Introduction to Carbohydrates Metabolism

1 . Dietary carbohydrates include starch , sucrose , lactose and indigestible fiber .
2 .The major product of digestion of carbohydrates is glucose , but some galactose and fructose are also produced .
3 . Glucose is the major fuel source that is oxidized by cells for energy .
4 . Fructose and galactose are converted to intermediates in the pathways by which glucose is metabolized .
5 . Glycogen is the major storage form of carbohydrate in animals , the largest stores are in muscle and liver (muscle glycogen is used to generate ATP for muscle contraction) (liver glycogen is used to maintain blood glucose during fasting or exercise) .

Stages of carbohydrates metabolism

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1 . Glycolysis (Glycolytic pathway)(Embden Meyerhof pathway)

Can be defined as a sequence of reactions for the breakdown of glucose to two molecules of pyruvic acid under aerobic conditions or lactate under anaerobic conditions along with the production of small amount of energy , this occurs in the cytoplasm of all the cells of the body .

2 . krebs cycle (Citric acid cycle)(Tricarboxylic acid cycle)

Is a series chemical reactions used by all aerobic organisms to release stored energy through the oxidation of acetyl CoA derived from carbohydrates , fats and proteins into CO_2 and ATP . In eukaryotic cells , the CAC occurs in the matrix of the mitochondrion . In prokaryotic cells , such as becteria , which lack mitochondria , the CAC reaction sequence is performed in the cytosol with the proton gradient for ATP production being across the cells surface (plasma membrane) rather than the inner membrane of the mitochondrion .

3 . Glycogenesis (anabolic reaction):

Is the process of glycogen synthesis in which glucose molecules are added to chains of glycogen for storage . This process is activated by insulin in response to high glucose levels .

4 . Glycogenolysis (catabolic reaction):

Is the breakdown of glycogen to glucose – 1 – phosphate and glycogen $_{(n-1)}$ by the enzyme glycogen phosphorylase in the liver , muscle and the kidney . This process occurs to provide glucose when necessary .

5 .Gluconeogenesis

Is the process of synthesizing glucose from non-carbohydrate precursors such as lactate , amino acids and glycerol , occurs mainly in the liver and kidneys . It is a particular importance when carbohydrate is not available from the diet .

6 . Other pathway such as pentose phosphate pathway for production of ribose and NADPH .

Sources of blood glucose

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1 . From CHO in the diet :

Most CHO in the diet form glucose , galactose and fructose . Upon digestion ,these are absorbed into the portal vein . In the liver , fructose and galactose are converted into intermediates in the pathway by which glucose is metabolized .

2 . From glucogenic compounds that undergo through gluconeogenesis :

A–Compounds that directly convert into glucose without significant recycling e.g. amino acids such as alanine .

B – Compounds that are products of the partial metabolism of glucose in certain tissues and move to liver and kidney

to resynthesize glucose e.g. lactate formed in skeletal muscle convert to glucose in Cori cycle .
3 . From liver glycogen by glycogenolysis .

Utilization of glucose

1 . Formation of glycogen in the liver (glycogenesis) .
2 . Formation of glycogen in the muscle and adipose tissues .
3 . Conversion to fat (lipogenesis) , occurs mainly in the adipose tissues .
4 . Oxidation to supply energy (glycolysis) .
5 . Synthesis of glycolipids , glycoproteins , lactose and nucleic acids .
6 . Extraction in the urine when blood glucose level exceeds renal threshold (abnormal) .

Phosphorylation of blood glucose

Glucose is phosphorylated to glucose-6-phosphate in a reaction that is common to the first reaction in the pathway of glycolysis from glucose .The reaction is catalyzed by :

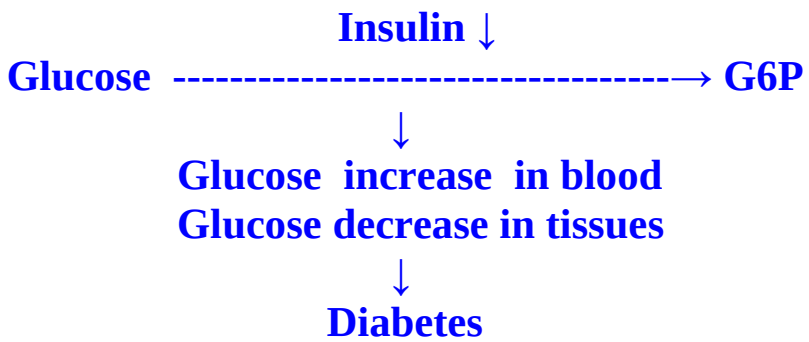
A . Hexokinase :

It is found in most tissues and is geared to provide glucose -6-phosphate for ATP production even when blood glucose is low .
a – Hexokinase has a low Km for glucose (about 0.1 mM) . Therefore , it is working near its maximum rate (Vmax.) even at fasting blood glucose levels (about 5 mM) .
b – Hexokinase is inhibited by its product , G-6-P . Therefore it is most active when G-6-P is being rapidly utilized .

B – Glucokinase :It is specific for glucose sugar , is found in the liver .
a – Glucokinase has a high Km for glucose (about 6 mM) . Therefore it is very active after a meal when glucose levels in the hepatic portal vein are high , and it is relatively inactive during fasting when glucose levels are low .
b – It is not inhibited by its product , G-6-P .

When glucose enters cells , it is converted to G-6-P,which is a pivotal compound in several metabolic pathways :
- The major fate of G-6-P is to enter the pathway of glycolysis , which produce pyruvate and generates NADH and ATP .
- G-6-P can be converted to G-1-P and then to UDP– glucose , which is used for the synthesis of glycogen .
- G-6-P can also enter the pentose phosphate pathway , which produces NADPH and ribose for nucleotide production .

The inactive hexokinase is converted into active hexokinase by the action of insulin .The function of insulin is to increase the entrance of glucose into the cell by stimulating the reaction of conversion (G → G6P) , thus if insulin is not present , then glucose will not be converted into G6P and cannot enter the cell ,while it remains in blood and causes diabetic .



Common problems associated with carbohydrate metabolism

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1 . Intestinal lactase deficiency :

Intestinal lactase deficiency is a common condition in which lactose cannot be digested and it oxidized by becteria in the gut , which produce gas and causing bloating and watery diarrhea .

2 . Hypoglycemia (low blood sugar) :

Is caused by the inability of the liver to maintain blood glucose levels .

Excessive alcohol ingestion can cause hypoglycemia , metabolism of alcohol increase levels of NADH in the liver , which inhibit gluconeogenesis .

3 . Diabetes mellitus :

Is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion , insulin action or both .

(Type 1 , or insulin–dependent diabetes mellitus, IDDM , results from the pancreases failure to produce enough insulin)(Type 2 , or noninsulin–dependent diabetes mellitus, NIDDM , begins with insulin resistance) .

4 . Lactic acidosis :

An increase of lactate levels in the blood cause an acidosis . This condition can result from hypoxia or alcohol ingestion .

5 . Galactosemia :

The appearance of high concentrations of galactose in the blood after lactose ingestion may be due to the galactokinase deficiency . In this conditions , galactose accumulates and is reduced to galactitol , which causes cataracts .

6 . Pyruvate kinase deficiency :

Deficiency of pyruvate kinase caused decreased production of ATP from glycolysis . RBCs have insufficient ATP for their membrane pumps , and a hemolytic anemia results .

Notes :

1 . The reaction of the phosphorylation is irreversible because the energy in glucose and ATP is higher than the energy in G6P , so there is loss of energy and reaction goes forward only .

2 . The blood glucose level is maintained with in these physiological limits by balance between two sets of factors :

A – Factors adding glucose to the blood .

B – Factors that remove glucose from the blood .

3 . Muscle glycogen cannot provide blood glucose by glycogenolysis due to lacks of the enzyme (glucose-6-phosphatase) .

4 . How to determine whether you have diabetes , prediabetes or neither : there are three possible tests :

a – The A1C test :

- **At least 6.5 % means diabetes .**
- **Between 5.7 % and 5.99 % means prediabtes .**
- **Less than 5.7 % means normal .**

b – The FPG (fasting plasma glucose) test :

- **At least 126 mg / dl means diabetes .**
- **Between 100 mg / dl and 125.99 mg / dl means prediabetes .**
- **Less than 100 mg / dl means normal .**

c – The OGTT (oral glucose tolerance test) :

- **At least 200 mg / dl means diabetes .**
- **Between 140 mg / dl and 199.9 mg / dl means prediabetes .**
- **Less than 140 mg / dl means normal .**