Pyruvate fates

After production of two pyruvate molecules from glycolysis (anaerobic condition). Depending upon the conditions the fates of pyruvate are:

1. Aerobic condition (in the presence of O2), the pyruvate will convert into :
   - ✓ Acetyl CoA for entry into mitochondria for citric acid cycle and electron transport chain.
2. Fermentation/ Anaerobic (in the absence of O2), the pyruvate will convert into:
   - ✓ **Lactic acid fermentation** via lactate dehydrogenase (LDH).
   - ✓ **Alanine transamination** via alanine aminotransferase (ALT).

Lactic acid (lactate) is a chemical byproduct of anaerobic respiration by muscles, brain cells and red blood cells catalyzed by lactate dehydrogenase (LDH). Lactic acid accumulation was once cause of muscle stiffness, fatigue, and soreness, although more recent research disagreed with such hypothesis. Lactic acid produced by fermentation must be removed by the blood circulation and brought to the liver for further metabolism.

When muscles degrade amino acids for energy needs, the resulting nitrogen is transaminated to pyruvate to form alanine via alanine aminotransferase (ALT).

Other fermentations products

1. Lactic acid fermentation is the pyruvate breaks down into lactic acid by bacteria specially in dairy products and our guts.
2. Acetic acid fermentation: is in two stage processes: Glucose is converted into ethanol anaerobically by yeast name (Saccharomyces cerevisiae), and second stage is ethanol is converted into acetic acid aerobically by bacteria name (acetobacter aceti).

Lipid

Lipids are a broad group of fatty, wax-like molecules found in the human body and other organisms. Lipids are organic compounds that are insoluble in water but soluble in organic solvents like chloroform, ether, benzene.

Monomers of the lipid

Fatty acids are the building blocks of all lipid types. Fatty acid consists of a straight chain of carbon atoms, with hydrogen atoms along the length of the chain and at one end of the chain and a carboxyl group (-COOH) at the other end. It is that carboxyl group that makes it an acid (carboxylic acid). Fatty acids classification based on the **number of double bond**:

1. **Saturated fatty acids** have Zero double bond like Stearic acid. This fatty acid is very stable, solid at room temperature. The tissues of animals contain large amounts of long-chain saturated fatty acids. Saturated fatty acid are ideal

for cooking because of their natural ability to withstand heat without being damaged such as butter.

2. **Monounsaturated fatty acids** have one double bond like Oleic acid. This fatty acid is liquid at room temperature, solidify in the refrigerator, less stable than a saturated fatty acid molecule. These are good for cooking, but only at very low temperatures such as olive oil, oil in almonds, hazelnuts, and avocados.
3. **Polyunsaturated fatty acids** have two or more double bonds like Linoleic acid. This type are liquid both at room temperature and in the refrigerator, and they should never be used for cooking such as vegetable oils, soybean oil, flax seed oil, and sunflower oil.
4. **Cis and trans unsaturated fatty acids** : Cis fats are the typical form of unsaturated fatty acids found in nature. In industrial products, the unsaturated fatty acid can be convert into saturated fatty acid by hydrogenation for economic advantages, but at high temperatures, during hydrogenation, the product still contains double bonds with hydrogen atom on incorrect position, these products called trans fats that raise the LDL (bad cholesterol).

Lipid classification

based on the structure :

1. Simple lipids (Esters of fatty acids with certain molecule)
   - ❖ Fats and Oils: which contain (fatty acids + glycerol) such as triglycerides, diglycerides and monoglyceride. A fat is solid at ordinary room temperature, but oil is liquid.
   - ❖ Waxes: which contain an ester of a long-chain of fatty acid + alcohol like some fruits , leaves, beeswax , protective coat in animals.
2. Compound lipids (Esters of fatty acids + Alcohol+ other groups like phosphate, Nitrogenous base, carbohydrate ,Protein):
   - ❖ Phospholipids (diglycerides): which contain two fatty acids + glycerol + phosphoric acid , found in the cellular membranes. Based on the type of alcohol:
     - ✓ Glycerphospholipids: Contain Glycerol as alcohol such as lecithin & cephalin
     - ✓ Sphingophospholipids: Contain sphingosine as alcohol such as sphingomyelin
   - ❖ Lipoprotein: lipid + protein complex. Based on the density, the types of lipoproteins are :
     - ✓ Chylomicron: is the largest lipoprotein molecule act to transport the triglycerides, cholesterol, phospholipid and protein into different tissues for storage.

- ✓ Very low-density lipoprotein (VLDL) transport the synthesized triglycerides from the liver to the adipose tissues for storage.
- ✓ Intermediate low-density lipoprotein (ILDL)
- ✓ Low -density lipoprotein (LDL) called **bad cholesterol** because it transport the cholesterol and other lipid molecules around the body tissues.
- ✓ High -density lipoprotein (HDL): called **good cholesterol** because it transport the cholesterol and other lipid molecules into the liver to be broken down.

❖ Glycolipids: which contain fatty acids + carbohydrates ,their role is to maintain the stability of the cell membrane and during immune response facilitate cellular recognition.

❖ Other compound lipids: Sulpholipids (brain and nervous tissues), Aminolipids and other Lipopolysaccharides

3. Derived lipids are the substances derived from simple and compound lipids by hydrolysis:
   - ✓ Ketone bodies
   - ✓ Eicosanoid
   - ✓ Steroids
   - ✓ Alcohol
   - ✓ Fatty acids
4. Miscellaneous lipids: vitamin E & K, carotenoids, squalene, hydrocarbons like pentacosone and Terpenes .

Function

1. Cell membrane molecules as receptors, antigens and membrane anchors for proteins
2. Steroid hormone synthesis like estrogens, androgens and cortisol
3. Bile production
4. Energy storage and utilization

Lipid metabolism

Exogenous lipid metabolism

Gastrointestinal lipolysis

1. In mouth: digestion of exogenous lipid begin in the mouth through chemical digestion by **lingual lipase (**secreted from **Ebner's glands)**.
2. In stomach: lipids continue to the stomach where chemical digestion continues by **gastric lipase** (secreted from gastric chief cells in the fundic mucosa in the stomach) and mechanical peristalsis digestion.
3. In small intestine:
   - ✓ **Bile acids** will emulsify lipid by broken down a large lipid molecules into small lipid aggregates.

- ✓ The hormone cholecystokinin (CCK) stimulate pancreas to secret **Pancreatic lipase** that act to hydrolysis of the triglycerides into free fatty acids and glycerol units to be absorbed into the small intestinal epithelial cells. Ingested cholesterol is not broken down by the lipases and stays intact until it enters the epithelium cells of small intestine.

4. Once the triglycerides are broken down into **free fatty acids and glycerol with cholesterol, and other molecules** will aggregate into structures called **micelles**. The micelles bump its contents to enter the brush border enterocytes by simple diffusion while the cholesterol enter to the enterocytes by special channels.
5. Inside the epithelial cell cytosol, free fatty acids and glycerol are recombined back into triglycerides, then **triglycerides** with **cholesterol,** phospholipid and proteins are packaged into bigger particles called **chylomicrons**.
6. Chylomicrons are leave the enterocytes via exocytosis into the space outside the cells. Chylomicrons are transport through lacteals into lymph, thoracic duct, and ultimately into the bloodstream then attach the cells.
7. Lipoprotein lipase in the luminal surface of capillary-endothelial cells hydrolyze the triglycerides of the chylomicron to release free fatty acid and glycerol across the cell membrane for direct use as energy source or recombined to form triglycerides for storage. After that the chylomicron remnant go to the liver for dissociation its remnant contents.

Endogenous lipid metabolism

1. Inside the liver, all the chylomicron remnants that dissociated will aggregates again to form **VLDL** that release from the liver to the blood until attach the cells and again to the lipoprotein lipase to hydrolyze the triglycerides into free fatty acid and glycerol for direct energy or storage.
2. The VLDL remnant called **IDL** back over to the liver. About 50% of IDL will be dissociated inside the liver, while other 50% will go to form **LDL**.
3. LDL will go back to the blood and enter the cells via receptor –mediated endocytosis to give up cholesterol and triglycerides . The cholesterol of LDL will use to several purposes like:
   - ✓ Synthesis of cell membrane
   - ✓ Making the sheath of the neurons
   - ✓ Synthesis of hormones like cortisol , aldosterone , testosterone and estrogen
   - ✓ Excess cholesterol will store in the cholesterol pool inside the cells
4. The excess cholesterol pool will remove from the cholesterol pool inside the cells by forming **HDL** that back over to the liver and utilize the cholesterol for bile synthesis.

Intracellular lipolysis

One triglyceride molecule yields three fatty acid molecules with as much as 16 carbons in each one, fat molecules yield more energy than carbohydrates.

The intracellular lipolysis are :

1. **Cytoplasmic Lipolysis**: in which triglycerides must be broken down by hydrolysis into fatty acids and glycerol that takes place in the cytoplasm.
2. **Fatty acid oxidation / beta-oxidation:** is the breakdown of fatty acids, begins in the cytoplasm:
   - ✓ Fatty acids are converted into **fatty acyl CoA** molecules.
   - ✓ The fatty acyl CoA combines with **carnitine** to create a **fatty acyl carnitine** molecule, which helps to transport the fatty acid across the mitochondrial membrane.
   - ✓ Once inside the mitochondrial matrix, the carnitine molecule spilt from the fatty acyl carnitine molecule to converted back into fatty acyl CoA and then into acetyl CoA.
   - ✓ The newly formed acetyl CoA enters the Krebs cycle and is used to produce ATP in the same way as acetyl CoA derived from pyruvate during glycolysis.
3. **The glycerol** that is released from triglycerides directly enters the glycolysis pathway through gluconeogenesis.
4. If excessive acetyl CoA that created from the oxidation of fatty acids the acetyl CoA is diverted to create **ketone bodies** specially in prolonged starvation or uncontrolled diabetes .

Lipid disorders

1. Dyslipidemia: abnormal lipoprotein levels (increase LDL and decrease HDL) in association with an increased risk of cardiovascular disease .
2. Hyperlipidemia: elevated blood lipid levels (total cholesterol, LDL, triglycerides)
3. Hypercholesterolemia: elevated total cholesterol> 200 mg/dL
4. Hypertriglyceridemia: elevated triglyceride levels
5. Hyperlipoproteinemia: elevated levels of a certain lipoprotein

Protein

Is a macromolecules found in our foods like meat, eggs, legumes and see foods. Found in our body for different functions.

The word derived from the Greek **proteios**, meaning "**holding first place**".

Monomers of protein

Amino acids

Amino acid have central carbon atom and amine group on one end and carboxylic acid group on the other end. All amino acids attach together between each amine group and carboxylic acid group of the other via **peptide linkage**.

There are about 20 different amino acids that occur naturally in proteins, each have assigned to them both three-letter (can be upper or lower case) and one-letter codes (upper case).

1. lysine
2. methionine
3. phenylalanine
4. histidine
5. isoleucine
6. leucine
7. threonine
8. tryptophan
9. valine
10. alanine
11. asparagine
12. aspartic acid
13. glutamic acid
14. cysteine
15. glutamine
16. glycine
17. proline
18. arginine
19. serine
20. tyrosine

- ✓ **Essential Amino Acids:** the first 1-9 amino acid must be obtained from dietary protein.
- ✓ **Nonessential Amino Acids:** the body can synthesize the 10-13 amino acids naturally.
- ✓ **Conditionally Nonessential Amino Acids** : the 14-20 that they will produce under only a healthy conditions but they convert to essential with diseases.

Protein structure

1. Primary Structure is the linear sequences of amino acids to form a protein back bone by peptide bonds. Primary structure appears with N-terminal and C-terminal.

2. Secondary Structure refers to the coiling or folding of a polypeptide chain that gives the protein a new forms via hydrogen bonds between hydrogen atom of amine group (NH) with oxygen atom of carboxylic acid group. The common types are alpha helix and beta sheet

3. Tertiary Structure : it is a 3-D structure of the polypeptide chain of protein by mixing of both secondary structures alpha helix and beta sheets like membrane bound proteins. The forces are:
   - ✓ Hydrophobic interactions.
   - ✓ Hydrogen bonds.

- ✓ Ionic bonds.
- ✓ Disulfide bonds

4. Quaternary Structure: refers to an interactions between multiple tertiary polypeptide chains. Each polypeptide chain is referred to as a subunit. For example, Hemoglobin contains four subunits.

Protein classification

On the basis of shape:

- ✓ **Fibrous protein**: threadlike structures to form fibers like collagen, actin, and myosin, keratin in hair, claws, feathers.
- ✓ **Globular proteins**: They are made up of polypeptides that are coiled about themselves to form oval or spherical molecules and soluble in water like albumin, insulin, and oxytocin.

On the basis of Constitution

- ✓ **Simple proteins**: These proteins are made up of amino acids only such as albumins, globulins, prolamins.
- ✓ **Conjugated proteins**: These are complex proteins that are combined with the non–amino acid substance called as a prosthetic group like:
  1. Nucleoproteins: Combination of protein and nucleic acid
  2. Glycoproteins: Combination of proteins and carbohydrate.
  3. Chromoproteins: Combination of proteins and colored pigments.
  4. Lipoproteins: Combination of proteins and lipids.
  5. Metalloprotein: Combination of proteins and metal ions.
  6. Phosphoprotein: Combination of proteins and phosphate group.
- ✓ **Derived proteins**: These are proteins that formed from simple or conjugated **proteins** by physical or chemical effectors like denatured protein and peptides.

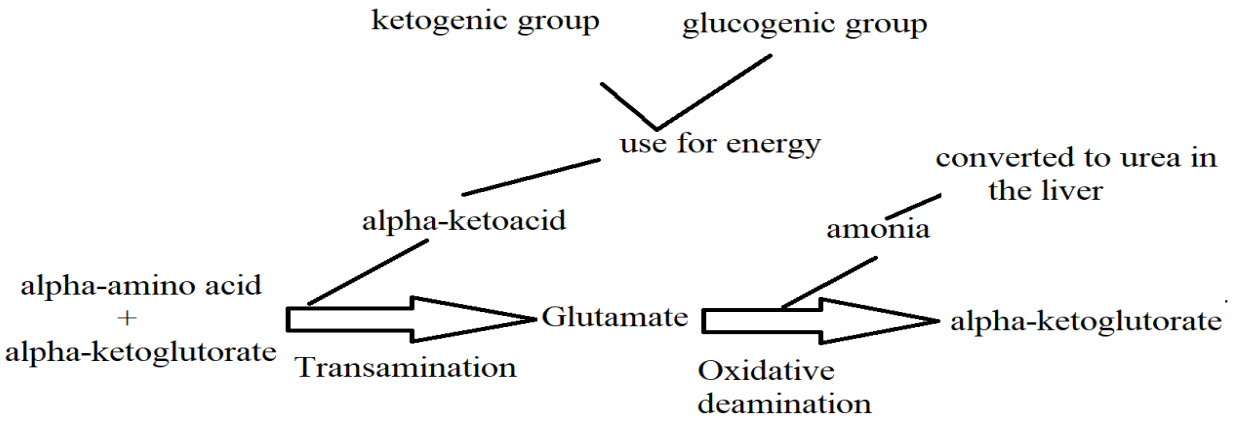
Functions of Proteins

1. Structural functions: are the building blocks of the body such as outer membrane of all cells in the human body, hair, skin, and contraction of muscles and movement of food through the digestive system.
2. Protective: are the main constituent of antibodies that protect the body against antigens to preventing infections.
3. Hormonal regulation: Hormones play a vital role in regulating muscle mass, sex hormones, growth and development.
4. Enzymes: that regulate many different biochemical reactions that are occurring in the body.

Protein metabolism

Proteolysis

1. In stomach: the digestion of protein will be start in the stomach by secretion of **HCL and pepsin** to break down the polypeptide bonds.
2. In small intestine:
   - ✓ The pancreas secret **trypsin, chymotrypsin and carboxypeptidase** to hydrolysis of large polypeptide bonds into small polypeptide bonds (di, tri peptide bonds).
   - ✓ Brush border enzymes: **dipeptidases** for hydrolysis of dipeptide bonds. **Amino peptidases** for hydrolysis of peptide bones from amino group.
   - ✓ After above enzyme activity , the polypeptides bonds will be di, tri peptide bonds and individual amino acids.
   - ✓ Start the absorption into the enterocytes then into the live via hepatic portal system:
     - Di and Tripeptide bonds will absorb via H- transporter channels then inside the cell it will be under further break down into individual amino acids by intracellular **peptidases**.
     - Individual amino acids will absorb via Na transport channels.
3. In liver: the liver will either :
   - ✓ Use the amino acids for protein synthesis by itself,
   - ✓ Send the amino acids to the muscles for protein synthesis there,
   - ✓ Or, the excess amino acid will be undergo catabolism, because the amino acids cannot be stored like glucose and fatty acid, The amino acid catabolism are:
     a. Transamination, oxidative deamination process and urea cycle.
     b. Uses of energy production via alpha-keto acid by :
        - Converting into Acetyl Co A to form fatty acids, that amino acid is called **ketogenic** group which are only two amino acids (lysine and Leucine).
        - Converting into pyruvate or oxaloacetate to form glucose molecule, that amino acid is called **glucogenic** group



Protein metabolism disorders

1. Kwashiorkor
2. Marasmus
3. Amyloidosis
4. Gout
5. Albinism