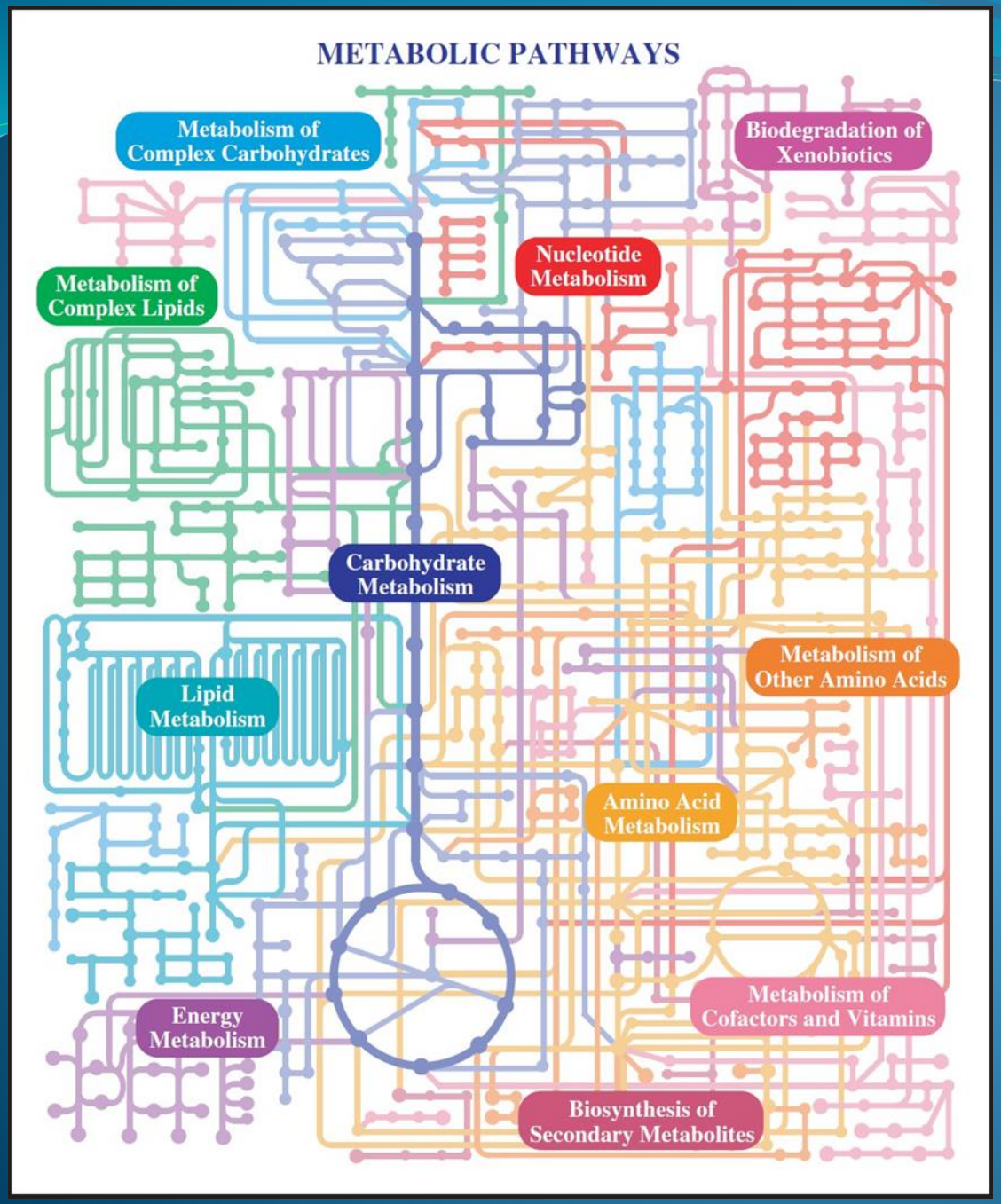


BIOENERGETICS AND METABOLISM

Cellular Respiration

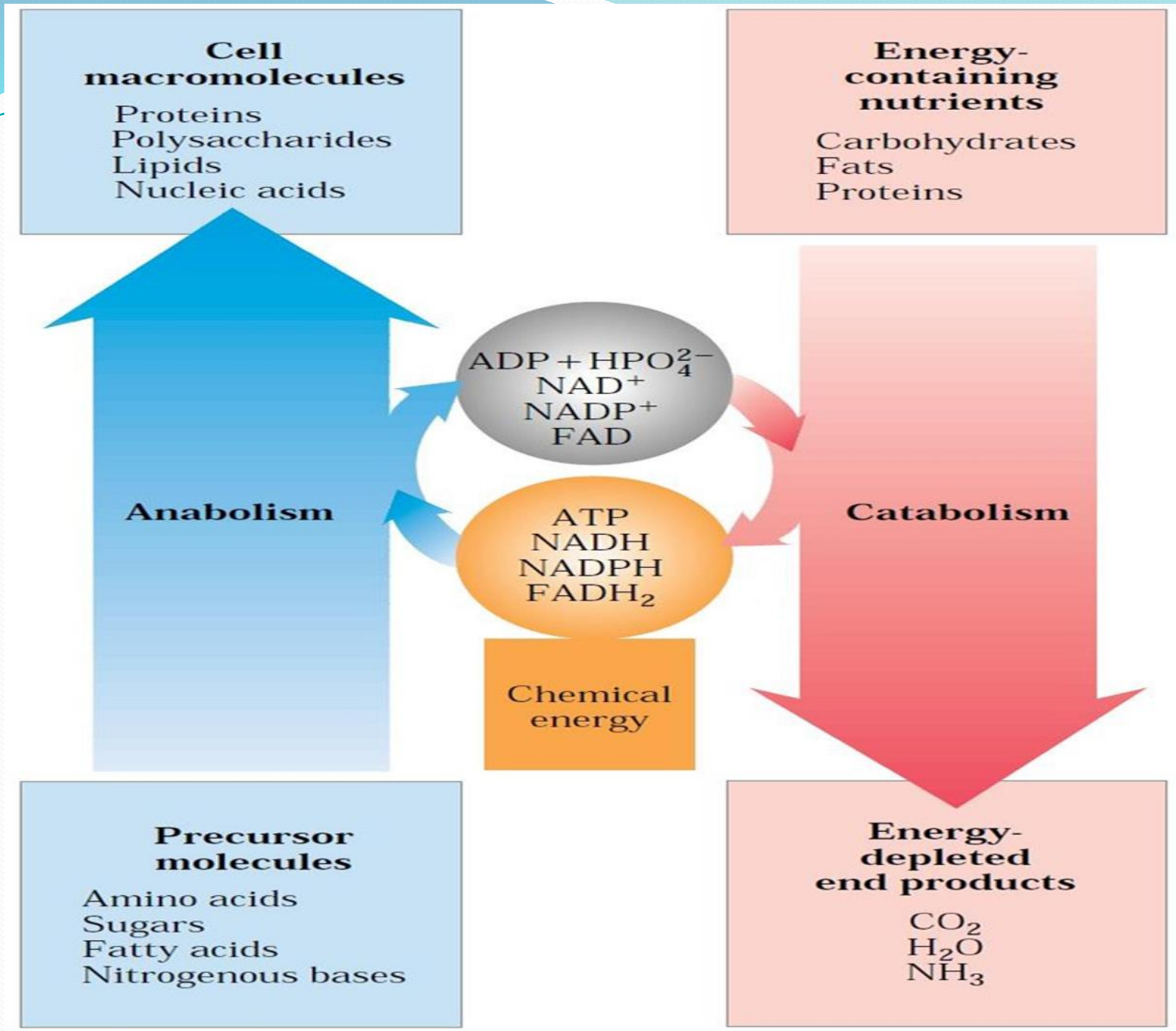
Bioenergetics

- It describes how living organisms acquire and transform energy in order to perform biological work through the study of different biological processes that lead to production and utilization of energy (ATP, GTP, .)

Metabolism

- It is the summation of chemical reactions involved in maintaining the living state of the organism.
- Divided into two categories:
    - Catabolism - the breakdown of molecules to obtain energy
    - Anabolism - the synthesis of all compounds needed by the cells

- Metabolism is closely linked to nutrition and the availability of nutrients.


Cell macromolecules
Proteins
Polysaccharides
Lipids
Nucleic acids
Energy-containing nutrients
Carbohydrates
Fats
Proteins
Anabolism
ADP + HPO_4^{2-}
NAD^+
$NADP^+$
FAD
ATP
NADH
NADPH
$FADH_2$
Chemical energy
Catabolism
Precursor molecules
Amino acids
Sugars
Fatty acids
Nitrogenous bases
Energy-depleted end products
CO_2
H_2O
NH_3

Types of cell respiration

- Aerobic cell respiration, with the participation of (O_2) with the production of 30 ATP molecules/glucose molecule; and anaerobic cell respiration, without the participation of (O_2) which uses other inorganic molecules as an oxidant instead with production of only 2 molecules of ATP/glucose molecule.

Phases of cell respiration

- The three phases of aerobic cell respiration are glycolysis, TCA cycle and electron transport chain.

Entropy

- It is the measure of a system's thermal energy per unit temperature that is unavailable for doing useful work.

Enthalpy

- It is defined as a state function that depends only on the prevailing equilibrium state identified by the system's internal energy, pressure, and volume, it simplifies the description of energy transfer.
- At constant pressure, the enthalpy changes equals the energy transferred from the environment through heating or work other than expansion work. It is measured as the change in enthalpy ΔH. The ΔH is a positive change in endothermic reactions and negative in heat- releasing exothermic processes.

Redox Reaction

- An oxidation-reduction reaction is any chemical reaction in which the oxidation number of a molecule, atom, or ion changes by gaining or losing an electron.

High Energy Phosphate

- ATP is formed after the binding of one phosphate molecule (phosphorylation) to one ADP molecule for storing energy in the produced ATP molecule. When ATP provides energy to the cellular metabolism, it releases one of its phosphate ions and ADP reappears.

- ADP can also release more phosphate ions and generate AMP or even non-phosphorylated adenosine. Adenosine production from ATP is used in tissues that need urgent supply oxygen, such as in the heart during a myocardial infarction (heart attack). This is because adenosine creates a local vasodilator effect, thus providing faster vasodilation than other physiological methods.

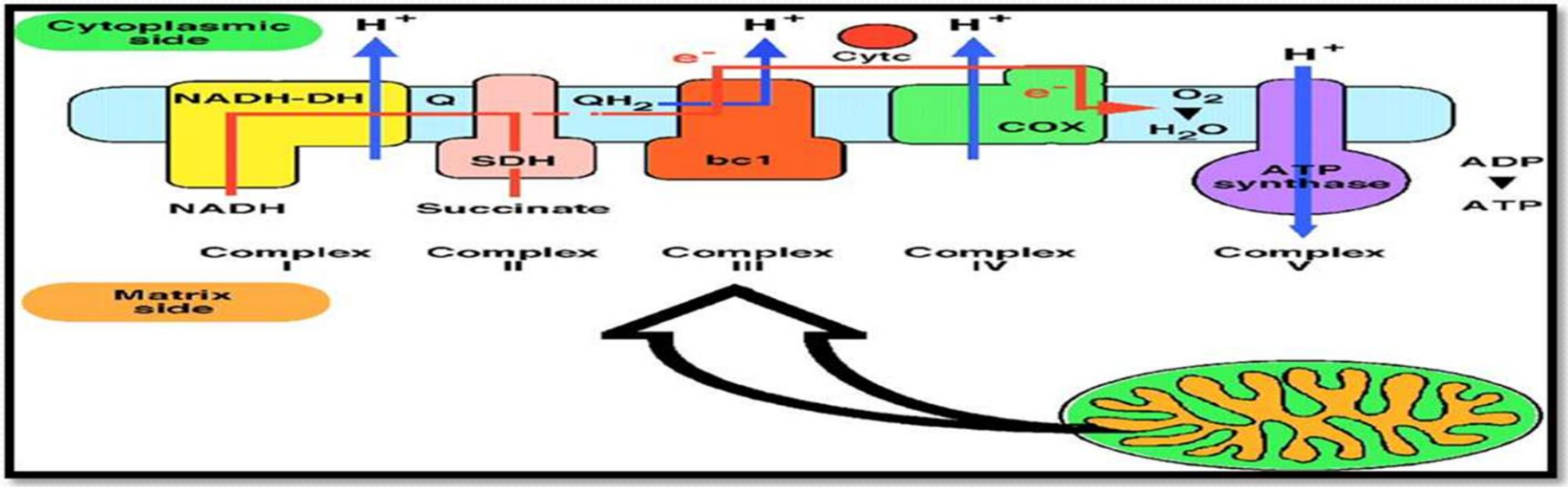
Oxidative phosphorylation

- This is the process in which ATP is formed as a result of the transfer – of electrons from NADH or FADH2 to O2 by a series of electron carriers. Electrons are passed from one member of the transport chain to another in a series of redox reactions.
- Energy released in these reactions is captured as a proton gradient, which is then used to make ATP in a process called chemiosmosis.
- Together, the electron transport chain and chemiosmosis make up oxidative phosphorylation. This process, which takes place in mitochondria, is the major source of ATP in aerobic organisms

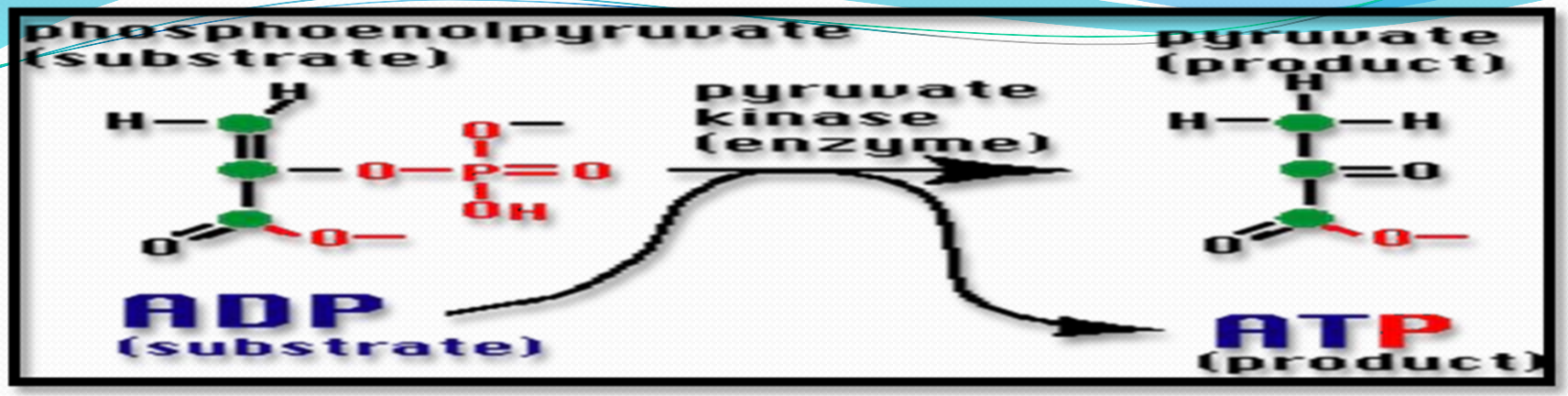
Electron Transport Chain

- ETC is a series of complexes that transfer electrons from electron donors to electron acceptors via redox reactions, and couples this electron transfer with the transfer of protons (H+ ions) across a membrane to create an electrochemical proton gradient that drives the synthesis of ATP.

- The molecules of ETC include peptides, enzymes, and others.
- The final acceptor of electrons in the electron transport chain during aerobic respiration is O2.



Substrate level phosphorylation



- The difference between substrate level phosphorylation and oxidative phosphorylation
- Substrate-level phosphorylation is directly phosphorylating ADP with a phosphate and energy provided from a coupled reaction. Oxidative phosphorylation is when ATP is generated from the oxidation of NADH and FADH2 and the subsequent transfer of electrons and pumping of protons.

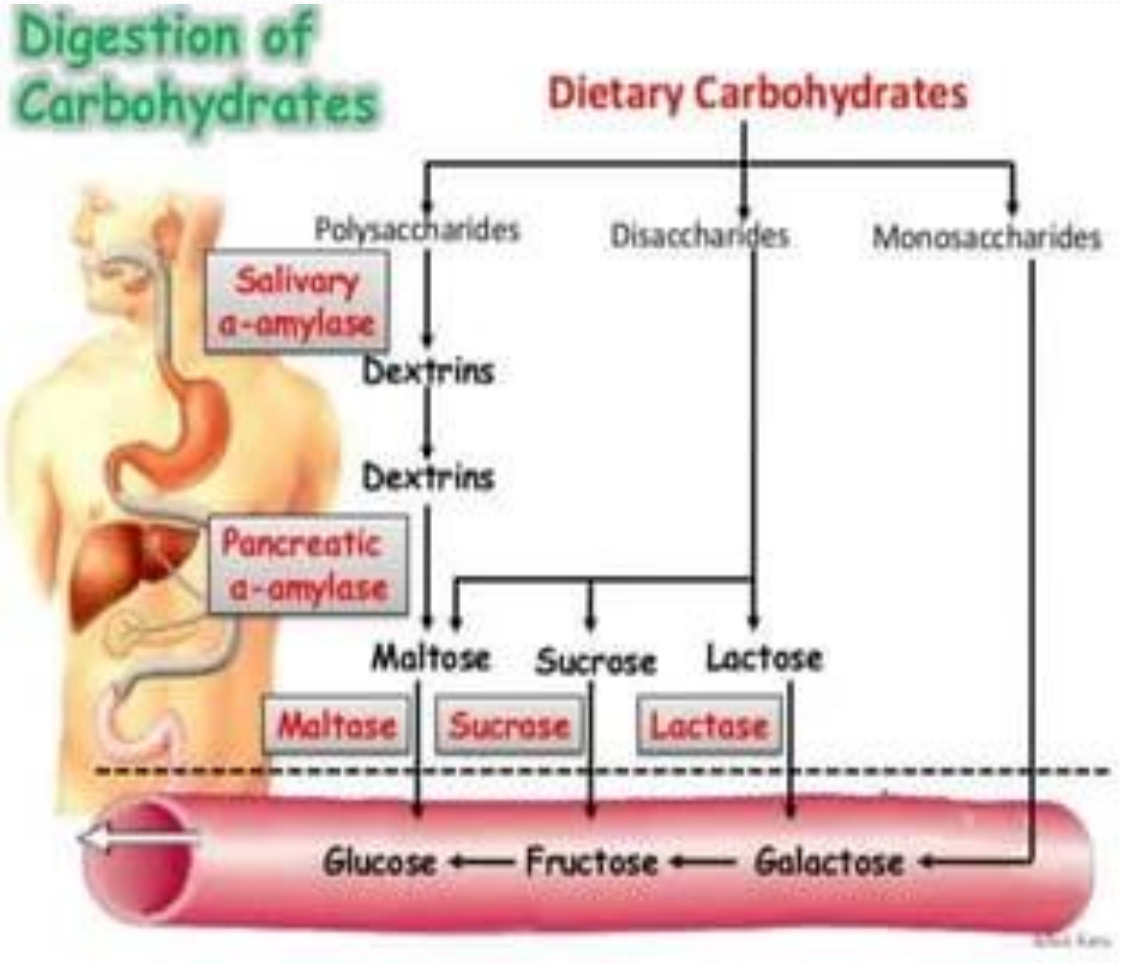
Carbohydrates metabolism

Stages of Carbohydrate Metabolism

Stage 1: Digestion and hydrolysis - break down large molecules to smaller ones that enter the bloodstream.

Stage 2: Degradation - breaks down molecules to two- and three-carbon compounds.

Stage 3: Oxidation of small molecules in the citric acid cycle and electron transport provide ATP energy.

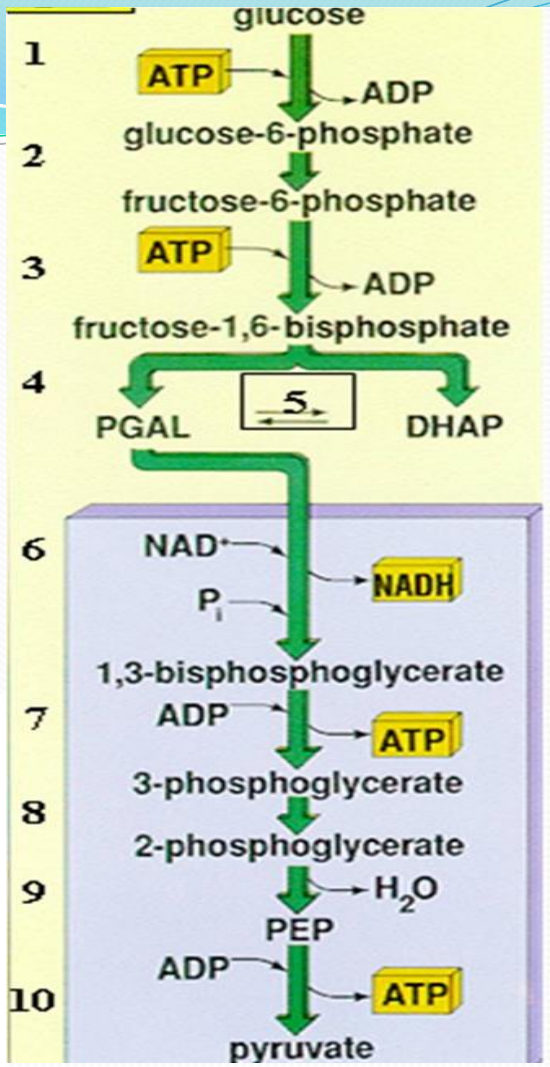


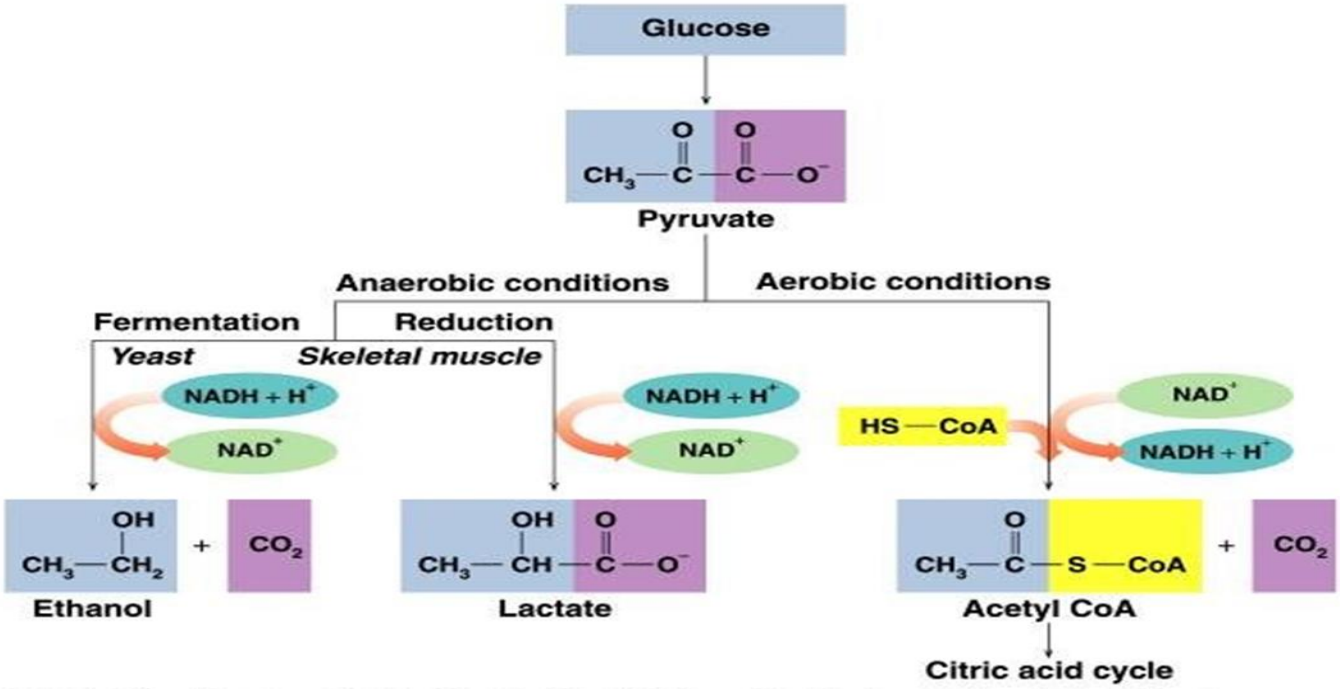
Stage 2: Glycolysis

- Glycolysis is a metabolic pathway that degrades glucose (a six-carbon) to pyruvate (a three-carbon molecules).
- It is an anaerobic process (no oxygen) and occur in the cytoplasm.
- It is divided into two stages:

A- five reactions and consume energy

B- five reactions that produce energy

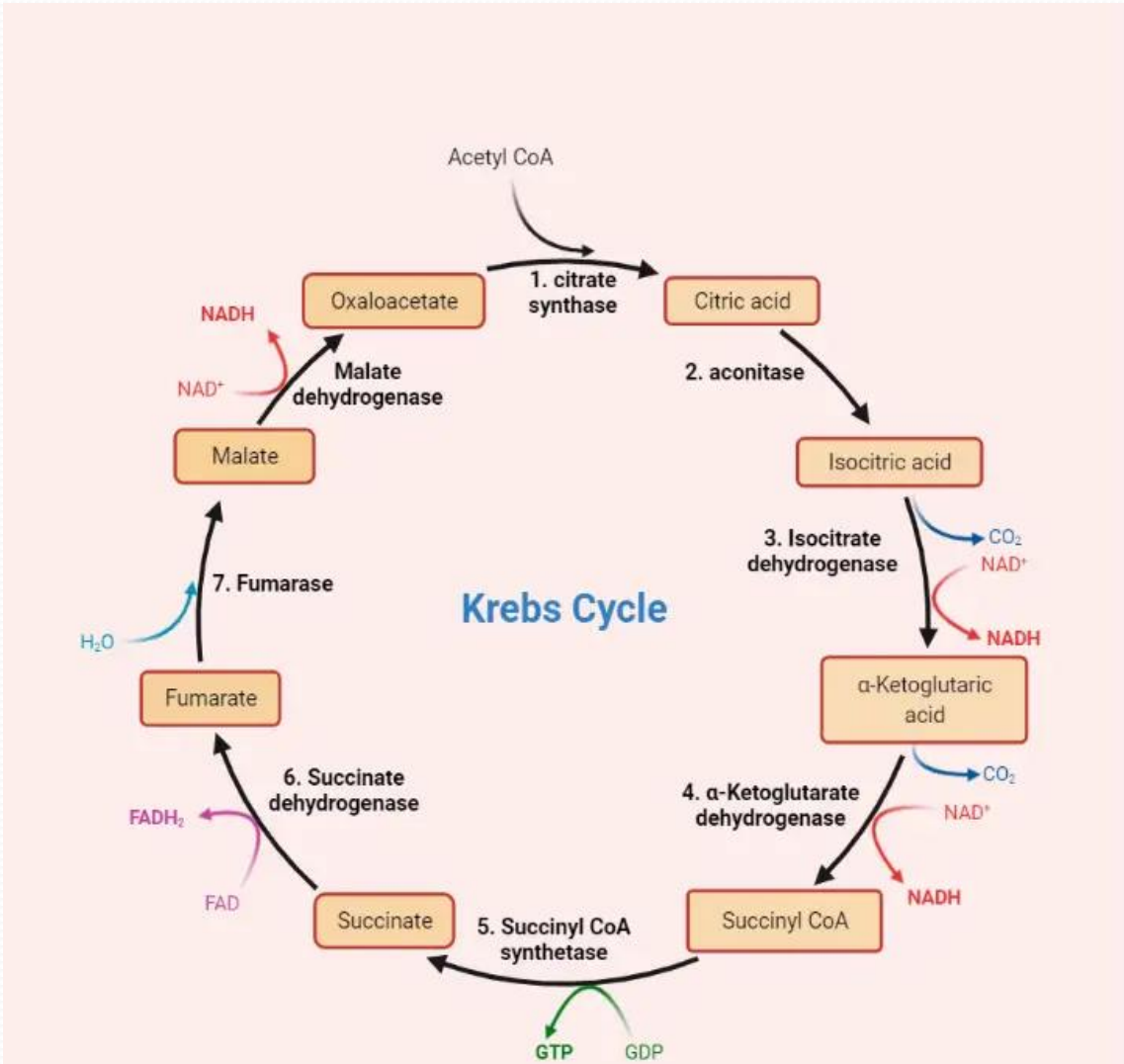




The Fate of pyruvate produced from glycolysis

TCA cycle

- It needs oxygen, so it occurs in all aerobic organisms.
- It is called citric acid cycle or the Krebs cycle.
- It generates energy through the oxidation of acetyl-CoA derived from carbohydrates, fats and proteins into CO2 and chemical energy in the form of ATP
- It occurs only in mitochondria

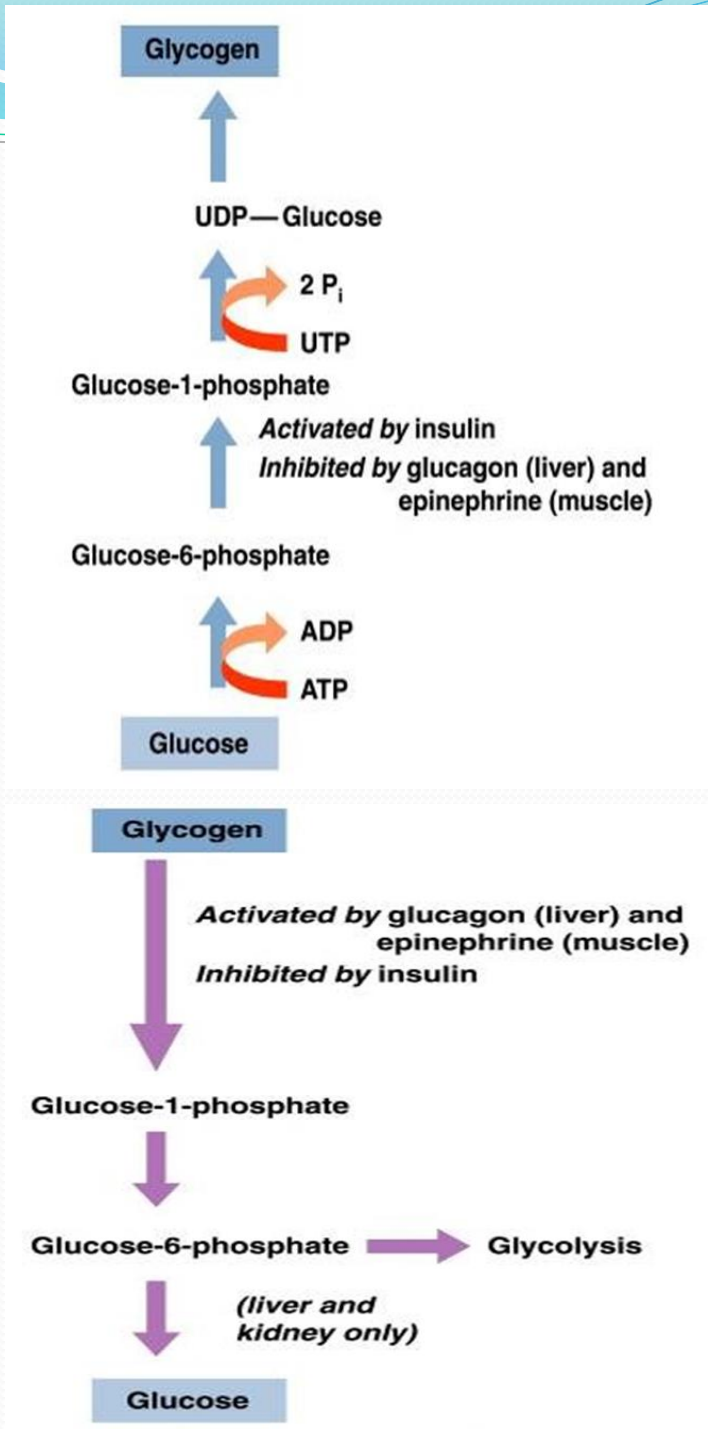


Glycogenesis

- It is the storing of glucose by converting it to glycogen in liver and muscles.
- It operates when high levels of glucose- 6-phosphate are formed in the first reaction of glycolysis.
- It does not operate when energy stores (glycogen) are full, which means that additional glucose is converted to body fat

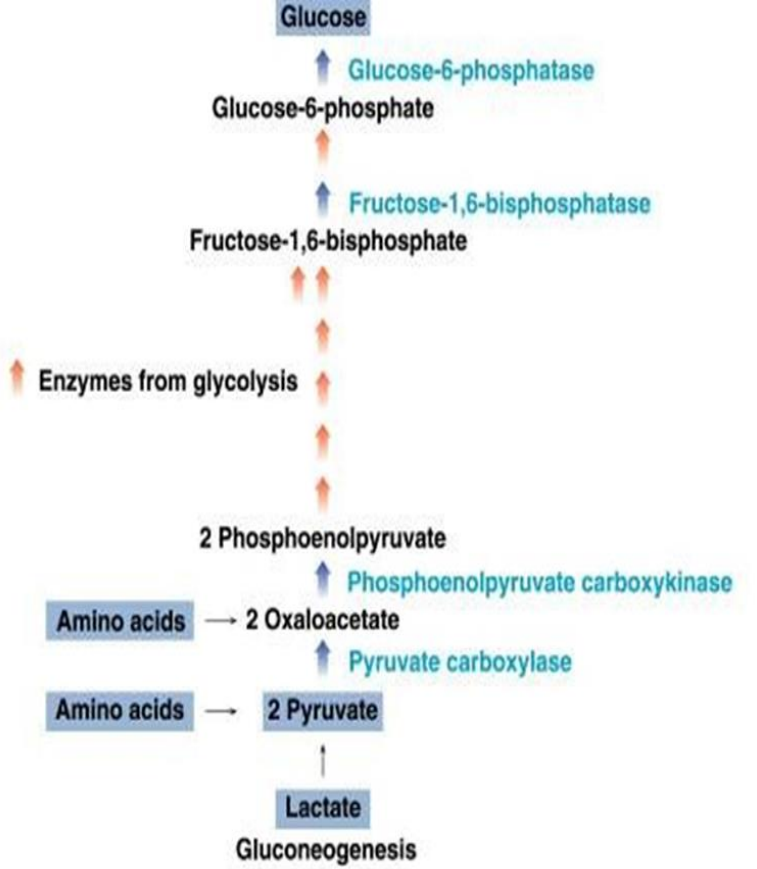
Glycogenolysis

- Glycogen stores in liver and muscles is broken down to glucose.
- Glucose molecules are removed one by one from the end of the glycogen chain to yield glucose-1- phosphate.
- It occurs when the blood glucose level is decreasing to less than the lower limit (70 mg%) to compensate this decrease.



Gluconeogenesis

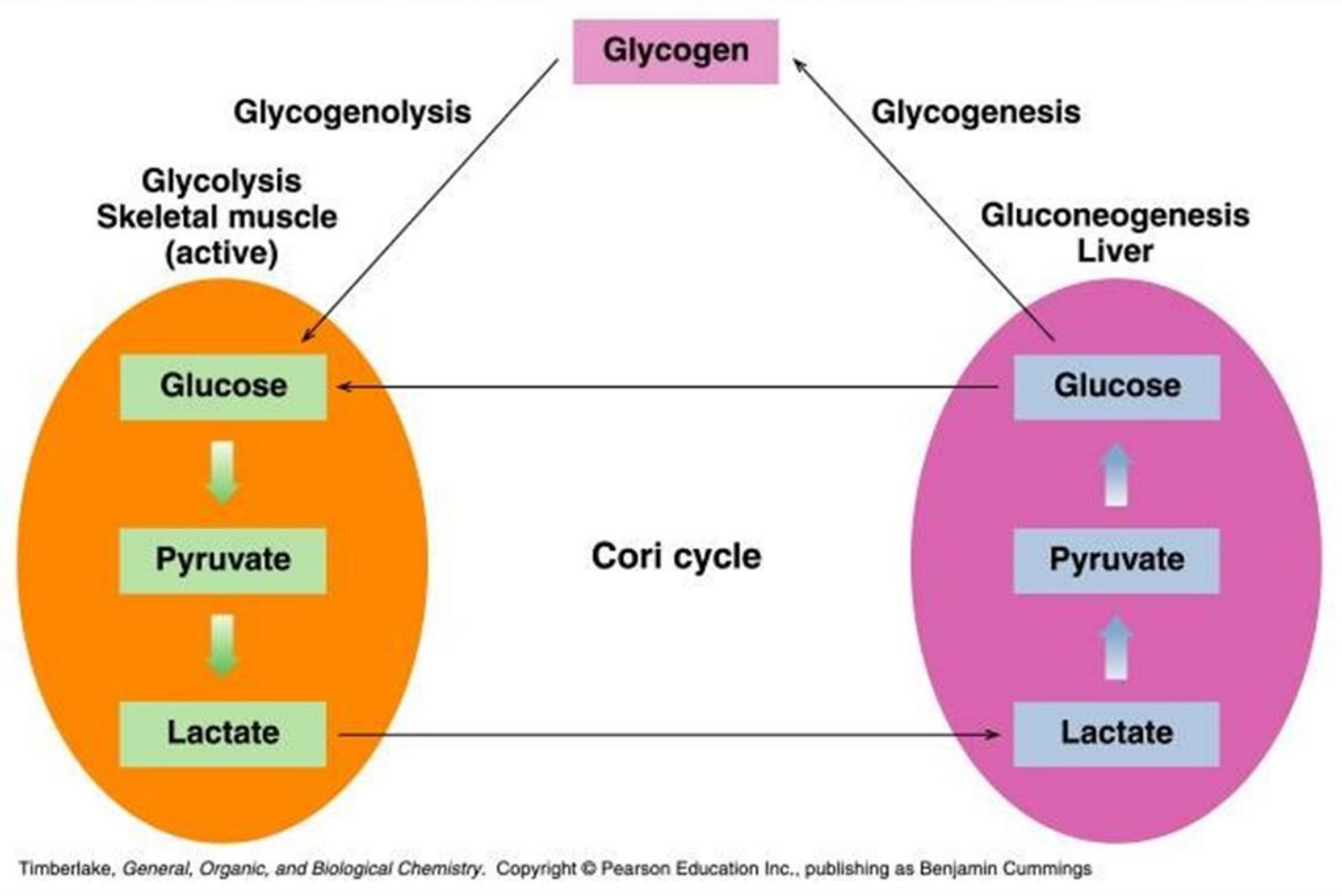
- It is the generation of glucose from certain non-carbohydrate carbon substrates like the metabolic products of carbohydrates, amino acids and lipid.
- It occurs when glycogen stores are depleted as a result of starvation or if the body can not utilize glucose as in the case of diabetes



Pentose Phosphate Pathway (PPP)

- The pentose phosphate pathway is a metabolic pathway parallel to glycolysis.
- It generates NADPH and pentoses as well as ribose 5- phosphate, the last one a precursor for the synthesis of nucleotides.

Pathways for Glucose



Lipid Metabolism

- Lipid metabolism is referred to the synthesis and degradation of lipids within the cells, either break down or storage of fats for energy.
- These fats are obtained from consuming food and absorbing them or they are synthesized by an animal's liver.
- Minimal amount of fat is essential in our food :
  - For essential fatty acids synthesis .
  - Help Fat-soluble vitamins absorption.
  - As a Source of energy: 1 gm supplies 9.1 calories

- Just like glucose Metabolism, the end-products of fatty acid metabolism are carbon dioxide, water and ATP.

- However, complete combustion of fatty acids requires glucose to convert it in to carbon dioxide, water and ATP, otherwise ketones are produced.

Table 1. Steps of lipid digestion and absorption

Step	Location	Enzymes
1. Minor digestion (TAGs → DAGs + FFA)	mouth and stomach	lingual/ gastric lipase
2. Major digestion (all) TAG → MAG + 2FFA (PL) CE → chol. + ester (CE) PL → FA + lysoPL (PLA)	lumen of the small intestines	pancreatic lipase (+colipase) cholesterol esterase phospholipase A_2
3. Formation of mixed micelles (uses bile salts as biological detergent)	lumen of the small intestines	N/A
4. Passive absorption of lipolytic products	into intestinal epithelial cell	N/A
5. Assembly and export of chylomicrons	from intestinal cells to the lymphatics	N/A

Fatty Acid Synthesis

- Start in cytoplasm with help of acetyl-CoA and NADPH produced from mitochondria and Pentose phosphate Pathway (PPP) respectively using enzyme fatty acid synthases.

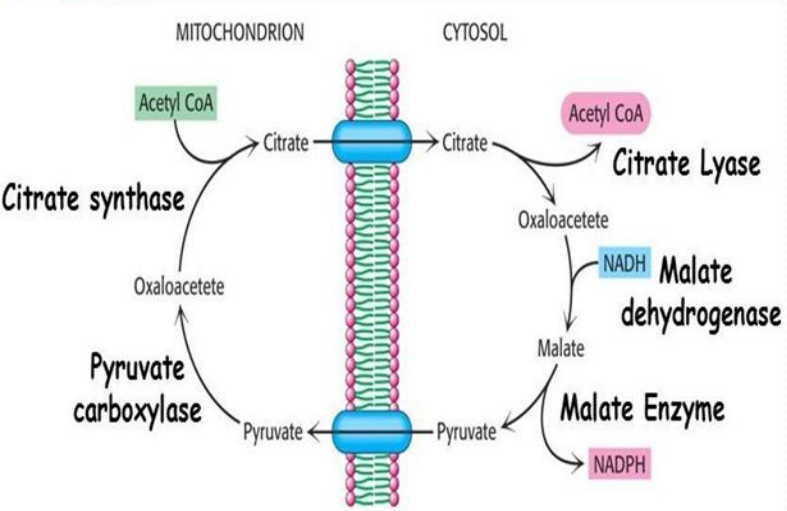
- First acetyl-CoA transported from mitochondria through citrate—malate- pyruvate –Shuttle in form of citrate, which further breaks into Acetyl-CoA and Oxaloacetate.

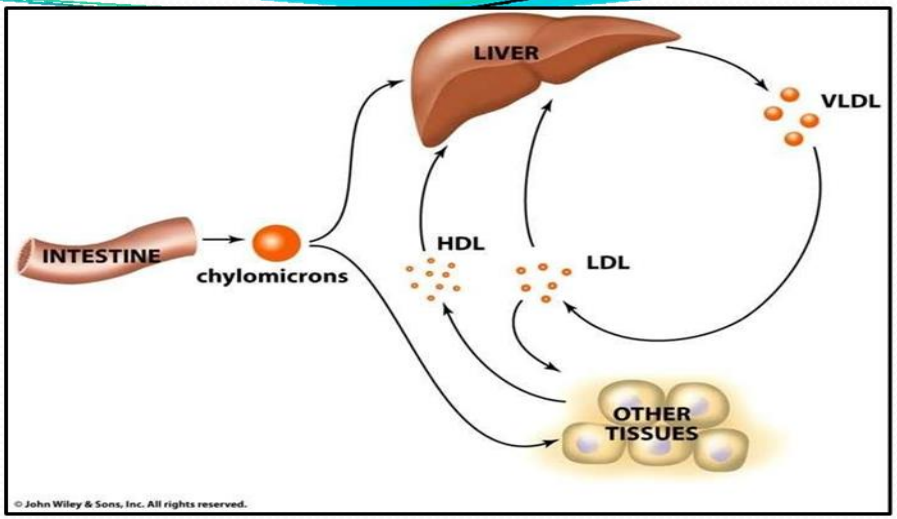
- Only small chain fatty acids get synthesized in to cytoplasm, so the synthesis of long chain fatty acids like Triacylglycerol required specialized organ like Liver.

- The liver is the major site for converting excess carbohydrates and proteins into fatty acids and triglyceride. The liver synthesizes large quantities of cholesterol and phospholipids.

- After synthesis, VLDL lipoproteins are then exported through blood circulation and stored in adipose tissue.

- A small fraction is also converted to small ketone molecules that are exported via the circulation to peripheral tissues, where they are metabolized to yield energy
- The conversion of carbohydrates to fatty acids is called lipogenesis.
- Lipogenesis is the metabolic process through which acetyl-CoA is converted to triglyceride for storage in fat.





Lipolysis

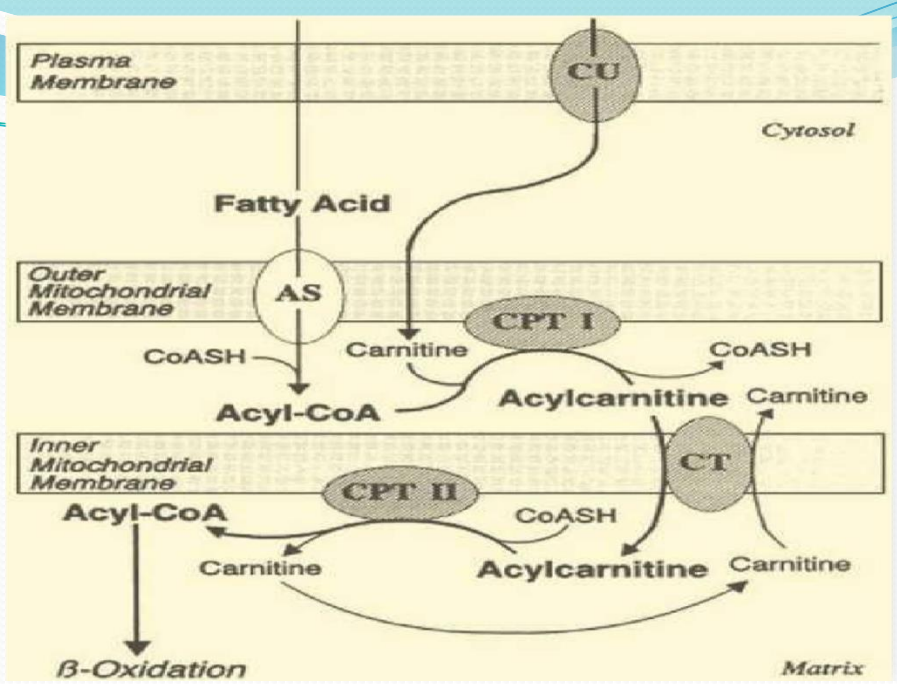
- It is the catabolic process leading to the breakdown of triacylglycerol (TAGs) into FFAs and glycerol. After release into the blood, FFAs are transported and taken up by other tissues to be utilized for β-oxidation and subsequent ATP generation. Some FFAs do not leave the fat cell and are re-esterified into intracellular TAG.

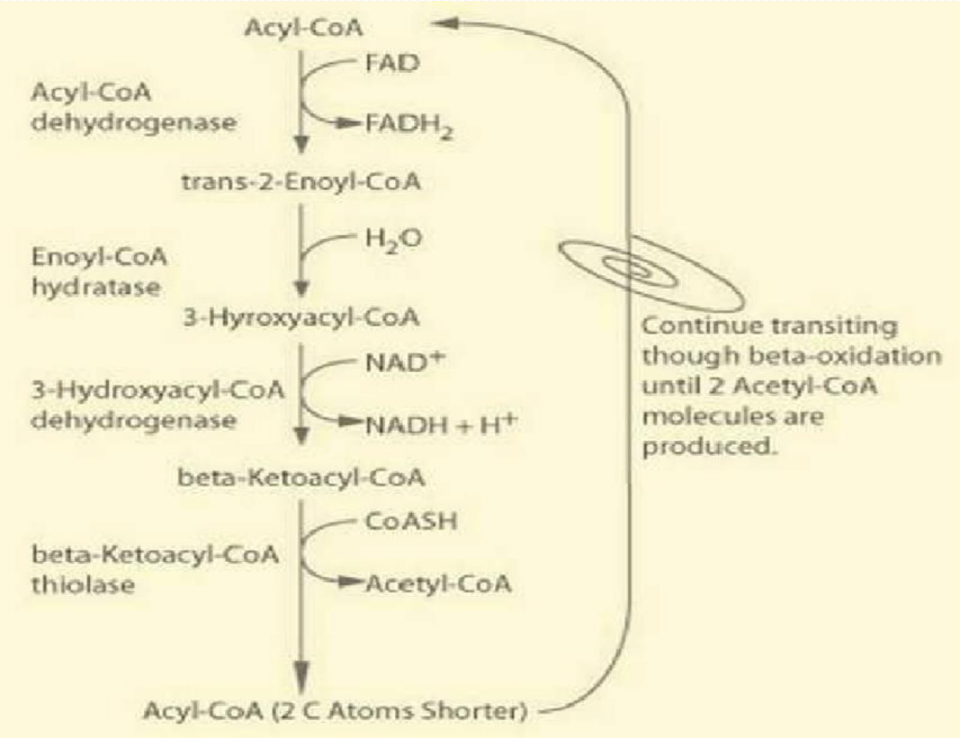
- During lipolysis, intracellular TAG undergoes hydrolysis through the action of lipases including HSL, and monoacylglycerol lipase that can hydrolyze TAGs and FAs.

- Lipolysis is regulated by the ANS and by several humoral factors, such as catecholamines (phosphorylation of HSL), glucocorticoids, natriuretic peptides, and growth hormone

Beta Oxidation of fatty acids

- A saturated acyl CoA is degraded by a recurring sequence of four reactions:
  - Oxidation by FAD
  - Hydration
  - Oxidation by NAD+, and
  - Thiolysis by Co ASH
- The fatty acyl chain is shortened by two carbon atoms as a result of these reactions, and generation of
  - FADH2,
  - NADH, and
  - acetyl CoA





Ketogenesis

- It is the biochemical process by which organisms produce a group of substances collectively known as ketone bodies by the breakdown of fatty acids and ketogenic amino acids.
- The three ketone bodies, each synthesized from acetyl-CoA molecules, are:

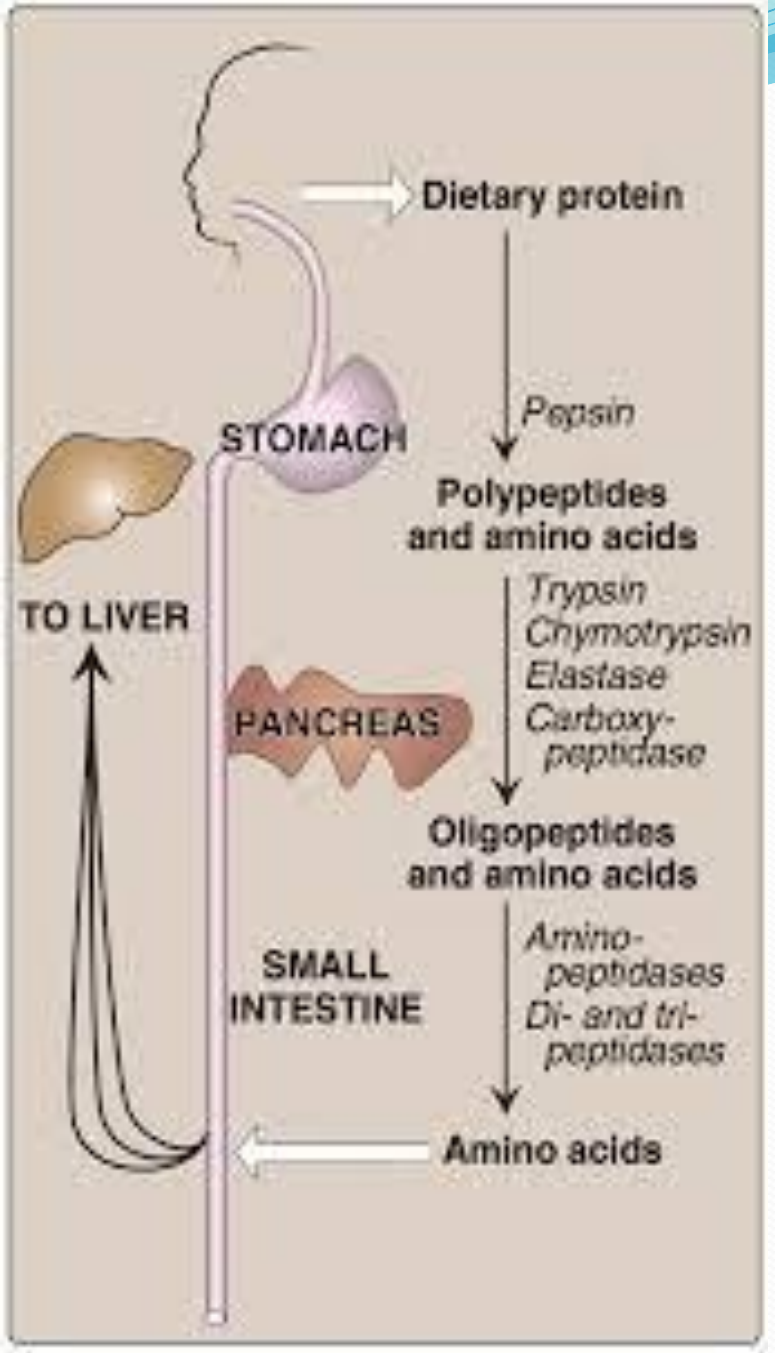
Acetoacetate, which can be converted by the liver into β- hydroxybutyrate, or spontaneously turn into acetone

Acetone, is generated through the decarboxylation of acetoacetate, either spontaneously or through the enzyme acetoacetate decarboxylase..

β-hydroxybutyrate is generated through the action of the enzyme D-β-hydroxybutyrate dehydrogenase on acetoacetate

Protein metabolism

- Proteins are too large to be absorbed. The dietary proteins are hydrolyzed to amino acids by proteolytic enzymes, which can be easily absorbed.
- Proteolytic enzymes responsible for degrading proteins are produced by three different organs; stomach, pancreas and the small intestine



Unlike fats and carbohydrates, amino acids are not stored by the body. Therefore, amino acids must be:

1. Obtained from the diet.
2. Synthesized de novo.
3. Produced from normal protein degradation.

- **The first phase of catabolism** involves the removal of the α-amino groups (by trans-amination and oxidative deamination),forming ammonia and the corresponding α-ketoacid—the "carbon skeletons" of amino acids.

A portion of the free ammonia is excreted in the urine, but most is used in the synthesis of urea.

- **In the second phase of amino acid catabolism**, the carbon skeletons of the α-keto acids are converted to common intermediates of energy producing, metabolic pathways. These compounds can be metabolized to C02 and water, glucose, fatty acids, or ketone bodies by the central pathways of metabolism

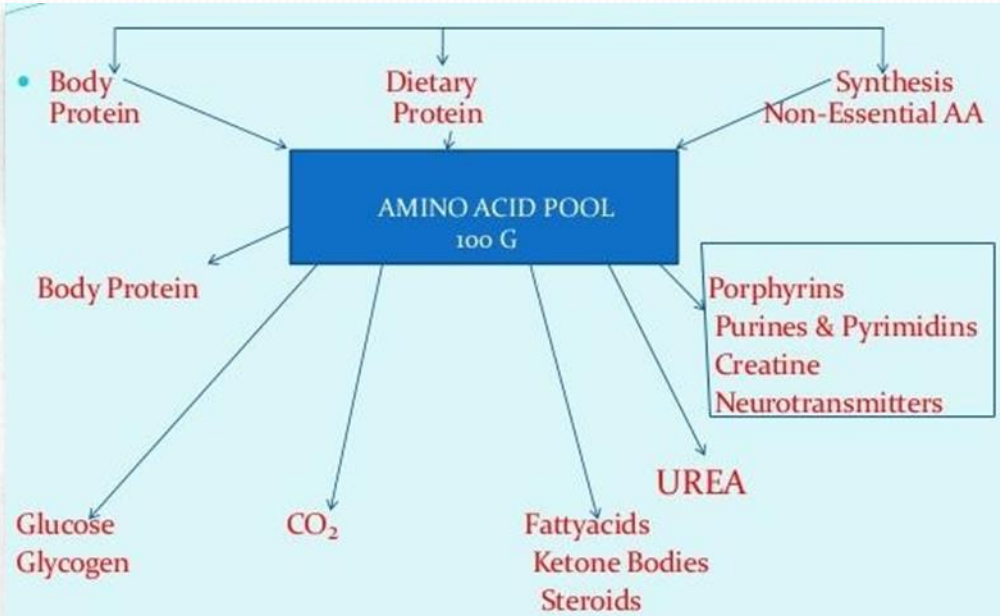
OVERALL NITROGEN METABOLISM

Nitrogen enters the body in a variety of compounds present in food.

Nitrogen leaves the body as urea, ammonia, and other products derived from amino acid metabolism.

Conversely the amino pool is depleted by three routes:

1. Synthesis of body protein.
2. Amino acids consumed as precursors of essential nitrogen containing small molecules.
3. Conversion of amino acids to glucose, glycogen, fatty acids or CO_2.



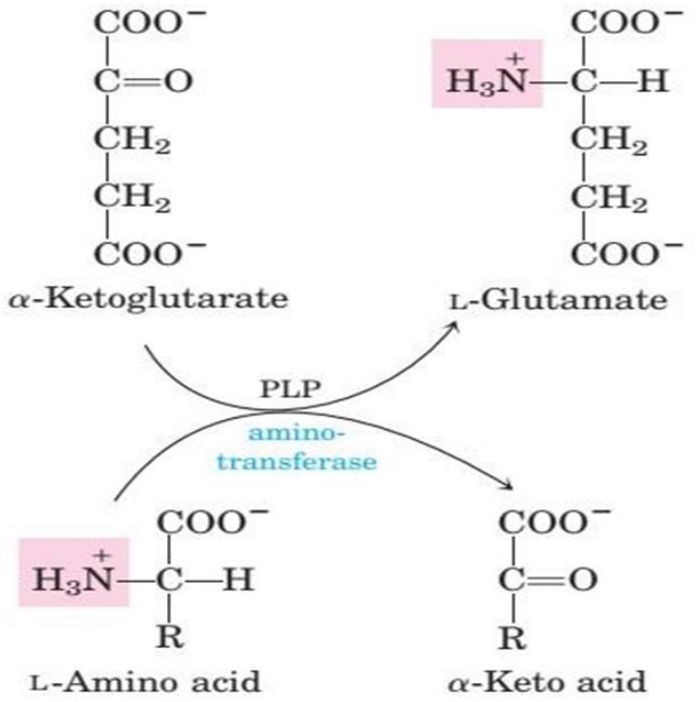
Catabolism Steps of the Amino acids

- Step1: Transport of amino acids in to the cells: The transport of amino acids occurs from the extracellular fluids in to the cells by active transport systems, driven by the hydrolysis of ATP. There are seven different transport systems are known for amino acids in the cells .
- Step 2: Transamination: It is a very crucial steps of the catabolism, removing of the α-amino group is essential for producing energy from any amino acid after that removal of remaining carbon skeletons is being metabolized .

Mechanism:

The first step in the catabolism of most amino acids is the transfer of their α-amino group to α-ketoglutarate .

The products are an α-keto acid (derived from the original amino acid) and glutamate



Step3. Oxidative deamination:

- After the transamination reactions that transfer amino groups, oxidative deamination occurs by glutamate dehydrogenase results in the liberation of the amino group as free ammonia from Glutamate.
- This reaction is occurs in the liver.
- The α-keto acids enter the central pathway of energy metabolism and ammonia in urea synthesis, liberated after oxidative deamination.
- Glutamate is a unique amino acid that only undergoes rapid oxidative deamination, that is catalyzed by glutamate dehydrogenase.
- The glutamate dehydrogenase of mammalian liver has the unusual capacity to use either NAD+ or NADP+ as cofactor