Clinical Biochemistry lecture 1
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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

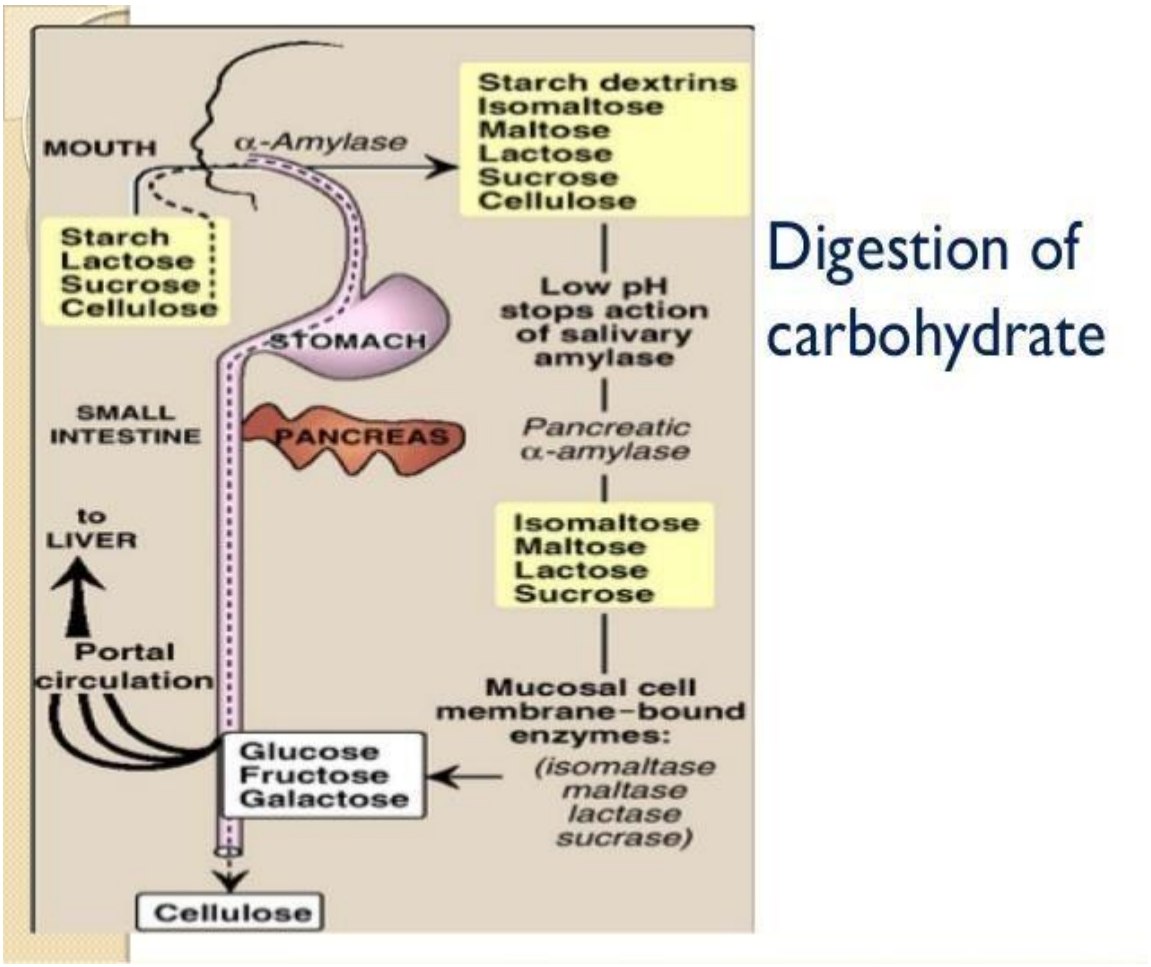
Anabolic reaction	catabolic reaction
1. synthesis of complex molecules molecules from simple compound. proteins	1.break down of large Such as polysaccharides,
2. energy is needed for synthesis CO2, (endergonic reaction)	into small molecules like, NH3, H2O. 2. liberated energy. (exergonic reaction)

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): α- amylase, hydrolysis **starch** to dextrin and maltose.
2. **stomach** ---------- no digestion is seen in stomach
3. **small intestine:** it is the major site of digestion of CHO, pancreatic amylase hydrolyze dextrin into maltose.
4. **intestinal mucosal :** mucosal cell membrane – bound enzymes , the site where disaccharides hydrolyze.

Maltose —maltase→ glucose +
glucose Sucrose —sucrase→ glucose + fructose
Lactose —lactase→ glucose + galactose



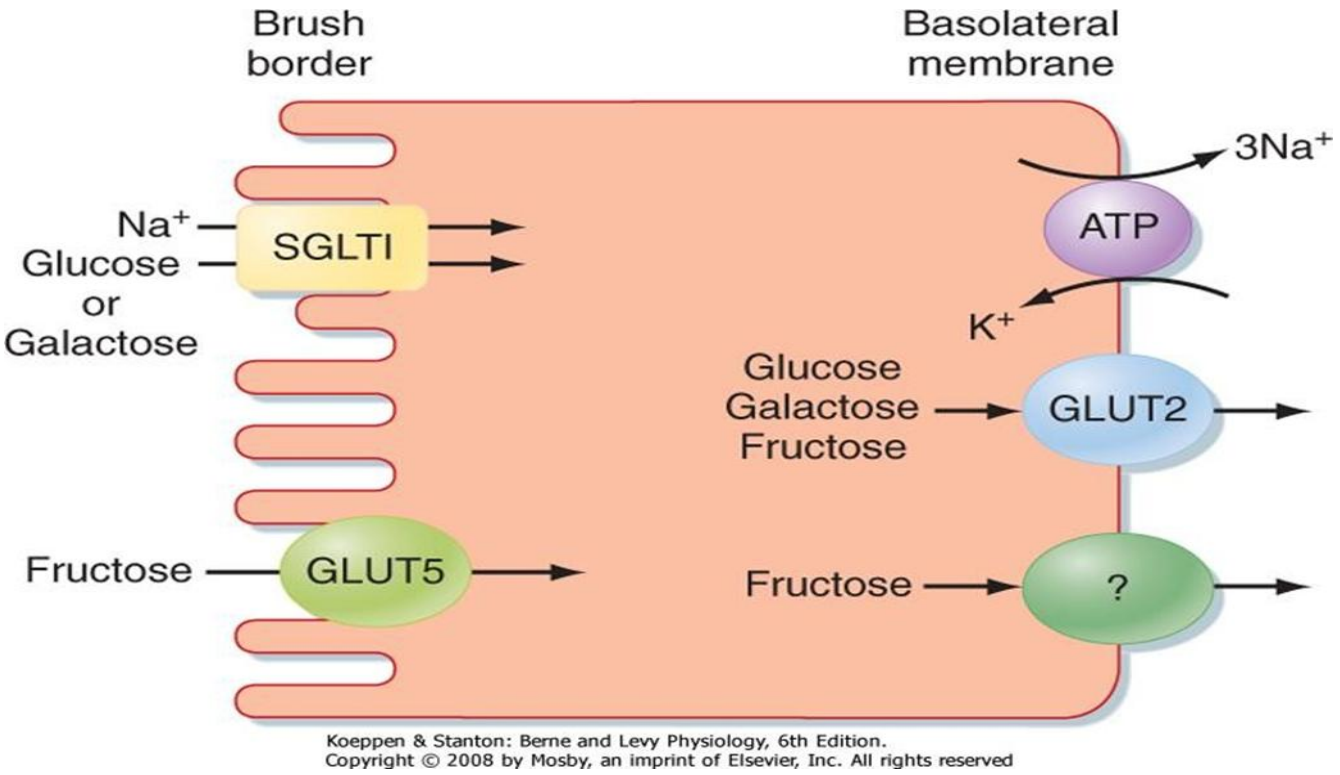
Digestion of carbohydrate

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

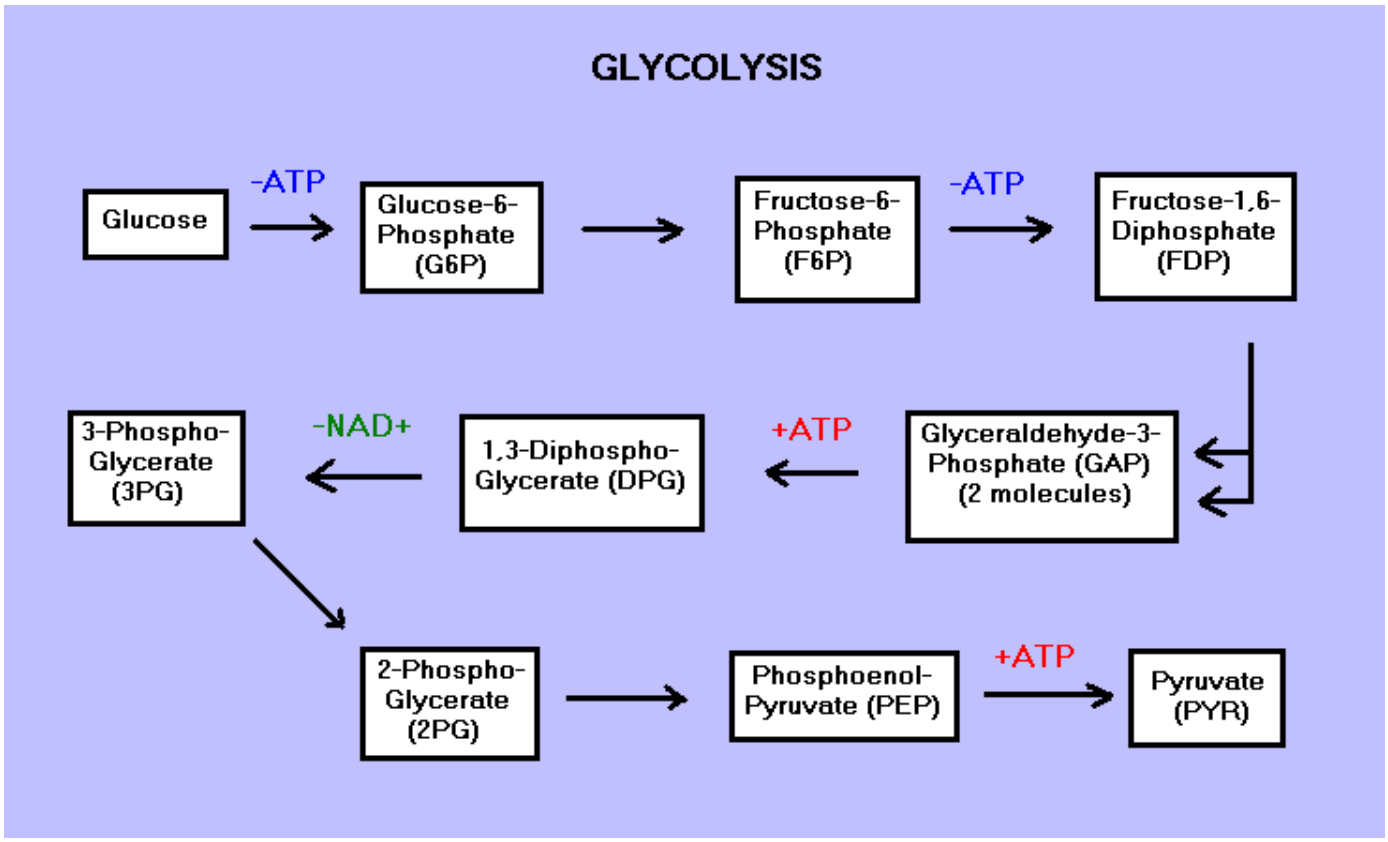
In the liver, glucose undergoes **variety of chemical changes depending upon the physiological need of the body.**

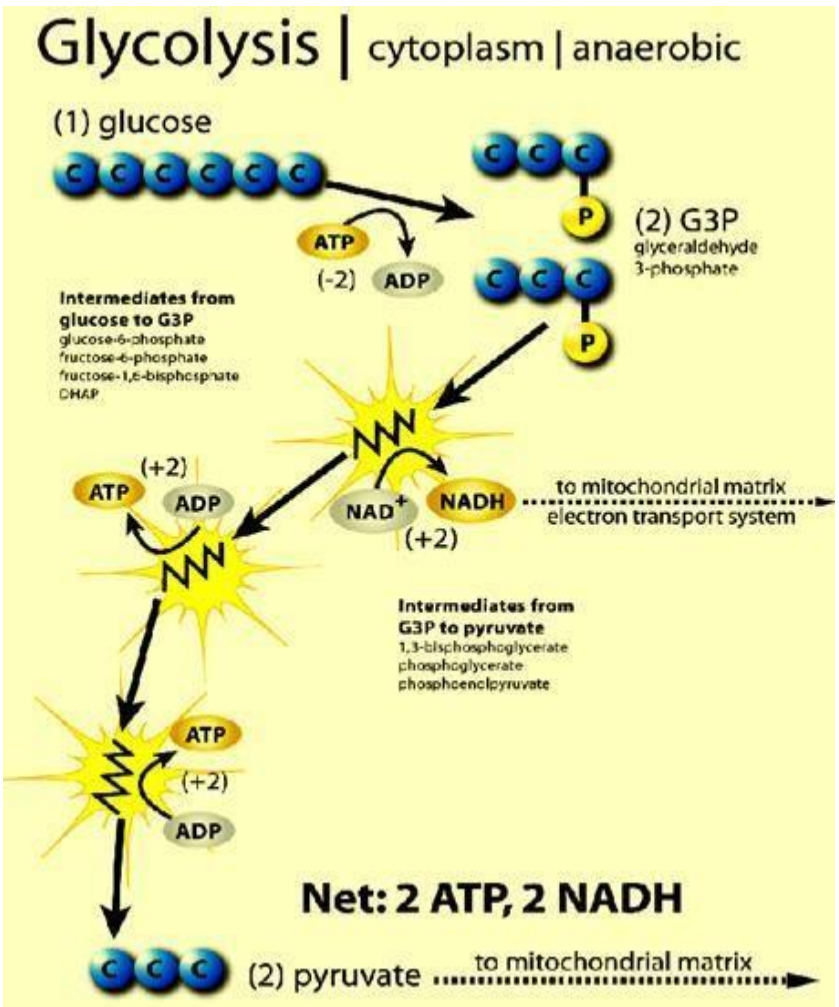
1. **Body needs for energy**: glucose oxidized completely to **CO2, H2O and energy** by (**glycolysis** and **citric acid cycle**).
2. **Excess glucose may be converted to glycogen**, deposit in liver, muscle tissues By **(glycogenesis**).
3. To maintain glucose blood level, liver glycogen reconverted 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 deoxyribose for synthesis of nucleic acids.
6. **in muscle contraction**, only partial degradation of glucose may take place, resulting in formation of lactic acid disposed of 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.
9. The overall process of glycolysis is:
10. $\text{Glucose} + 2\ NAD^+ + 2\ ADP + 2\ P_i \rightarrow 2\ \text{Pyruvate} + 2\ NADH + 2\ H^+ + 2\ ATP + 2\ H_2O$


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)

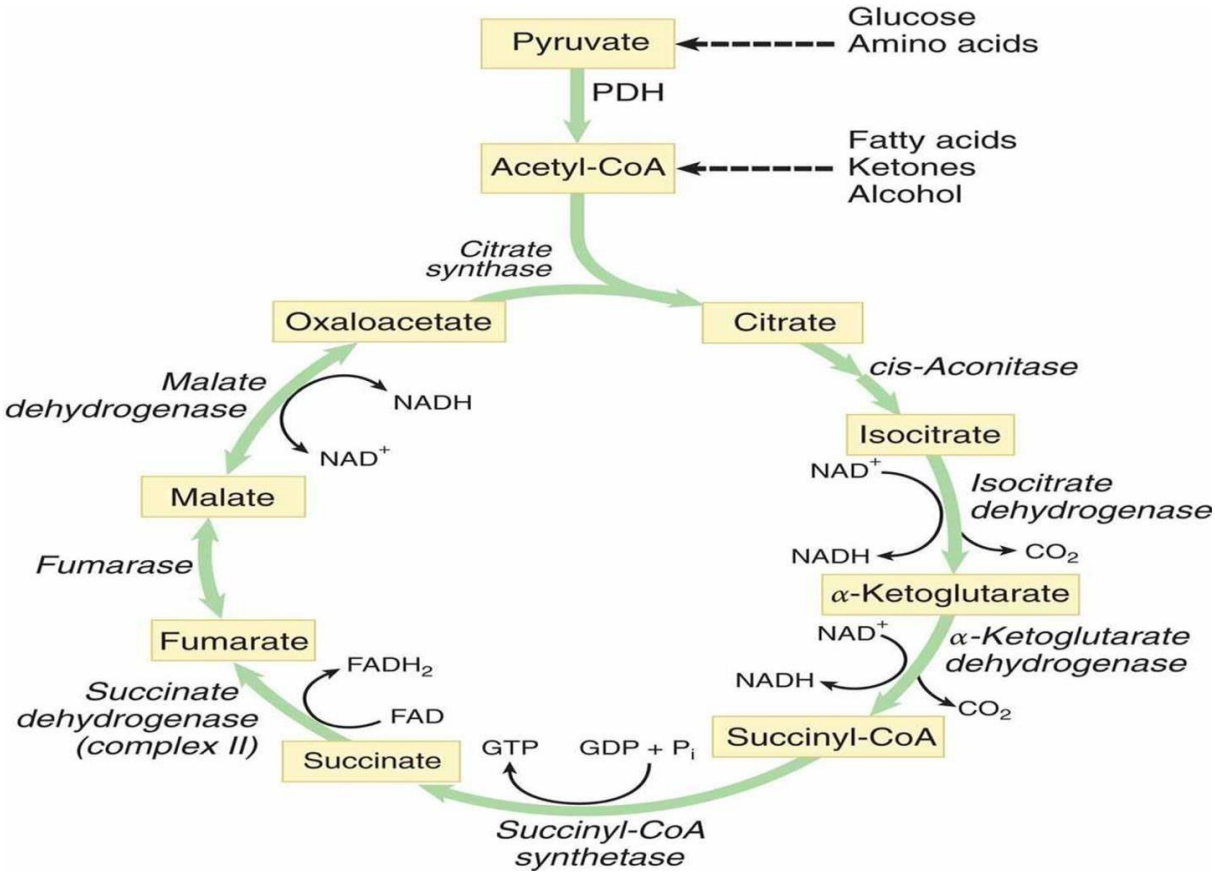

Glycolysis | cytoplasm | anaerobic
(1) glucose
ATP
(-2)
ADP
(2) G3P
glyceraldehyde 3-phosphate
Intermediates from glucose to G3P
glucose-6-phosphate
fructose-6-phosphate
fructose-1,6-bisphosphate
DHAP
(+2)
ATP
ADP
NAD+
NADH
(+2)
to mitochondrial matrix
electron transport system
Intermediates from G3P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



ATP generated in TCA cycle

Conversion 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

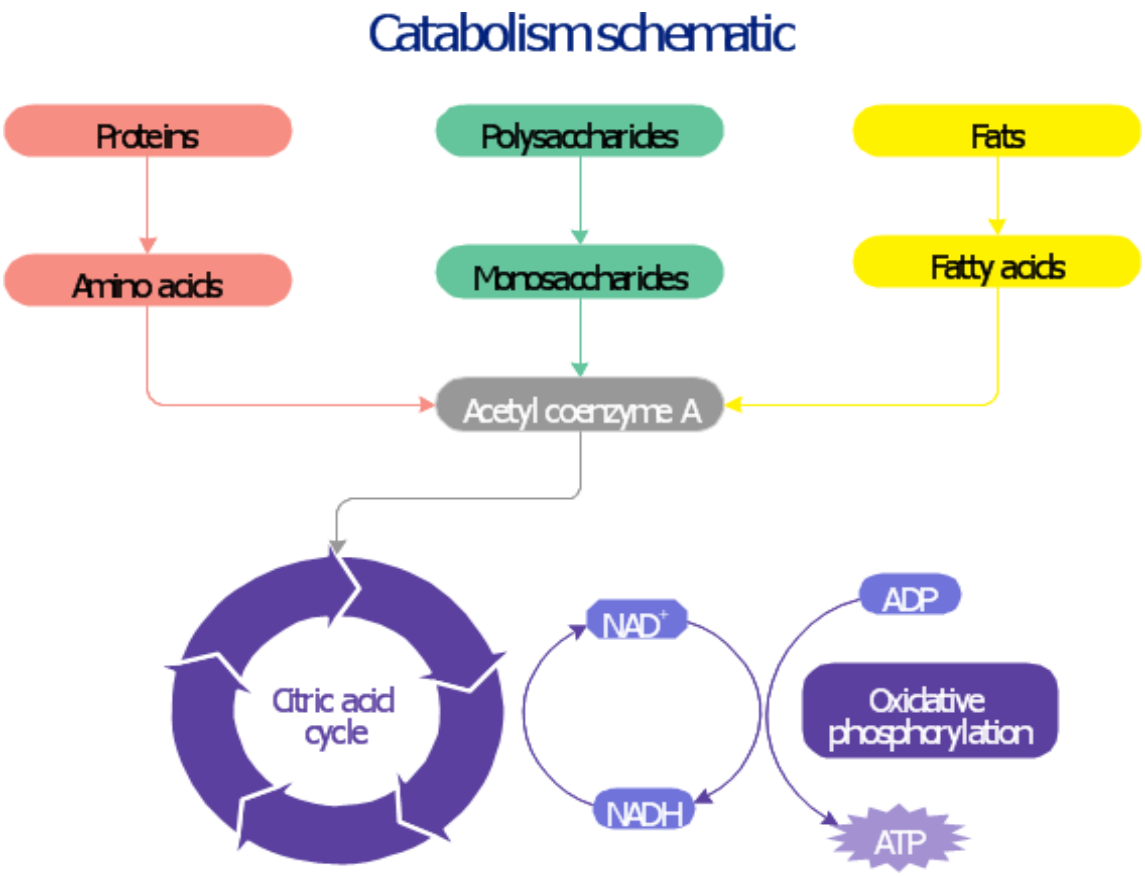
Krebs cycle, tricarboxylic acid cycle TCA

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 hormones** and **adrenaline**.

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