Carbohydrate Metabolism

Definition of Metabolism:

The chemical processes occurring within a living cell or organism that are necessary for the maintenance of life. All these are called anabolism and catabolism.

Metabolism

Anabolic reaction	**catabolic reaction**
1. synthesis of complex molecules from simple compound.	1.break down of large molecules Such as polysaccharides, proteins
2. energy is needed for synthesis (endergonic reaction)	Into small molecules like, CO_2, NH_3, H_2O.
	2. liberated energy. (exergonic reaction)

Digestion and absorption:

Digestion of CHO is accomplished by the enzymes of digestive fluids, saliva, pancreatic juice and intestinal juice.

1. mouth: salivary glands secrete saliva

Saliva contains: **α- amylase** (ptyalin), **water** 99.5% and **glycoprotein** as food lubricant.

α- amylase, hydrolysis **starch** to dextrin and maltose.

PH of α- amylase = 5.8 – 7.1 less than 4.0 is in active

2. stomach ---------- no digestion is seen in stomach , amylase is in active

Because the PH of stomach (1 - 2) very acidic.

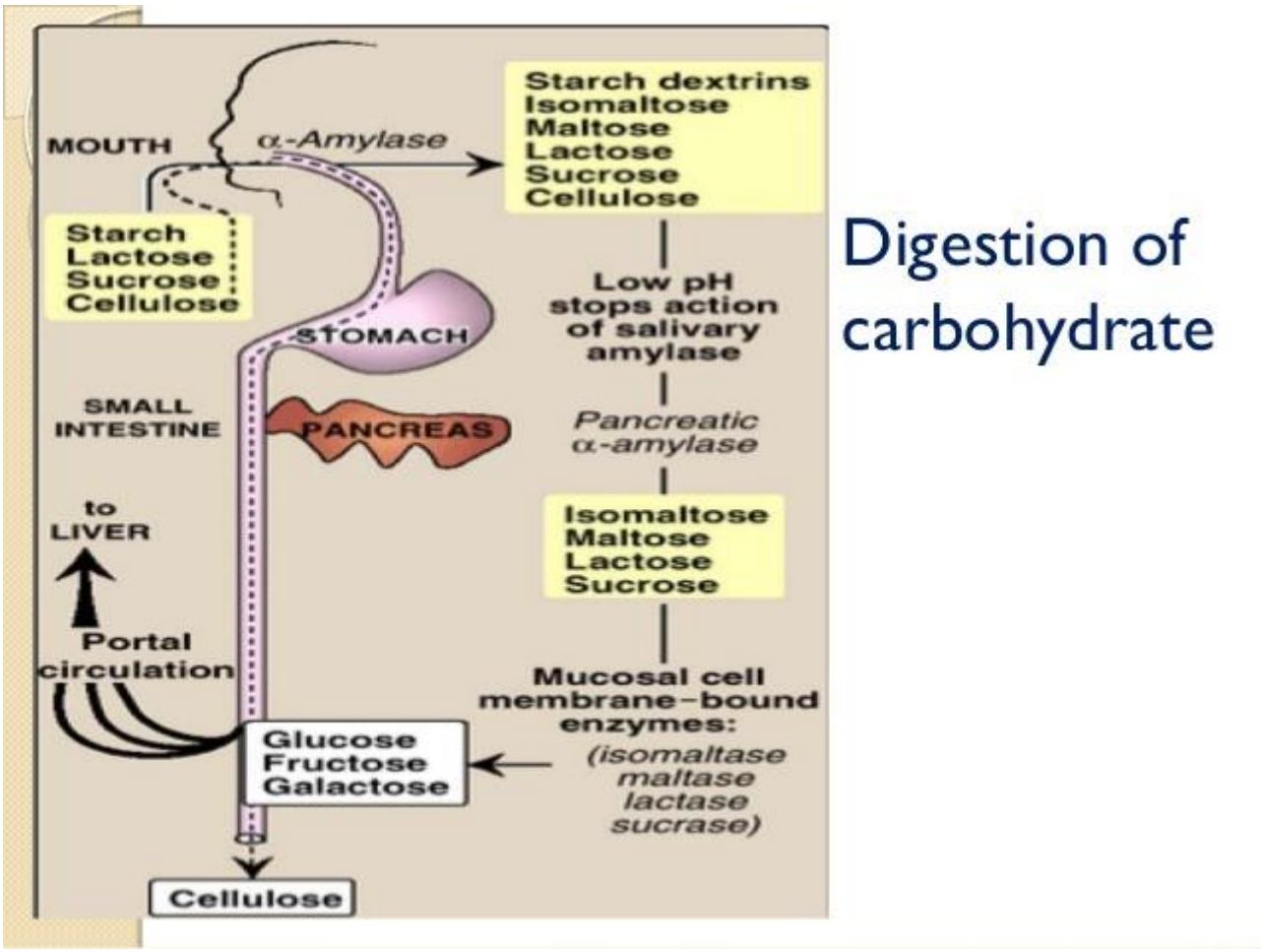
3. small intestine: it is the major site of digestion of CHO, pancreatic amylase hydrolyze dextrin into maltose. The optimum PH of amylase = 7.1

4. intestinal mucosal : mucosal cell membrane – bound enzymes , the site where disaccharides hydrolyze.

Maltose $\xrightarrow{\text{maltase}}$ glucose + glucose

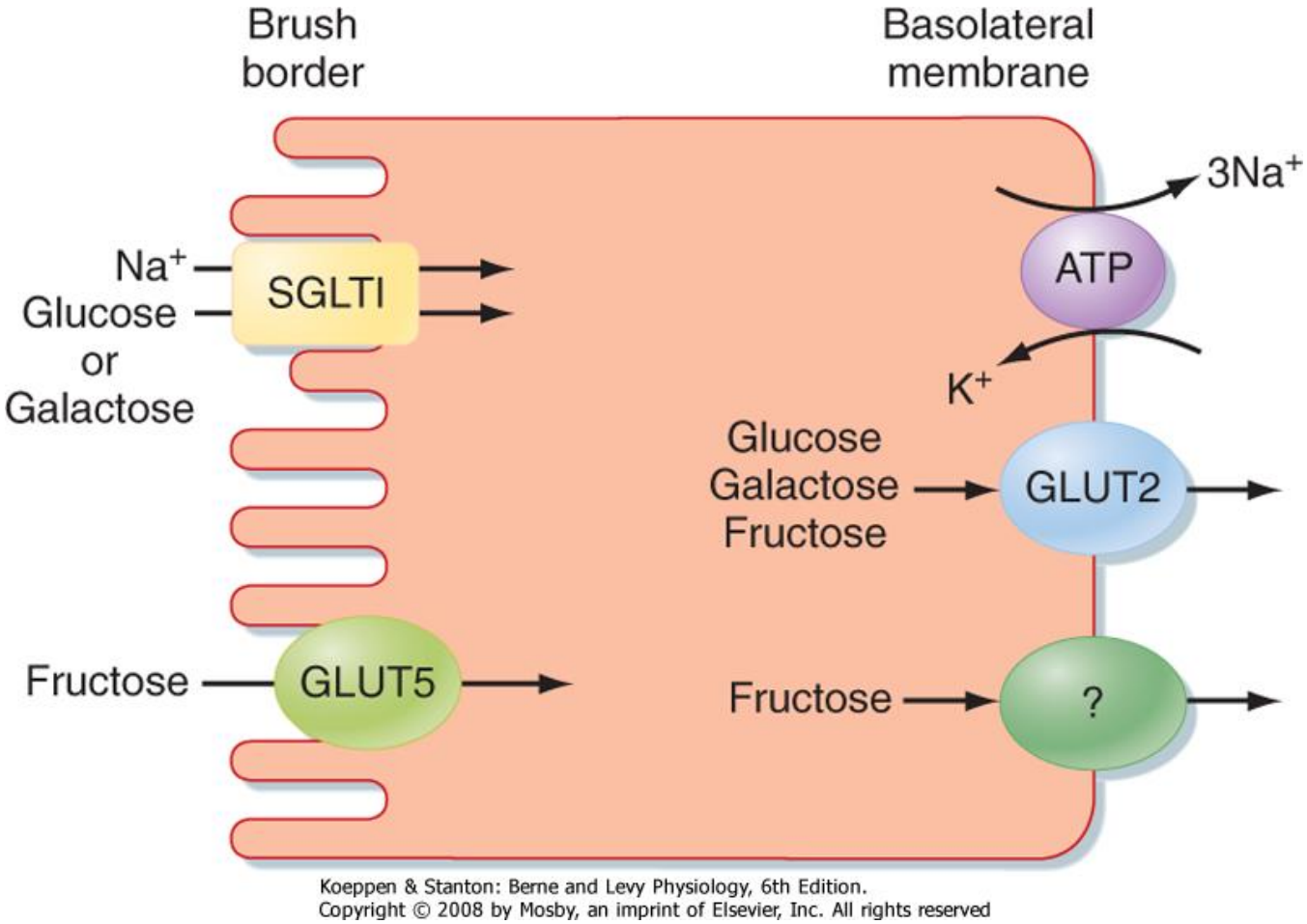
Sucrose $\xrightarrow{\text{sucrase}}$ glucose + fructose

Lactose $\xrightarrow{\text{lactase}}$ glucose + galactose



Absorption of Carbohydrates

Intestine



Absorption of Carbohydrates:

1. transport into epithelial cells (of the villi)

glucose and galactose are transported by **active transport**, while **fructose** is transported by **facilitated diffusion.**

2. transport from epithelial cells into the blood stream is by **facilitated diffusion.**

Fate of glucose after absorption

In the liver, glucose undergoes **variety of chemical changes depending upon the physiological need of the body.**

1. Body need for energy: glucose oxidized completely to **CO2, H2O and energy** by (**glycolysis** and **citric acid cycle**).

2. Excess glucose may be converted to glycogen, deposit in liver, muscle tissues By **(glycogenesis**).

3. To maintain glucose blood level, liver glycogen reconverted to glucose enters blood By **(glycogenolysis).**

4. excess glucose after conversion to glycogen , **convert to fatty acids stored in adipose tissue as triglycerides (lipogenesis).**

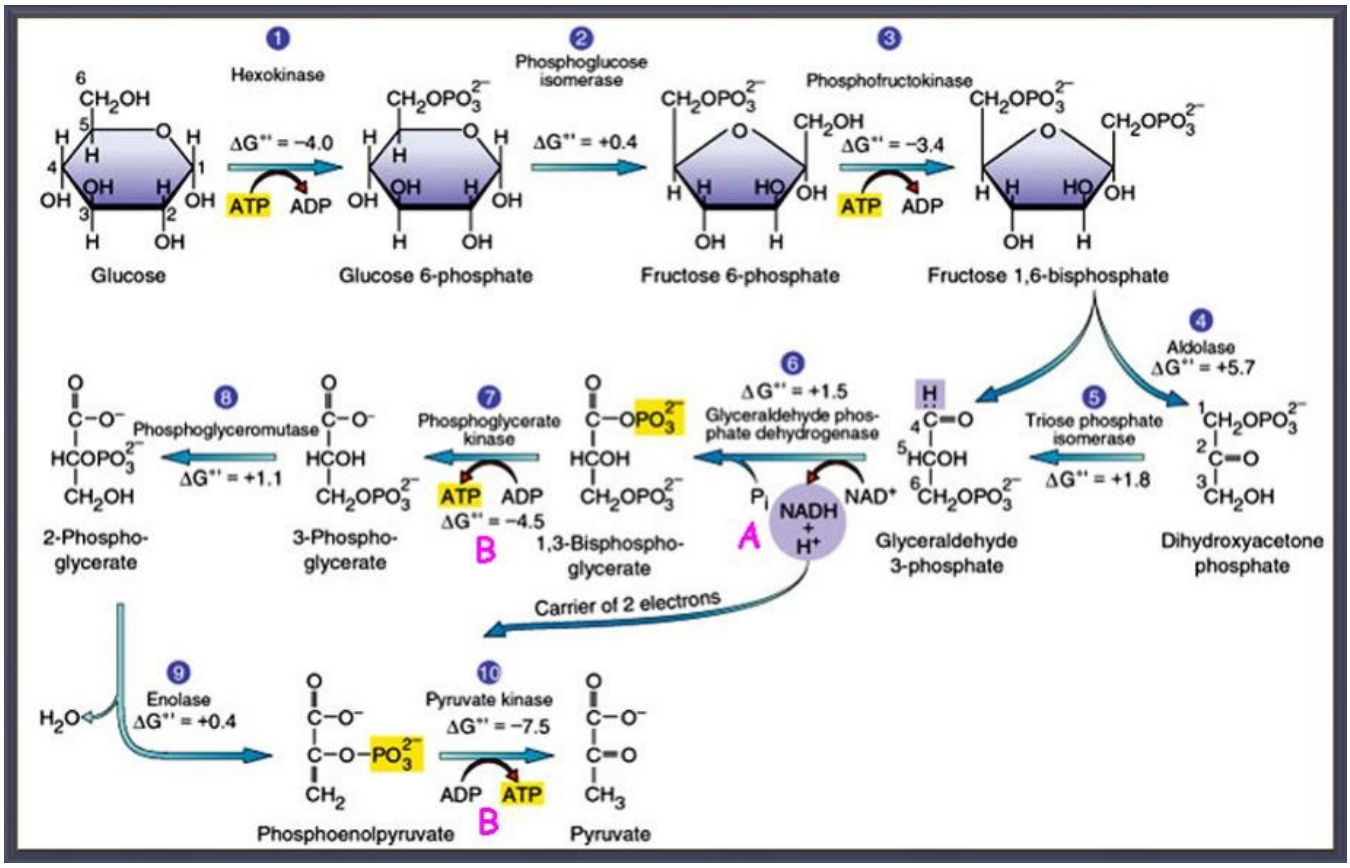
5. small amounts of glucose may be utilized for the synthesis of ribose and deoxyribosee for synthesis of nucleic acids.

6. in muscle contraction, only partial degradation of glucose may take place, resulting in formation of lactic acid disposed off by the liver.

The metabolism of CHO may be subdivided in the following categories.

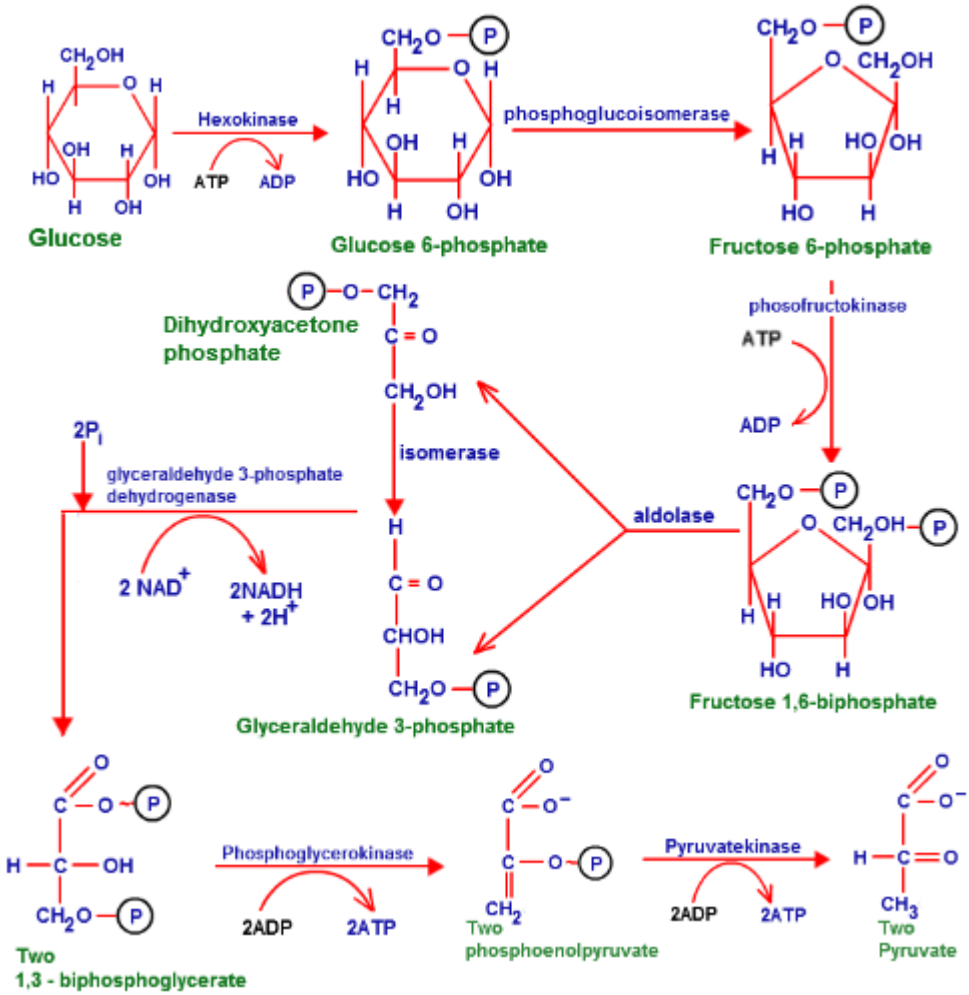
Glycolysis: (from *glycose*, an term for glucose + *-lysis* degradation)

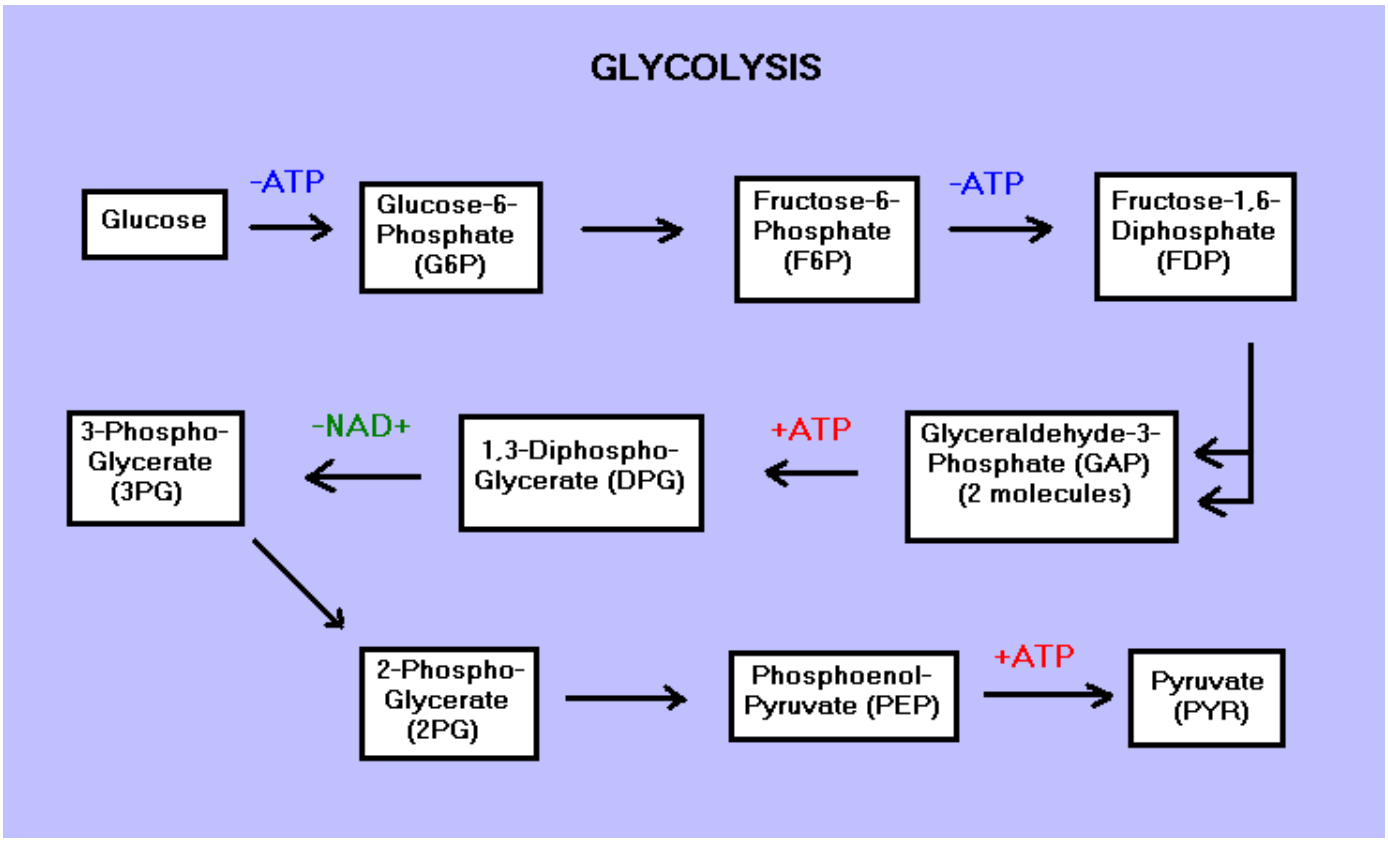
1. It is the metabolic pathway that converts glucose $C_6H_{12}O_6$, into pyruvate.
2. The free energy released in this process is used to form the high-energy molecules ATP and NADH.
3. Glycolysis is an oxygen independent metabolic pathway, said to be anaerobic.
4. Glycolysis occurs in the cytosol (cytoplasm) of the cell.
5. The most common type of glycolysis is the Embden–Meyerhof–Parnas (EMP), which was discovered by Gustav Embden, Otto Meyerhof, and Jakub Karol Parnas.
6. The glucose in the blood circulation, when enter the cell become phosphorylated given by ATP (Activation by phosphate group).
7. This phosphorylation occurs on the cell membrane by the action of two enzymes.
    1. specific enzyme (glucokinase) in the liver.
    2. nonspecific enzyme (hexokinase), Present in liver and other extra hepatic cell
8. Glu-6- p is an important compound for several metabolic pathways. The reaction is irreversible.

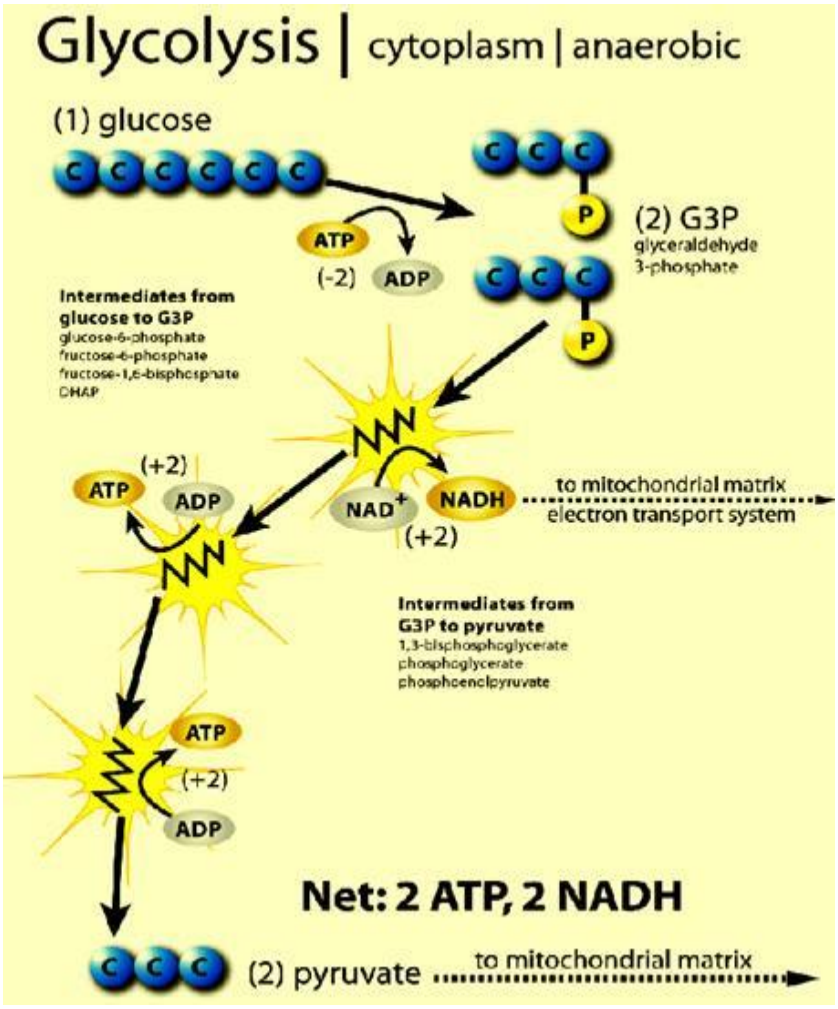


The overall process of glycolysis is:

$$\text{Glucose} + 2\ NAD^+ + 2\ ADP + 2\ P_i \rightarrow 2\ \text{Pyruvate} + 2\ NADH + 2\ H^+ + 2\ ATP + 2\ H_2O$$




GLYCOLYSIS
Glucose
-ATP
Glucose-6-Phosphate (G6P)
Fructose-6-Phosphate (F6P)
-ATP
Fructose-1,6-Diphosphate (FDP)
Glyceraldehyde-3-Phosphate (GAP) (2 molecules)
+ATP
1,3-Diphospho-Glycerate (DPG)
-NAD+
3-Phospho-Glycerate (3PG)
2-Phospho-Glycerate (2PG)
Phosphoenol-Pyruvate (PEP)
+ATP
Pyruvate (PYR)


Glycolysis | cytoplasm | anaerobic
(1) glucose
ATP
(-2)
ADP
(2) G3P
glyceraldehyde 3-phosphate
Intermediates from glucose to G3P
glucose-6-phosphate
fructose-6-phosphate
fructose-1,6-bisphosphate
DHAP
(+2)
ATP
ADP
NAD+
NADH
(+2)
to mitochondrial matrix
electron transport system
Intermediates from G3P to pyruvate
1,3-bisphosphoglycerate
phosphoglycerate
phosphoenolpyruvate
ATP
(+2)
ADP
Net: 2 ATP, 2 NADH
(2) pyruvate
to mitochondrial matrix

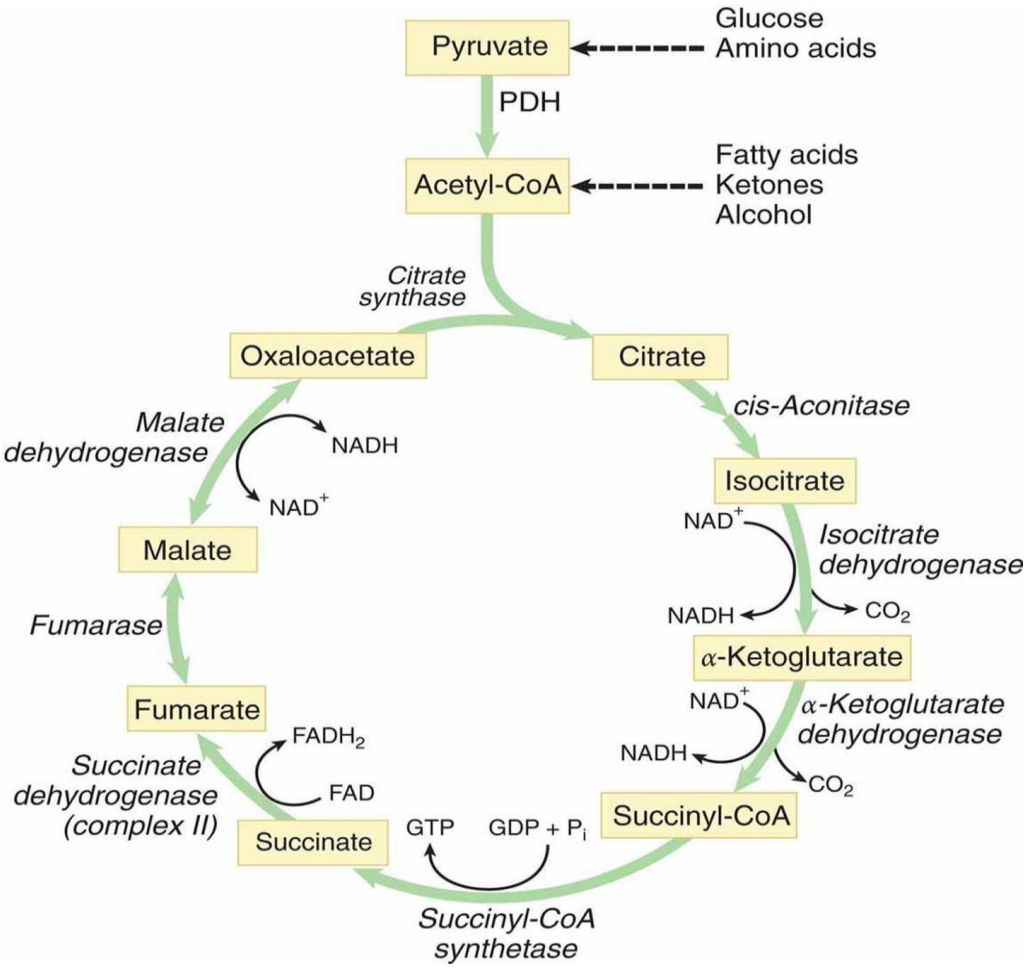
Energy production: The net of ATP molecules during glycolysis is equal to (8).

ATP used	1.	(glu ⟶ glu-6-pho)	1 ATP
	2.	(F-6-pho ⟶ F-1,6 - di pho)	1 ATP
ATP gain	Gly-3- pho ⟶	1,3-diphoGly	NADH × 2
	1,3 -diphoGlyc ⟶	3phoGly	1 ATP × 2
	PEP ⟶	pyruvate	1 ATP × 2

Net of ATP from anaerobic glycolysis 10 – 2 = 8 ATP

Formation of lactate from pyruvate is the major steps in **RBCs, lens and cornea, kidney, medulla, and leukocytes.**

Tricarboxylic Acid Cycle (TCA) OR Krebs Cycle:



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ATP generated in TCA cycle

Convertion of :

pyruvic acid to acetyl COA 1 NADH = 3ATP

Isocitric acid to α-ketoglutarate	1NADH	=3ATP
α –ketoglutarare to succinyl COA	1NADH	=3ATP
Succinyl COA to succinic acid	1GTP	=1ATP
Succinic acid to fumeric acid	1FAD	=2 ATP
Malic acid to oxaloacitic acid	1NADH	=3ATP
	total	15 ATP

Net ATP produced per glucose molecule = 15 × 2= 30 ATP

Total ATP per glucose (aerobic oxidation + anaerobic) 30 + 8= 38 ATP

Citric acid cycle

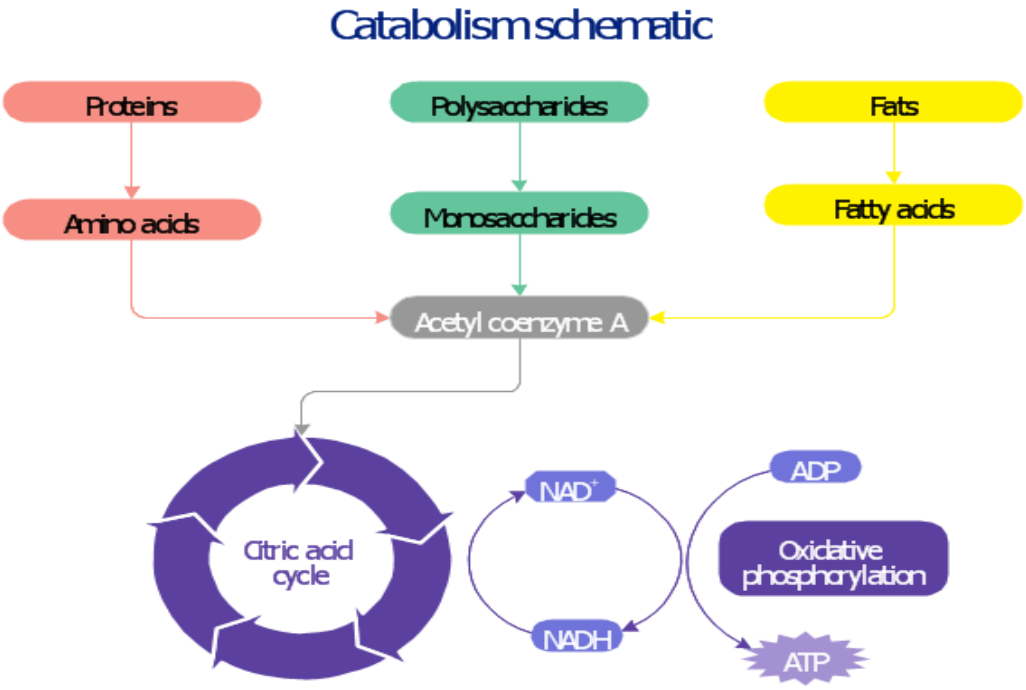
Krebs cycle, tricarboxylic acid cycle TCA

The central function is the oxidation of acetyl CoA to CO2

- It is the final common pathway for oxidation of fuel molecules
- Acetyl Co is derived from the metabolism of fuel molecules as amino acids, fatty acids, and carbohydrates.
- Citric acid cycle is also an important source of precursors
  - Some intermediates are precursors of amino acid
  - One of the intermediates is used in the synthesis of porphorins
  - Another is used in the synthesis of fatty acids and sterols.
- Citric Acid Cycle located in the mitochondrial matrix

(c) Glycolysis and citric acid cycle

Glycolysis		**Citric acid cycle (Krebs cycle)**	
1.	It is a linear pathway.	1.	It is a cyclic pathway.
2.	It occurs in the cell cytoplasm.	2.	It occurs in the mitochondrial matrix.
3.	It occurs in both aerobic and anaerobic respiration.	3.	It occurs in aerobic respiration.
4.	One glucose molecule breaks down to generate 2 $NADH_2$ and 2 ATP molecules.	4.	It produces 6 $NADH_2$, 2 $FADH_2$, and 2 ATP molecules on breakdown of two acetyl-coA molecules.



Glycogenesis (glycogen synthesis): formation of glycogen from glucose.

1. Glycogen is serves as an energy store primarily in muscle and liver, when glucose and ATP are present in relatively high amounts.

2. the excess of insulin promotes the glucose conversion into glycogen for storage in liver and muscle cells.

3. It is stored in the form of granules **cytoplasm** in the cell.

4. The concentration of glycogen in **muscle is low** (1-2 % fresh weight) compared to the levels **stored in the liver** (up to 8% fresh weight).

5. Glycogen is an **energy reserve** that can be quickly mobilized to meet a sudden need for glucose.

Difference between muscle and liver glycogen

	Liver glycogen	Muscle glycogen
Amount	-	More
Source	Glucose and other precursors	Glucose only
Hydrolysis	Give blood glucose	Give lactic acid
Starvation	Converted into blood glucose	Not affected
Muscular exercise	Depleted later on	Depleted first

Glycogenolysis: biochemical breakdown of glycogen to glucose.

1. take place in the cells of muscle and liver tissues in response to hormonal and neural signals.

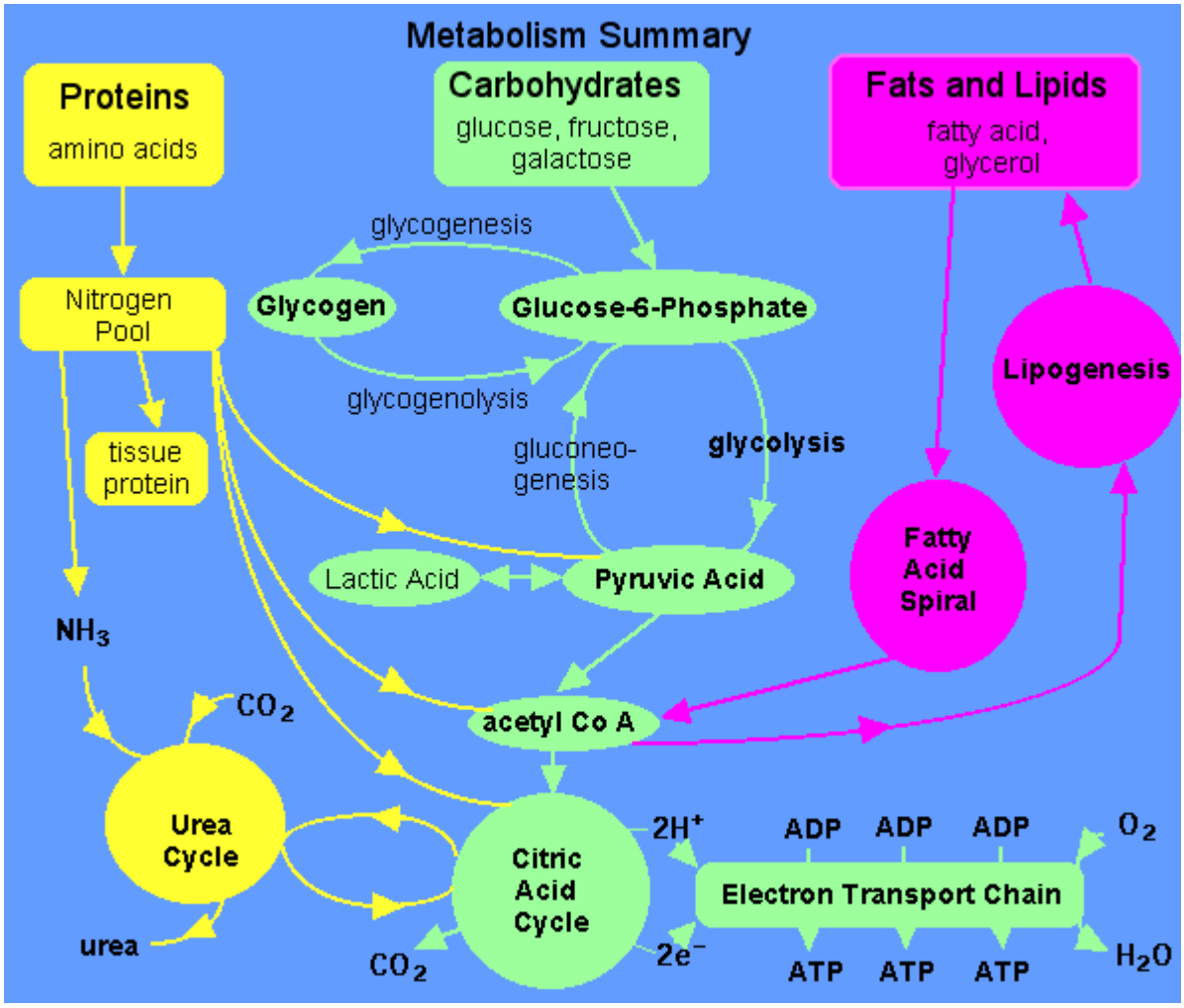
2. Glycogenolysis occurs in the cytoplasm and is stimulated by **glucagon** and **adrenaline hormones.**

3. glycogenolysis plays an important role in the **adrenaline-induced fight-or-flight** response and the **regulation of glucose levels in the blood.**

4. The enzymes required for this process are **glycogen phosphorylase**, **debranching enzyme, and amylo-α-1, 6-glucosidase.**

Gluconeogenesis: is the process of producing glucose from non-carbohydrate sources.

1. 6 ATP molecules are consumed per molecule of glucose produced.
2. most reactions of the gluconeogenesis take place in the ***cytoplasm*** while two reactions occur in the **mitochondria**
3. It mainly occurs in hepatocytes in liver.
4. The molecules that provide substrates for gluconeogenesis include ***proteins***, ***lipids*** and **pyruvate.**
5. Muscle proteins are degraded to form ***amino acids***, These amino acids are called '**glucogenic amino acids.**
6. **Pyruvate** is produced by ***glycolysis*** under ***anaerobic*** conditions.
7. ***glycerol*** produced during the ***hydrolysis*** of fat stores or ingested fats



Regulation (homeostasis) of blood glucose level:

The blood sugar level is maintained by two factors .

a.factors adding glucose to blood (increase blood glucose level).

- from diet (intestinal absorption).
- glycogenolysis (liver).
- gluconeogenesis.
- lipolysis
- conversion of fructose and galactose into glucose

b. factors remove glucose from blood (decrease blood glucose level).

- glycogen formation in liver and muscle (glycogenesis).
- glycolysis in liver(oxidation of glucose).
- convertion of glucose to fat in adipose tissue(lipogenesis).
- B-oxidation (supply energy).
- synthesis of glycoprotein.
- excretion in urine (diabetes)

Hormones decrease blood glucose level

1. insulin secreate from β-cells of pancreas.

causes the liver to convert more glucose into glycogen (this process is **called glycogenesis**).

2. about **2/3 of body cells (primarily muscle and fat tissue cells)** take up glucose from the blood, thus decreasing blood sugar..

Hormones increase blood glucose level

1.glucagon

in very heavy exercise or lack of food for extended periods, the Alpha cells of the pancreas release glucagon, a hormone act to increase blood glucose levels. They convert **glycogen** into glucose (this process is **called glycogenolysis).**

2. Epinephrine, also known as **adrenalin** or **nor adrenaline**, is a hormone, neurotransmitter and medication

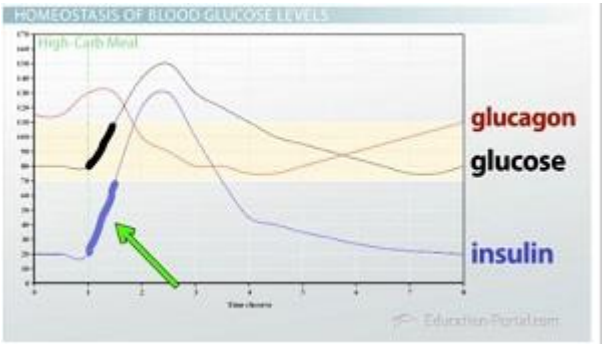
a. Enhances release of glucose from glycogen **(glycogenolysis**).

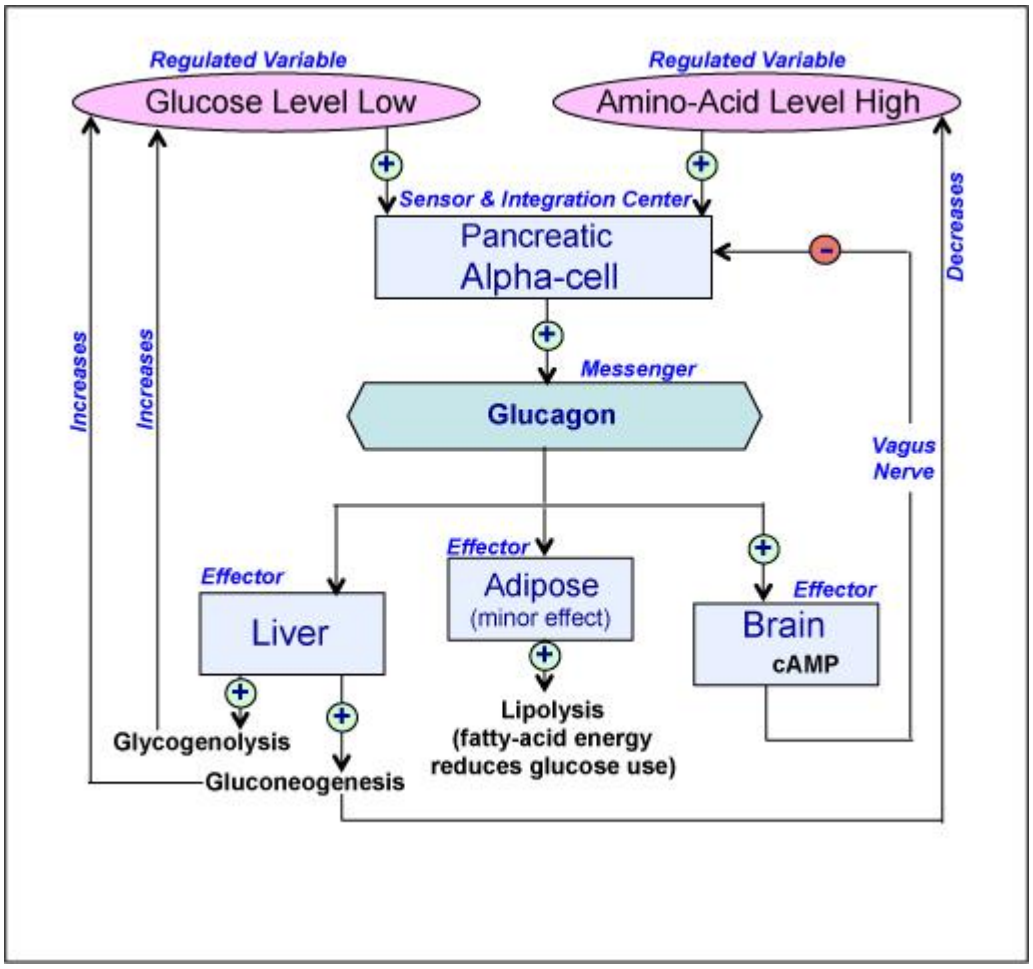
b. Enhances release of fatty acids from adipose tissue **(lipolysis).**

3. Cortisol, Enhances **(gluconeogenesis)** ; Antagonizes **Insulin.**

4. Thyroxine, Enhances release of glucose from glycogen; Enhances absorption of sugars from intestine

5. ACTH, Enhances release of fatty acids from adipose tissue **(Lipolysis).**





BLOOD SUGAR LEVEL CHART

	FASTING	JUST ATE	3 HOURS AFTER EATING
NORMAL	80-100	170-200	120-140
PRE-DIABETIC	101-125	190-230	140-160
DIABETIC	126+	220-300	200+

Abnormalities in blood glucose level:

- **1.Hyperglycemia:** Hyperglycemia is an abnormally high blood glucose (blood sugar) level.
- Hyperglycemia is a hallmark sign of **diabetes** (both **type 1 diabetes** and **type 2 diabetes)** and **prediabetes.**
- **Diabetes** is the most common cause of hyperglycemia.

- **Causes of hyperglycemia**
- **pancreatitis**, **Cushing's syndrome**, **pancreatic cancer, certain medications**, and **severe illnesses.**
- **Common symptoms of diabetes:**
- 1. Urinating often. 2. Feeling very thirsty. 3. Feeling very hungry - even though you Eating.
  4. Extreme fatigue. 5. Blurry vision. 6. Weight loss - even though you are eating more (type 1)
  7. Tingling, pain, or numbness in the hands/feet (type 2)
  8. Cardiac arrhythmia

Treatment: This is done by a combination of proper **diet**, **regular exercise**, and **insulin** or other medication such as **metformin.**

2. Hypoglycemia:

abnormally low level of sugar (glucose) in the blood. Hypoglycemia is not a disease in itself.

The brain needs a continuous supply of glucose to **function** because it can neither store nor manufacture glucose.

Hypoglycemia is not a disease, it is commonly linked with **diabetes** or caused by other conditions.

Common symptomes of low sugar levels: include **hunger, trembling, heart racing, nausea**, and **sweating**.

Causes of hypoglycemia:

1. medication:

Quinine, a drug used for **malaria**, can also cause hypoglycemia. Salicylates, which are used for treating **rheumatic disease**, and propanolol for (**high blood pressure**)

2. Alcohol abuse if somebody has been drinking heavily.

3. Some liver diseases -hepatites can cause hypoglycemia.

4. Kidney disorders

5. Some disorders of the **adrenal and pituitary glands** can lead to hypoglycemia.

6. Not eating enough - people with eating disorders, such as **anorexia nervosa**, may find that their blood sugar levels drop dramatically.

7. Insulinoma - this is a **tumor in the pancreas** which can make the pancreas produce too much insulin.

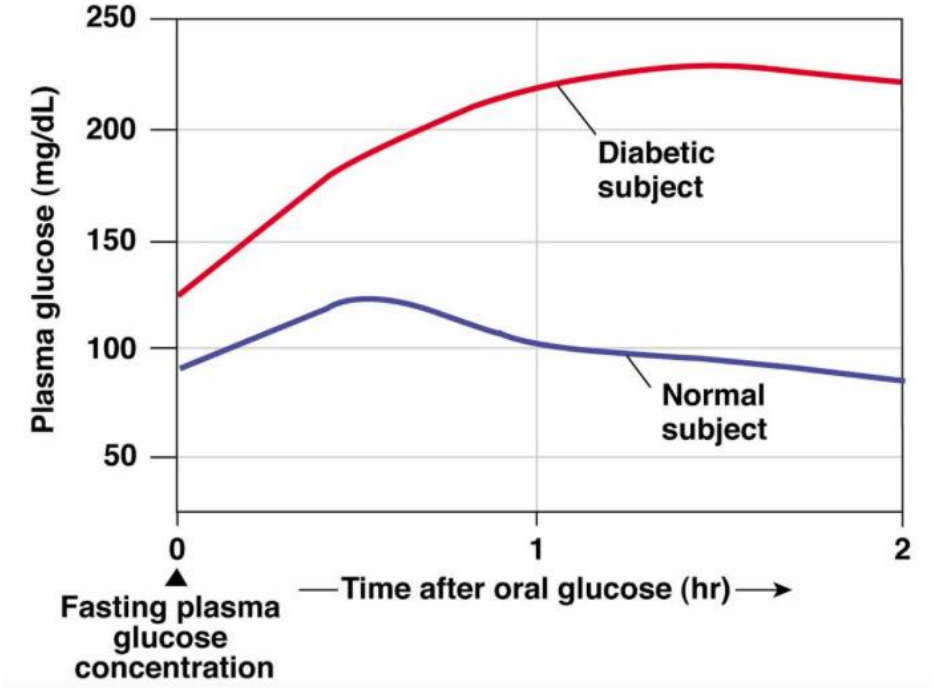
Test used in determining blood sugar:

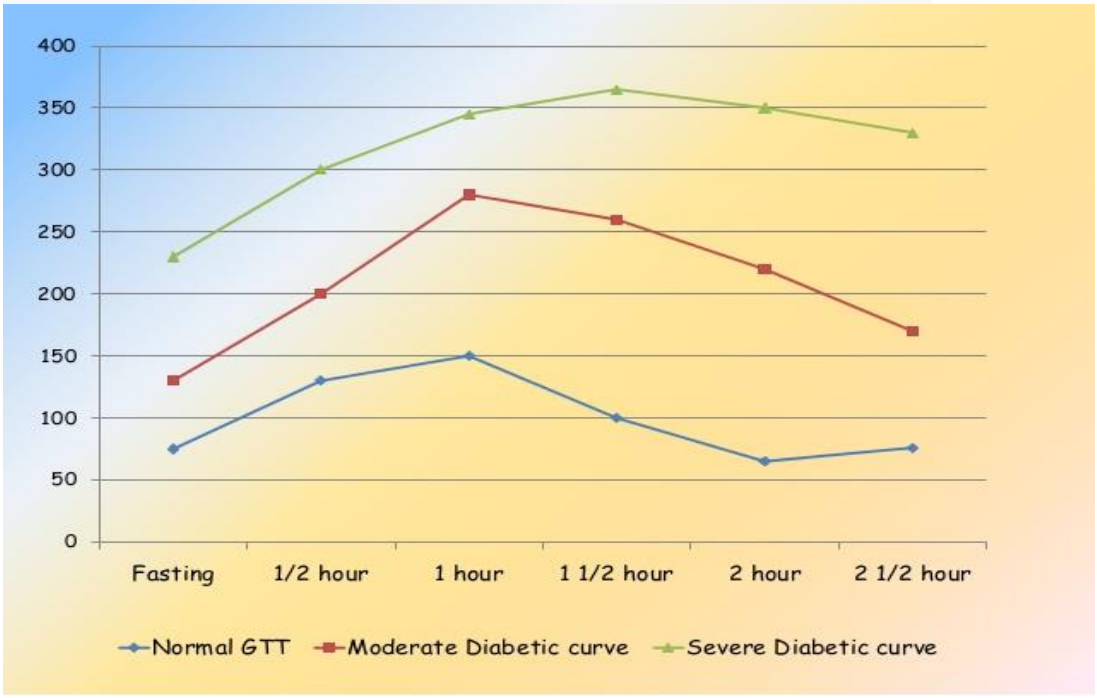
1. Fasting blood sugar (F.B.S).

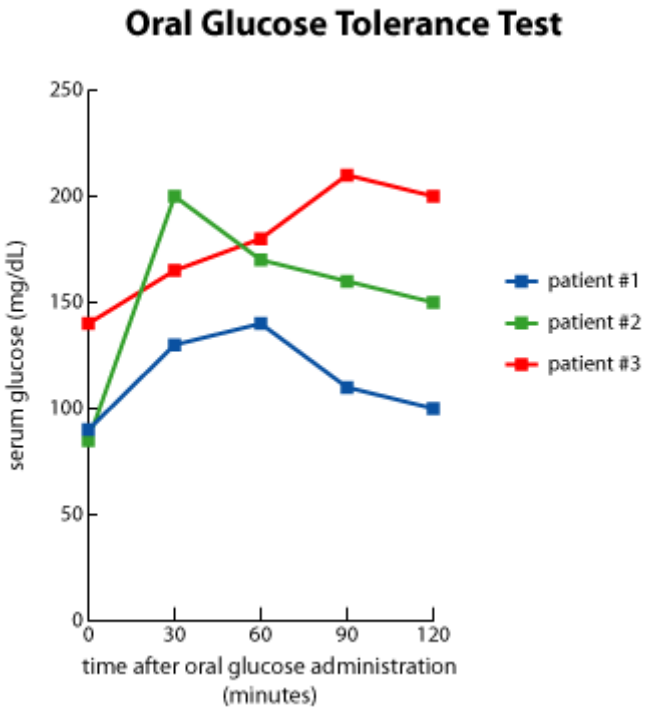
2. Random blood sugar (R.B.S).

3. 2hrs postprandial test

4. Oral glucose tolerance test (OGTT).


250
200
150
100
50
Plasma glucose (mg/dL)
Diabetic subject
Normal subject
0
1
2
Fasting plasma glucose concentration
Time after oral glucose (hr)


400
350
300
250
200
150
100
50
0
Fasting
1/2 hour
1 hour
1 1/2 hour
2 hour
2 1/2 hour
Normal GTT
Moderate Diabetic curve
Severe Diabetic curve



A. Normal blood sugar level= 70 – 100 mg/ dl or 80 – 110 mg/dl

B. Conditions in which blood sugar level is raised.

1.diabetes melletus 2.hyperthyrodism. 3.hyperadrenalism 4.thyrotoxicosis

C. Conditions in which blood sugar level is low.

1. Overdose of insulin treatment of diabetes melletus.
2. hypothyrodism

D. Kidney threshold of glucose equal = 180 mg/dl

E. Hormones regulate blood glucose level (insulin).

F. **The functions of insulin are:**

1. excess glucose in the bloodstream, known as hyperglycemia, insulin encourages the storage of glucose as glycogen in the liver, muscle (glycogenesis).
2. in fat cells(adipose tissues) synthesis of triglycerides (lipogenesis).
3. Build muscle following sickness or injury.
4. Enhance learning and memory of the brain functions.

Disorders in CHOs metabolism

1.Lactose intolerance:It is a condition in which people have symptoms due to the decreased ability to digest lactose, a sugar found in milk products.

Symptoms:

Abdominal pain, bloating, diarrhea, gas, and nausea. **These typically start between half and two hours after drinking milk**.

Severity depends on the amount a person eats or drinks. It does not cause damage to the gastrointestinal tract

Causes.

1. due to not enough of the enzyme lactase present in the small intestine to break lactose down in to glucose and galactose.

2. Primary lactose intolerance is when the amount of lactase decline as people age.

3. Secondary lactose intolerance is due to injury in the small intestine from **infection**, **celliac disease**, **inflammatory bowel disease.**

4. Developmental lactose intolerance may occur in premature babies and usually improves over a short period of time.

2. Galactosemia It is a hereditary disease that results in a **defect in, or absence of, galactose-metabolizing enzymes**. This inborn error leaves the body unable to metabolize galactose, **allowing toxic levels of galactose to build up in human body blood, cells, and tissues or urine .**

Symptoms: lethargy, vomiting, diarrhea, failure to thrive, and jaundice. None of these symptoms are specific to galactosemia.

A galactosemia test: is a blood test (from the heel of the infant) or urine test that checks for three enzymes that are needed to change galactose sugar that is found in milk into glucose.

endogenous production of galactose can cause symptoms development of:

cataract, renal failure, cirrhosis, cognitive, neurologic, and female reproductive complications.

3. Glycogen storage disease (GSD):

Accumulation of glycogen in liver or muscle or other tissues, due to the defects in the processing of glycogen synthesis or breakdown within muscles, liver.

GSD has two types of causes:

1. Genetic GSD is caused by any inborn error of metabolism (genetic defect of enzymes).
2. Acquired GSD is caused by intoxication.