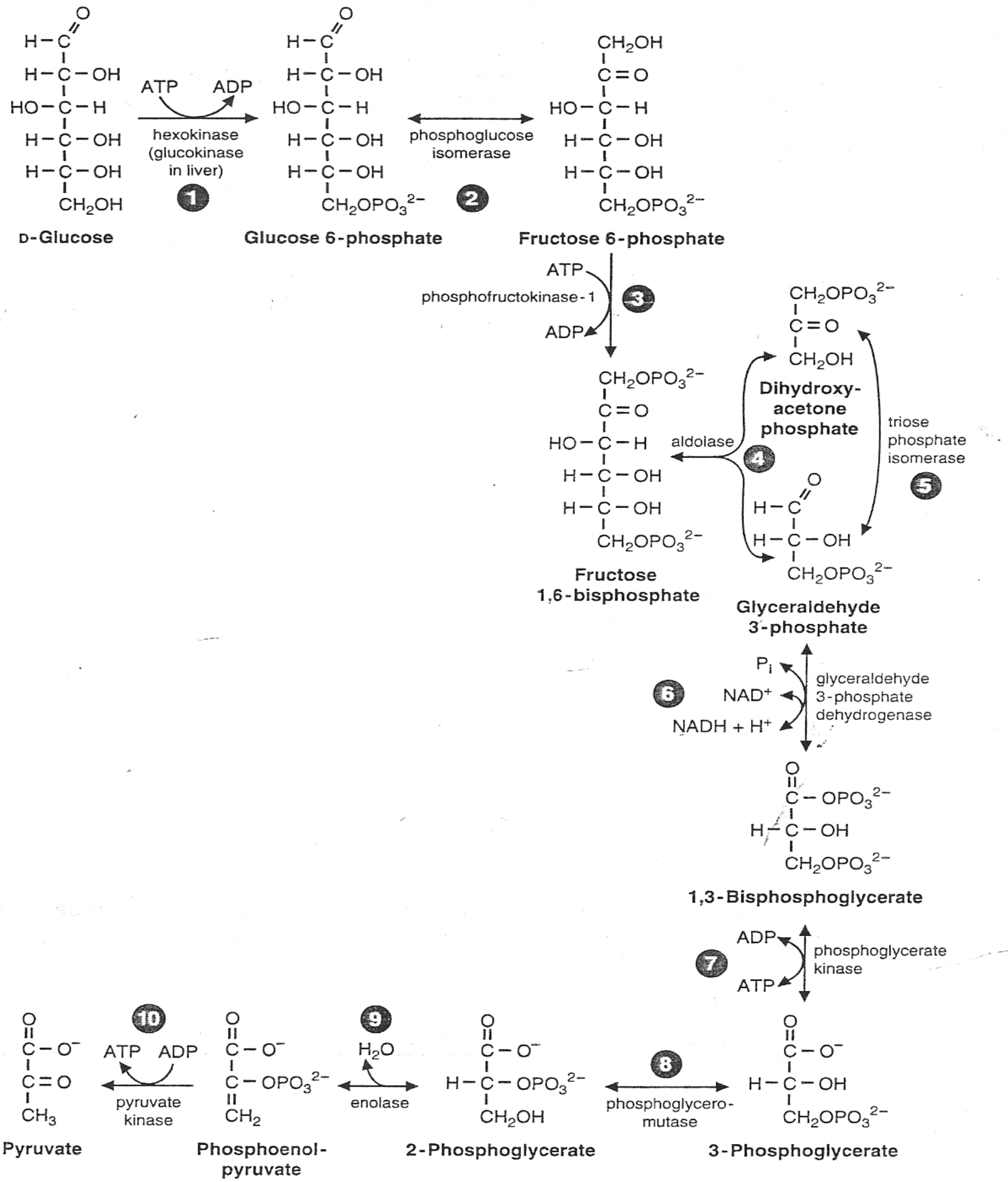

Figure 5-17. The reactions of glycolysis. The numbers correspond with those in V B in the text. These reactions occur in the cytosol.

Differences between hexokinase and glucokinase:

Hexokinase	Glucokinase
1-Non – specific, can phosphorylate any of the hexoses.	**1-** specific, can phosphorylated glucose only.
2- Found almost in all tissues.	**2-** Found only in liver.
3- Found in foetal as well as in adult liver.	**3-** Found in adult liver, not in foetal liver.
4- More stable.	**4-** Physiologically more labile.
5- Allosteric inhibition by G-6-P.	**5-** Not inhibited by G-6-P.
6-Km is low , hence high affinity for glucose.	**6-** Km is high , low affinity for glucose.
7-Not very much influenced by diabetic state or fasting.	**7-**Depressed in fasting and in diabetes. Glucokinase is deficient in patients of DM.
8- No change with glucose feeding.	**8-** Increased by feeding of glucose after fasting.
9- Inhibited by glucocorticoids and GH (growth hormone), insulin doesn't affect it.	**9-** Inhibited by glucocorticoids and GH. Synthesis is induced by insulin.
10- Main function to make available glucose to tissues for oxidation at lower blood glucose level.	**10- Main function is to clear glucose from blood after meals and at blood levels greater than 100 mg/dl.**