HORMONES

It is a chemical substance which is produced in one part of the body, enters the circulation and is carried to distant target organs and tissues to modify their structures and functions.

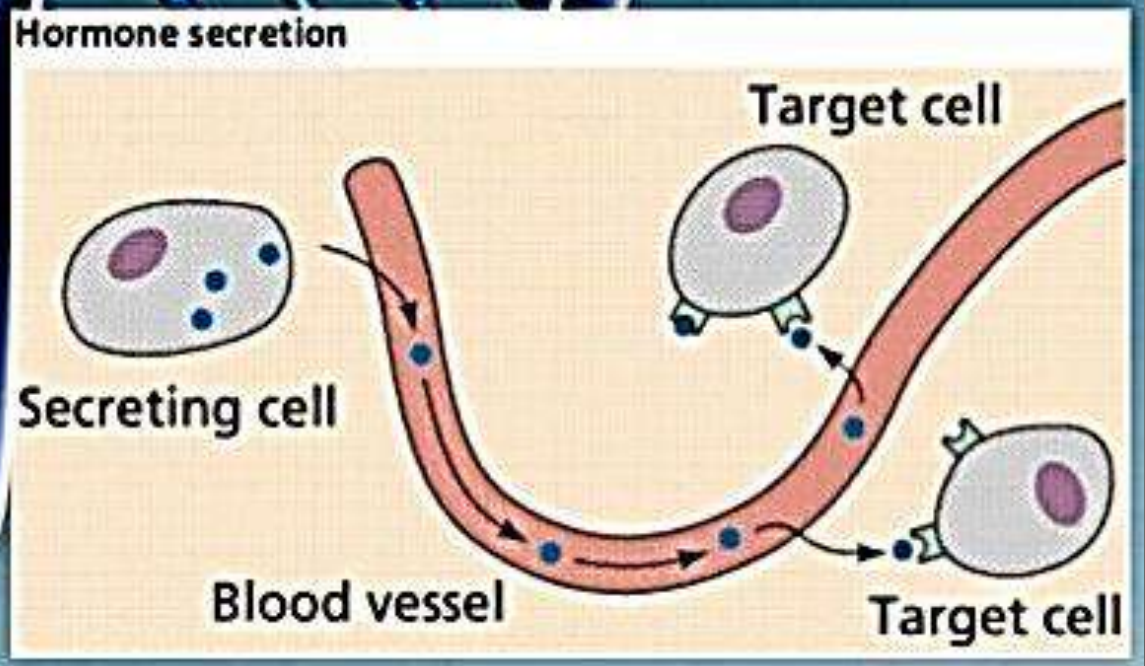
The word hormone is derived from a Greek word "Hormacin" which means to "Excite". Hormones are strictly speaking stimulating substances and act as body catalysts. The hormones catalyse and control diverse metabolic processes, despite their varying actions and different specifities depending on the target organ.

HORMONE SECRETION

Hormones in animals are often transported in the blood. Endocrine hormone molecules are secreted (released) directly into the bloodstream, while exocrine hormones (ecto-hormones) are secreted directly into a duct, and from the duct they either flow into the bloodstream or they flow from cell to cell by diffusion

Hormone secretion can be stimulated and inhibited by:

- Other hormones (stimulating or releasing hormones)
- Plasma concentrations of ions or nutrients
- Neurons and mental activity
- Environmental changes, E.g. Change in light or temperature.



EFFECT OF HORMONES

Hormones have the following effects on the body:

- Stimulation or inhibition of growth
- Mood swings
- Activation or inhibition of the immune system
- Regulation of metabolism
- Preparation of the body for fighting, fleeing, mating, and other activities
- Preparation of the body for a new phase of life, such as puberty, parenting, and menopause
- Control of the reproductive cycle
- Hunger cravings
- Hormone may also regulate the production and release of other hormones.
- Hormone signals control the internal environment of the body through homeostasis.

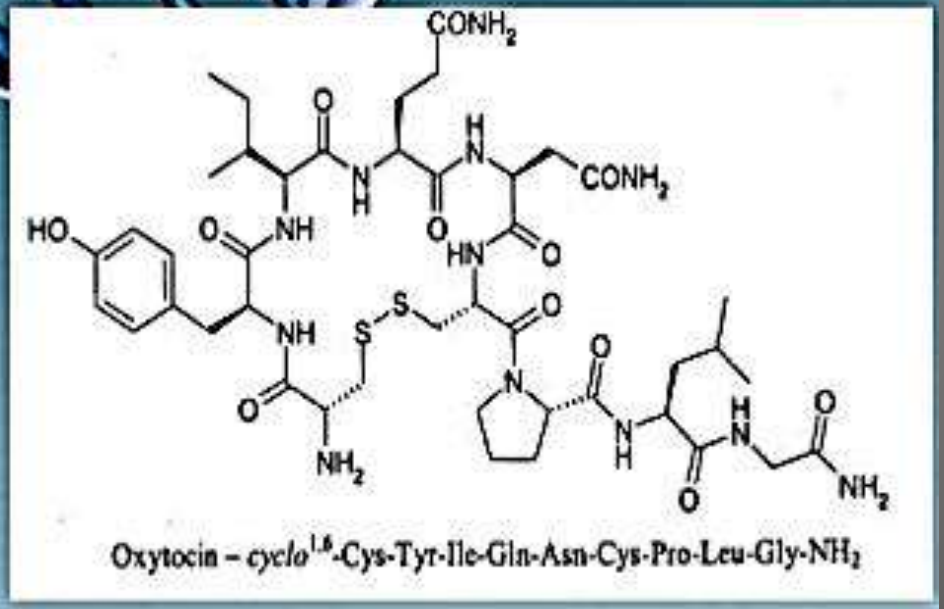
CLASSIFICATION OF HORMONES

Most commonly, hormones are categorized into four structural groups, with members of each group having many properties in common:

- Peptides and proteins
- Amino acid derivatives
- Steroids

1. PEPTIDES AND PROTEINS:

Peptide and protein hormones are products of translation. They vary considerably in size and post-translational modifications, ranging from peptides as short as three amino acids to large, multi-subunit glycoproteins. Peptide hormones are synthesized in endoplasmic reticulum, transferred to the Golgi and packaged into secretory vesicles for export. E.g. Oxytocin.



Oxytocin – *cyclo*[1,6]-Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH_2

2. AMINO ACID DERIVATIVES:

There are two groups of hormones derived from the amino acid, tyrosine:

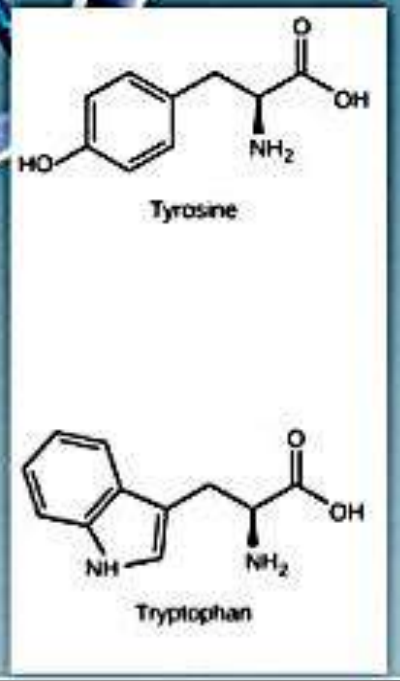
· Thyroid hormones are basically a "double" tyrosine with the critical incorporation of 3 or 4 iodine atoms.

· Catecholamine include epinephrine and norepinephrine, which are used as both hormones and neurotransmitters.

Two other amino acids are used for synthesis of hormones:

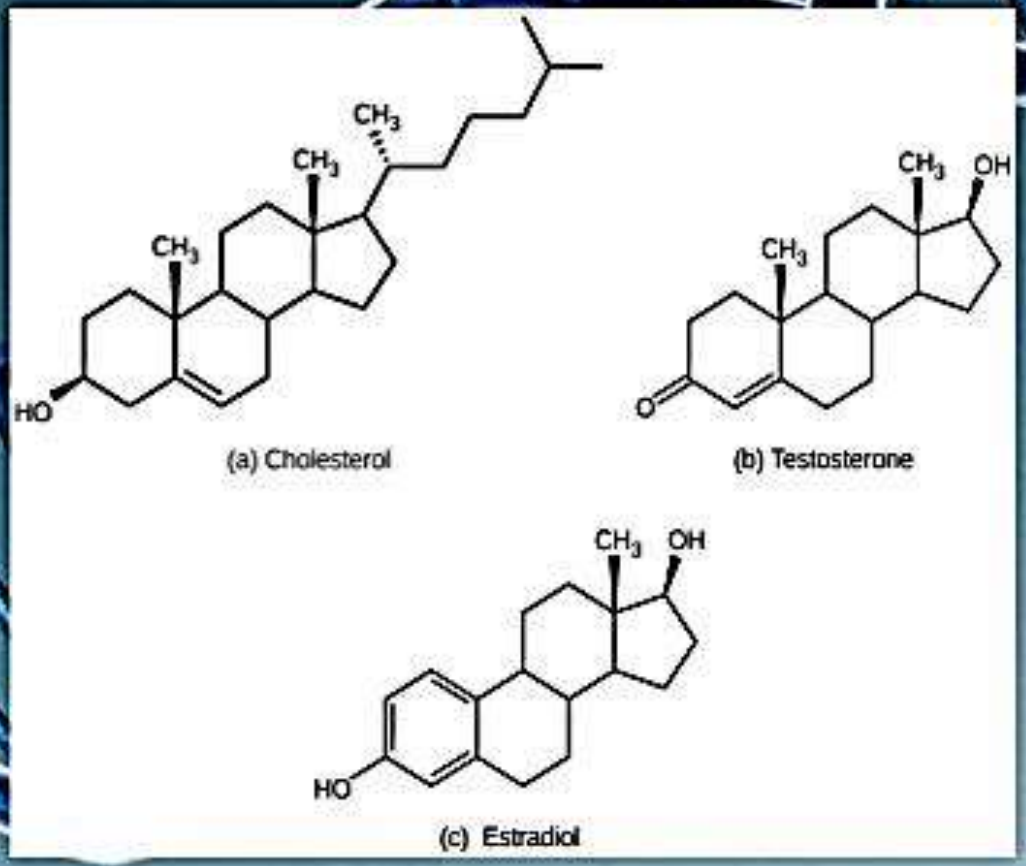
· Tryptophan is the precursor to serotonin and the pineal hormone melatonin.

· Glutamic acid is converted to histamine.



3. STEROIDS:

Steroids are lipids and, more specifically, derivatives of cholesterol. Examples include the sex steroids such as testosterone and adrenal steroids such as cortisol.



ACTION OF MECHANISIM

Understanding mechanism of action is not only of great interest to basic science, but critical to understanding and treating diseases of the endocrine system and in using hormones as drugs.
There are two fundamental mechanisms by which a hormone can change its target cell. These mechanisms are:

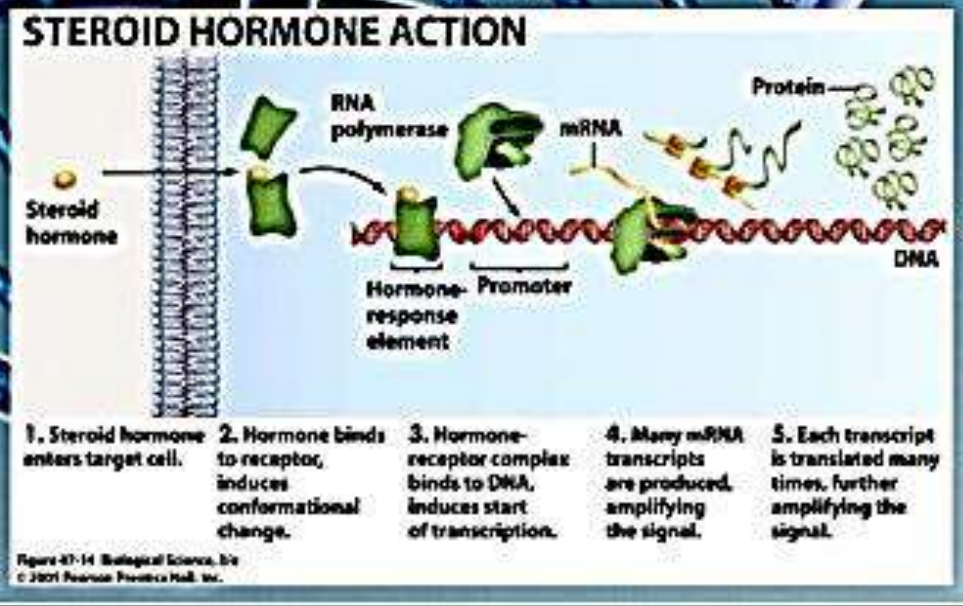
1. ACTIVATION OF ENZYMES AND OTHER DYNAMIC MOLECULES:

Most enzymes fluctuate between conformational states that are catalytically active versus inactive. Many hormones affect their target cells by inducing such transitions, usually causing an activation of one of more enzymes. Because enzymes are catalysts and often serve to activate additional enzymes, a seemingly small change induced by hormone receptor binding can lead to widespread consequences within the cell.

2. MODULATION OF GENE EXPRESSION:

Stimulating transcription of a group of genes clearly can alter a cell's phenotype by leading to a burst of synthesis of new proteins. Similarly, if transcription of a group of previously active genes is shut off, the corresponding proteins will soon disappear from the cell.

More specifically, when a receptor becomes bound to a hormone, it undergoes a conformational change which allows it to interact productively with other components of the cells, leading ultimately to an alteration in the physiologic state of the cell.



HORMONE RECEPTORS

Despite the molecular diversity of hormones, all hormone receptors can be categorized into one of two types, based on their location within the cell:

LOCATION OF RECEPTOR	CLASSES OF HORMONES	PRINCIPLE MECHANISM OF ACTION
Cell surface receptors (plasma membrane)	Proteins peptides, catecholamine and eicosanoids (water soluble)	Generation of second messengers which alter the activity of other molecules, usually Enzymes, within the cell.
Intracellular receptors (cytoplasm and/or nucleus)	Steroids and thyroids hormones (lipid soluble)	Alter transcriptional activity of responsive Genes.

THE FINAL EFFECTS OF HORMONES ACTION

1. Change the permeability of cell membrane.
2. Accelerate the penetration of substrates, enzymes, coenzymes into the cell and out of cell.
3. Acting on the allosteric centers, affect the activity of enzymes (Hormones penetrating membranes).
4. Affect the activity of enzymes through the messengers (cAMP). (Hormones that can not penetrate the membrane).
5. Act on the genetic apparatus of the cell (nucleus, DNA) and promote the synthesis of enzymes (Steroid and thyroid hormones).

FACTORS REGULATING HORMONE ACTION

Action of a hormone at a target organ is regulated by four factors:

1. Rate of synthesis and secretion: The hormone is stored in the endocrine glands.
2. In some cases, specific transport systems in plasma.
3. Hormone-specific receptors in target cell membranes which differ from tissue to tissue.
4. Ultimate degradation of the hormones usually by the liver or kidneys.

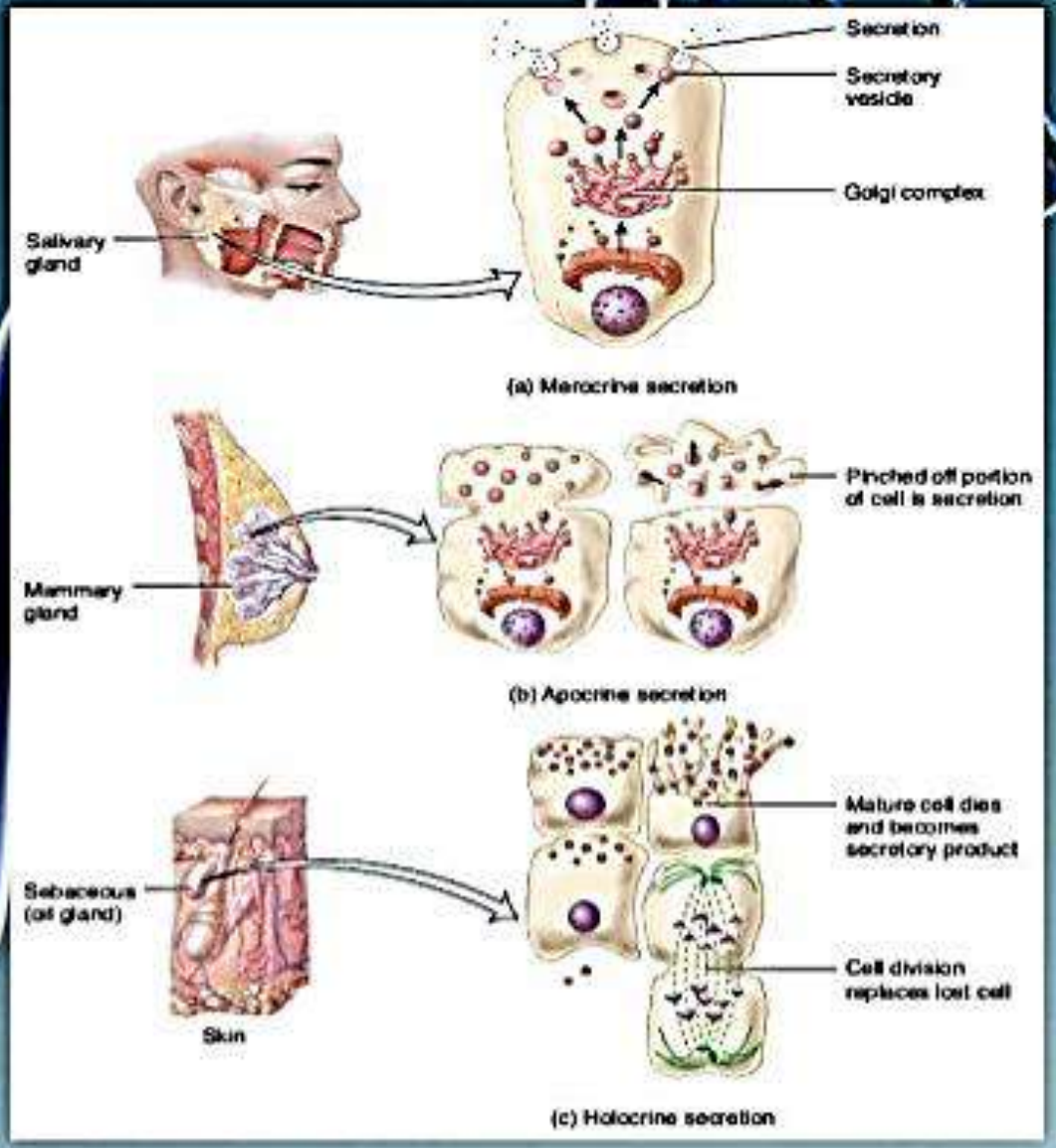
ENDOCRINE HORMONES

Endocrine glands produce endocrine hormones which have certain effects on our bodies.

Gland	Hormones produced	Effect of Hormone
Pineal gland	Melatonin	Affects reproductive development and daily physiologic cycles
Pituitary gland	Growth hormone	Controls growth of bones and muscles
	Anti-diuretic hormone	Increases reabsorption of water in kidneys
	Gonadotrophins	Controls development of ovaries and testes
Thyroid gland	Thyroxine	Controls rate of metabolism and rate that glucose is used up in respiration, and promote growth
Adrenal gland	Adrenaline	Prepares the body for emergencies: increases heart rate and rate and depth of breathing, raises blood sugar level so more glucose is available for respiration, diverts blood from gut to limbs
Pancreas	Insulin	Converts excess glucose into glycogen in liver.
	Glucagon	Converts glycogen back to glucose in liver
Ovaries	Oestrogen	Controls ovulation and secondary sexual characteristics.
	Progesterone	Prepares the uterus lining for receiving an embryo.
Testes	Testosterone	Controls sperm production and secondary sexual characteristics
Thymus	Thymosin	Promotes production and maturation of white blood cells

EXOCRINE HORMONES

These are exocrine glands in which exocrine hormones are present:



GLUCAGON
(PROTEIN HORMONE)

INTRODUCTION:

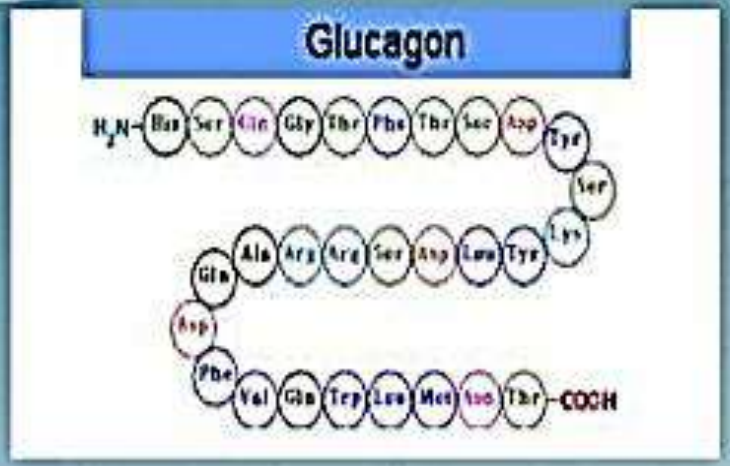
Glucagon is a hormone produced by α-cells of islets of Langerhans of pancreas and is an important hormone involved in:

- Rapid mobilization of hepatic glycogen to give glucose by glucogenolysis
- To a lesser extent FA from adipose tissue.

Thus, it act as a hormone required to mobilise metabolic substrates from storage depots.

CHEMISTRY:

Glucagon has been purified and crystallized from pancreatic extracts and also the hormone has been synthesized. It is a polypeptide containing 29 amino acids.



ESTROGEN
(STEROID HORMONE)

INTRODUCTION:

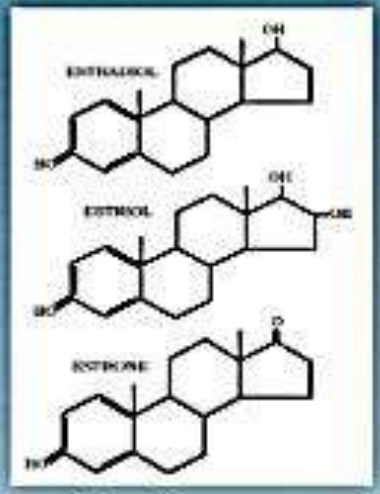
Estrogen are hormones capable of producing certain biological effects. They include:

- Growth of female genetic organs
- The appearance of female secondary sex characteristics
- Growth of the mammary duct system and numerous other phenomena which vary some what in different species.

CHEMISTRY:

The naturally occurring estrogens in humans are:

- β-Estradiol
- Estrone
- Estriol



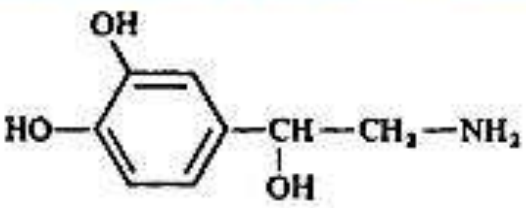
EPINEPHRINE & NOREPINEPHRINE (AMINO ACID DERIVATIVE)

INTRODUCTION:

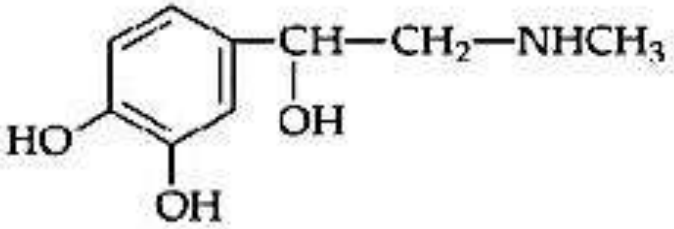
They are the hormones secreted from adrenal gland from adrenal medulla. They help in fight and flight responses.

CHEMISTRY:

- The naturally occurring forms are levorotatory.
- They don't have -COOH group.
- They act as neurotransmitters.
- They are stored in the form of granules.



NOREPINEPHRINE



EPINEPHRINE

SIMILARITIES & DISSIMILARITIES OF HORMONES & ENZYMES

SIMILARITIES:

- Both act as body catalysts.
- Both are required only in small quantities.
- Both are not used up during the reaction.

DISSIMILARITIES:

- Hormones are produced in an organ other than that in which they ultimately perform their action.
- They are secreted in blood prior to use.
- Structurally they are not only proteins. Few hormones are protein in nature, few are small peptides. Some are derived from amino acids while some are steroids in nature.

IMPORTANCE OF HORMONES

- Our bodies rely on hormones to function properly. Any problems affecting hormonal balance will affect our lives. Some things hormones are responsible for include: simulation of growth, control of cell's life span, control of **immune system**, metabolism regulation, control of phases of life, self preservation reactions, sexual functions, reproductive cycle.

- Hormones are chemical messengers in the body which control certain processes in the body, such as reproduction and homeostasis.

For example, insulin is a hormone in homeostasis which controls the concentration of glucose in the blood by causing its conversion into a insoluble substance. Without it (as in Type 1 diabetes), the blood sugar level would rise uncontrollably.


THANKYOU ☺

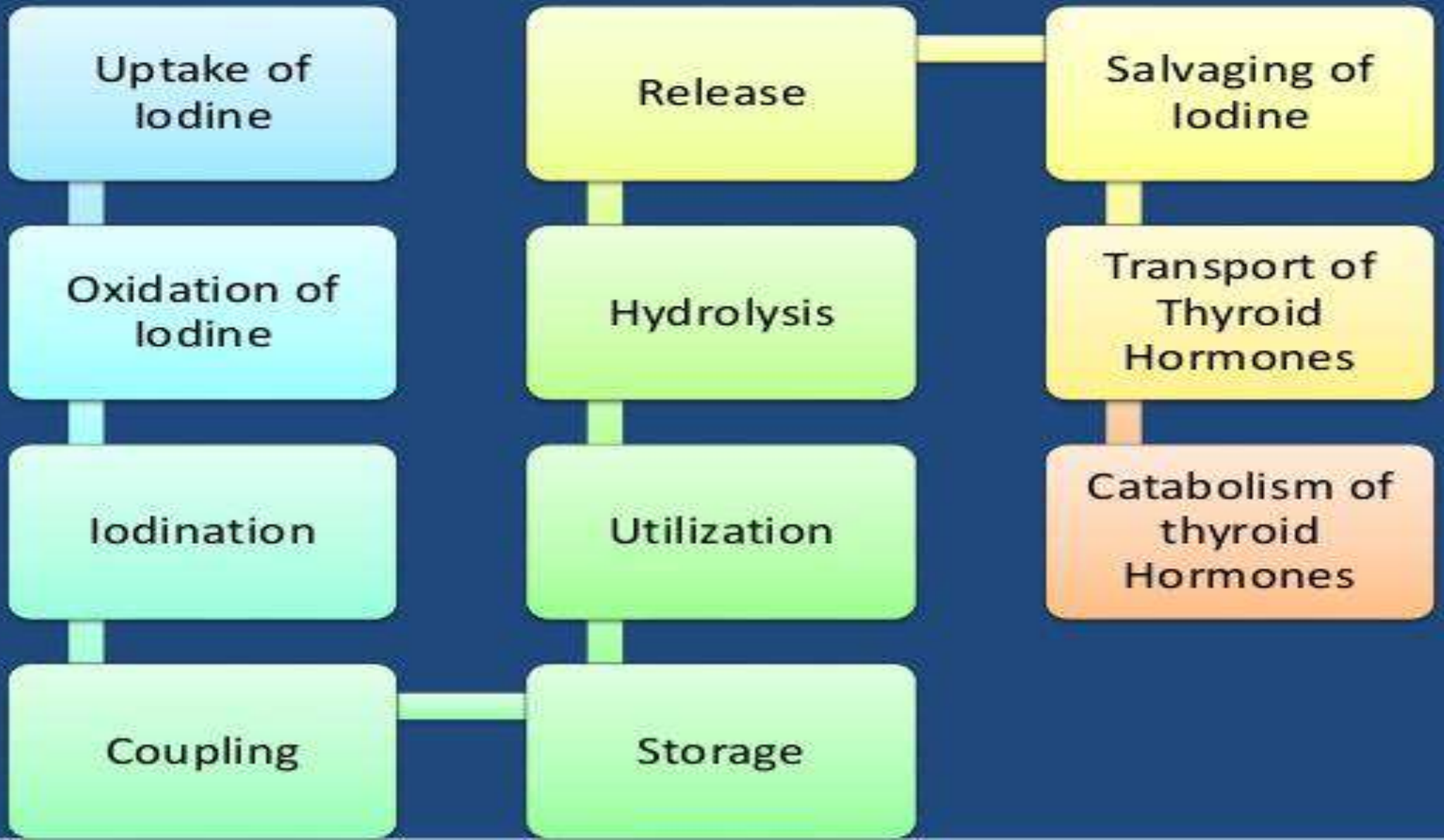
Thyroid Hormone

- Secreted by the thyroid gland
- Gland secret major hormone;
  - Thyroxine (T4)
  - Triiodothyronine (T3)
- Controlled by the primarily TSH (Thyroid stimulating hormone) secreted by the ant Pituitary gland.
- Gland also secrete calcitonin (imp hormone in calcium metabolism).

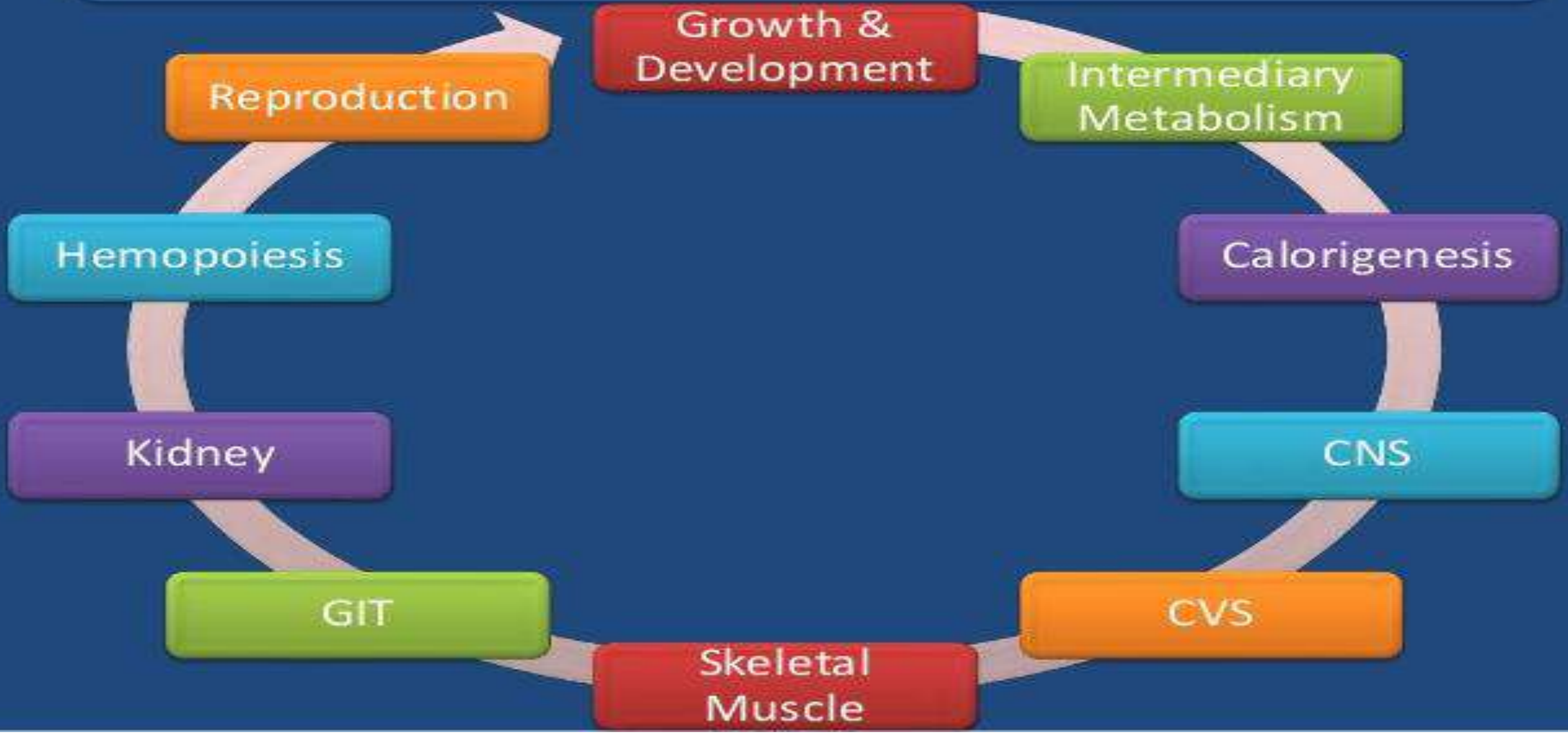
Iodine metabolism

- Iodine is required for the formation of thyroid (150-200µg/day) (sr 5-10 µg/dL)
- About 80% is stored in Thyroid gland.
- Ingredients which prevent the utilization of Iodine are called as Goitrogens.

Synthesis & secretion of Thyroxin



Effect of Thyroid Hormones



Effect of Thyroid Hormones

Lipid metabolism

- Fat mobilization.
- Oxidation of FA
- Inversely related to hormone levels.

Carbohydrate metabolism

- Enhance insulin dependent glucose entry
- Increased gluconeogenesis & glycogenolysis.

Growth

- For normal growth.

Development

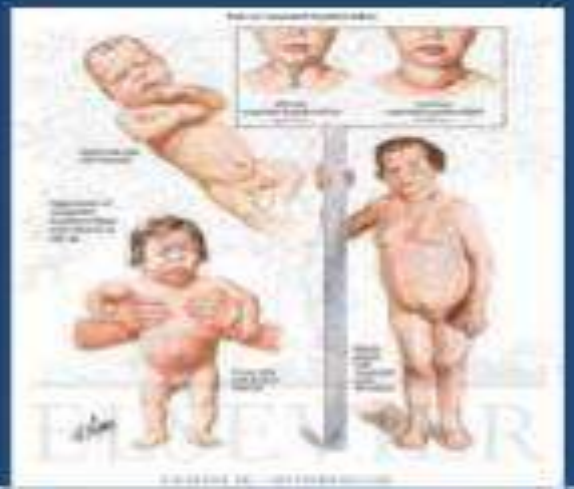
- Physical and mental development in fetal, neonatal, young and adult.

Other effect

- Cardiovascular
- Central nervous system
- Reproductive system
- Hemopoiesis
- Skeletal, GIT, Kidney

Thyroid Disorders

- Cretinism
- Hyperthyroidism
- Hypothyroidism
- Euthyroid Goiter

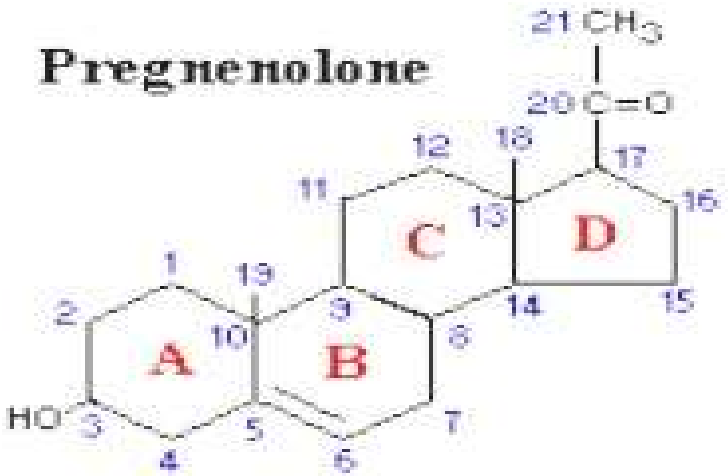


Steroid Hormones

- Steroid hormones: produced in the adrenal cortex, testis, ovary, and some peripheral tissues (adipose tissue, the brain!)
- All steroid hormones share a typical (but not identical) ring structure.

Steroid hormones

- All steroid hormones are derived from cholesterol and differ only in the ring structure and side chains attached to it.
- All steroid hormones are lipid soluble



Types of steroid hormones

- **Glucocorticoids**; cortisol is the major representative in most mammals
- **Mineralocorticoids**; aldosterone being most prominent
- **Androgens** such as testosterone
- **Estrogens**, including estradiol and estrone
- **Progestogens** (also known a progestins) such as progesterone

Steroid hormones

- Steroid hormones are not water soluble so have to be carried in the blood complexed to specific binding globulins.
- Corticosteroid binding globulin carries cortisol
- Sex steroid binding globulin carries testosterone and estradiol
- In some cases a steroid is secreted by one cell and is converted to the active steroid by the target cell: an example is androgen which secreted by the gonad and converted into estrogen in the brain

Functions of Steroid Hormones

- Steroid hormones play important roles in:
  - carbohydrate regulation (glucocorticoids)
  - mineral balance (mineralocorticoids)
  - reproductive functions (gonadal steroids)

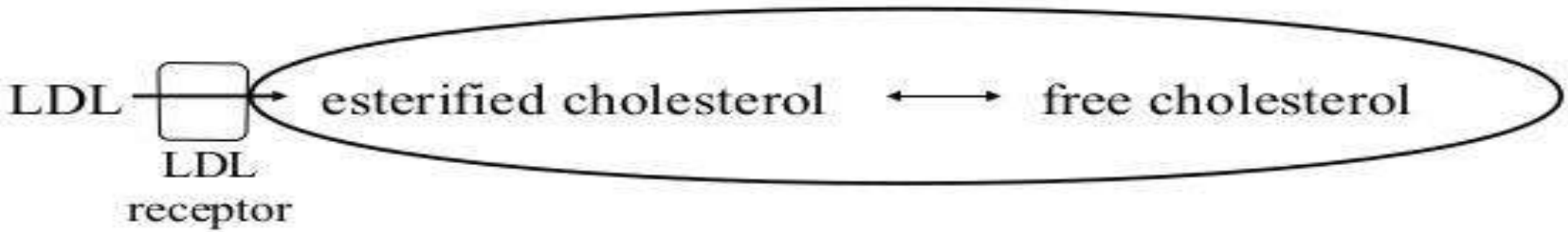
- Steroids also play roles in inflammatory responses, stress responses, bone metabolism, cardiovascular fitness, behavior, cognition, and mood.

Sources of Cholesterol for Steroid Synthesis

- Cholesterol is also taken up by the cell in the form of low density lipoprotein (LDL).

  - LDL is a complex composed of cholesterol, phospholipids, triglycerides, and proteins (proteins and phospholipids make LDL soluble in blood).

  - LDL is taken into cells via LDL receptors, and broken down into esterified cholesterol, and then free cholesterol:



Adrenal Steroids

- The adrenal glands are located immediately superior to the kidneys.
- There are three classes of adrenal steroids:
  - mineralocorticoids,
  - glucocorticoids, and
  - androgens

Parathyroid Hormone

- provides a powerful mechanism for controlling extracellular calcium and phosphate concentrations by regulating:

- ✓ intestinal reabsorption
- ✓ renal excretion
- ✓ exchange between the extracellular fluid and bone of these ions.

- **Excess activity** of the parathyroid gland causes rapid **absorption of calcium salts** from the bones, with resultant **hypercalcemia** in the extracellular fluid;

- conversely, **hypofunction** of the parathyroid glands causes **hypocalcemia**, often with resultant **tetany**.

Chemistry of Parathyroid Hormone

- synthesized in the form of a **preprohormone**
- cleaved to a **prohormone**
- then to the **hormone itself with 84 amino acids** by the endoplasmic reticulum and Golgi apparatus
- finally is **packaged in secretory granules** in the cytoplasm of the cells.

Effect on Ca^+ and Phosphate Concentrations in the ECF

- suddenly infusing PTH

- ✓ **calcium** ion concentration begins to **rise** and reaches a plateau in about 4 hours.

- ✓ the **phosphate** concentration, however, **falls** more rapidly than the calcium rises and reaches a depressed level within 1-2 hours.

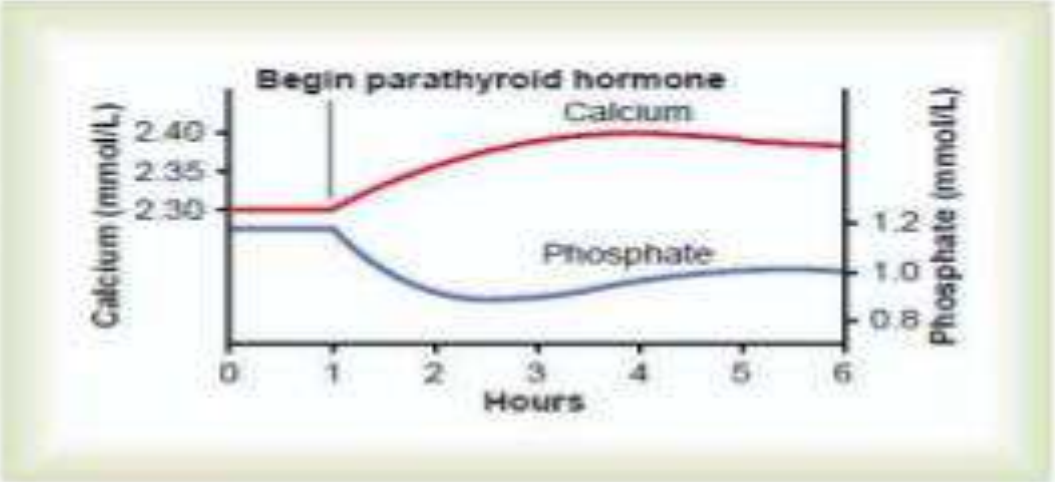


Figure 79–10

Approximate changes in calcium and phosphate concentrations during the first 5 hours of parathyroid hormone infusion at a moderate rate.

- PTH ↑calcium and phosphate absorption from the bone
- PTH ↓excretion of calcium by the kidneys.
- PTH ↑renal phosphate excretion **

** an effect that is usually great enough to override increased phosphate absorption from the bone.

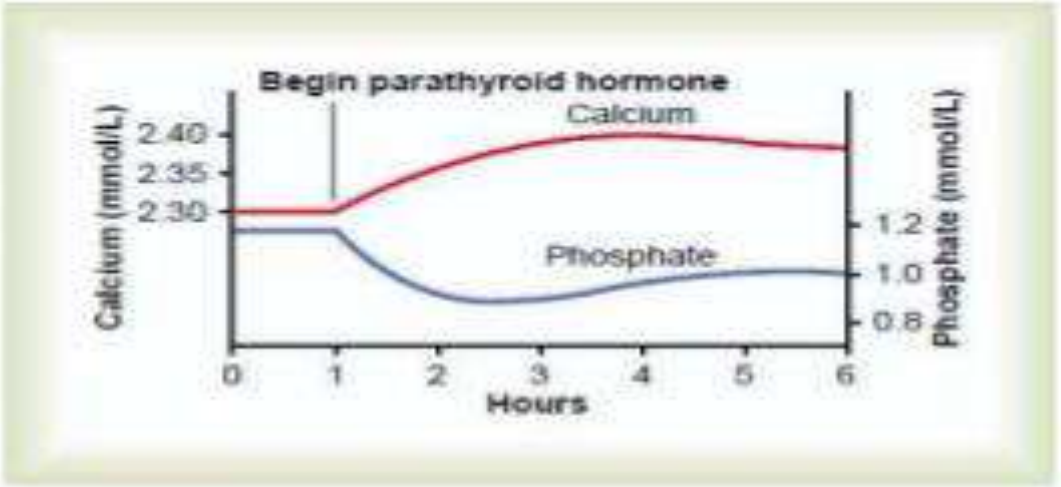


Figure 79–10

Approximate changes in calcium and phosphate concentrations during the first 5 hours of parathyroid hormone infusion at a moderate rate.

PTH ↑calcium and phosphate absorption from the bone

First phase	Second phase
rapid	**slow**
Minutes-hours	Days-weeks
Activation of already existing **osteocytes /osteoblasts**	Proliferation of **osteoclasts**
Receptor protiens on octeocytes/osteoblasts that bind PTH and activate calcium pump	Activated osteocytes/osteoblasts send **secondary signals** to osteoclasts
Promote **calcium and phosphate** absorption	Osteoclastic absorption of **bone** itself

Disorders of PTH

- hypoparathyroidism
- Primary hyperparathyroidism
- Secondary hyperparathyroidism

Hypoparathyroidism

- ↓PTH→↓Ca^+ reabsorption from bone→↓ Ca^+ level in body fluids

- Bone remains strong

- If parathyroid glands are suddenly removed:
  - ✓ Ca^+ levels fall from 9.4mg/dl to 6-7 within few days
  - ✓ **Phosphate** concentration may **double**
  - ✓ **↓Ca^+→tetany**

- **Laryngeal muscles tetany**→obstructs respiration →death

Hypoparathyroidism

- Treatment

- ✓ hypoparathyroidism is usually **not treated with PTH** administration.
- ✓ large quantities of **vitamin D** daily
- ✓ 1-2 grams of **Calcium**
- ✓ **1,25-dihydroxycholecalciferol**

Primary Hyperparathyroidism

- **Osteoblastic activity** in the bones also **increases** greatly in attempt to make up for the old bone absorbed by the osteoclastic activity.

- When the osteoblasts become active, they secrete large quantities of **alkaline phosphatase**. Therefore, one of the important diagnostic findings in hyperparathyroidism is a high level of plasma alkaline phosphatase.

Primary Hypeparathyroidism

- **Tumor in parathyroid glands** (females mainly)→ excess PTH → **↑Ca concentration in ECF. ↓Phosphate**
- In severe hyperparathyroidism the bone may be eaten away entirely.
- Indeed, the reason a hyperparathyroid person seeks medical attention is often a broken bone.

Kidney stones

- **Mild hyperparathyroidism** leads to formation of kidney stones(calcium phosphate, calcium oxalate stones)

- Kidney stones are more common in alkaline urine(low solubility in alkaline media)→**treatment include acidotic diet & acidic drugs.**

Secondary hyperparathyroidism

- high levels of PTH occur as a compensation for **hypocalcemia**
- this contrasts with primary hyperparathyroidism, which is associated with hypercalcemia.
- caused by **vitamin D deficiency** or **chronic renal disease** in which the damaged kidneys are unable to produce sufficient amounts of the active form of vitamin D

CLINICAL SIGNIFICANCE of Proteins in Blood and urine

Lac.3

By
Dr. Muna M. Yaseen

Objective

1. Type of proteins in blood
2. Clinical Diagnostic & Utility

of Proteins Measurements in blood

3. Causes of Proteinuria

- **Proteins** are Polypeptide group of nutrients in human body. All enzymes, receptors, membrane channels such as those of Na-K, Ca channels, coagulation factors and peptide hormones

(GH, prolactin,...),..., etc. are proteins in nature.

- All proteins are synthesized in the liver, with exception of complement systems

(C1-C9 these are components of immune system synthesized by liver and macrophages), and Immunoglobulin's (Igs) (by plasma cells of immune system).

- Proteins may be linear structural (such as collagen component of connective tissue) or globular functional such as enzymes & peptide hormones.

Amounts of proteins in blood depend on balance:

rate of synthesis ↔ (rate of catabolism + rate of clearance).

However, protein distribution between the Intravascular (IV) and Extra vascular compartments is also important and therefore blood protein concentrations are affected by dehydration & over hydration.

Proteins in blood involved two types:

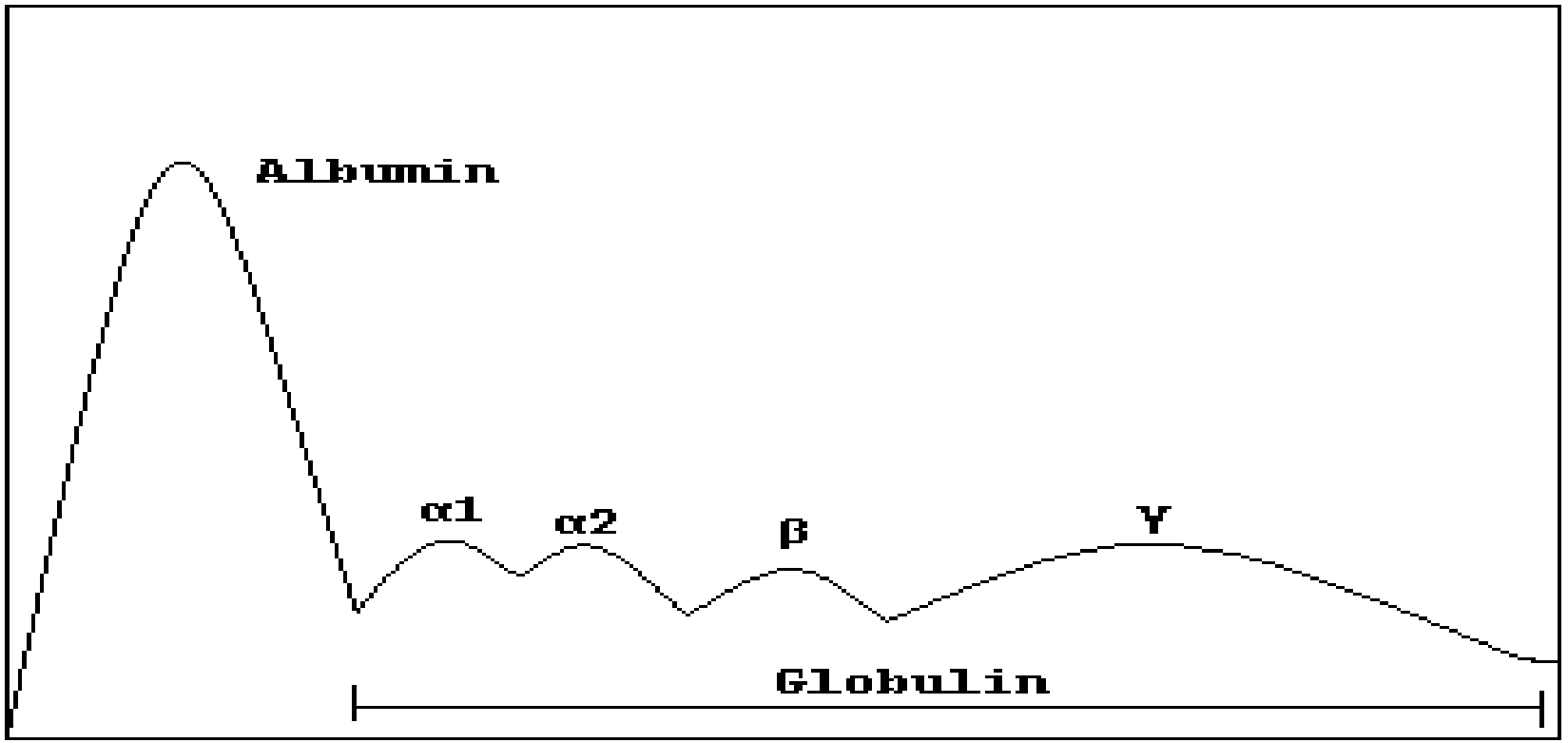
Albumin & total Globulin.

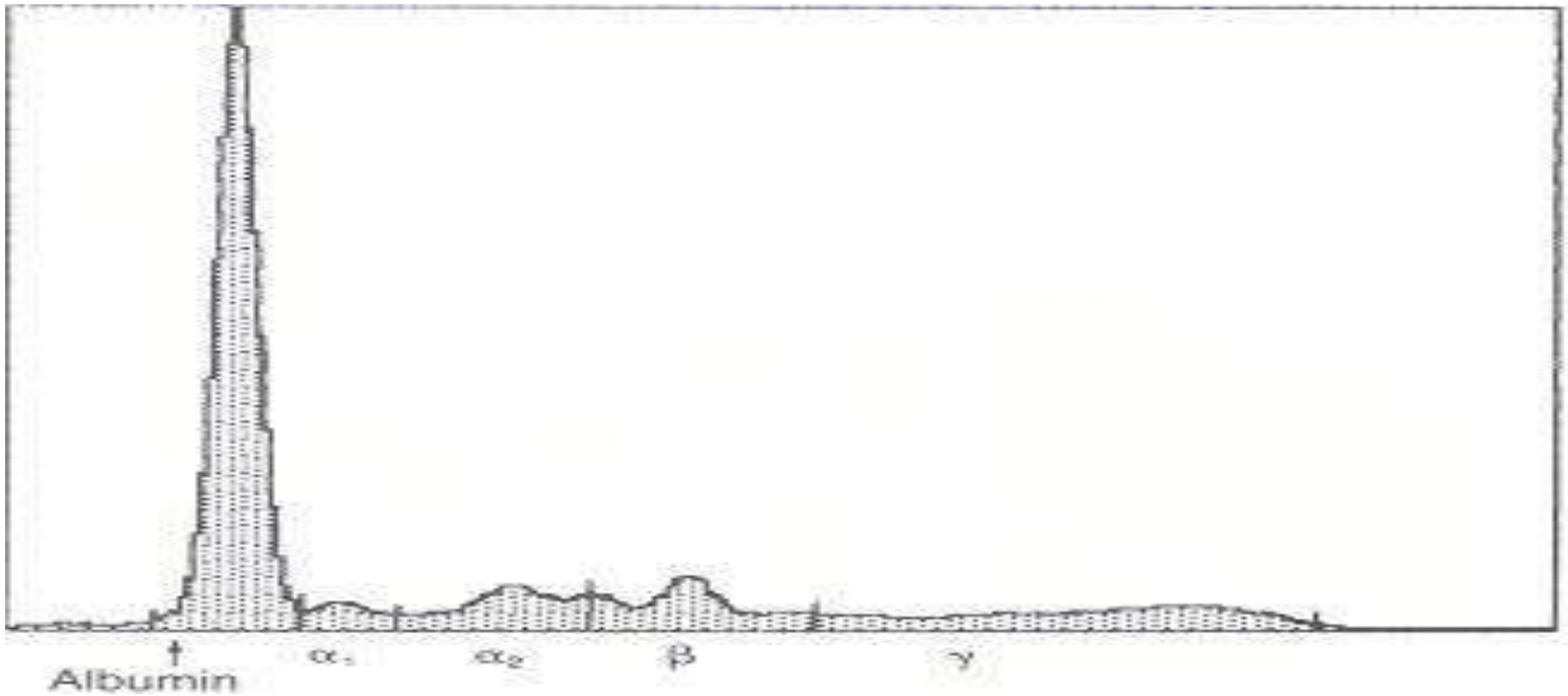
Albumin is the major single protein accounts to 60 % of total serum protein,

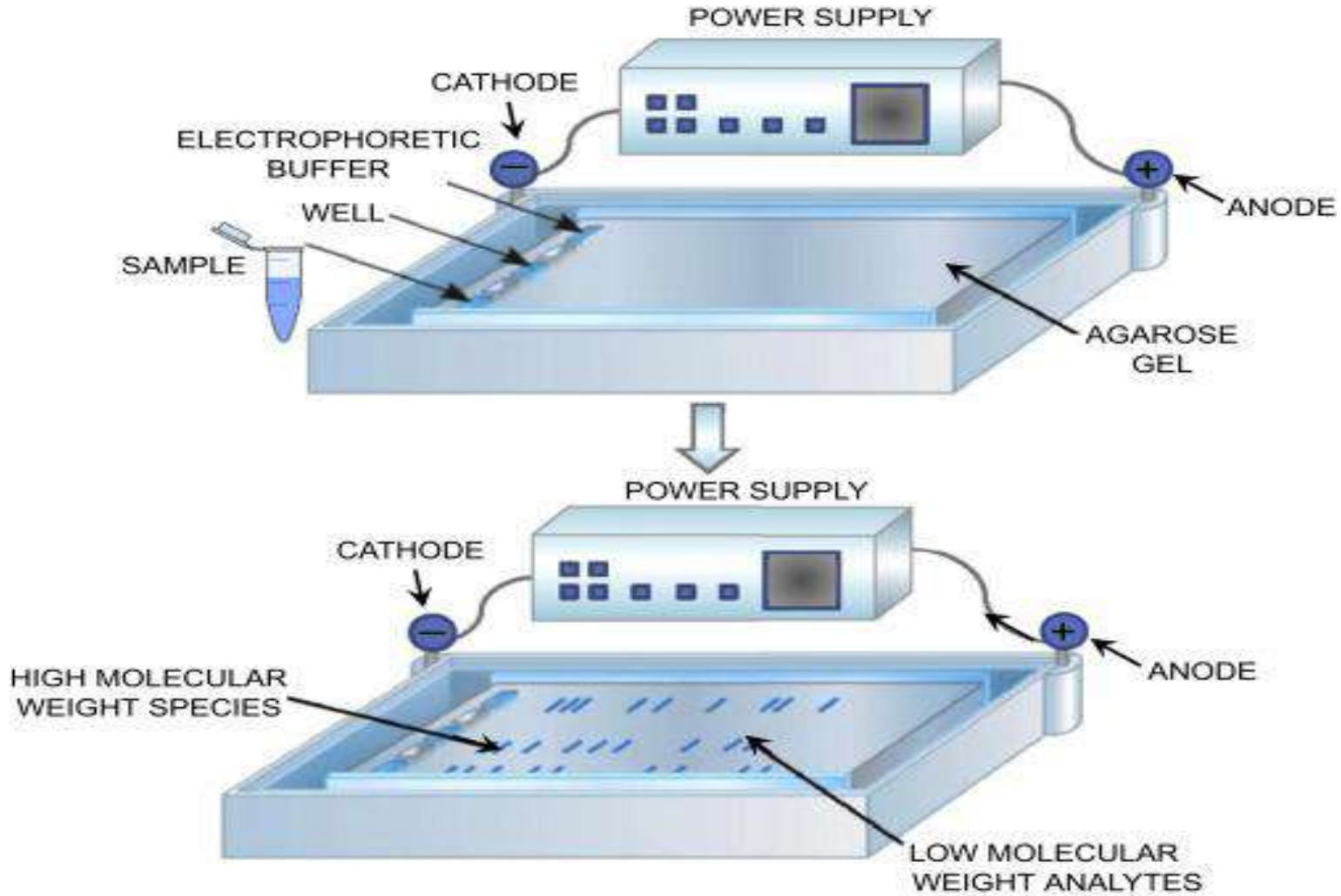
while globulin is consisted of 4-5 fractions**; α 1, α 2, β 1, β 2, and γ globulins**.

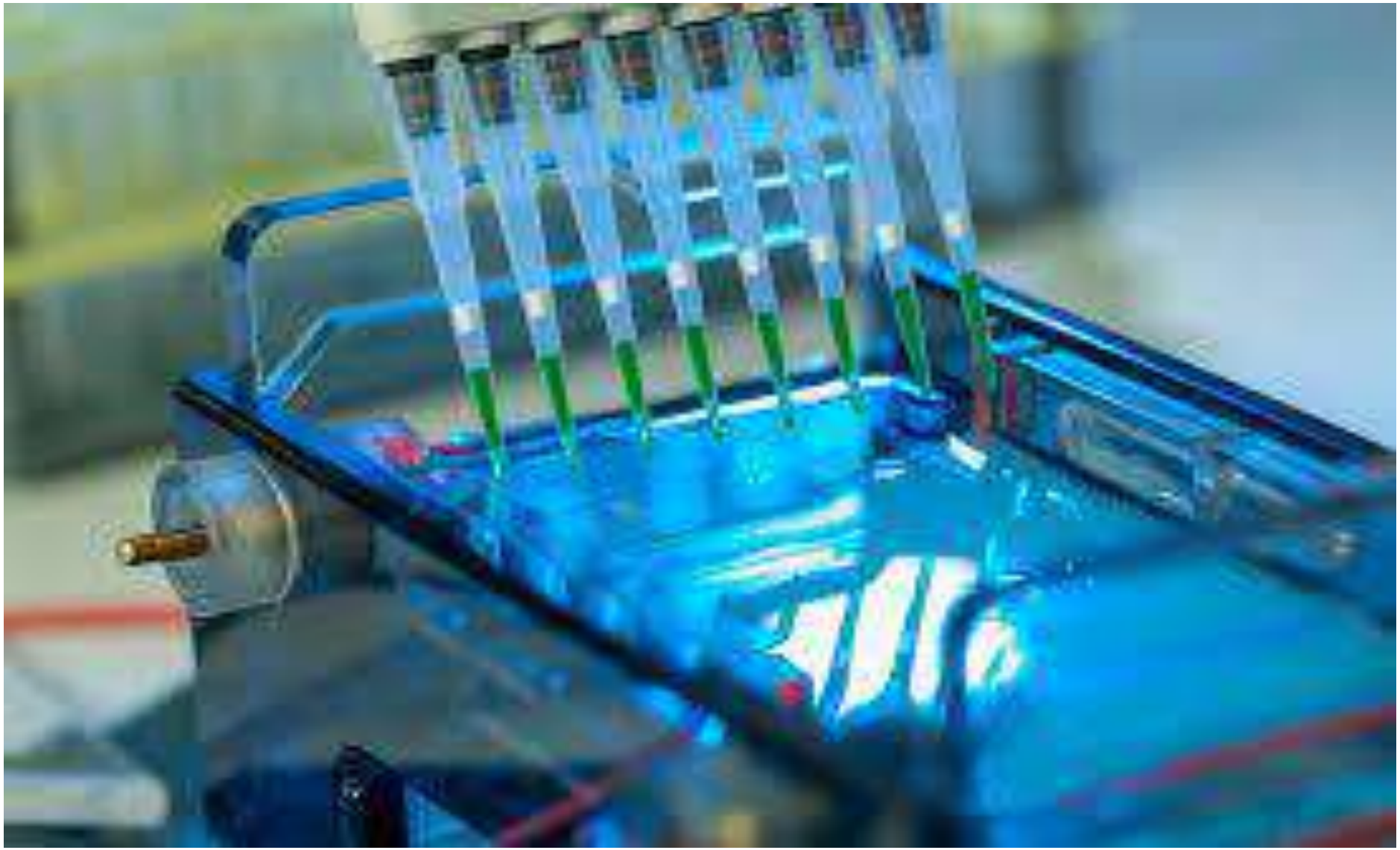
These Proteins components are separated by **electrophoresis technique** in which serum is introduced to filter paper in a media of PH 8.6 to make protein which are polar substances negatively charged. Then electrical current is passed into media and the serum proteins are separated **according to their MW and charge intensity** into five–six fractions or bands: **albumin, α1- globulin, α2-globulin, β-globulin (may be β1 & β2), and γ globulin**.

Total Serum Protein=S. albumin + total serum globulin.


Albumin
α1
α2
β
γ
Globulin


Albumin
α1
α2
β
γ


POWER SUPPLY
CATHODE
ELECTROPHORETIC BUFFER
WELL
SAMPLE
ANODE
AGAROSE GEL
POWER SUPPLY
CATHODE
ANODE
HIGH MOLECULAR WEIGHT SPECIES
LOW MOLECULAR WEIGHT ANALYTES

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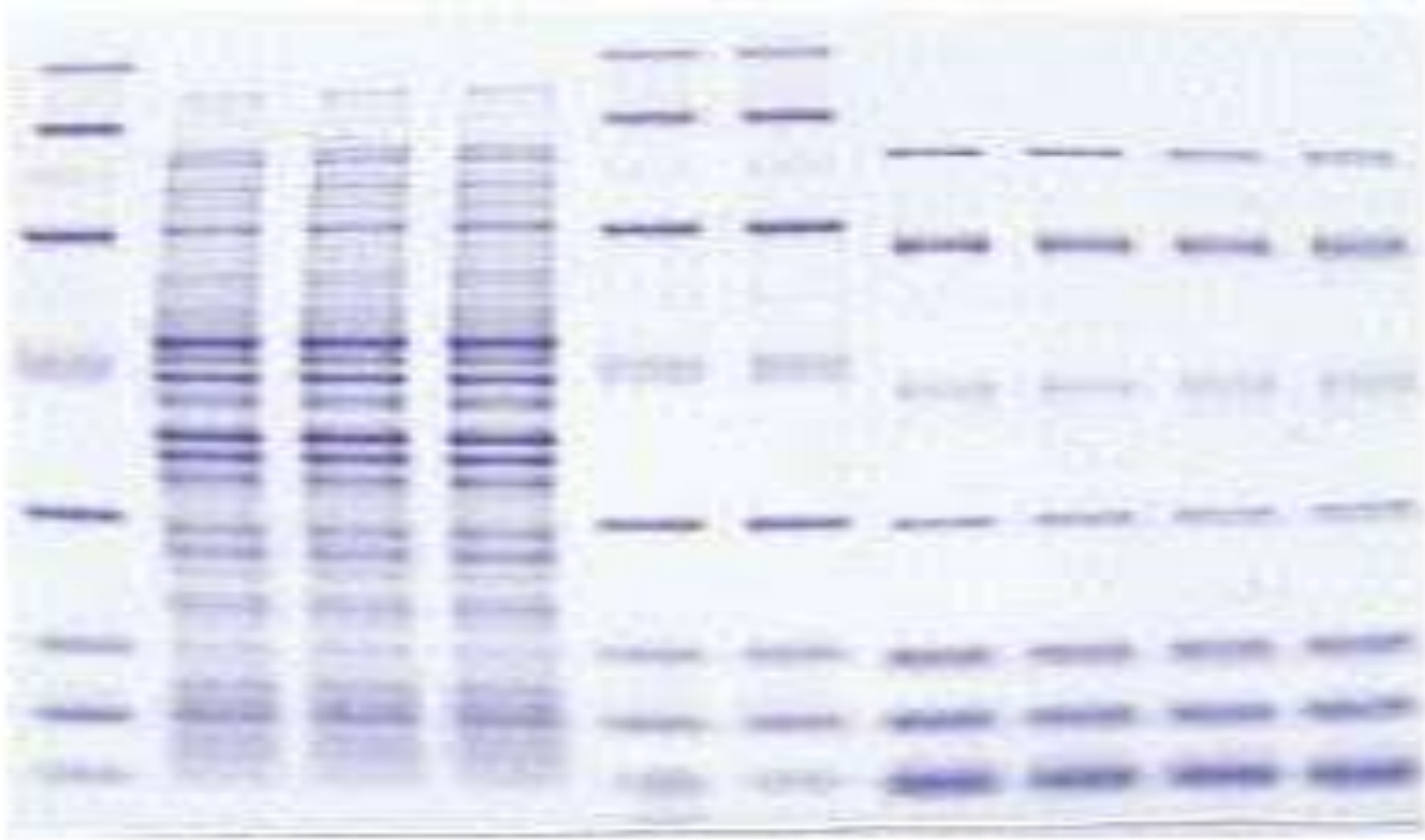
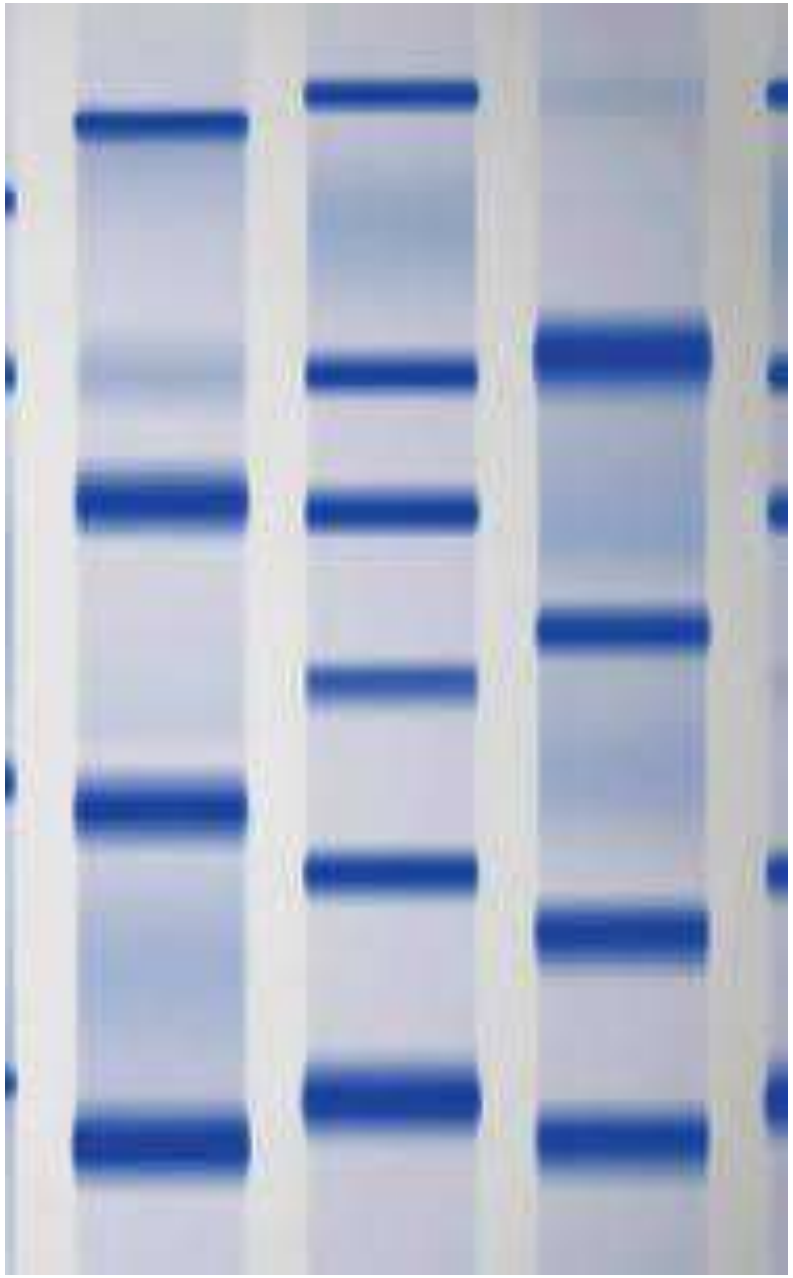
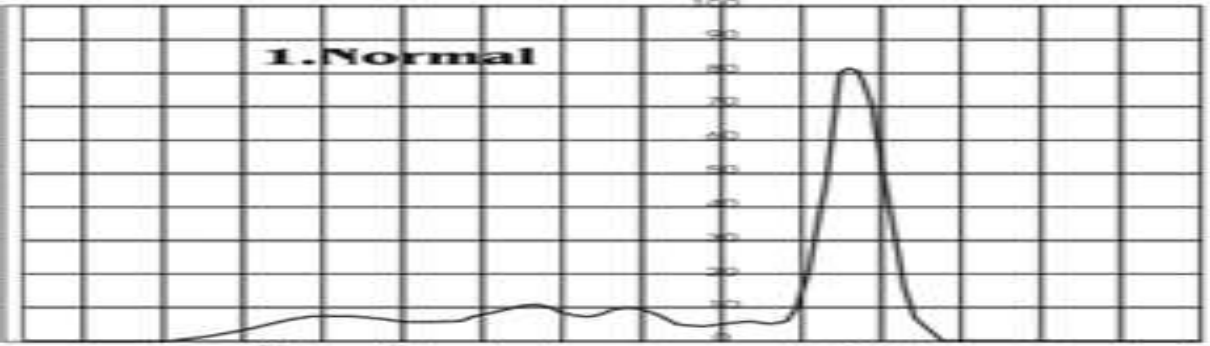
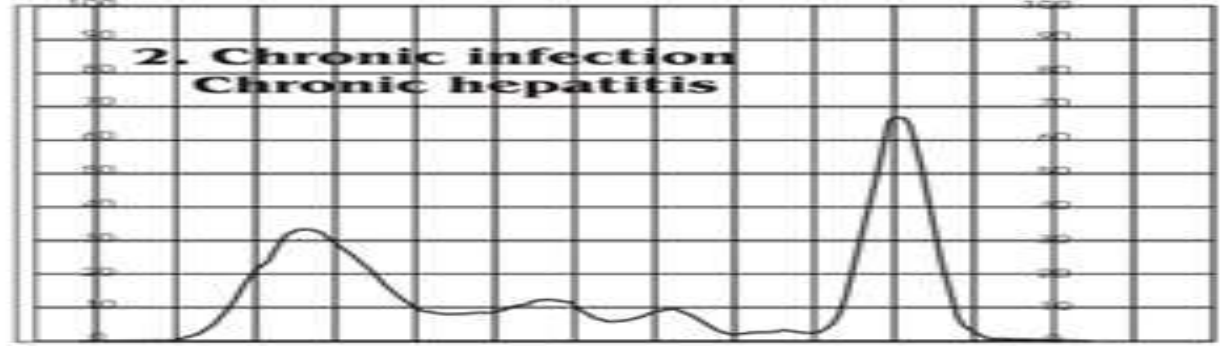
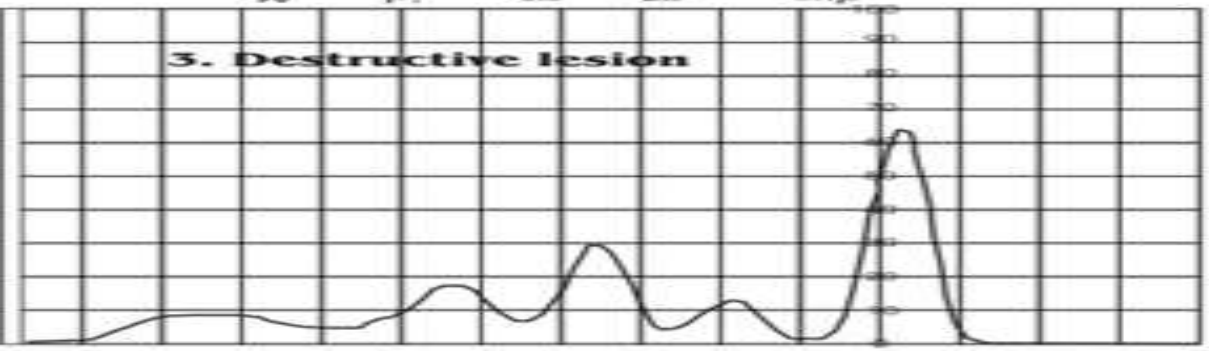
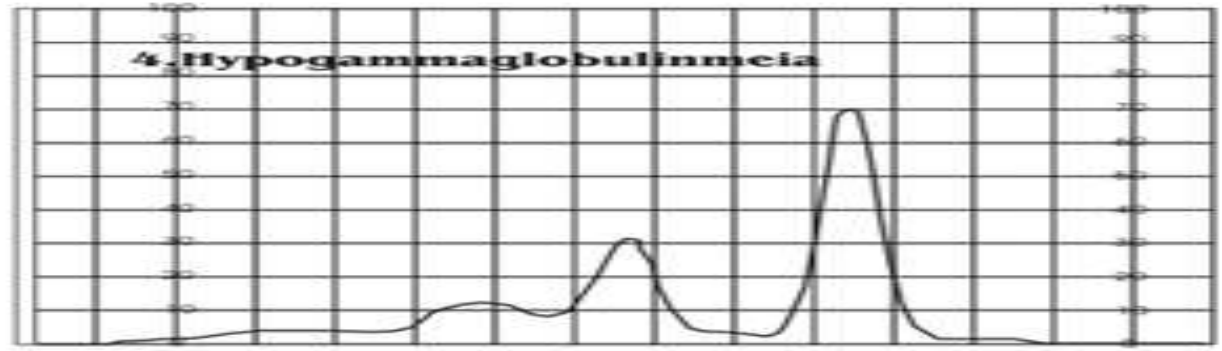


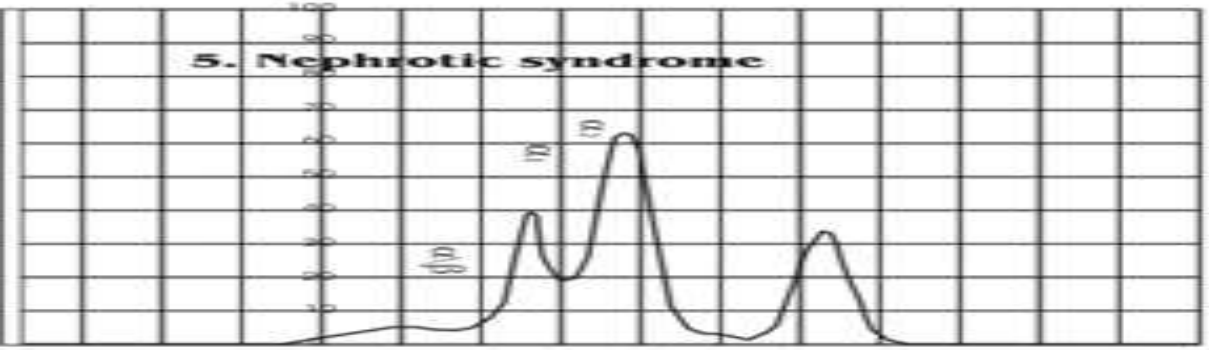


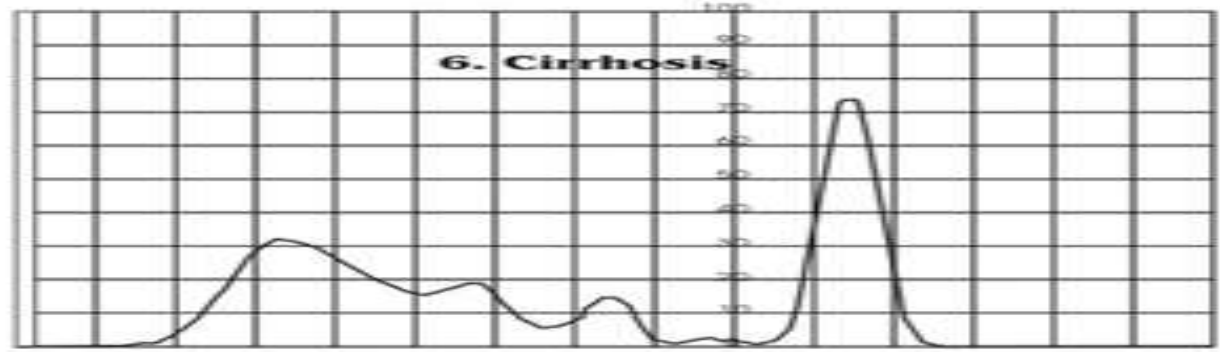

1.Normal
χ
β2
α2
α1
α\β

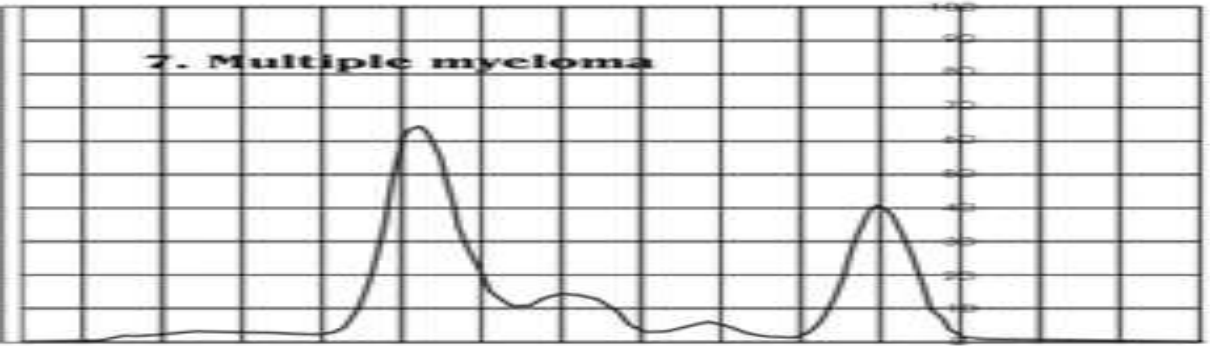

2. Chronic infection
Chronic hepatitis

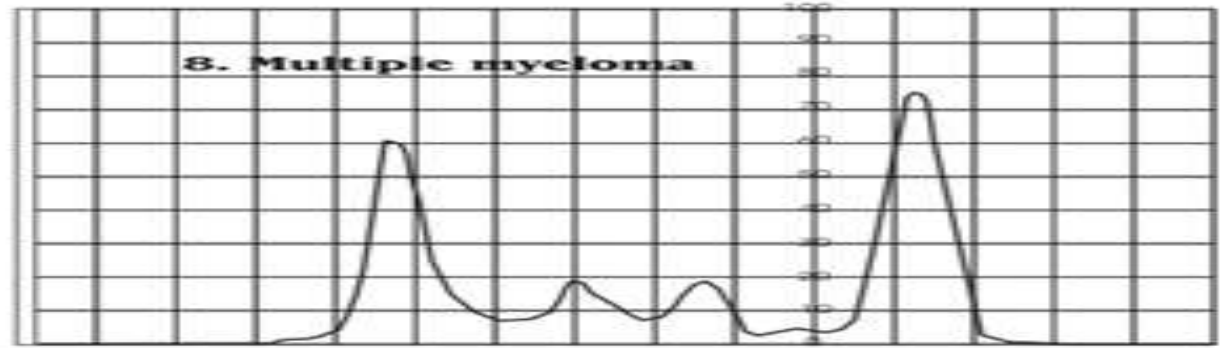

3. Destructive lesion


4.Hypogammaglobulinmeia


5. Nephrotic syndrome
α\β
α1
α2


6. Cirrhosis


7. Multiple myeloma


8. Multiple myeloma

Hyperproteinemia

are rare and are of no clinical significance value and may obtained from prolonged vein stasis during blood collection, posture (due to fluid redistribution) and from excessive dehydration.

Hypoalbuminemia:

It is clinically an important condition because albumin is one of the major components of osmotic colloid pressure of blood vessels and involved in normal fluid distribution between the Intravascular and Extra vascular compartments and in maintenance of normal blood pressure.

Albumin is also the major transporter substance in the blood; transporting bilirubin, fatty acids, steroid drugs, steroid & thyroid hormones,

Hypoalbuminemia

1. Chronic liver disease ; liver cirrhosis

2. Advanced kidney disease; Nephroteic syndrome &Chronic renal failure

3. Malnutrition (Kwashiorkor & Marasmus diseases) and Malabsorption like in Tropical intestinal diseases; Celiac disease

4. Loss through Enteropathy

5. skin lesions; extensive burns.

Clinical consequences Hypoalbuminemia :

1. edema due to migration of fluid from IV to interstitum compartment

2. transporting and binding capacity defects; such as for fatty acids, bilirubin, steroid Hs and drugs which may leads to toxicity with appropriate dose.

Analbuminemia is a rare disorder characterized by low blood albumin (s. albumin 10 gram/l; but of no edema or other symptoms and signs).

Globulin

This include 4-5 fractions (alpha 1, alpha 2, beta, and gamma fractions).

Increased in globulin may be due to increased in one or more of its fractions;α,β, and γ.

The α-1 and -2 include :

α1 -Antitrypsin,

haptoglobin,

ceruloplasmin,

C- reactive protein(CRP),

α2- macroglobulin.... etc.

α1-Antitrypsin(AAT)

- Protease inhibitor that binds to, and inactivates macrophage enzymes like trypsin, limit their actions during infection, and protects the body.
- **Deficiency** is associated with

– Pulmonary emphysema.

– Liver Cirrhosis (direct hyperbilirubinemia; Jaundice is one of tests used in investigation of prolonged neonatal)

•α1 -Fetoprotein(AFP)

– Principal fetal protein, used in screening for fetal abnormalities (neural tube defects) and in adult for liver
carcinoma investigation.

α2 -Macroglobulin

- Largest non-immunoglobulin in blood ~750 KD
- Protease inhibitor
- Increased in Nephrotic syndrome (largest in size)

(α -globulin) Ceruloplasmin (Cp)

- Copper transporting protein
- Participates in plasma redox reactions like Fe+2 Fe+3.
- serum CP measurement is used in investigation of Wilson's disease (Liver cirrhosis-Copper storage disease) in

which serum Cp level is decreased due to genetic defect in incorporation of Cu with apoceruloplasmin in the liver,

leading to precipitation of toxic Cu ion and damage of liver .

(α2) Haptoglobin

- Binds to, and preserves hemoglobin and its content of iron during hemolysis.
- Hemolytic diseases can deplete haptoglobin levels (α2) .

(β) Transferrin

- Iron transporting protein
- Transferrin is increased in iron deficiency anemia.

Apotransferrin + Fe+3=Transferrin

B2 -Microglobulin BMG

- Smallest blood protein (MW=11.8K)

- BMG is filtered through the glomerulus, but is reabsorbed by

renal tubules.

- Urinary BMG levels are a sensitive measure of renal tubular function

γ -Region

- Includes Immunoglobulin's (IgG, IgM, IgA, IgD & IgE).

They are involved in specific immune system.

- CRP is the most sensitive indicator of Acute Phase Reaction (non specific early immune defense system)

– Serum CRP (high sensitive -CRP) increased in Inflammation, trauma, infection, etc.

Protein in urine

normally less than 100 mg/day of proteins appears in urine,

in kidney disease this value increased according to degree of kidney damage which

reflect mainly the glomerular damage.

Normally glomerulus is permeable to

proteins of MW < 60 KD (D Dalton unit of

MW.

In kidney damage(mainly of glomerulus) excess amounts of proteins of large MW>60 KD will pass in the urine and may reach 5-50 gr/day.

Presence of low MW of proteins, like BMG in the urine

indicates the renal tubules damage as these tubules normally catabolize and reabsorbed the low MW proteins. In tubules damage these proteins will escape from the damaged tubules and appear in the urine(Low MW).

Amino Acids Metabolism

Lac.1

By

Dr. Muna M. Yaseen

- **Proteins are the most abundant organic molecules of the living system.**
- **They occur in the every part of the cell and constitute about 50% of the cellular dry weight.**
- **Proteins form the fundamental basis of structure and function of life.**
- **In 1839 Dutch chemist G.J.Mulder while investing the substances such as those found in milk, egg, found that they could be coagulated on heating and were nitrogenous compounds.**

- **The term protein is derived from a Greek word *proteios,* meaning first place.**
- ***Berzelius (Swedish chemist)* suggested the name proteins to the group of organic compounds that are utmost important to life.**
- **The proteins are nitrogenous macromolecules composed of many amino acids.**

Biomedical importance of proteins:

- Proteins are the main structural components of the cytoskeleton. They are the sole source to replace nitrogen of the body.
- Bio chemical catalysts known as enzymes are proteins.
- Proteins known as immunoglobulins serve as the first line of defense against bacterial and viral infections.

- Several hormones are protein in nature.
- Structural proteins like actin and myosin are contractile proteins and help in the movement of muscle fibre.

  Some proteins present in cell membrane, cytoplasm and nucleus of the cell act as receptors.
- The transport proteins carry out the function of transporting specific substances either across the membrane or in the body fluids.

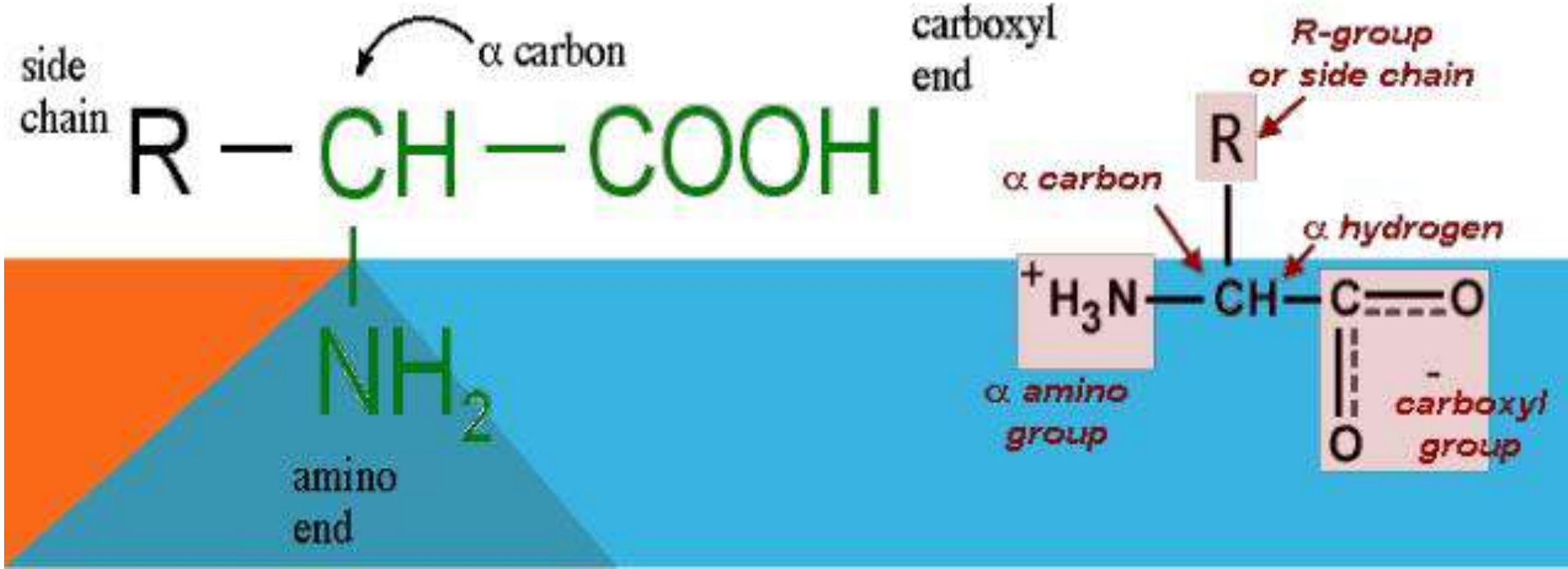
- **Storage proteins bind with specific substances and store them, e.g. iron is stored as ferritin.**
- **Few proteins are constituents of respiratory pigments and occur in electron transport chain, e.g. Cytochromes, hemoglobin, myoglobin**
- **Under certain conditions proteins can be catabolized to supply energy.**
- **Proteins by means of exerting osmotic pressure help in maintenance of electrolyte and water balance in the body.**

OBJECTIVES

- Digestion and absorption of proteins and amino acids
- Introduction to amino acids, structure and types
- Amino acid and nutrition
- General and individual Amino acid metabolism; and inborn errors of metabolism
- Metabolism of ammonia
- Clinical significance of amino acid and ammonia metabolism

WHAT IS AMINO ACID?

Amino acids are derivatives of carboxylic acids formed by substitution of α-hydrogen for amino functional group



WHAT DO AMINO ACIDS DO?

- Amino acids are essential to life, have a role in metabolism, and are important in nutrition.
- They form short polymer chains called peptides, as well as longer chains that are called polypeptides or proteins.
- About 75 percent of the human body is made up of chains of amino acids, which is why they are so vital to how your system functions.
- All the chemical reactions that occur in the body depend on amino acids and the proteins they build.

TYPES OF AMINO ACIDS

Amino acids are classified as

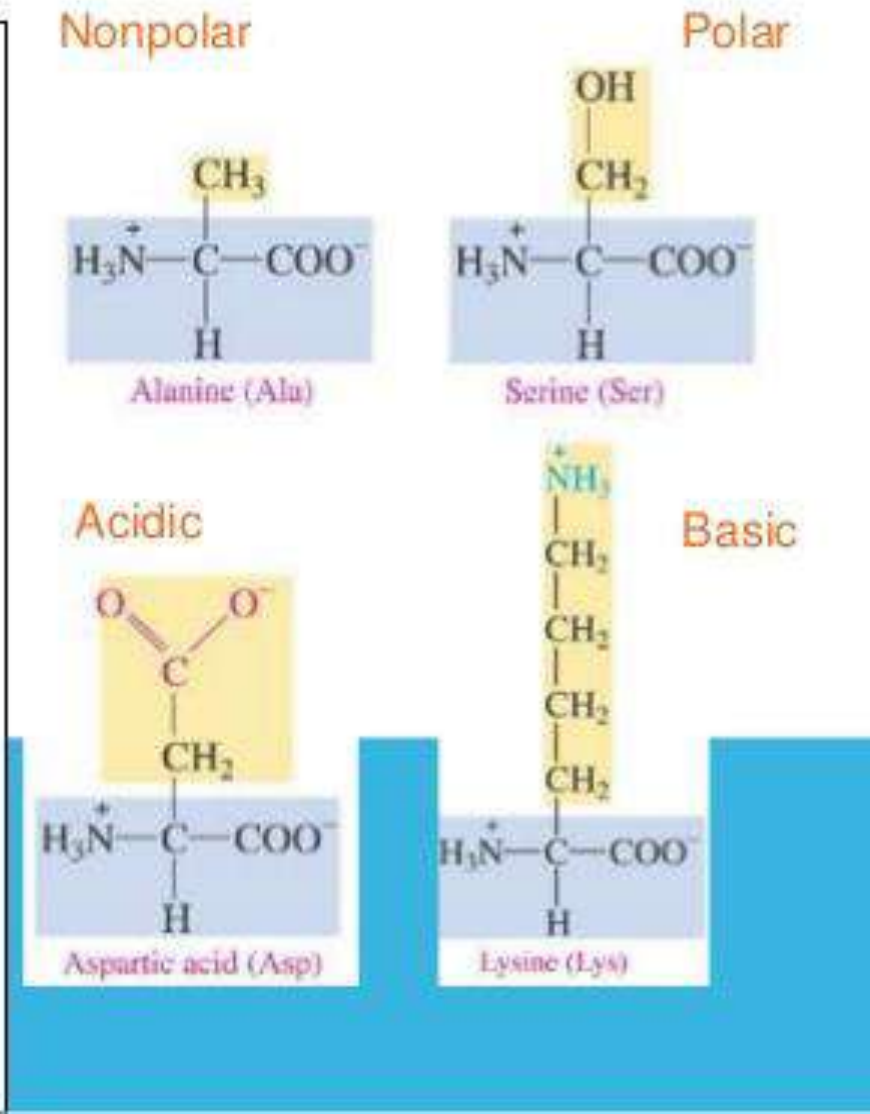
Nonpolar (hydrophobic) with hydrocarbon side chains.

Polar (hydrophilic) with polar or ionic side chains.

Acidic (hydrophilic) with acidic side chains.

Basic (hydrophilic) with

$-NH_2$ side chains.



- non-essential amino acids

  - can be synthesized by an organism

  - usually are prepared from precursors in 1-2 steps

- Essential amino acids

  - cannot be made endogenously

  - must be supplied in diet

    eg. Leu, Phe.....

Nutritionally-Essential amino acids :

Lysine, Leucine, Isoleucine, Valine, Methionine, Phenylalanine,

Threonine, Tryptophan

Nutritionally Nonessential amino acids: Alanine, glycine, aspartate , glutamate, serine, tyrosine, cysteine, proline , glutamine, aspargine

N.B. Histidine & arginine are semi essential. They are essential only for infants growth, but not for old children or adults where in adults histidine requirement is obtained by intestinal flora & arginine by urea cycle

PROTEIN DIGESTION

Digestive Tract of protein

- Proteins are generally too large to be absorbed by the intestine and therefore must be hydrolyzed to the amino acids
- The proteolytic enzymes responsible for hydrolysis are produced by three different organs: the stomach、pancreas and small intestine (the major organ)

Stomach

- HCl (parietal cells) and Pepsinogen (chief cells)
- The pH of gastric juice is around 1.0. Food is retained in the stomach for 2-4 hrs
- HCl kills microorganisms, denatures proteins, and provides an acid environment for the action of pepsin
- **Autocatalysis**: pepsinogen is converted to active pepsin(*Pepsin A)* by HCl

Pancreas and small intestine

- **Endo**peptidase (pancreas)

  Trypsin: carbonyl of arg and lys

  Chymotrypsin: carbonyl of Trp, Tyr, Phe, Met, Leu

  Elastase: carbonyl of Ala, Gly, Ser

  Exopeptidase (pancreas)

  Carboxypeptidase A:amine side of Ala, Ile, Leu, Val

  Carboxypeptidase B: amine side of Arg, lys

- Aminopeptidase (small intestine):

  cleaves N-terminal residue of oligopeptidaes

PROTEIN ABSORPTION

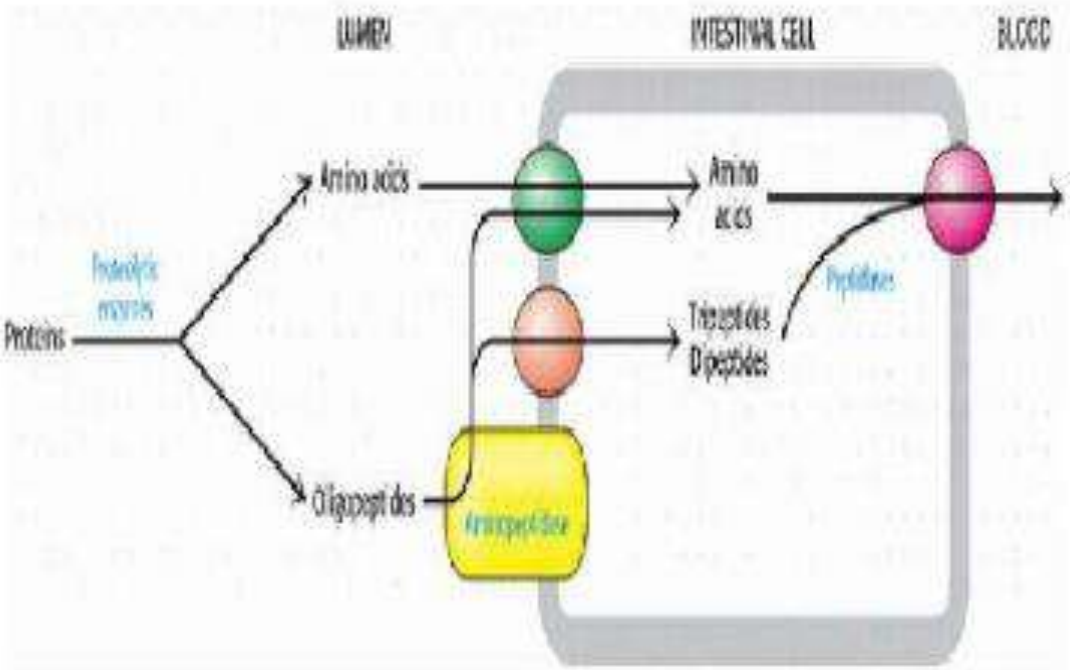
*L-amino acids are actively transported across the intestinal mucosa (need carrier, Na + pump,

Na+ ions, ATP).

Different carrier transport systems are: a) For neut amino acids.
b) For basic amino acid and cysteine.
c) For imino acids and glycine.

d) For acidic amino acids.
e) For B-amino acids (B-alanine & taurine).

*D-isomers transported by simple diffusion.



Nitrogen Balance (NB):

- **Nitrogen balance** is a **comparison between**

  Nitrogen intake (in the form of dietary protein)

  and

  Nitrogen loss (as **undigested protein** in feces ,

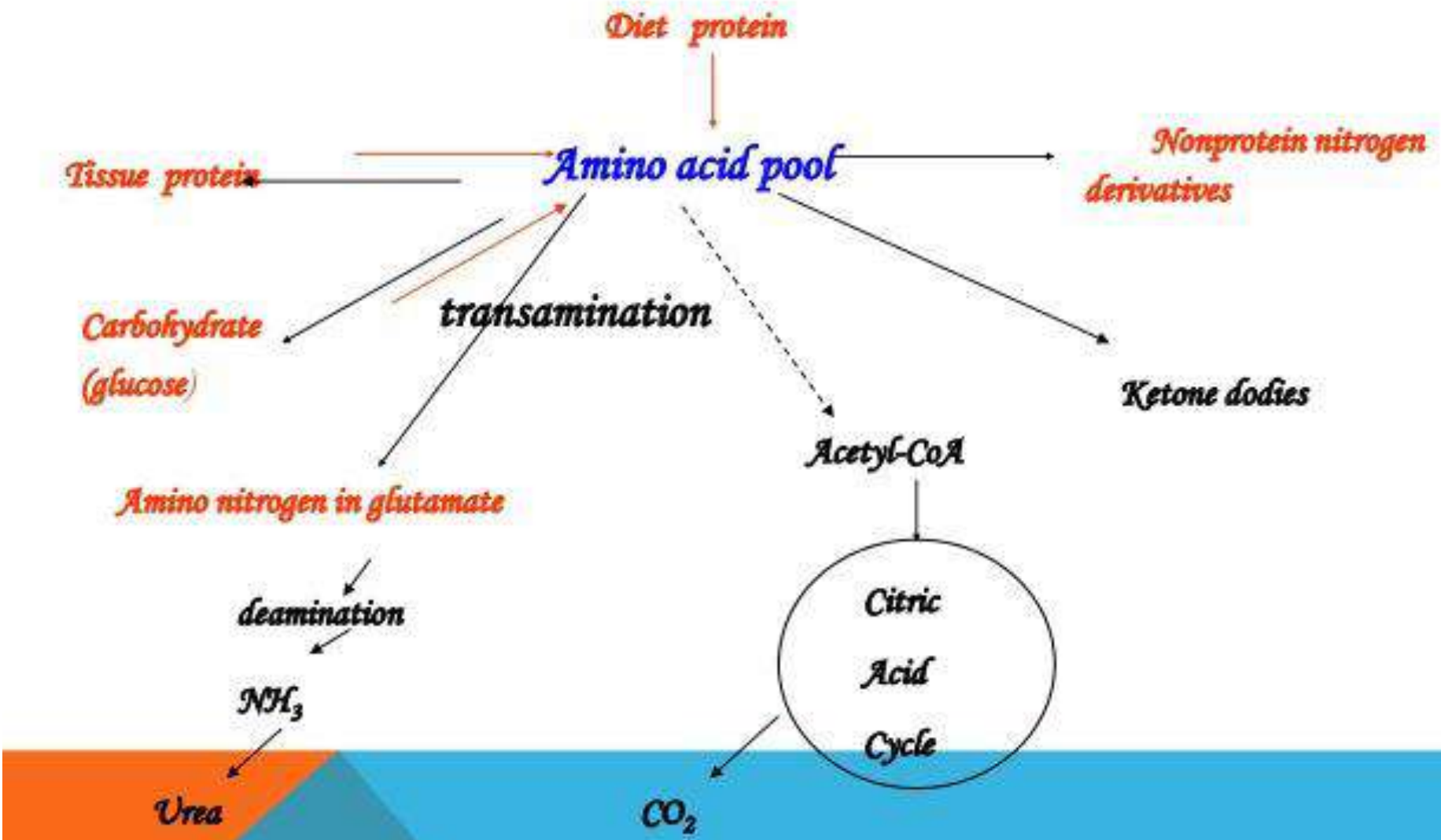
  NPN as urea, ammonia, creatinine & uric acid in urine, sweat & saliva & **losses** by hair, nail, skin).

- NB is important **in** defining

  1.overall protein metabolism of an individual

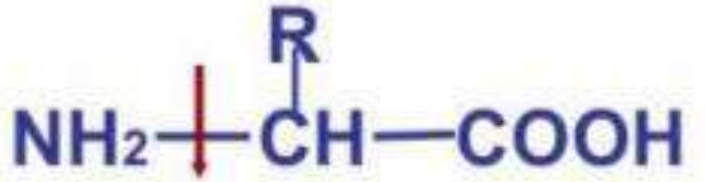
  2.nutritional nitrogen requirement.

AMINO ACID METABOLISM



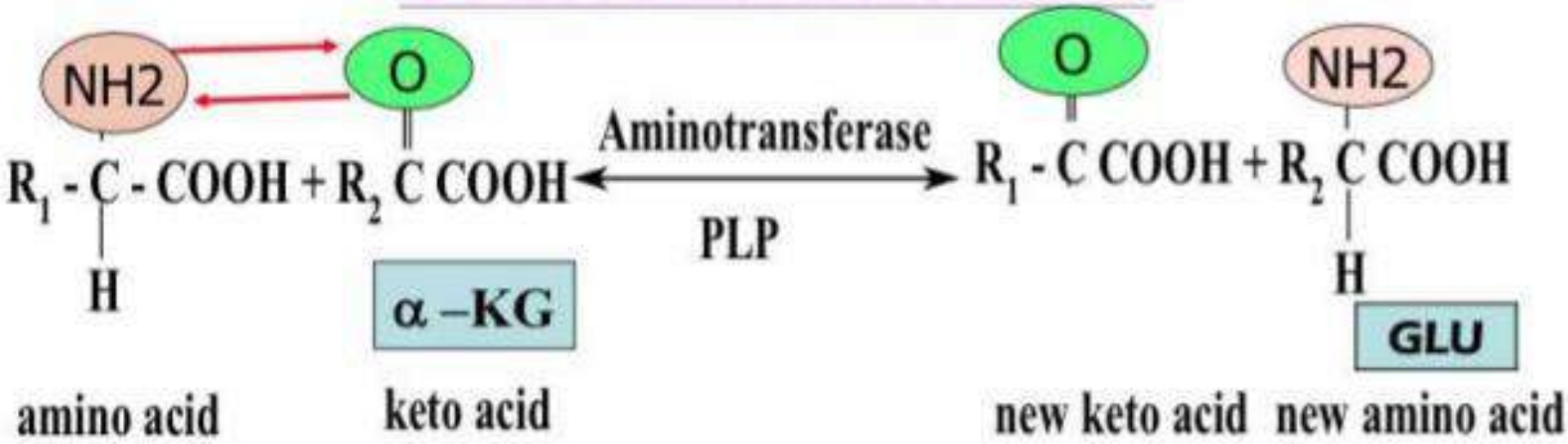
Overview of the protein metabolism

Metabolism OF AMINO ACIDS:



1. **Removal of amonia** by :
   - Deamination → **Oxidative deamination**
     1) glutamate dehydrogenase in mitochondria
     2) amino acid oxidase in peroxisomes
     Direct deamination (nonoxidative)
     1) dea. by dehydration ($-H_2O$)
     2) dea. by desulhydration ($-H_2S$)
   - Transamination (GPT & GOT)
   - and transdeamination.
2. **Fate of carbon-skeletons of amino acids**
3. **Metabolism of ammonia**

Transamination:



Aminotransferases are **active** both in cytoplasm and mitochondria e.g.:

1. **Aspartate aminotransferase (AST)**, Glutamate oxaloacetate transaminase **(GOT),**

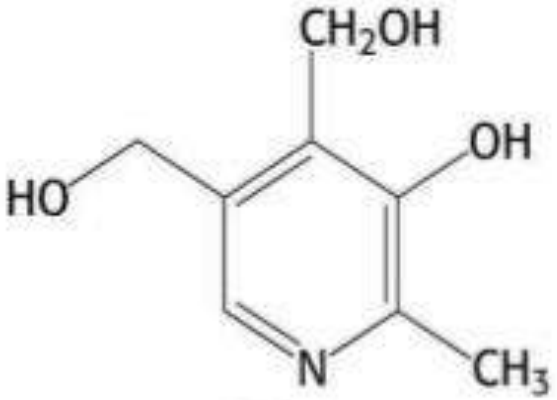
2. **Alanine aminotransferase (ALT)**, Glutamate pyruvate transaminase, **(GPT)**

In all transamination reactions, α-ketoglutarate (α –KG) acts as amino group acceptor.

Most, but not all amino acids undergo transamination reaction with few exceptions **(lysine, threonine and imino acids)**

Mechanism of transamination

All aminotransferases require the prosthetic group ***pyridoxal phosphate (PLP),*** which is derived from ***pyridoxine (vitamin B_6).***

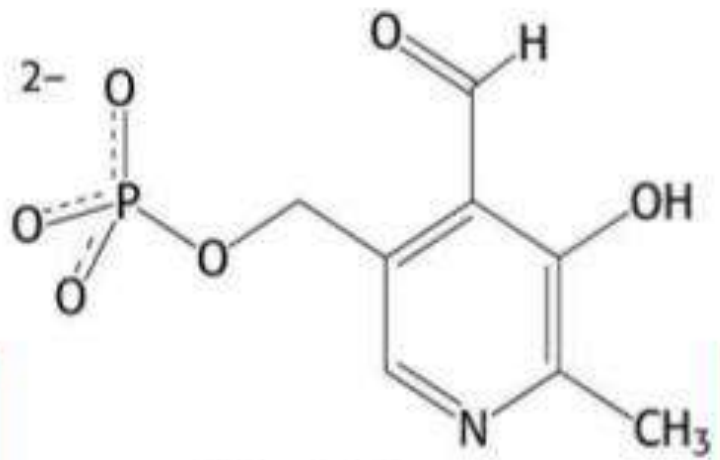


Pyridoxine (Vitamin B_6)

Ping-pong kinetic mechanism

First step: the amino group of amino acid is transferred to pyridoxal phosphate, forming pyridoxamine phosphate and releasing ketoacid.

Second step: α-ketoglutarate reacts with pyridoxamine phosphate forming glutamate



Pyridoxal phosphate (PLP)

B. Oxidative Deamination

- L-glutamate dehydrogenase (in mitochondria)

Glu + NAD^+ (or $NADP^+$) + H_2O ⇆ NH_4^+ + a-ketoglutarate + NAD(P)H +H^+

Requires NAD^+ or $NADP^+$ as a cofactor

Plays a central role in AA metabolism

THE FATE OF CARBON-SKELETONS OF AMINO ACIDS

a) Simple degradation:

(amino acid → Common metabolic intermediate)

Alanine → Pyruvate

Glutamate → α-ketoglutarate

Aspartate → Oxaloacetate

b) Complex degradation:

(amino acid--- Keto acid----- **complex** pathway---- Common metabolic intermediate)

Amino acids whose ketoacids are metabolized via **more complex** pathway **e.g. Tyrosine, Lysine, Tryptophan**

c) Conversion of one amino acid into another amino acid before degradation:

Phenylalanine is converted to **tyrosine** prior to its further degradation.

Metabolism of the Common Intermediates

1. ***Oxidation:*** all amino acids can be oxidized in **TCA** cycle with **energy** production
2. ***Fatty acids synthesis:*** some amino acids provide **acetyl CoA** e.g. leucine and lysine (ketogenic amino acids).
3. ***Gluconeogenesis:*** ketoacids derived from amino acids are used for synthesis of **glucose** (is important in starvation).

Glucogenic	*Ketogenic*	*Glucogenic&Ketogenic*
Ala, Ser, Gly, Cys, Arg, His, Pro, Glu, Gln, Val, Met, Asp, Asn.	Leu , Lys	Phe,Tyr,Trp,Ile,Thr

METABOLISM OF AMMONIA

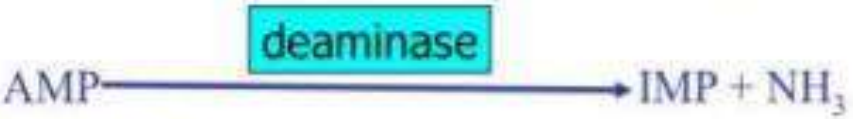
Ammonia is formed in body from:

a) From amino acids: 1.Transdeamination in liver (NOT T.A.)

2.amino acid oxidases and amino acid deaminases in liver and kidney.

b) Deamination of physiological amines: by monoamine oxidase.

c) Deamination of purine nucleotides: especially adenine nucleotides



d) Pyrimidine catabolism.

e) From bacterial action in the intestine **on dietary protein & on urea in the gut.**

NH3 is also produced by glutaminase on glutamine .

TRANSPORT OF AMMONIA TO THE LIVER

Two mechanism are available for the transport of ammonia from peripheral cells to liver for detoxification

The first uses glutamine synthetase to combine glutamate with ammonia

The second , used primarily by muscle, involves transamination of pyruvate to Alanine

GLUTAMATE AND GLUTAMINE RELATIONSHIP

Ammonia Nitrogen can be transported as glutamine.

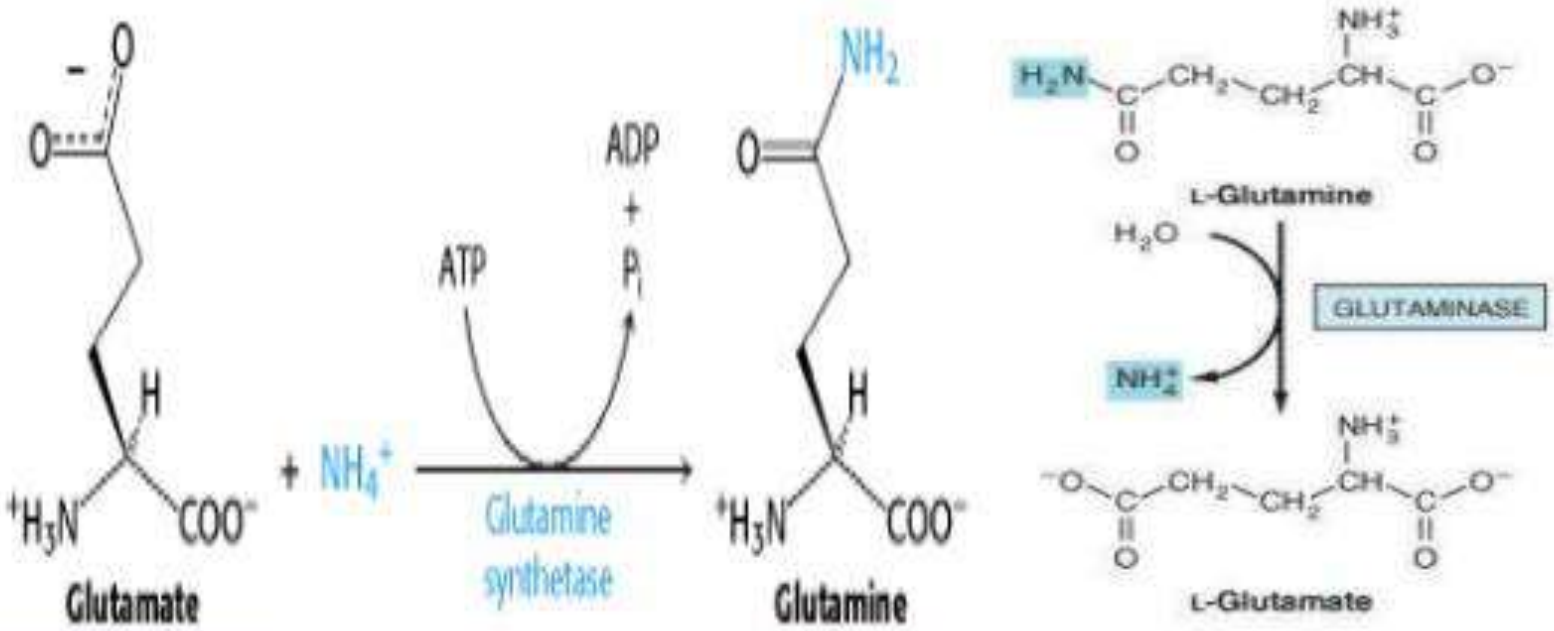
This is the first line of defense in brain cells.

Glutamine synthetase catalyzes the synthesis of glutamine from glutamate and NH_4^+ in an ATP-dependent reaction

The nitrogen of glutamine can be converted to urea in liver by the action of glutaminase in liver

Hydrolytic release of the amide nitrogen of glutamine as ammonia, catalyzed by glutaminase favors glutamate formation.

GLUTAMATE AND GLUTAMINE RELATIONSHIP



The concerted action of glutamine synthase and glutaminase thus catalyzes the interconversion of free ammonium ion and glutamine

GLUCOSE ALANINE CYCLE AND ROLE OF GLUTAMATE

The transport of amino group of amino acids also takes place in the form of Alanine.

Nitrogen is transported from muscle to the liver in two principal transport forms.

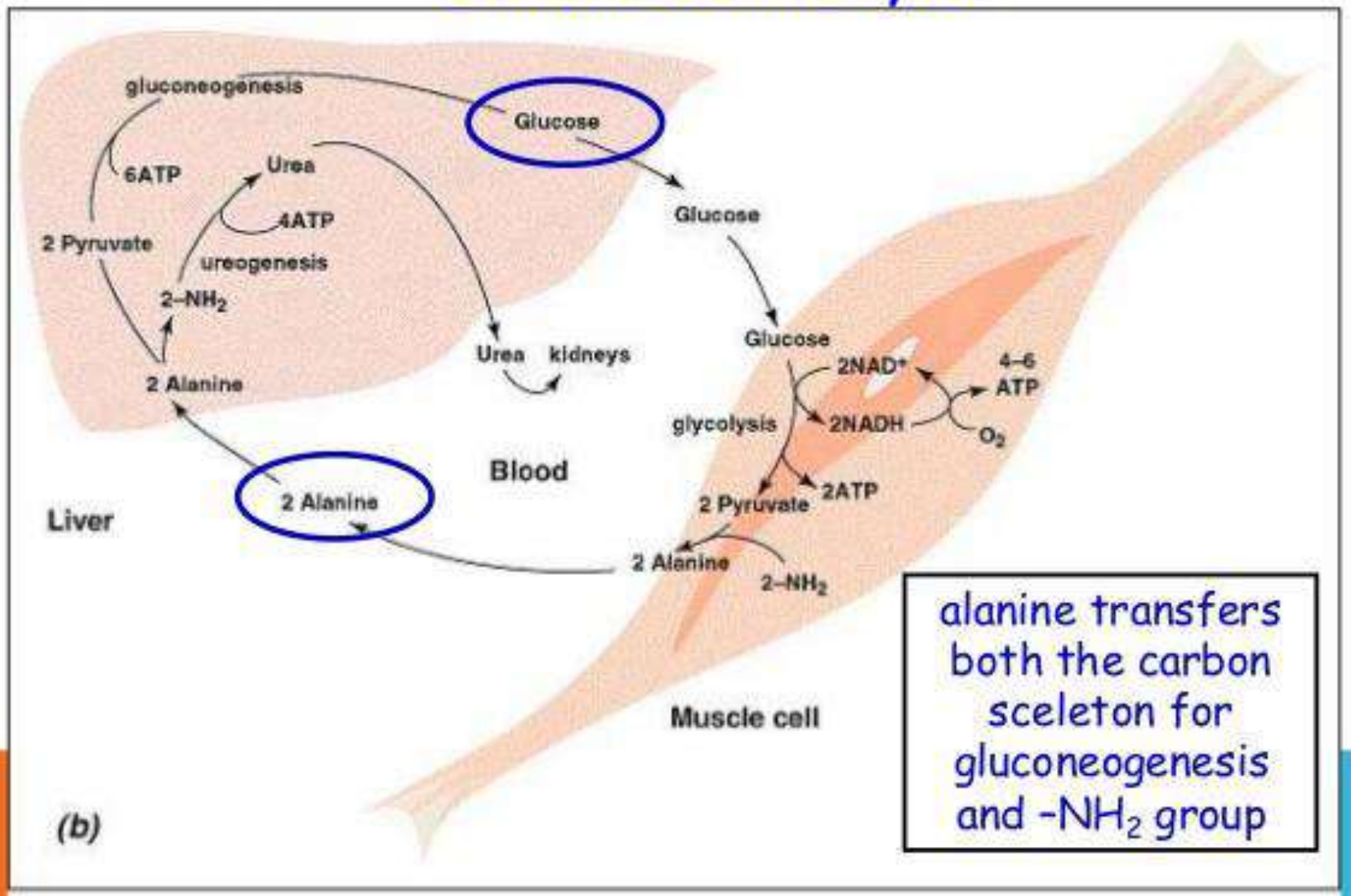
Glutamate is formed by transamination reactions, but the nitrogen is then transferred to pyruvate to form alanine, which is released into the blood.

The liver takes up the alanine and converts it back into pyruvate by transamination.

The pyruvate can be used for gluconeogenesis and the amino group eventually appears as urea.

This transport is referred to as the *alanine cycle.*

Glucose-alanine cycle

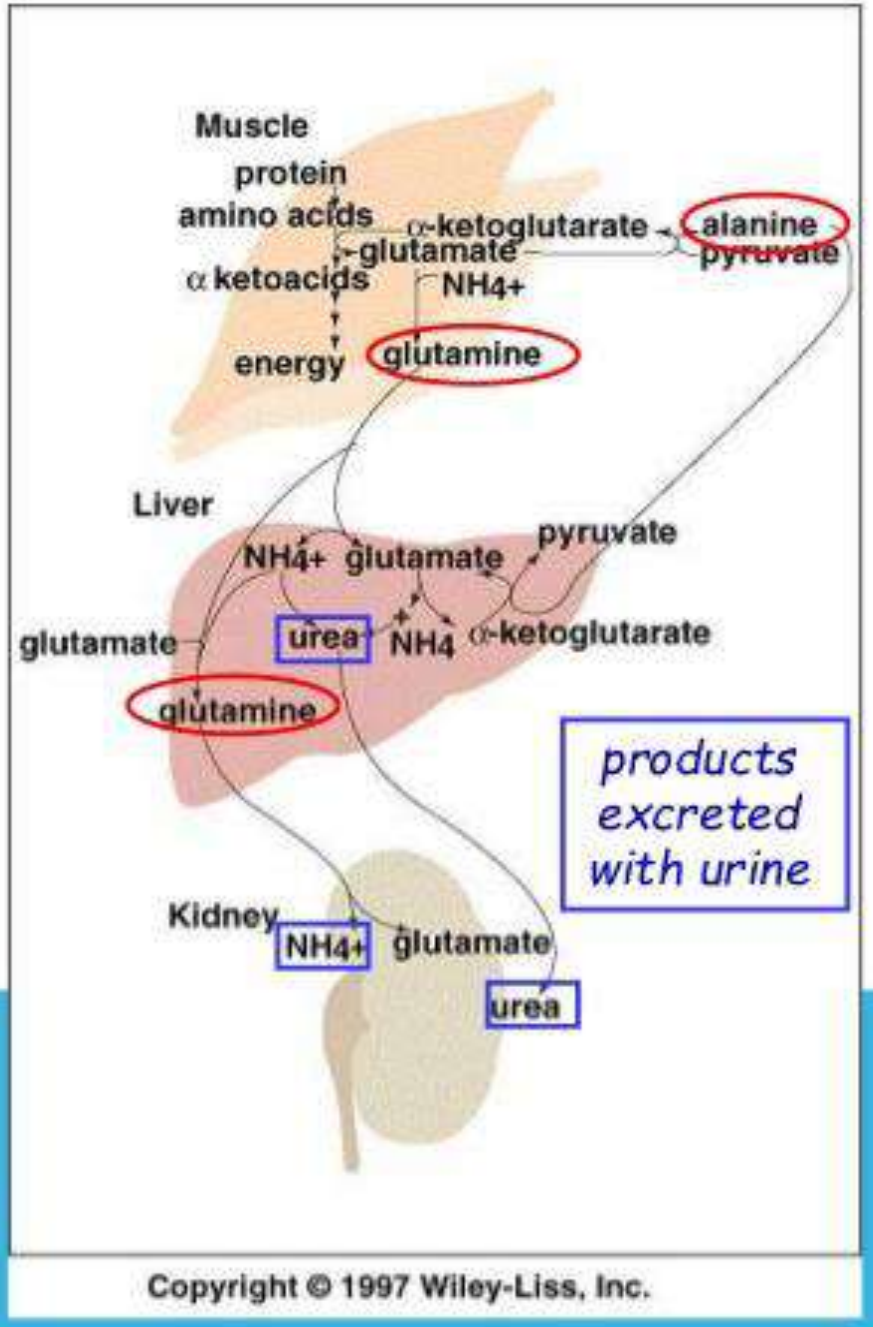


alanine transfers both the carbon sceleton for gluconeogenesis and -NH_2 group

The figure was adopted from Devlin, T. M. (editor): Textbook of Biochemistry with Clinical Correlations, 4th ed. Wiley-Liss, Inc., New York, 1997. ISBN 0-471-15451-2

Transport of amino nitrogen

from degraded muscle proteins



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AMMONIA INTOXICATION

The ammonia produced by enteric bacteria and absorbed into portal venous blood and the ammonia produced by tissues are rapidly removed from circulation by the liver and converted to urea.

Thus, only traces (10–20 g/dL) normally are present in peripheral blood.

This is essential, since ammonia is toxic to the central nervous system.

Should portal blood bypass the liver, systemic blood ammonia levels may rise to toxic levels.

This occurs in severely impaired hepatic function or the development of collateral links between the portal and systemic veins in cirrhosis.

AMMONIA INTOXICATION

Excess of ammonia depletes glutamate and hence GABA level in brain

To compensate for glutamate, alpha keto glutarate is used , the decrease concentration of which subsequently depresses TCA and thus deprives brain cells of energy.

Excess Glutamine is exchanged with Tryptophan , a precursor of Serotonin , resulting in hyper excitation.

Symptoms of ammonia intoxication include tremor, slurred speech, blurred vision, coma, and ultimately death.

UREA (ORNITHINE) CYCLE

detoxification pathway (NH_3 is toxic for brain)

proceeds only in the liver

localized in mitochondria /cytoplasm

carbamoyl phosphate synthetase I (= mitoch.)

can acidify an organism (consumes HCO_3^-)

needs energy (3 ATP, but 4 energy rich bonds)

connected with citrate cycle through fumarate

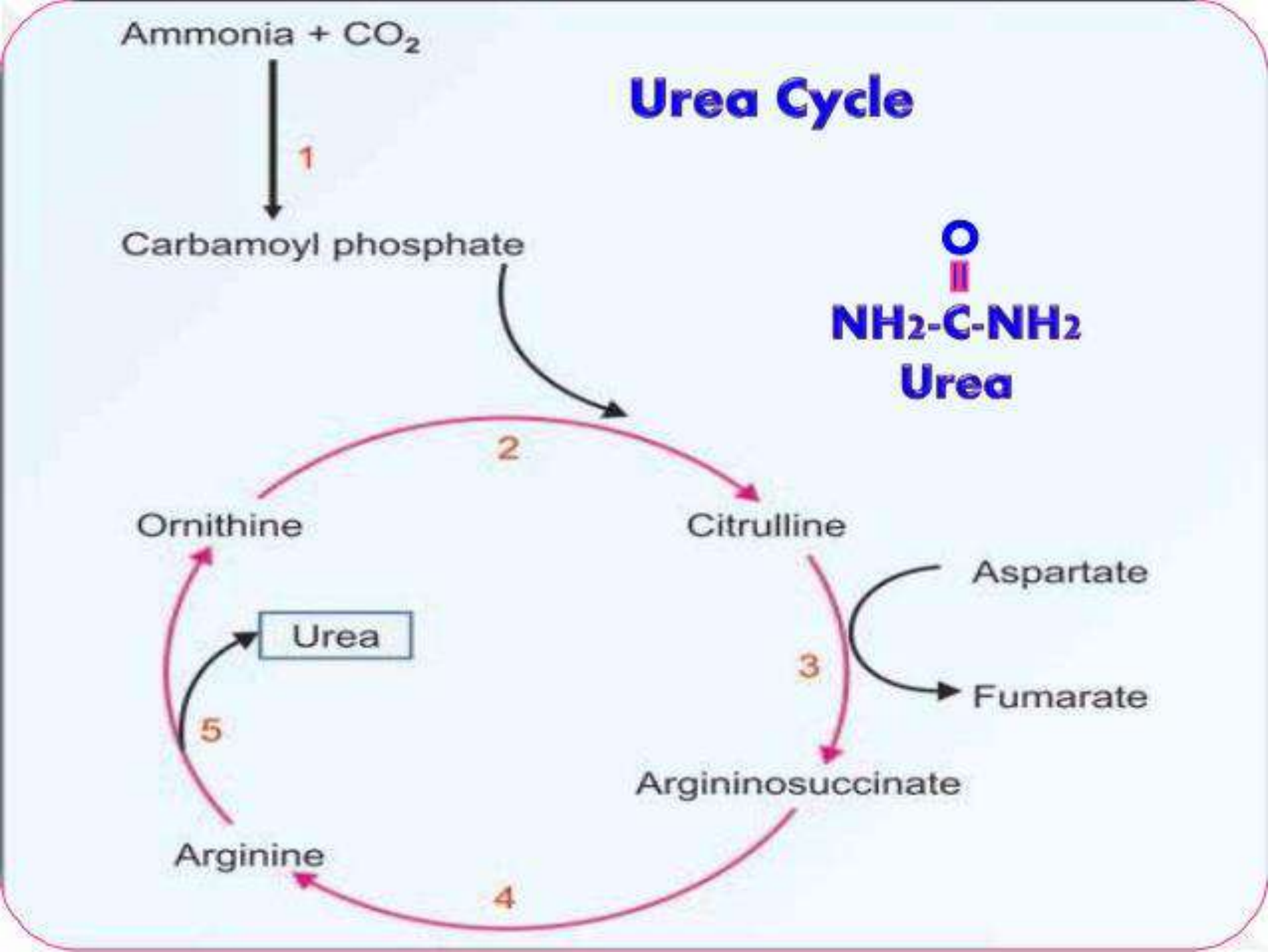
urea is end product of $-NH_2$ metabolism (→ urine)

Urea Cycle

- The urea cycle is the first metabolic pathway to be elucidated.
- The cycle is known as Krebs–Henseleit urea cycle.
- Ornithine is the first member of the reaction, it is also called as Ornithine cycle.
- Urea is synthesized in liver & transported to kidneys for excretion in urine.

- The two nitrogen atoms of urea are derived from two different sources, one from ammonia & the other directly from the a-amino group of aspartic acid.
- Carbon atom is supplied by CO_2
- Urea is the end product of protein metabolism (amino acid metabolism).

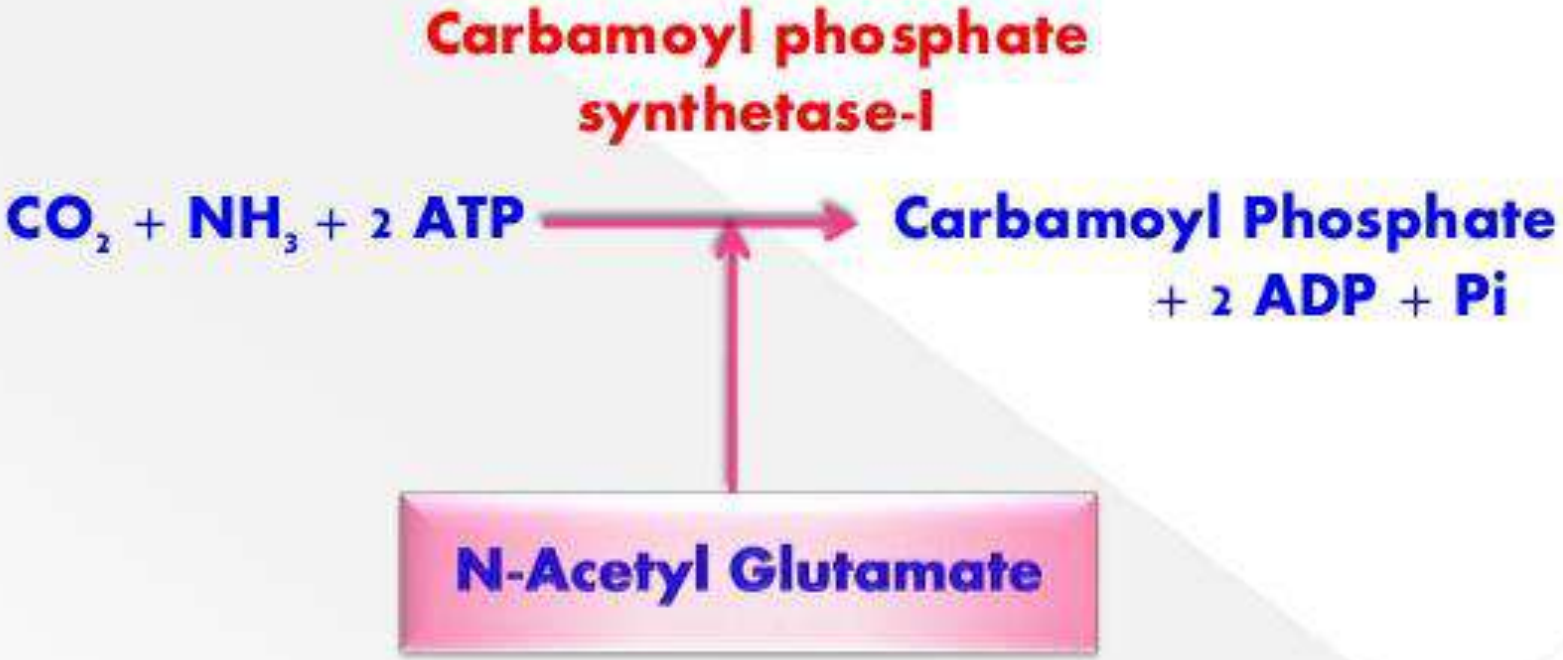
- Urea accounts for 80-90% of the nitrogen containing substances excreted in urine.
- Urea synthesis is a five-step cyclic process, with five distinct enzymes.
- The first two enzymes are present in mitochondria while the rest are localized in cytosol.


Ammonia + CO_2
1
Carbamoyl phosphate
Urea Cycle
NH_2-C-NH_2
Urea
2
Ornithine
Citrulline
Aspartate
Urea
3
Fumarate
5
Argininosuccinate
Arginine
4

Step: 1 Formation of carbamoyl phosphate

- Carbamoyl phosphate synthase I (CPS I) of mitochondria catalyses the condensation of NH_4^+ ions with CO_2 to form carbamoyl phosphate.
- This step consumes two ATP & is irreversible.
- It is a rate-limiting.

Step: 1 Formation of carbamoyl phosphate



Step 2: Formation of Citrulline

- The second reaction is also mitochondrial.
- Citrulline is synthesized from carbamoyl phosphate & ornithine by ornithine transcarbamoylase.
- Ornithine is regenerated & used in urea cycle.

- Ornithine & citrulline are basic amino acids. (Never found in protein structure due to lack of codons).
- Citrulline is transported to cytosol by a transporter system.
- Citrulline is neither present in tissue proteins nor in blood; but it is present in milk.

Step 2: Formation of Citrulline

Step 3: Formation of Arginosuccinate

- Citrulline condenses with aspartate to form arginosuccinate by the enzyme Arginosuccinate synthetase.
- Second amino group of urea is incorporated.
- It requires ATP, it is cleaved to AMP & PPi
- 2 High energy bonds are required.
- Immediately broken down to inorganic phosphate (Pi).

Step:4 Formation of Arginine or cleavage of Arginosuccinate

- The enzyme Argininosuccinase or argininosuccinate lyase cleaves arginosuccinate to arginine & fumarate (an intermediate in TCA cycle)
- Fumarate provides connecting link with TCA cycle or gluconeogenesis.

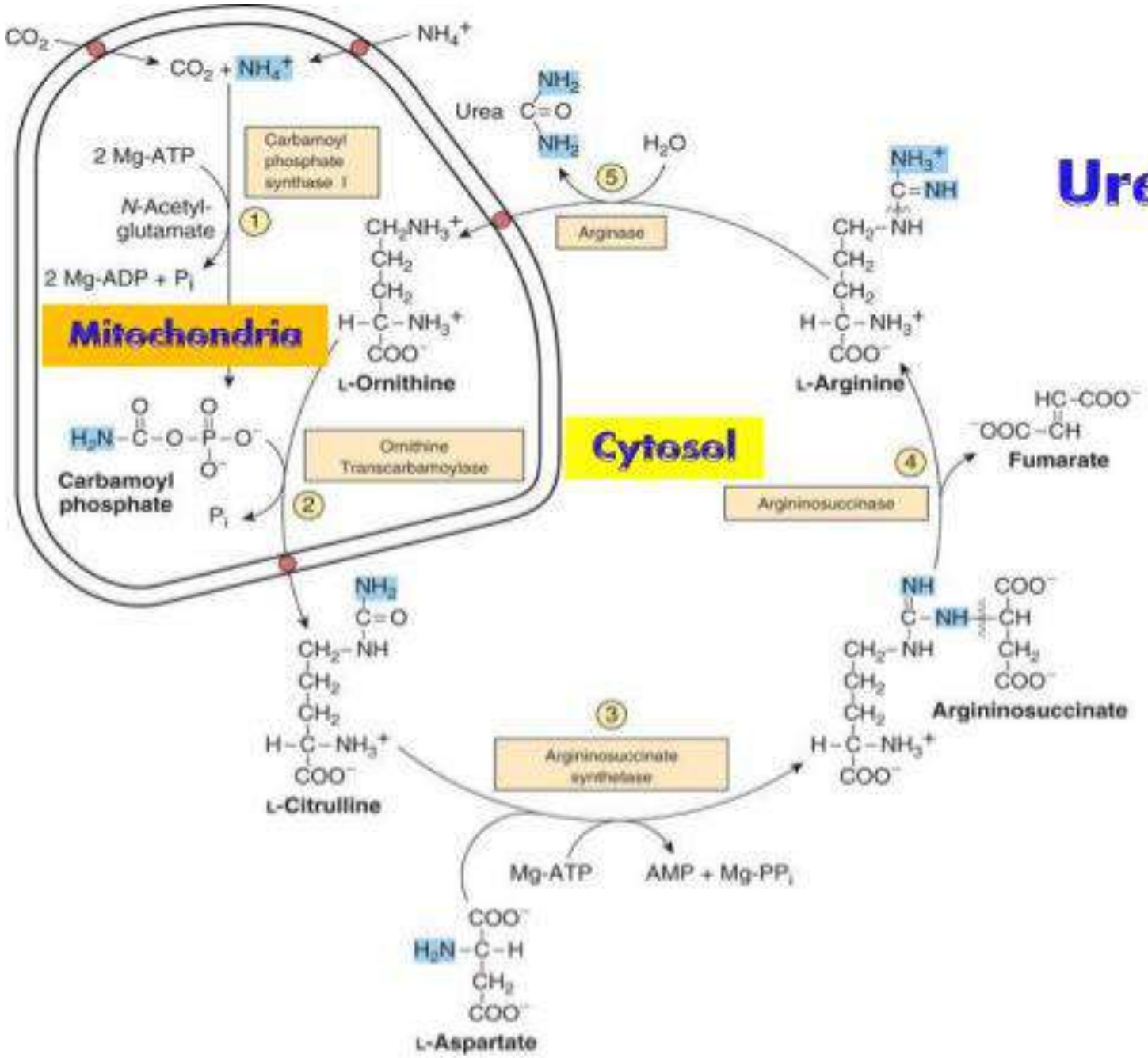
- The fumarate is converted to oxaloacetate via fumarase & MDH & transaminated to aspartate.
- Aspartate is regenerated in this reaction.

Step 5: Formation of Urea

- **Arginase is the 5th and final enzyme that cleaves arginine to yield urea & ornithine.**
- **Ornithine is regenerated, enters mitochondria for its reuse in the urea cycle.**
- **Arginase is activated by Co^{2+} & Mn^{2+}**
- **Ornithine & lysine compete with arginine (competitive inhibition).**

- Arginase is mostly found in the liver, while the rest of the enzymes (four) of urea cycle are also present in other tissues.
- Arginine synthesis may occur to varying degrees in many tissues.
- But only the liver can ultimately produce urea.

Urea Cycle


CO_2
NH_4^+
$CO_2 + NH_4^+$
2 Mg-ATP
Carbamoyl phosphate synthase I
N-Acetyl-glutamate
1
2 Mg-ADP + P_i
Mitochondria
Carbamoyl phosphate
P_i
Ornithine Transcarbamoylase
2
L-Ornithine
Cytosol
Urea
H_2O
5
Arginase
L-Arginine
4
Fumarate
Argininosuccinase
Argininosuccinate
3
Argininosuccinate synthetase
L-Citrulline
Mg-ATP
AMP + Mg-PP_i
L-Aspartate

Energetics of Urea Cycle

- The overall reaction may be summarized as:
- $NH_3 + CO_2 + Aspartate \rightarrow Urea + fumarate$
- 2ATPs are used in the 1st reaction.
- Another ATP is converted to AMP + PPi in the 3rd step, which is equivalent to 2 ATPs.
- The urea cycle consumes 4 high energy phosphate bonds.
- Fumarate formed in the 4th step may be converted to malate.

- Malate when oxidised to oxaloacetate produces 1 NADH equivalent to 2.5 ATP.
- So net energy expenditure is only 1.5 high energy phosphates.
- The urea cycle & TCA cycle are interlinked & it is called as "urea bicycle".

Disposal of urea

- Urea produced in the liver freely diffuses & is transported in blood to kidneys & excreted.
- A small amount of urea enters the intestine where it is broken down to CO_2 & NH_3 by the bacterial enzyme urease.
- This ammonia is either lost in the feces or absorbed into the blood.

Regulation of urea cycle

1. Mitochondrial carbamoyl phosphate synthetase I (CPS I)

CPS I catalyzes the first committed step of the urea cycle

CPS I is also an allosteric enzyme sensitive to activation by N-acetylglutamate（AGA） which is derived from glutamate and acetyl-CoA

Urea Cycle Defects and Hyperammonemia—

(1) Hereditary Hyperammonemia (genetic deficiencies of Urea cycle enzymes)

- Ornithine carbamyl transferase (OTC) deficiency (X linked)
- Carbamyl phosphate synthetase I (CPS I) deficiency
- Citrullinemia (enzyme defect?)
- Arginosuccinic Aciduria (enzyme defect?)
- Argininemia (not severe why?)(enzyme defect?)

- N-acetylGlu synthase deficiency

Urea Cycle Defects and Hyperammonemia

(2) **Acquired Hyperammonemia-------**

a) Liver disease---- (cirrhosis , hepatitis)
b) High protein diet

Clinical significance of blood urea:

- Elevated in renal insufficiency.
- Decreased in hepatic failure.

CHOLESTEROL METABOLISM

By
Dr. Muna M. Yaseen

CHOLESTEROL

→ Cholesterol is a **light yellow crystalline solid**

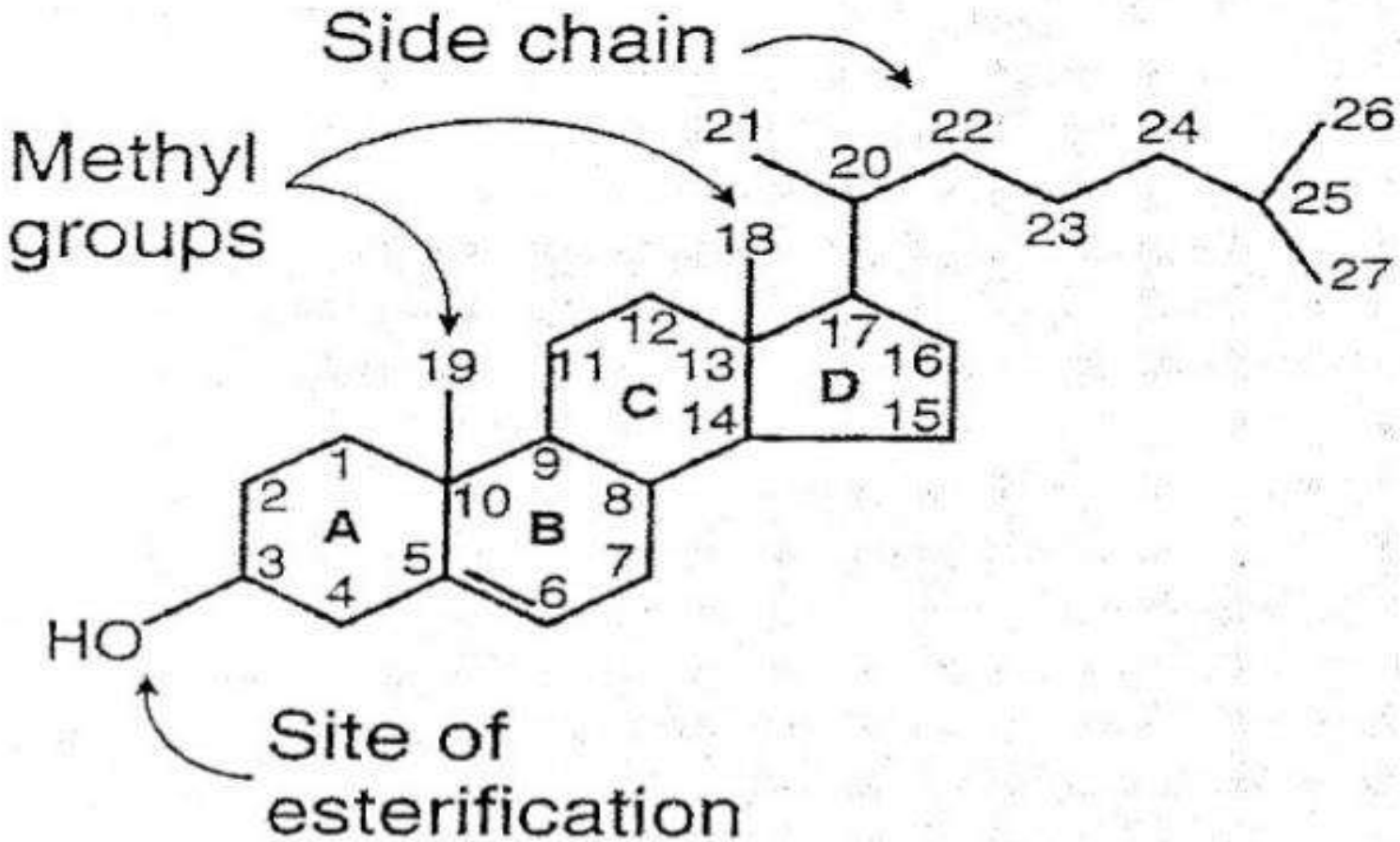
→ It is a **27 Carbon compound**

→ contains ***cyclopentano perhydro phenanthrene*** ring

→ **One hydroxyl group (OH) at 3rd position**

→ **Double bond** between **5 & 6 Carbons**

→ **8 Carbon side chain** at 17th Carbon



Cholesterol

Significance of Cholesterol

1) Normal level ***150 – 200 mg/dl*** . Increased levels increases the risk for ***Atherosclerosis***
2) Important ***component of cell membranes*** which affects fluid state of membrane
3) It is used to ***Insulate Nerve fibers***.
4) ***Bile acids*** (24 Carbon) are derived from Cholesterol
5) ***Steroid hormones*** (21 'C' glucocorticoids, 19 'C' androgens and 18 'C' estrogens) are produced from cholesterol
6) ***Vitamin D*** formed from Cholesterol

Biosynthesis of Cholesterol

Major sites – ***Liver, Adrenal Cortex, testis, ovaries*** and ***Intestine***

80% by Liver

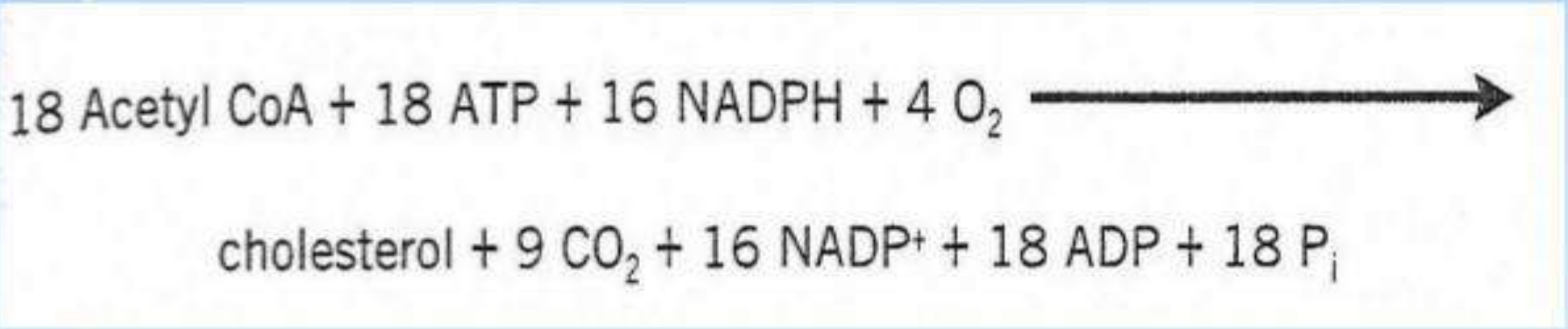
The enzymes involved in synthesis are located partly in ***cytoplasm*** and ***endoplasmic reticulum***.

Requirements:

1) Acetate of **acetyl CoA** provides all the carbon atoms of cholesterol
2) Reducing equivalents by **NADPH**
3) Energy from **ATP**.

De novo Synthesis of Cholesterol

- Primary site: liver (~1g/d)
  - Secondary sites: adrenal cortex, ovaries, testes
- Overall equation:



Cholesterol Synthesis in 5 stages

1) Synthesis of **HMG CoA (6 c)**
2) Formation of **mevalonate (6 C)**
3) Production of **Isoprenoid Units (5 C)**
4) Synthesis of **squalene (30 C)**
5) Conversion of **Squalene to cholesterol (27 C)**

2C ► 6C ► 6C ► 5C ► 10C ► 15C ► 30C ► 27C

Step I : Condensation

Two molecules of Acetyl CoA condense to form **Acetoacetyl CoA**

Enzyme: ***Acetoacetyl CoA Synthase***

Step II : *Production of HMG CoA*

One acetyl CoA condenses with Acetoacetyl CoA to form ***β-hydroxy β-methyl glutaryl CoA*** (HMG CoA)

Enzyme: ***HMG CoA Synthase***

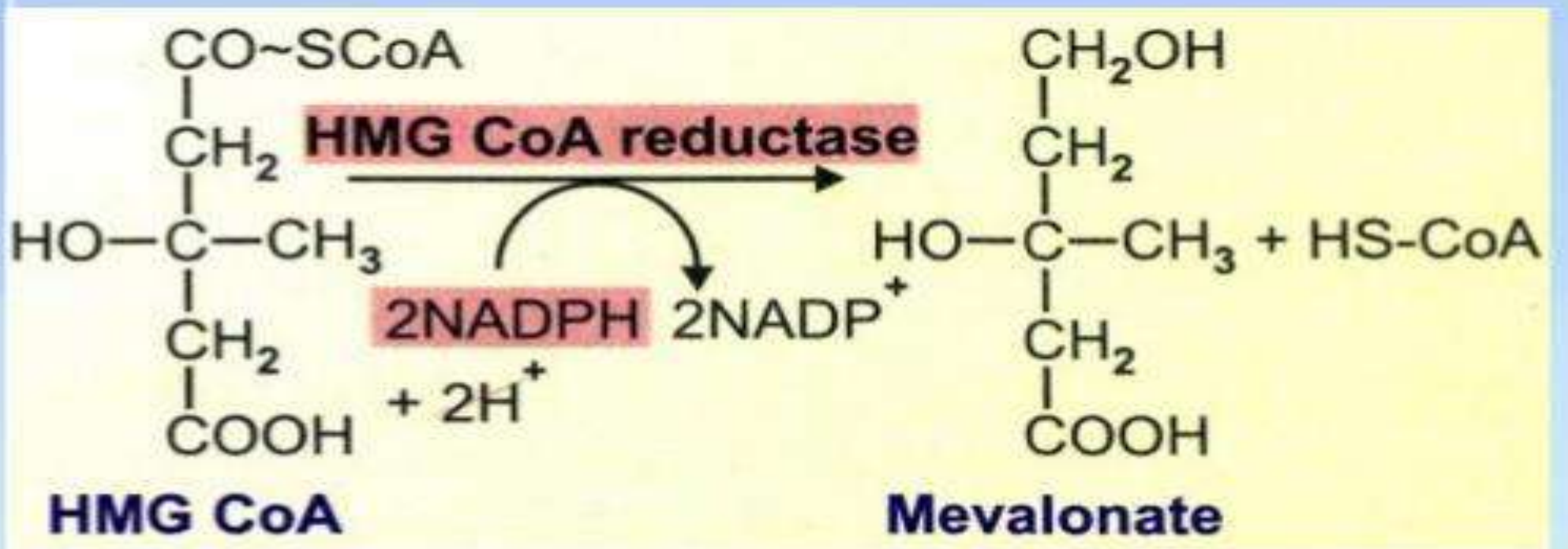
Step III – Regulating Step

Formation of **Mevalonate**

Reduction of HMG CoA to Mevalonate

Enzyme: ***HMG CoA reductase***

requires 2 NADPH



Step 3 of cholesterol synthesis

Step 4 : Formation of Isoprenoid Unit (5 C)

Mevalonate is ***phorphorylated*** three times to form ***3" phospho 5" pyrophospho mevalonate***, requires 3 ATP.

This undergoes **decarboxylation** to form ***Isopentanyl Pyrophosphate*** (5 C)

Step 5: Synthesis of Squalence (30 C)

Isopentanyl pyrophosphate Isomerizes to form

Di methyl allyl pyrophosphate

One molecule of **IPP** (5 C) condenses with **DMP** (5 C) to form **Geranyl pyrophosphate** (10 C)

One molecule of **IPP** (5 C) condenses with **GP** (10 C) to form **Farnesyl pyrophosphate (15 C)**

Two molecules of **Farnesyl pyrophosphate (15 C)** condenses to form **Squalene (30 C)**

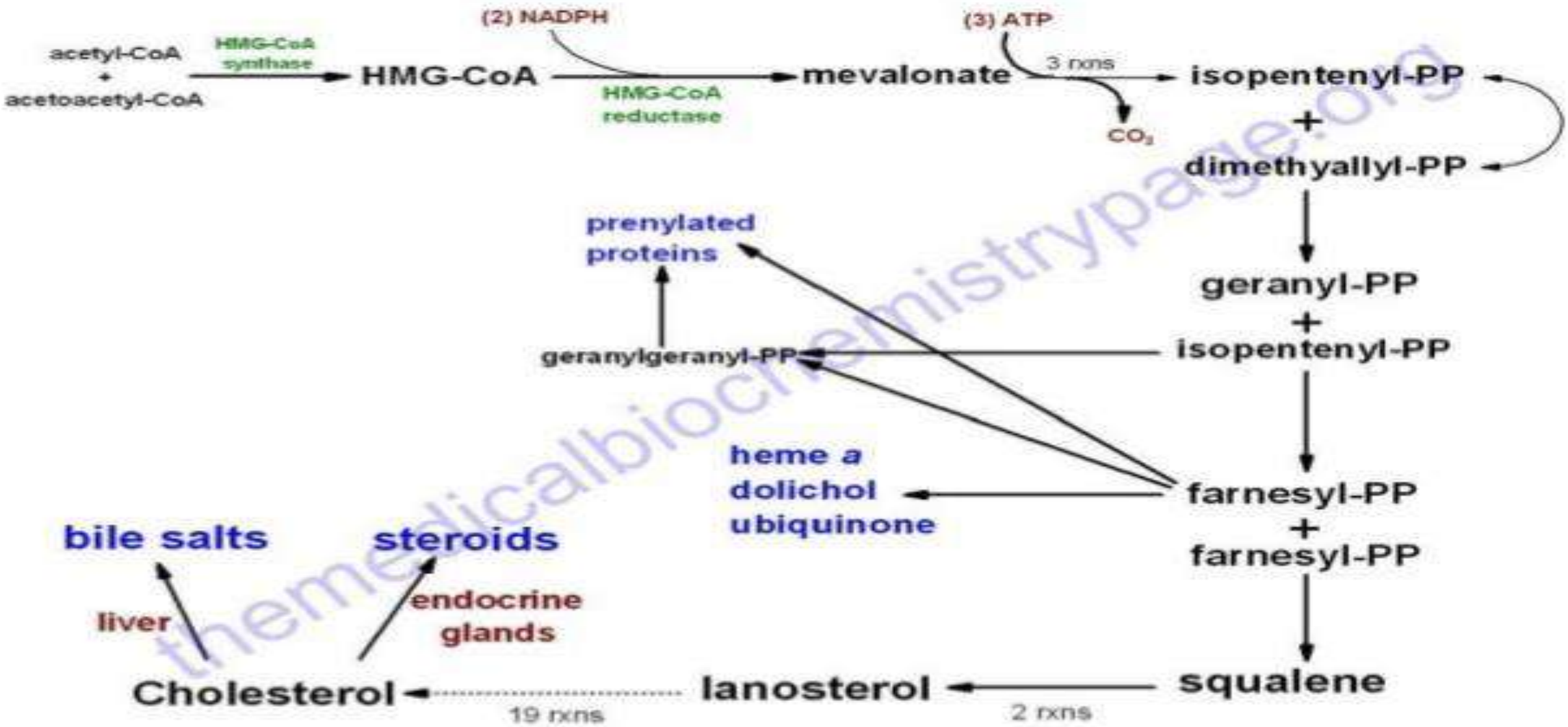
Step 6 : ***Cyclization***

Squalene undergoes oxidation and cyclization to form **Lanosterol**

Lanosterol first formed steroid compound.

2C ► 6C ► 6C ► 5C ► 10C ► 15C ► 30C ► 27C

Biosynthesis of Cholesterol



Regulation of Cholesterol Synthesis

HMG CoA reductase is the regulating Enzyme

1. **Feed back Inhibition:**

   The end product cholesterol in excess inhibits the gene which is responsible for production of HMG CoA reductase

2. **Hormonal regulation:**

   Glucogon & Glucocorticoids favor the formation of Inactive HMG CoA reductase, thus decreases the cholesterol synthesis

   Insulin increases cholesterol synthesis by enhancing the formation of active HMG CoA reductase.

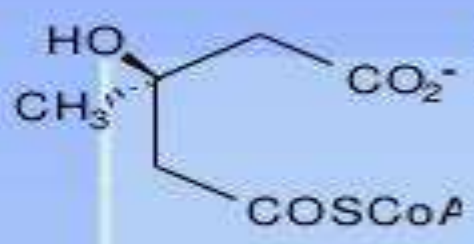
3. **Inhibition by drugs:**

Compactive

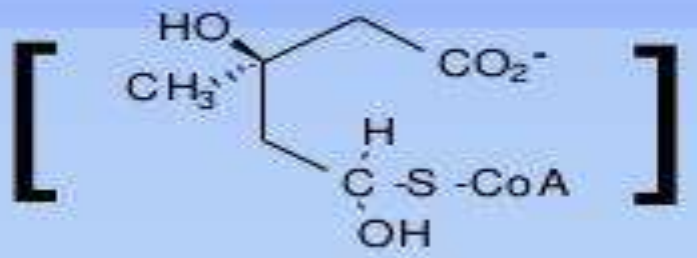
Lovastatin

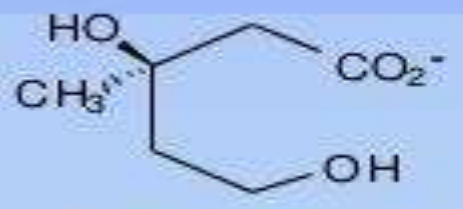
Competitive Inhibitors for HMG CoA reductase.

Inhibition of Cholesterol Biosynthesis

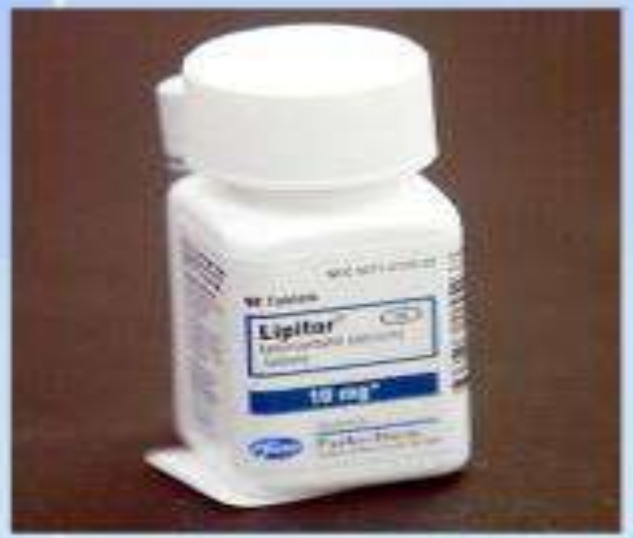


HMGCoA reductase





HMG CoA **Intermediate** **Mevalonate**



Atorvastatin (Lipitor):
resembles intermediate

Degradation of cholesterol

Cholesterol is not completely degraded to Co_2 & H_2o.

It is converted to **Bile acids**
Steroid hormones
Vitamin D

Bile acids:

24 Carbon compounds with steroid ring.

Helps in digestion & absorption of lipids.

Synthesis takes place in **Liver**

7-hydroxylase is the regulating Enzyme

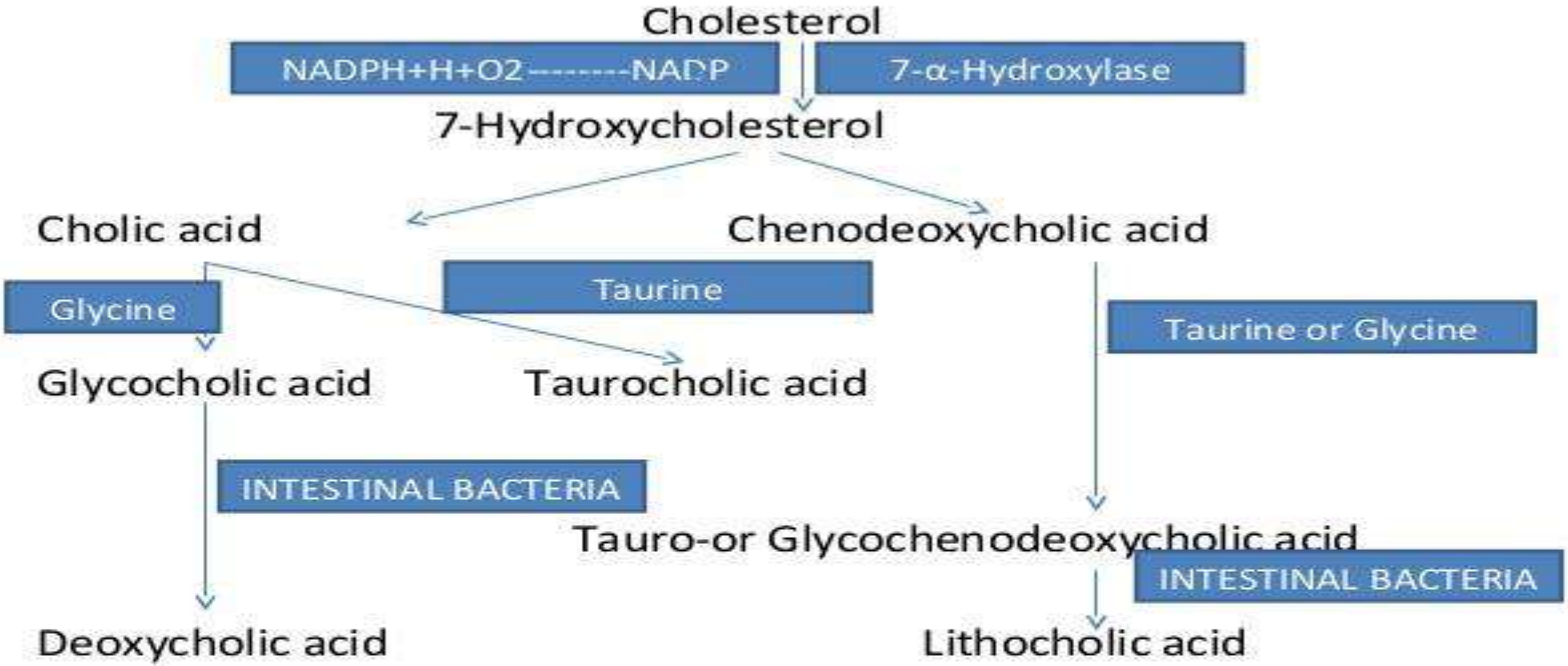
Primary Bile acids –

cholic acid, chenodeoxy cholic acid

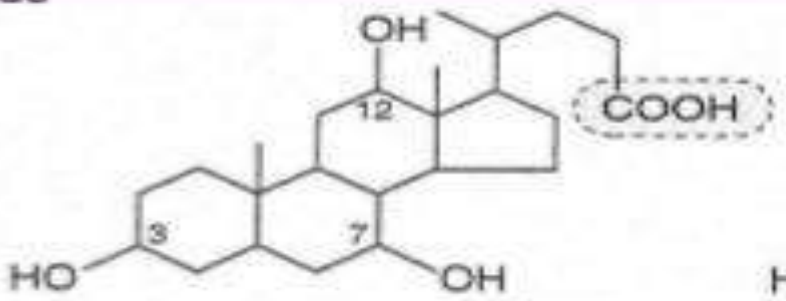
Secondary Bile acids –

deoxycholic acid, Lithocholic acid

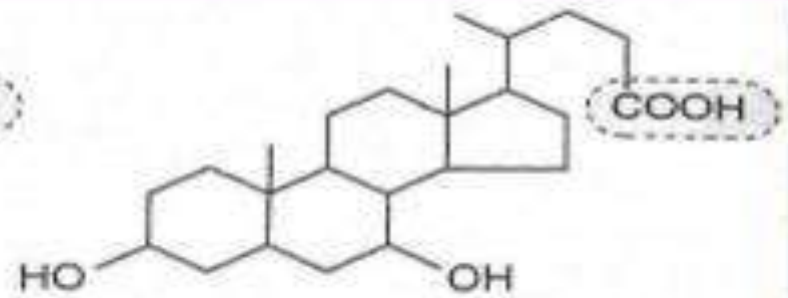
SYNTHESIS OF BILE ACIDS



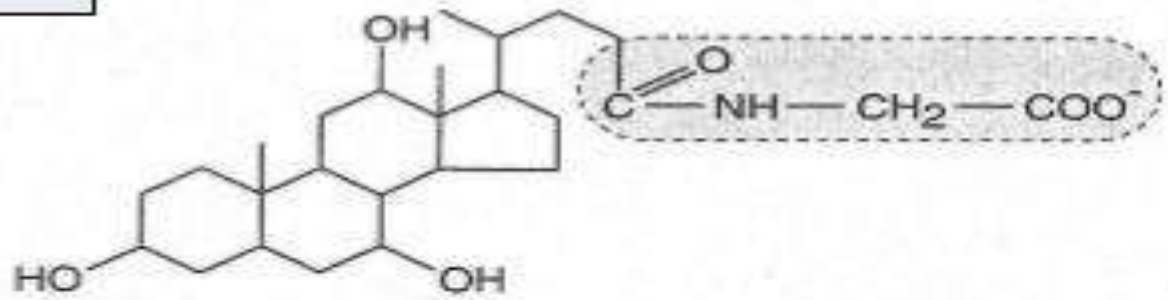
Bile acids



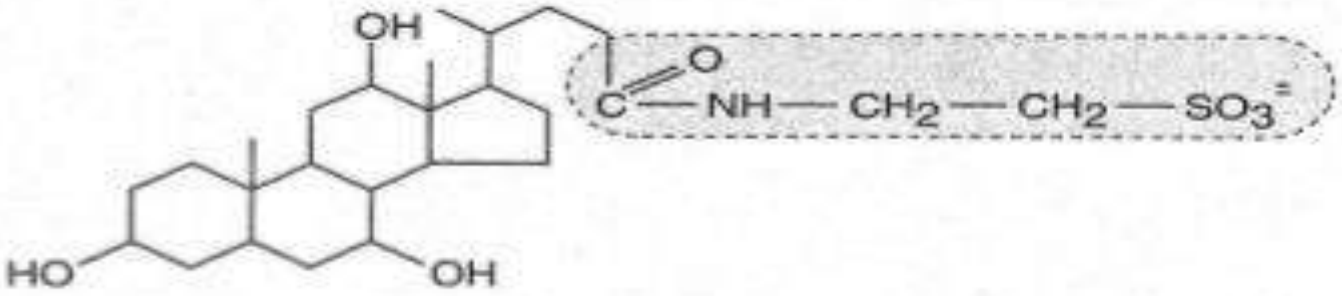
Cholic acid



Chenodeoxycholic acid



Glycholate



Taurocholate

Cholelithiasis: Bile salts and phospholipids are responsible to keep cholesterol in bile in a soluble state.

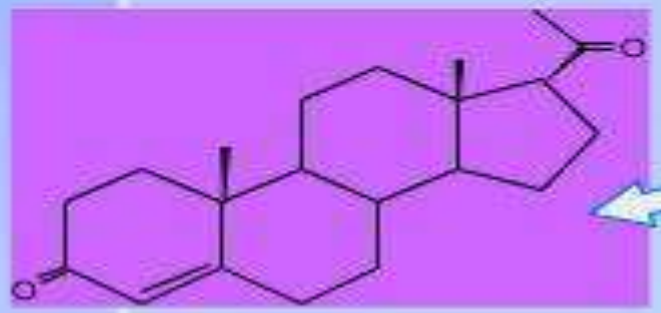
Deficiency of Bile salts, leads to precipitation of cholesterol into crystals in gall bladder resulting in Gall stones or cholelithiasis

Causes:

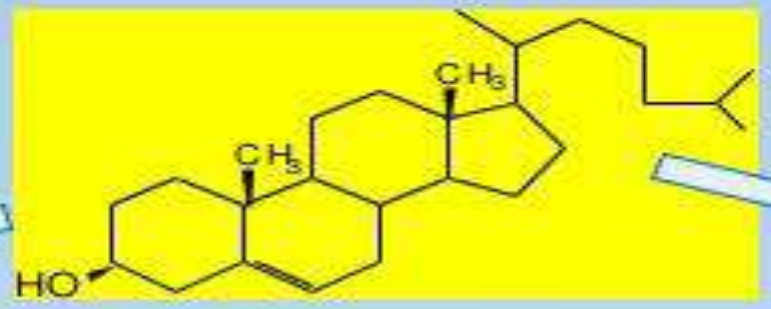
- Impairment in Liver
- Obstruction of biliary tract
- Defect in Enterohepatic circulation of bile salts

Transformations of Cholesterol:

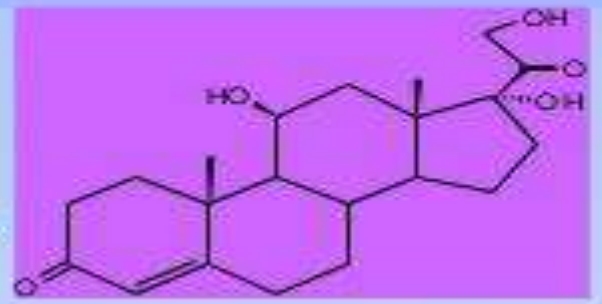
Steroid Hormones



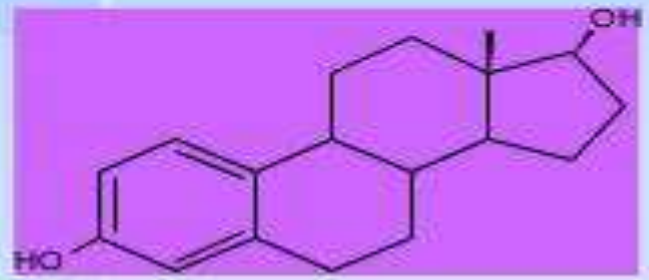
Progesterone



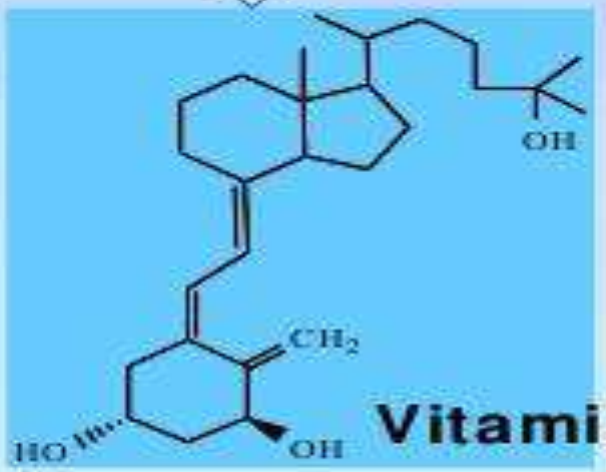
Cholesterol



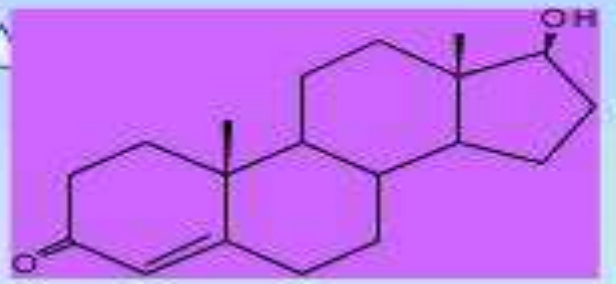
Cortisol



Estradiol



Vitamin D



Testosterone

HYPER CHOLESTEROLEMIA

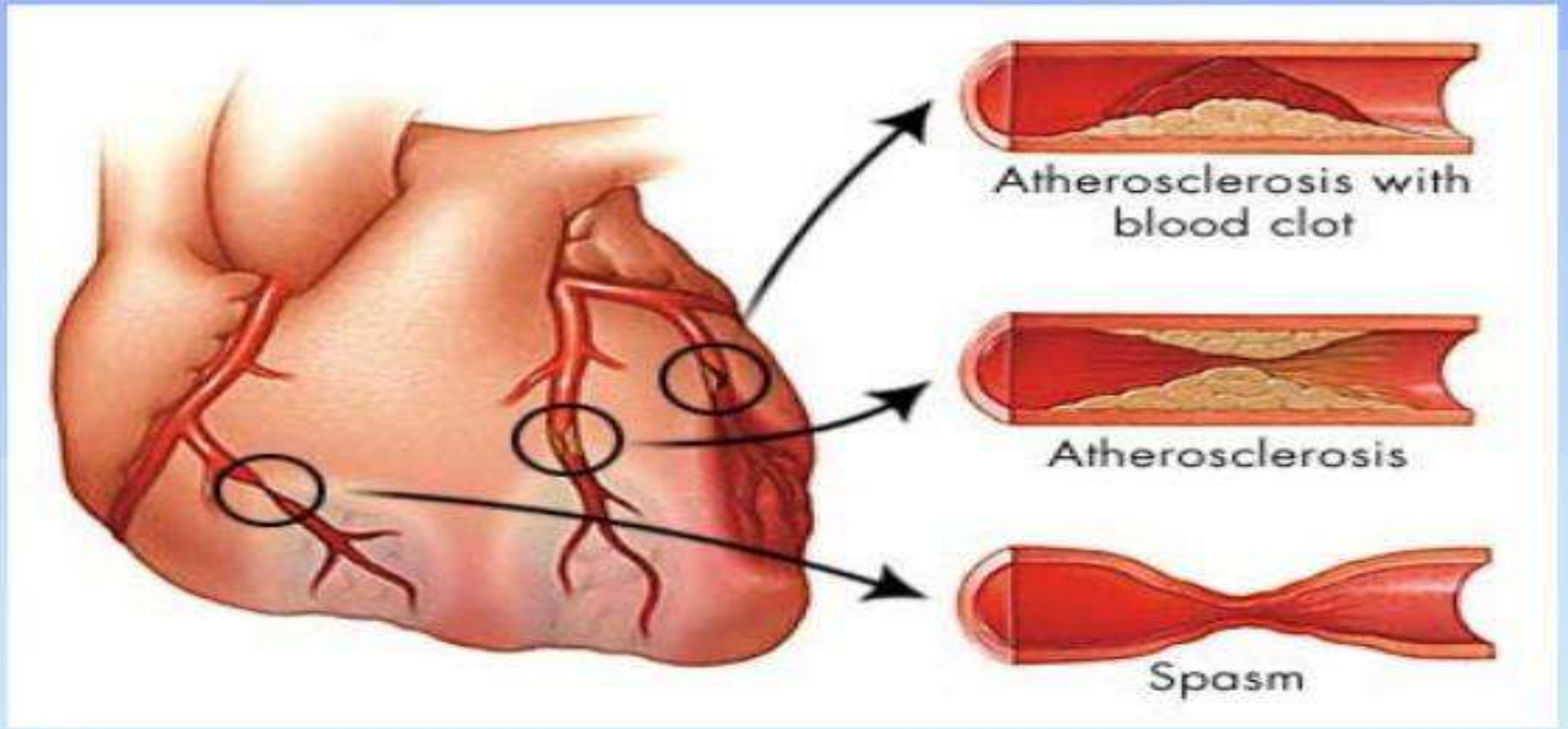
Serum cholesterol level is more than **200mg/dl** it is considered as Hypercholesterolemia

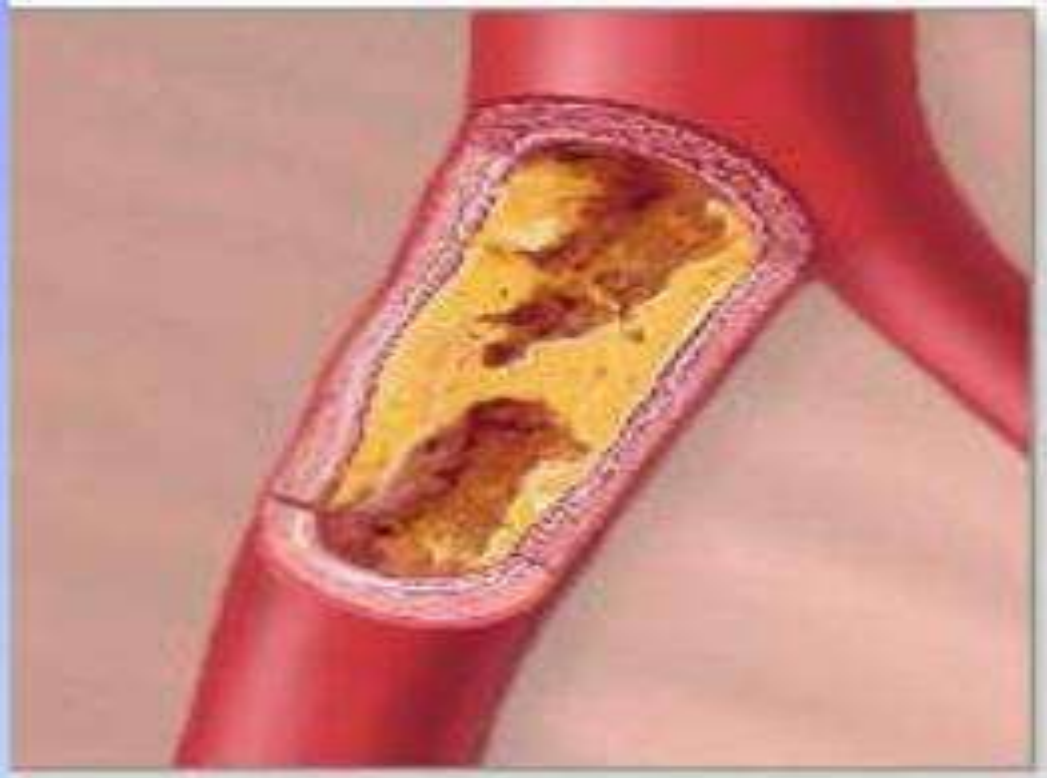
Causes-

1) **Diabetes mellitus**
2) **Hypothyroidism**
3) **Obstructive jaundice**
4) **Nephrotic syndrome**

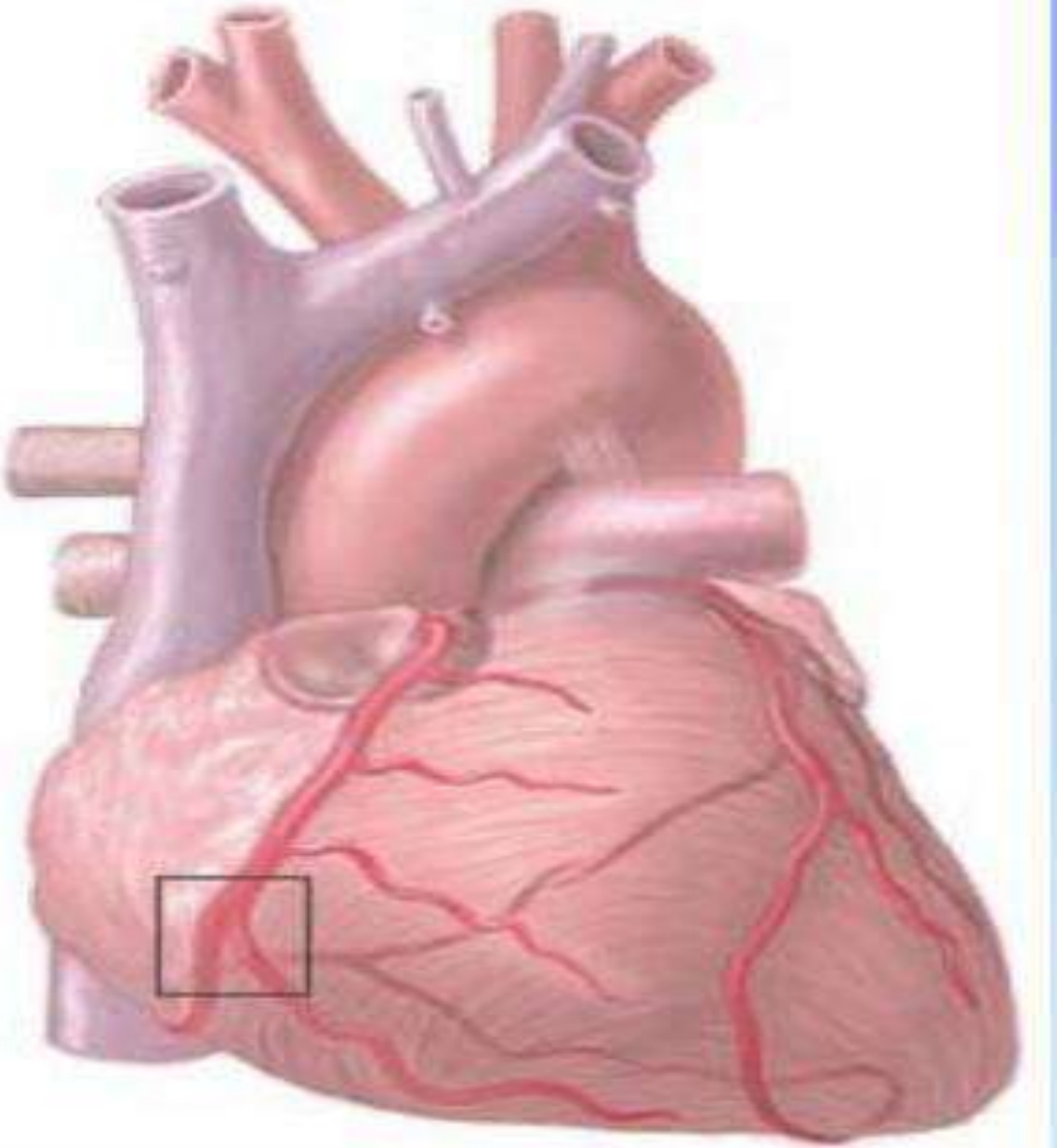
Atherosclerosis : Deposition of cholesterol esters and other lipids in the internal layers of arterial walls, leading to hardening and closure of coronary & cerebral arteries

ATHEROSCLEROSIS





Blockage in right coronary artery



Treatment for Hypercholesterolemia

1) Consumption of PUFA
2) Dietary fiber
3) Avoiding high carbohydrate diet
4) Drugs like Lovastatin
   Atorvastatin

} Inhibit HMG CoA reductase

Cholestyramine
Cholestipol

} bind with bile acid decreases Entero hepatic circulation

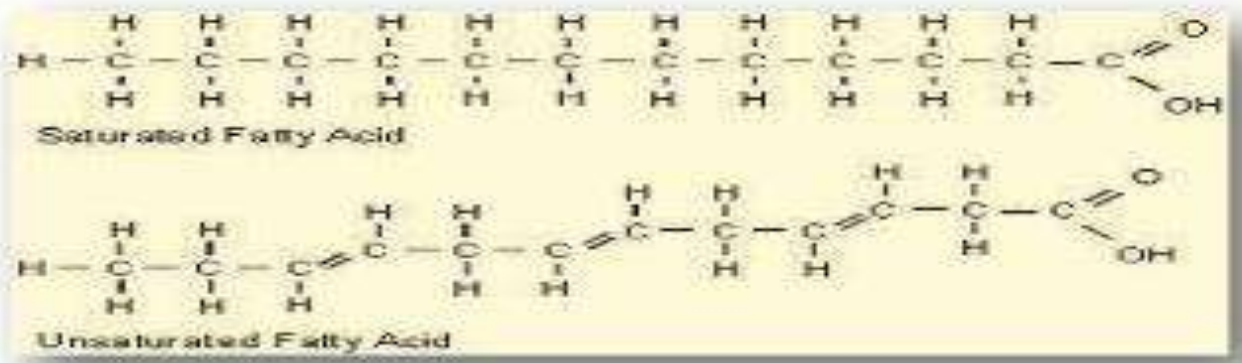
Oxidation of Fatty acids

by

Dr. Muna M. Yaseen

FATTY ACIDS

A fatty acid contains a long hydrocarbon chain and a terminal carboxylate group. The hydrocarbon chain may be saturated (with no double bond) or may be unsaturated (containing double bond).



- Fatty acids can be obtained from-
- Diet
- Adipolysis
- De novo synthesis

FUNCTIONS OF FATTY ACIDS

Fatty acids have four major physiological roles.

1) Fatty acids are **building blocks of phospholipids and glycolipids.**

2) Many proteins are modified by the **covalent attachment of fatty acids, which target them to membrane locations**

3) Fatty acids are **fuel molecules**. They are stored as triacylglycerols. Fatty acids mobilized from triacylglycerols are oxidized to meet the energy needs of a cell or organism.

4) Fatty acid **derivatives serve as hormones and intracellular messengers** e.g. steroids, sex hormones and prostaglandins.

TRIGLYCERIDES

- Triglycerides are **a highly concentrated** stores of energy because they are ***reduced* and *anhydrous*.**
- The yield from the complete oxidation of fatty acids is about 9 kcal g-1 (38 kJ g-1)
- Triacylglycerols are nonpolar, and are stored in a nearly anhydrous form, whereas much more polar proteins and carbohydrates are more highly

TRIGLYCERIDES V/S GLYCOGEN

- ***A gram of nearly anhydrous fat stores more than six times as much energy as a gram of hydrated glycogen,*** which is likely the reason that triacylglycerols rather than glycogen were selected in evolution as the major energy reservoir.
- The glycogen and glucose stores provide enough energy to sustain biological function for about 24 hours, whereas the **Triacylglycerol stores allow survival for several weeks.**

TRANSPORTATION OF FREE FATTY ACIDS

- Free fatty acids—also called unesterified (UFA) or nonesterified (NEFA) fatty acids—are fatty acids that are in the **unesterified state.**
- In plasma, longer-chain FFA are combined with **albumin,** and in the cell they are attached to a **fatty acid-binding protein.**
- **Shorter-chain fatty acids are more water-soluble and exist as the un-ionized acid or as a fatty acid anion.**
- By these means, free fatty acids are made accessible as a fuel in other tissues.

TYPES OF FATTY ACID OXIDATION

Fatty acids can be oxidized by-

1) Beta oxidation- Major mechanism, occurs in the mitochondria matrix. 2-C units are released as acetyl CoA per cycle.

2) Alpha oxidation- Predominantly takes place in brain and liver, one carbon is lost in the form of CO_2 per cycle.

3) Omega oxidation- Minor mechanism, but becomes important in conditions of impaired beta oxidation

4) Peroxisomal oxidation- Mainly for the trimming of very long chain fatty acids.

BETA OXIDATION

Overview of beta oxidation

A saturated acyl Co A is degraded by a recurring sequence of four reactions:

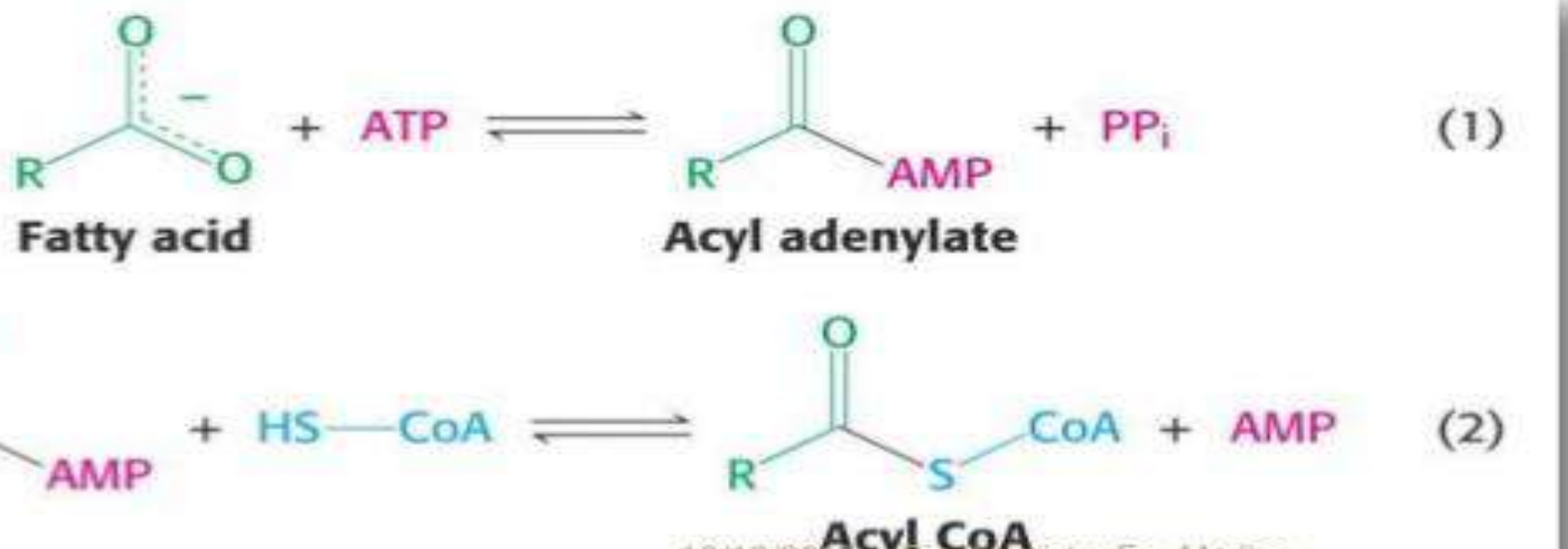
1) **Oxidation** by flavin adenine dinucleotide (FAD)
2) **Hydration,**
3) **Oxidation** by NAD^+, and
4) **Thiolysis** by Co ASH

BETA OXIDATION

- The fatty acyl chain is shortened by two carbon atoms as a result of these reactions,
- FADH2, NADH, and acetyl Co A are generated.
- Because oxidation is on the β carbon and the chain is broken between the α (2)- and β (3)-carbon atoms—hence the name – β oxidation .

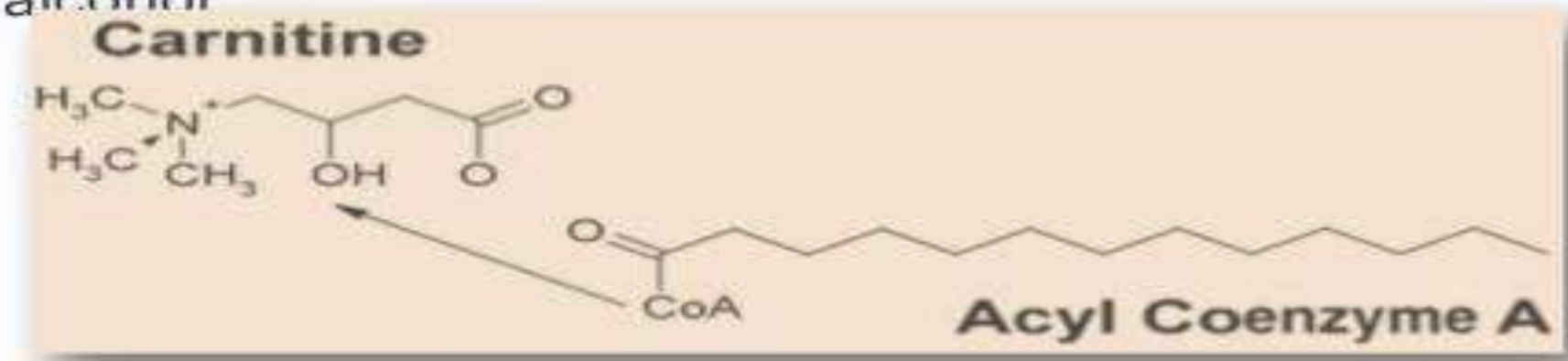
ACTIVATION OF FATTY ACIDS

Fatty acids must first be converted to an active intermediate before they can be catabolized. This is the only step in the complete degradation of a fatty acid that requires energy from ATP. The activation of a fatty acid is accomplished in two steps-



TRANSPORT OF FATTY ACID IN TO MITOCHONDRIAL MATRIX

- Fatty acids are activated on the outer mitochondrial membrane, whereas they are oxidized in the mitochondrial matrix.
- Activated long-chain fatty acids are transported across the membrane by conjugating them to *carnitine*, a zwitterionic alcohol



Carnitine (ß-hydroxy-Y-trimethyl ammonium butyrate), $(CH_3)_3N^+—CH_2—CH(OH)—CH_2—COO^-$, is widely distributed and is particularly abundant in muscle. Carnitine is obtained from foods, particularly animal-based foods, and via endogenous synthesis.

ROLE OF CARNITINE

1) The acyl group is to the hydroxyl group of carnitine to form *acyl carnitine*. This reaction is catalyzed by ***carnitine acyl transferase I***

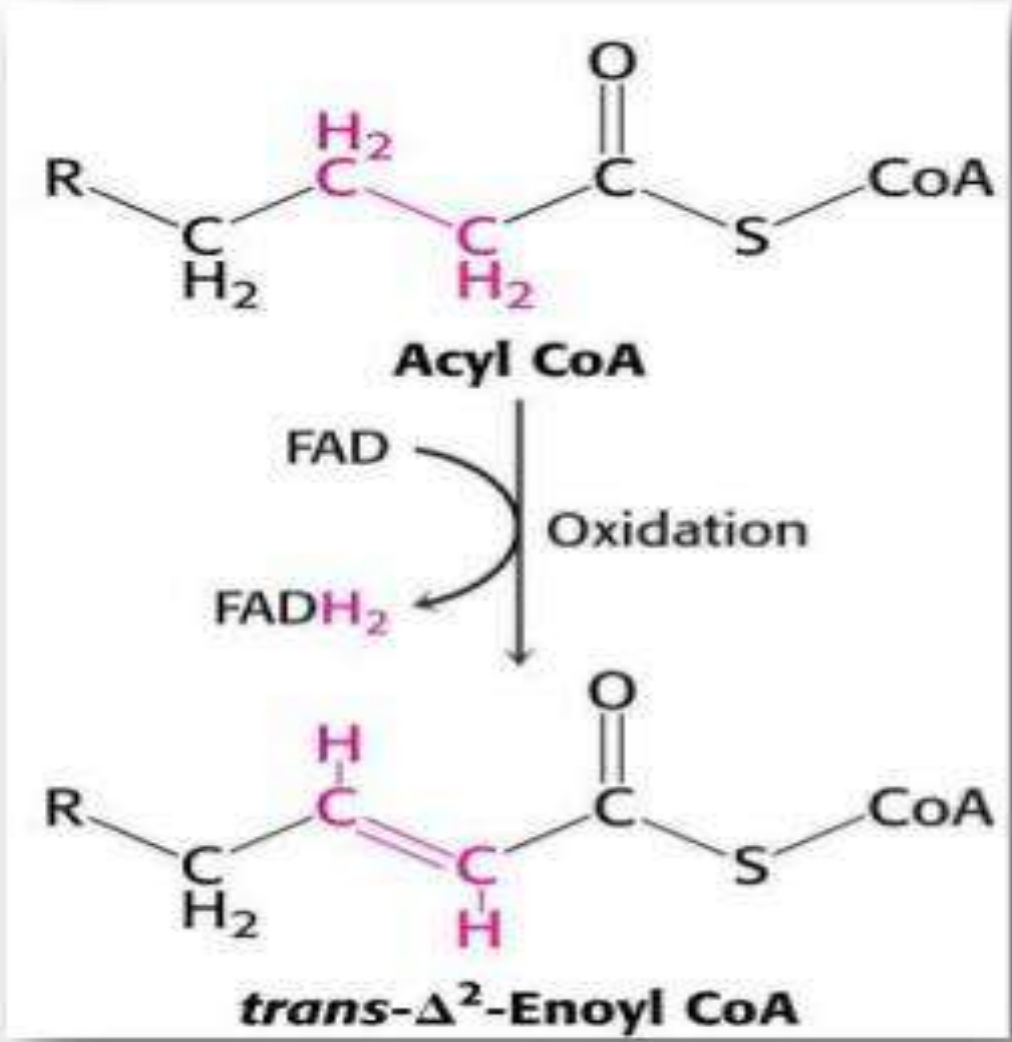
2) Acyl carnitine is then shuttled across the inner mitochondrial membrane by a **translocase.**

3) The acyl group is transferred back to CoA on the matrix side of the membrane. This reaction, which is catalyzed by ***carnitine acyl transferase II.***

Finally, the translocase returns carnitine to the cytosolic side in exchange for an incoming acyl carnitine

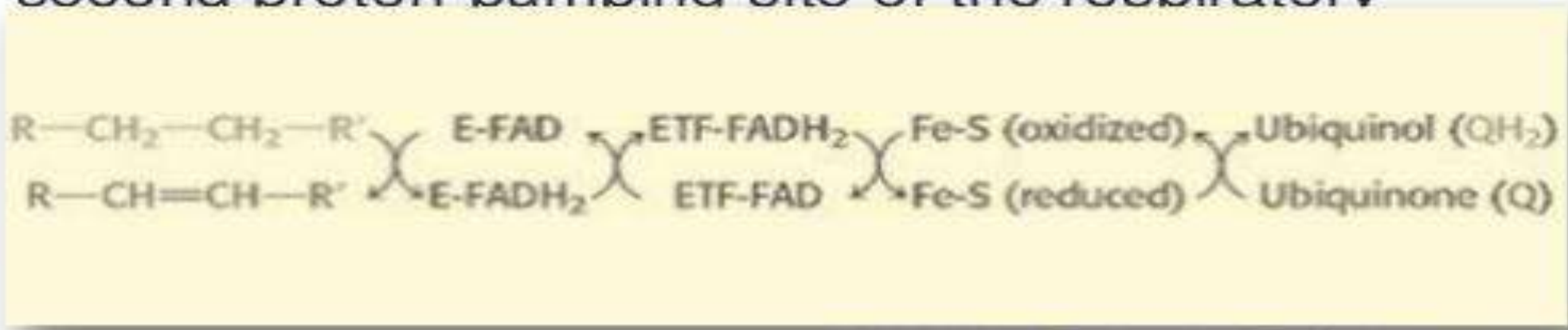
STEPS OF BETA OXIDATION

Step-1
Dehydrogenation-
The first step is the removal of two hydrogen atoms from the 2(α)- and 3(β)-carbon atoms, catalyzed by **acyl-CoA dehydrogenase** and requiring FAD. This results in the formation of Δ^2-*trans*-enoyl-CoA and $FADH_2$.

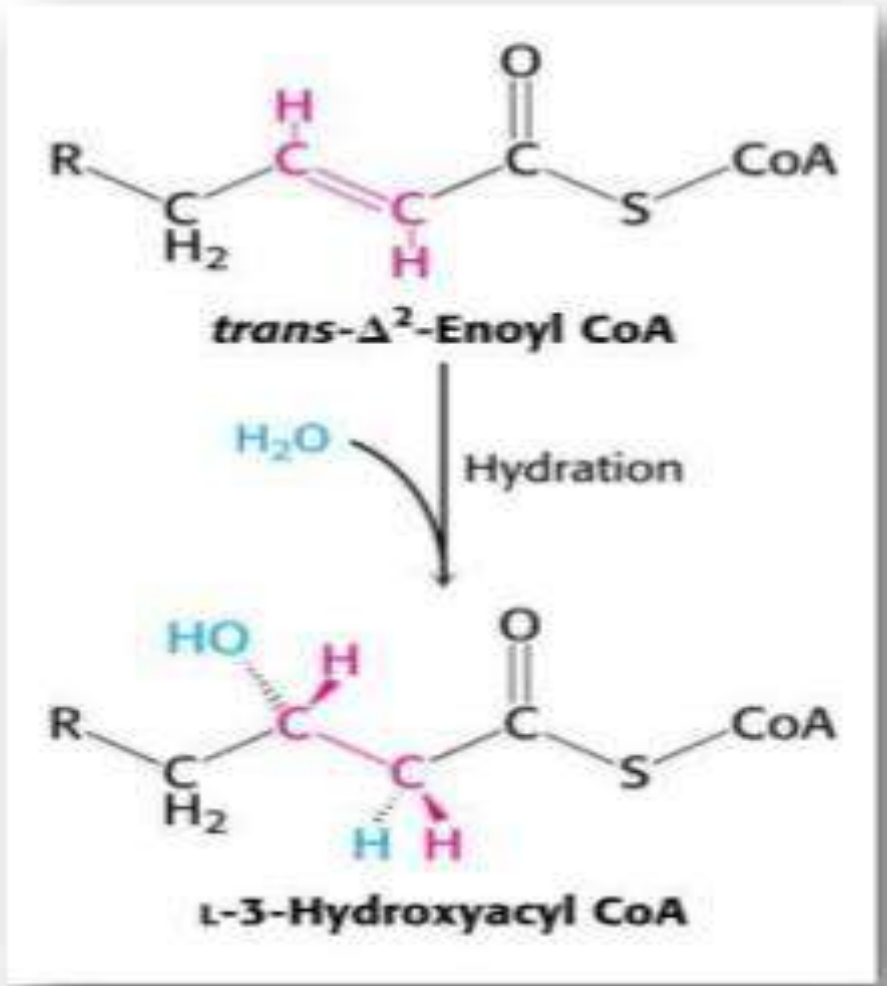


STEPS OF BETA OXIDATION

- Electrons from the FADH2 prosthetic group of the reduced acyl CoA dehydrogenase are transferred to ***electron-transferring flavoprotein*** **(ETF).**
- ETF donates electrons to ***ETF: ubiquinone reductase*, an iron-sulfur protein.**
- Ubiquinone is thereby reduced to ubiquinol, which delivers its high-potential electrons to the second proton-pumping site of the respiratory



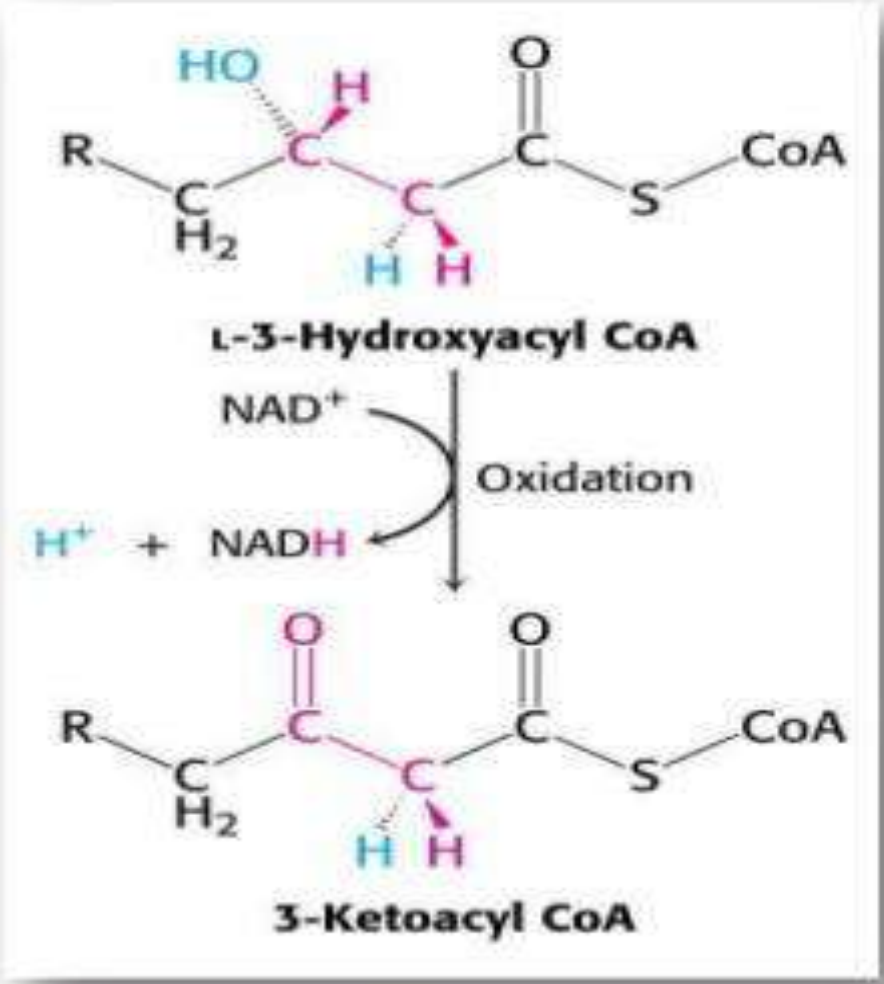
STEPS OF BETA OXIDATION



Step-2- Hydration

Water is added to saturate the double bond and form 3-hydroxyacyl-CoA, catalyzed by **Δ ²-enoyl-CoA hydratase.**

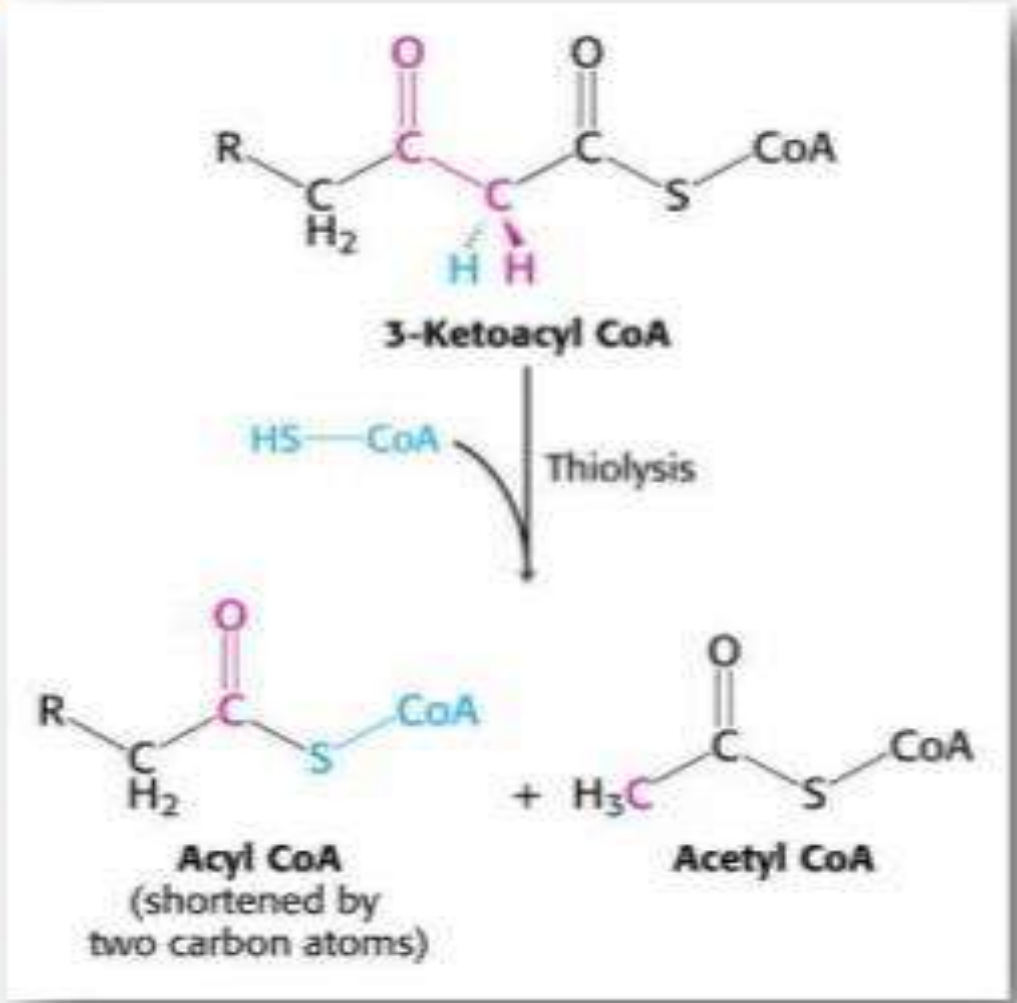
STEPS OF BETA OXIDATION



Step-3-dehydrogenation-

The 3-hydroxy derivative undergoes further dehydrogenation on the 3-carbon catalyzed by **L(+)-3-hydroxyacyl-CoA dehydrogenase** to form the corresponding 3-ketoacyl-CoA compound. In this case, NAD^+ is the coenzyme involved.

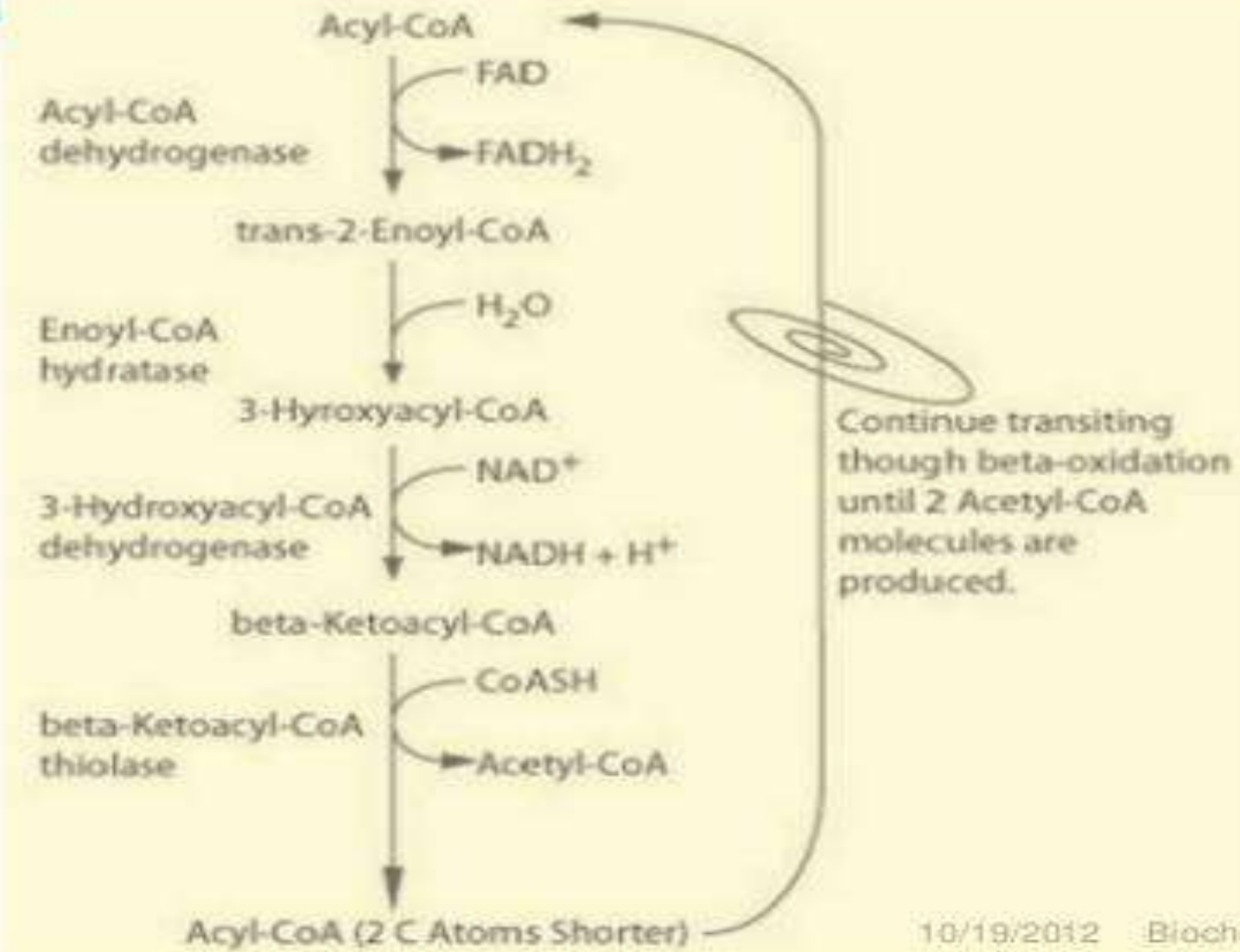
STEPS OF BETA OXIDATION



Step-4-
Thiolysis-

3-ketoacyl-CoA is split at the 2,3-position by **thiolase** (3-ketoacyl-CoA-thiolase), forming acetyl-CoA and a new acyl-CoA two carbons shorter than the original acyl-CoA molecule.

STEPS OF BETA OXIDATION



- The acyl-CoA formed in the cleavage reaction reenters the oxidative pathway at reaction 2.
- Since acetyl-CoA can be oxidized to CO_2 and water via the citric acid cycle the complete oxidation of fatty acids is achieved

BETA OXIDATION

The overall reaction can be represented as follows-

$$C_n\text{-acyl CoA} + FAD + NAD^+ + H_2O + CoA \longrightarrow C_{n-2}\text{-acyl CoA} + FADH_2 + NADH + \text{acetyl CoA} + H^+$$

BETA OXIDATION- ENERGY YIELD

Energy yield by the complete oxidation of one mol of Palmitic acid-

The degradation of palmitoyl CoA (C16-acyl Co A) requires seven reaction cycles. In the seventh cycle, the C4-ketoacyl CoA is thiolyzed to two molecules of acetyl CoA.

$$\text{Palmitoyl CoA} + 7\,\text{FAD} + 7\,\text{NAD}^+ + 7\,\text{CoA} + 7\,\text{H}_2\text{O} \longrightarrow 8\,\text{acetyl CoA} + 7\,\text{FADH}_2 + 7\,\text{NADH} + 7\,\text{H}^+$$

106 (129 As per old concept) ATP are produced by the complete oxidation of one mol of Palmitic acid.

BETA OXIDATION- ENERGY YIELD

2.5 ATPs per NADH = 17.5

1.5 ATPs per FADH2 = 10.5

10 ATPs per acetyl-CoA = 80

Total = 108 ATPs

2 ATP equivalents (ATP $\longrightarrow$ AMP + PPi

PPi $\longrightarrow$ 2 Pi)

consumed during activation of palmitate to Palmitoyl CoA

Net Energy output- 108-2 = 106 ATP

DISORDERS ASSOCIATED WITH IMPAIRED BETA OXIDATION

1) Deficiencies of carnitine or carnitine transferase or translocase

- Symptoms include muscle cramps during exercise, severe weakness and death.
- Muscle weakness related to importance of fatty acids as long term energy source
- Hypoglycemia and hypo ketosis are common findings
- Diet containing medium chain fatty acids is recommended since they do not require carnitine shuttle to enter mitochondria.

DISORDERS ASSOCIATED WITH IMPAIRED BETA OXIDATION

2) Jamaican Sickness- Jamaican vomiting sickness is caused by eating the unripe fruit of akee tree, which contains the toxin hypoglycin, that inactivates medium and short-chain acyl-CoA dehydrogenases, inhibiting β oxidation and thereby causing hypoglycemia.

3) Dicarboxylic aciduria is characterized by-

i) Excretion of C_6–C_{10} -dicarboxylic acids and

ii) **Nonketotic hypoglycemia** which is caused by lack of mitochondrial **medium chain acyl-CoA dehydrogenases.**

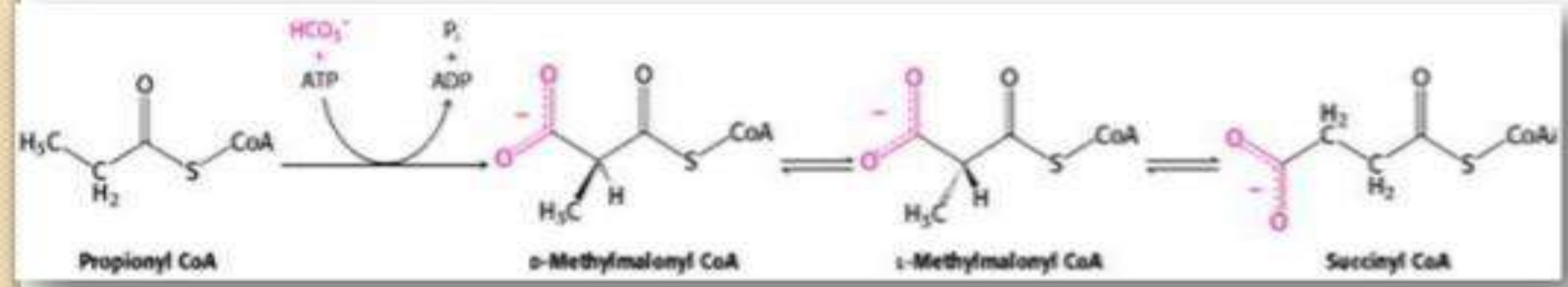
DISORDERS ASSOCIATED WITH IMPAIRED BETA OXIDATION

4) Acute fatty liver of pregnancy

- Manifests in the second half of pregnancy, usually close to term, but may also develop in the postpartum period.
- The patient developed symptoms of hepatic dysfunction at 36 weeks of gestation.
- Short history of illness, hypoglycemia, liver failure, renal failure, and coagulopathy are observed.
- Diagnosis is made based on an incidental finding of abnormal liver enzyme levels.
- Affected patients may become jaundiced or develop encephalopathy from liver failure, usually reflected by an elevated ammonia level.
- Profound hypoglycemia is common.

BETA OXIDATION OF ODD CHAIN FATTY ACIDS

Fatty acids with an odd number of carbon atoms are oxidized by the pathway of β-oxidation, producing acetyl-CoA, until a three-carbon (propionyl-CoA) residue remains. This compound is converted to Succinyl-CoA, a constituent of the citric acid cycle



The propionyl residue from an odd-chain fatty acid is the only part of a fatty acid that is glucogenic. Acetyl CoA cannot be converted into pyruvate or Oxaloacetate in animals.

Enzymes

Luc. 1

By

Dr. Muna M. Yaseen

Objective

- Definition
- Nomenclature
- Classification of enzymes
- Factors affecting enzyme activity.
- Application of enzyme inhibition.
- Isoenzymes.
- Enzyme in the Diagnosis of Pathology

- ***Definition***

Enzyme : It is a protein, catalyst, synthesized in all living cells that regulate a biochemical reaction without being changed.

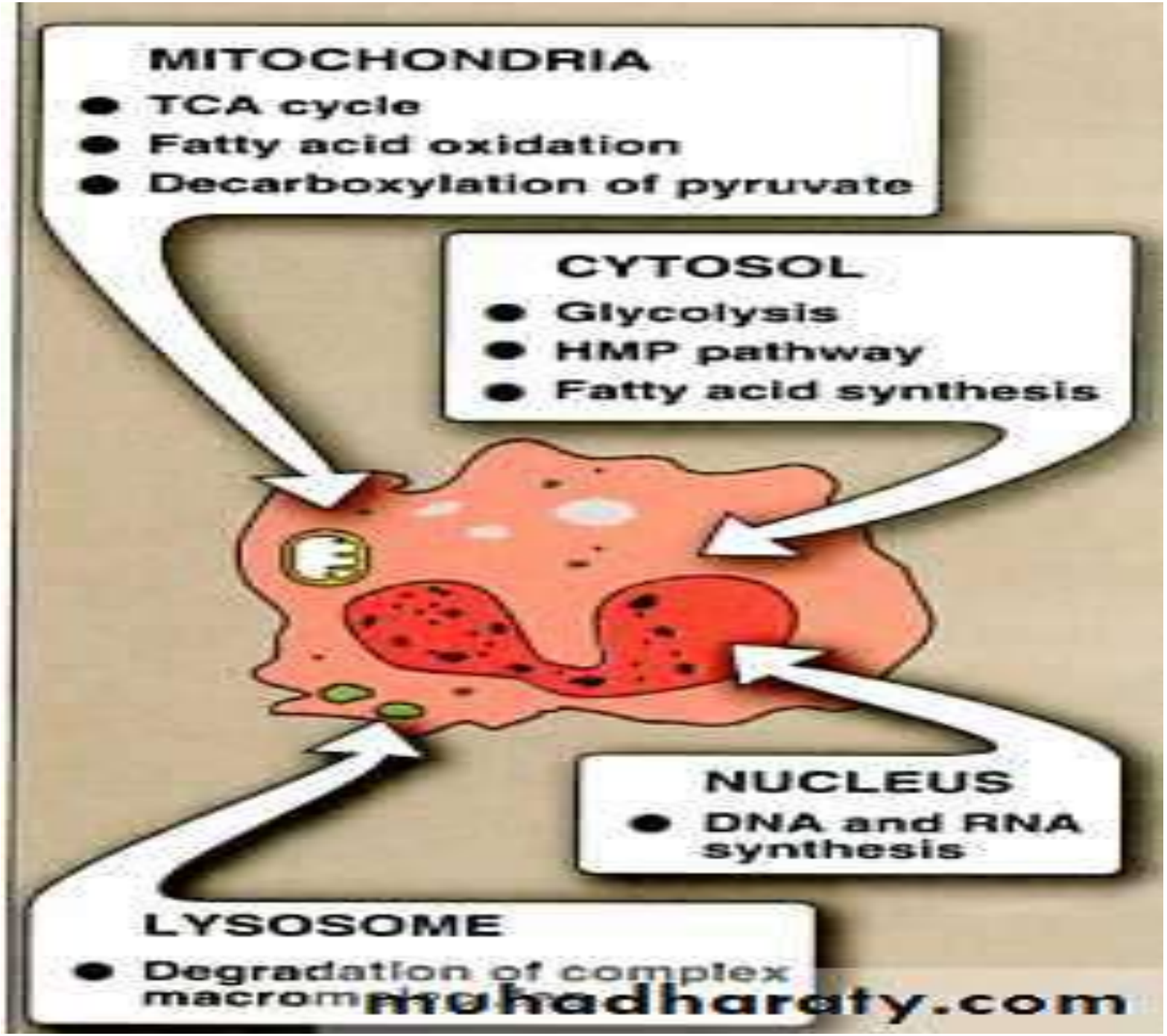
- ***Characteristics***

They are high catalytic rate.

They catalyze reaction without being changed.

They are very specific .

Enzyme distribution


MITOCHONDRIA
TCA cycle
Fatty acid oxidation
Decarboxylation of pyruvate
CYTOSOL
Glycolysis
HMP pathway
Fatty acid synthesis
NUCLEUS
DNA and RNA synthesis
LYSOSOME
Degradation of complex
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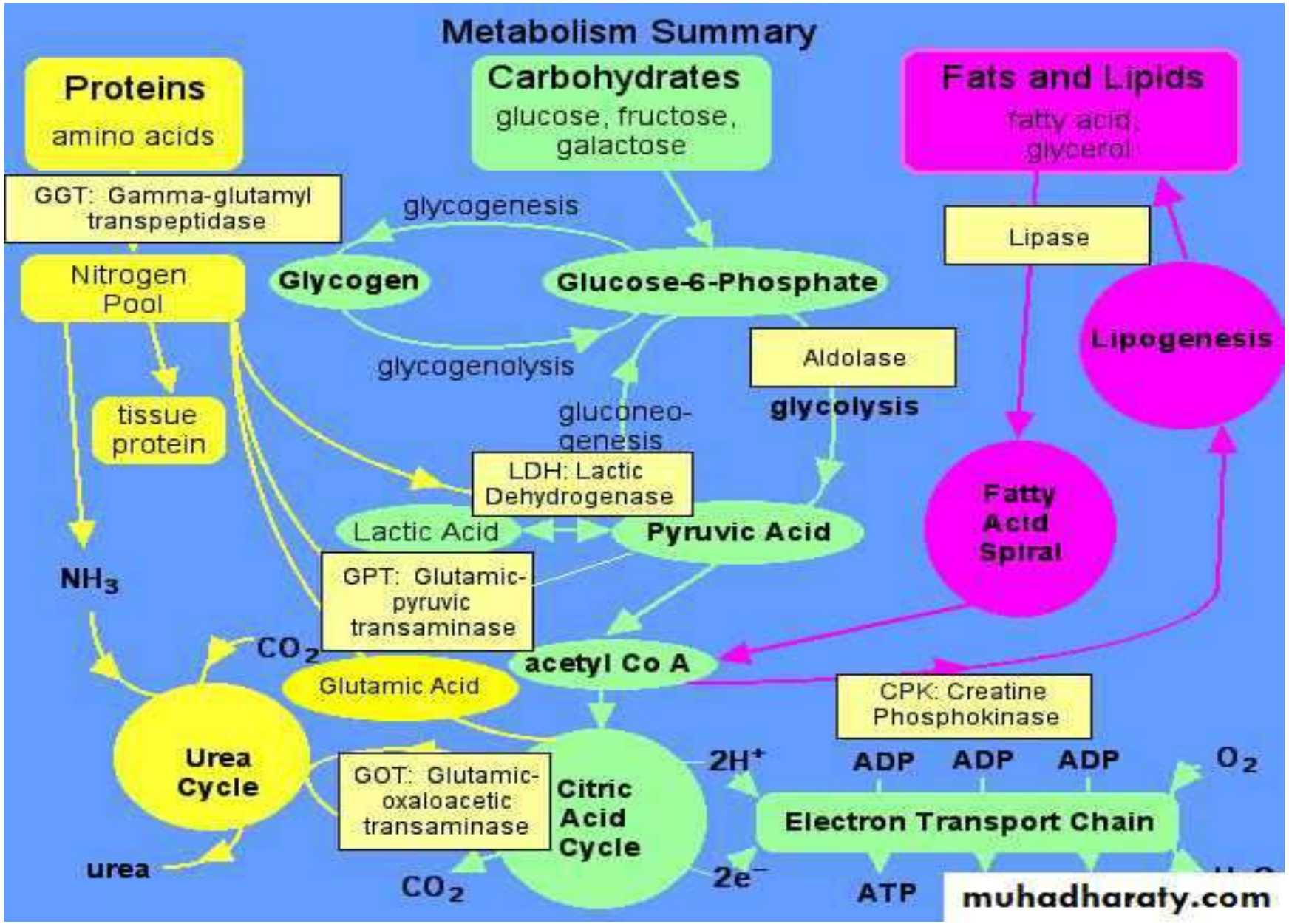

Metabolism Summary
Proteins
amino acids
Carbohydrates
glucose, fructose, galactose
Fats and Lipids
fatty acid, glycerol
GGT: Gamma-glutamyl transpeptidase
glycogenesis
Lipase
Nitrogen Pool
Glycogen
Glucose-6-Phosphate
Lipogenesis
glycogenolysis
Aldolase
tissue protein
gluconeo-genesis
glycolysis
LDH: Lactic Dehydrogenase
Fatty Acid Spiral
Lactic Acid
Pyruvic Acid
NH3
GPT: Glutamic-pyruvic transaminase
CO2
acetyl Co A
Glutamic Acid
CPK: Creatine Phosphokinase
Urea Cycle
2H+
ADP ADP ADP
O2
GOT: Glutamic-oxaloacetic transaminase
Citric Acid Cycle
Electron Transport Chain
urea
CO2
2e−
ATP
muhadharaty.com

Cofactor

Definition: A non-protein unit ,its presence is important in many enzymes.

Types:

1-Inorganic metals: Mn ,Zn ,Fe ,Cu.

2-Organic Complex (Coenzyme) .

Cofactors

Metal-activated enzymes:

- active in the presence of metal ions as K+, Mg+ or Ca++.

- Example: Kinase uses Mg++ , ATP.

Metalloenzyme:

- Firmly bound metal ion in the active site as Iron , copper , Zn & Co.

Examples:

1-Carbonic Anhydrase Zn.

2- Cytochrome oxidaseFe2+.

COENZYMES

Many enzymes require for their action on substrate, specific ,heat stable ,low M. wt.

and organic substance called ***coenzymes***

Enzyme which requires a coenzyme for its catalytic action is called ***apoenzyme*** and complete catalytic unit which

contain enzyme and its coenzyme is called ***holoenzyme.***

Catalytic unit (Apoenzyme + Coenzyme ==== Holoenzyme)

Apoenzyme: *inactive protein part.*

Cofactor: *Non protein part.*

Holoenzyme: *Active enzyme .*

Coenzyme itself may covalently or non covalently bound to enzyme and when coenzyme is covalent linked to its enzyme it will be then called ***PROSTHETIC GROUP.***

Majority of enzyme in the body required coenzyme in their action

(Nomenclature)

Unsystematic nomenclature:

1- Enzyme is named by adding (ase) to the name of the substrate e.g. (Urease).

2-Some other enzymes as (Trypsin ,pepsin) are known by their historic names.

one enzyme has one name or many enzymes have the same name.

Systematic Nomenclature

Adopted by **(IUB)** ; According to the type of reaction which is catalyzed.

It divided the enzymes into **6 classes.**

Classification of enzymes

Class no I Oxidoredoctase

Class no II Transferase

Class no III Hydrolases

Class no IV Lyases

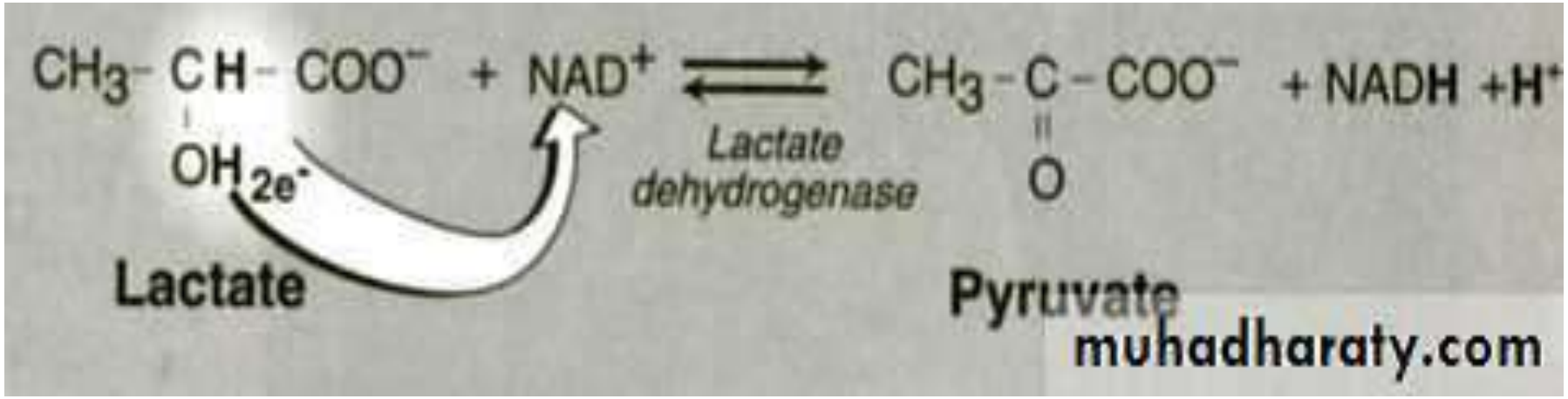
Class no V Isomerases cis and Trans

Class no VI Ligases

Class 1: Oxido-Reductase:

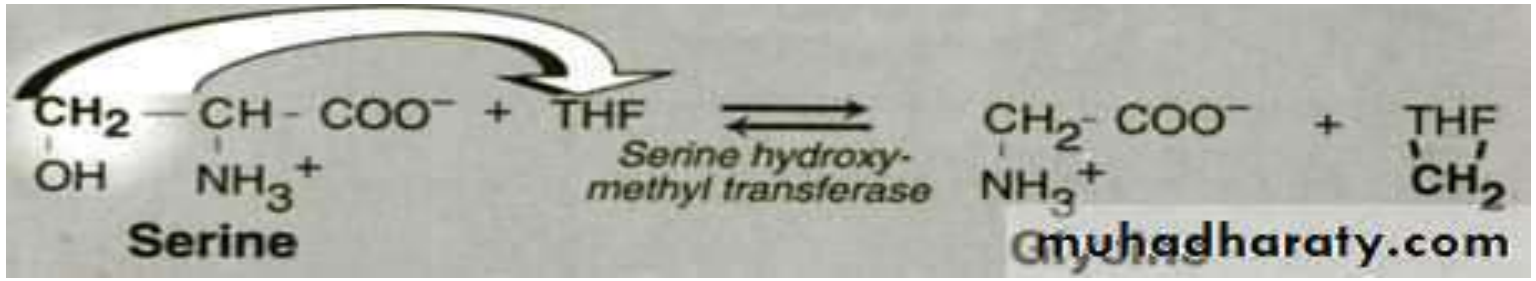
Catalyses Oxidation ,reduction reactions as : Dehydrogenase ,Oxidase ,Hydroxylase ,Peroxidase.

Usually they require coenzymes as : (NAD+,NADP+,FAD,FMN).



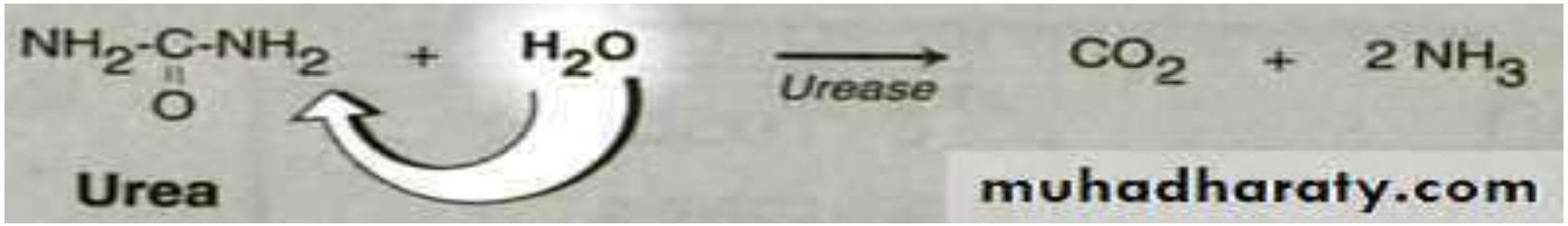
Class 2: Transferase

Catalyze transfer of functional group between donor & acceptor molecule as methyl , formyl ,carboxyl ,nitrogenous, phosphorus & sulfur containing groups



Class 3: Hydrolases

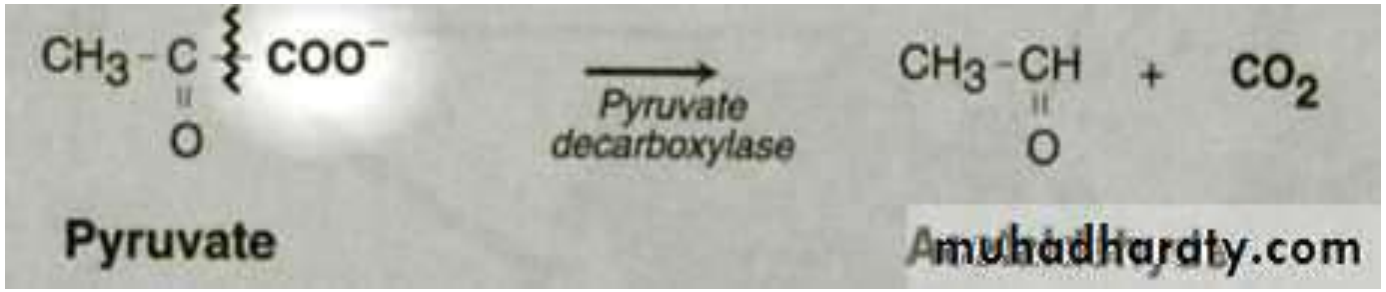
Catalyze hydrolytic reaction by adding H2Ocleavage of bond between C & others as : C-O , C-N & C-S.



Class 4 : Lyases

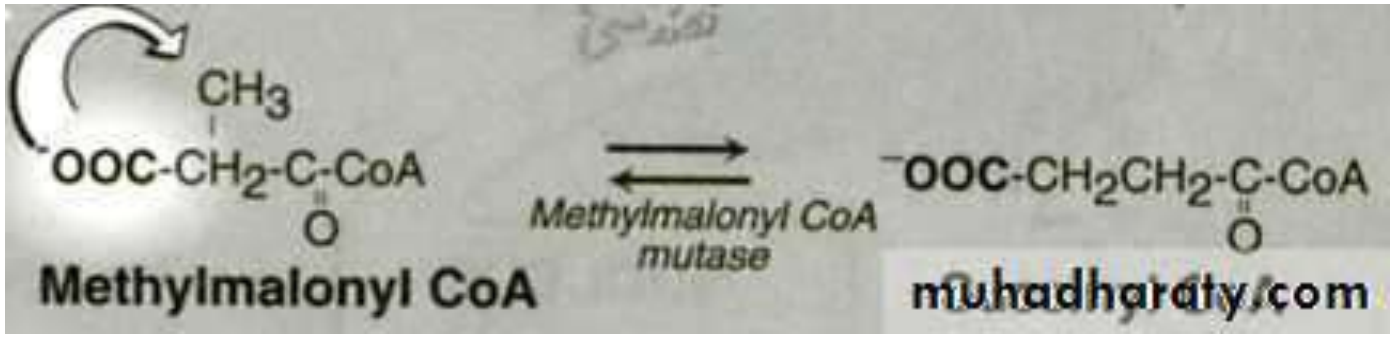
Catalyze non-hydrolytic reaction

Examples: Decarboxylase .



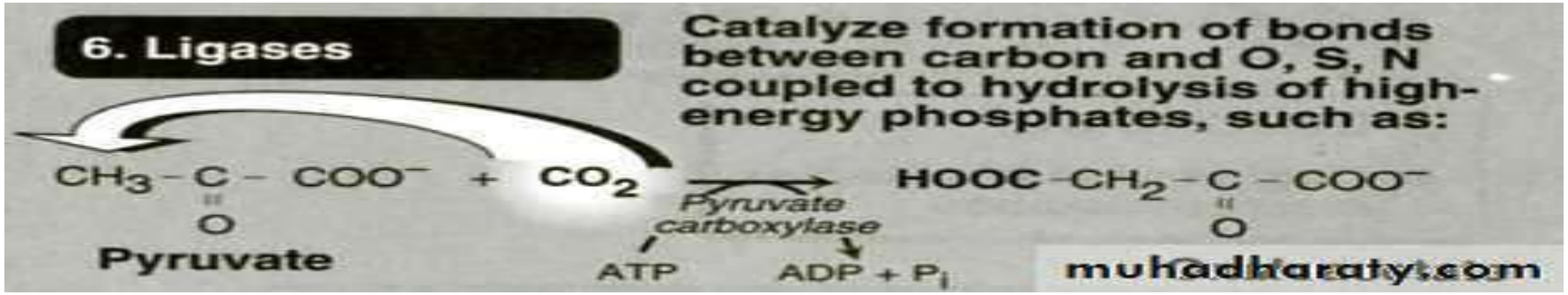
Class 5 : Isomerase

Catalyze transfer of groups within a molecule (rearrange).



Class 6:Ligase

Catalyze bond formation coupled to ATP-hydrolysis joining 2 molecules.



Substrate

The molecule being utilized and/or modified by a particular enzyme at its active site

Enzyme Specificity

The most significant properties in the enzyme catalytic reaction is the ability of the enzyme in catalyze one specific reaction and no other that is a characteristic of enzyme and when these enzyme is absent the respective reaction will not occur and this behavior is called ***specificity*** of enzyme and this behavior is usually appear in the following **TWO** properties:

I-optical specificity

II- Selective group

I-optical specificity

The enzyme has an absolute specificity in particular optical region of the substrate. Almost all human enzyme are being specific for an optical part of substrate . ex: enzyme acting on CHO. Metabolism (sugar breakdown)are usually specific for D-sugar not act on L-sugar or other enzyme acting on amino acid metabolism are usually acting on L- amino acid (not D-amino acid) with exception of D- amino acid oxidase in the kidney .

II- Selective group:

In this properties enzyme is usually affective on specific chemical group that is present in the structure of substrate. ex: glycosidase, glycosidase catalyze hydrolysis of Glycosidic bond between sugar and alcohol are highly specific for sugar portion not specific for alcohol.

Trypsin and pepsin act on peptide bond.

Some enzymes have a higher degree of specificity ex: amino peptidase act on amino group , carboxypeptidase act on carboxy end of peptide bond .

Chymotrypsin will act on peptide bond on which carboxy terminal end of peptide bond is being contributed to an aromatic a.a. Which may be phenyl alanine , tyrosine and tryptophan split of a.a one at a time from the carboxy or amino terminal end of polypeptide chain respectively.

Tyrosine

Tyrosine

CH NH2COOH

CH NH2COOH

CH2

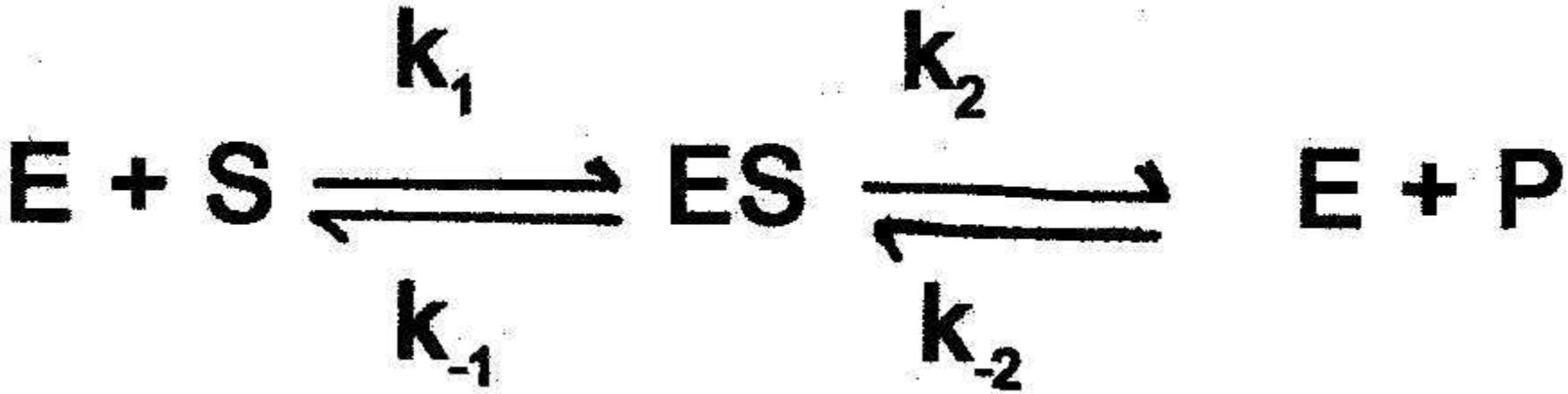
CH2

-HO

-HO

Enzyme velocity (V)

It is moles of product (P) appearing or substrate (S) disappearing per unit of time. (Mole / liter /sec.)



S = substrate P = product

E = enzyme

ES = enzyme-substrate complex

k_1, k_{-1}, k_2, k_{-2} are rate constants

Enzyme units

International unit (IU): a mount of enzyme that converts one micromole (µmol) of substrate per minute at 25°C under the optimal conditions of the measurement.

Katal: amount of enzyme that converts one mole of substrate to product/sec

(Active site)

Active site: is an important structural feature to recognize and to bind substrates.

It is very specific.

Catalytic Site:

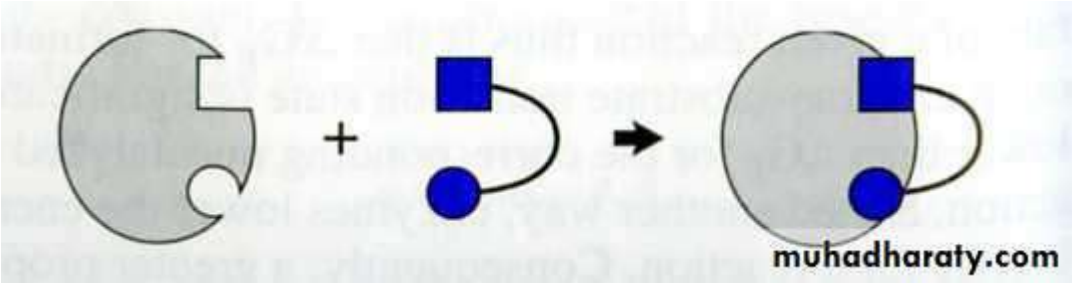
The large size of the enzyme molecule in comparison with substrate size that a small part or limited number of amino acids in the enzyme molecule is being responsible for the catalytic reaction these size is called ***CATALYTIC SITE*** or ***ACTIVE SITE*** or ***ACTIVE CENTER*** of the enzyme.

There are two theory or mode or type to explain the interaction between the substrate and enzyme.

Type I

The lock & key model:

- Enzyme fits substrate as a lock & key .
- Its rigid type.

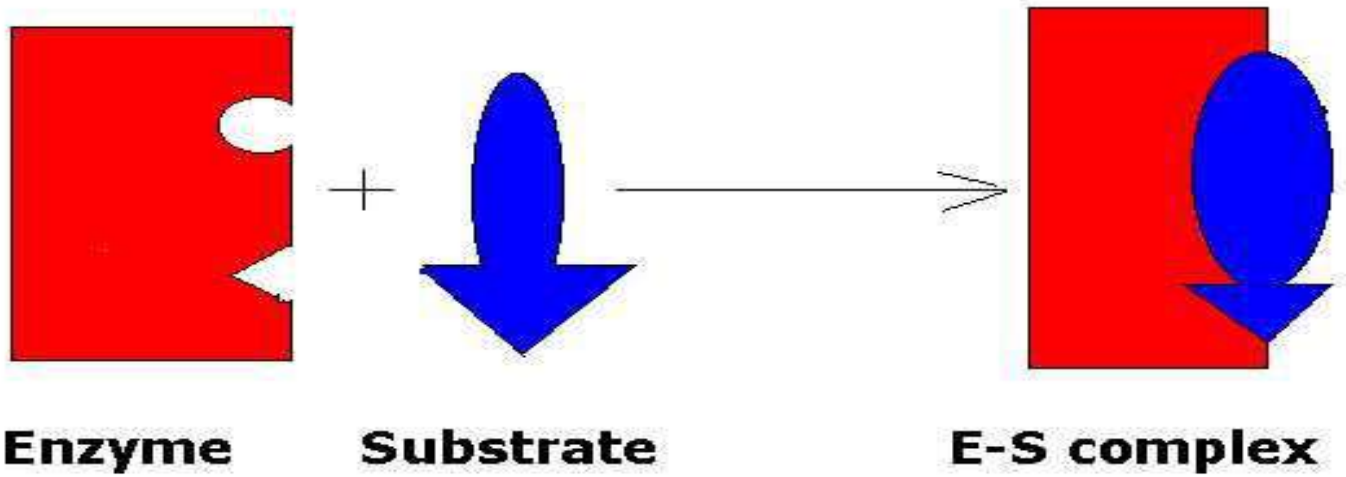


Type II Induced fit (Koshland model):

the substrate induces conformational changes in the active site rearrangement of the A.A Enzyme fits substrate exactly.

This type discovered by Koshland in which there is a source of flexibility in substrate – enzyme binding in which certain physical changes take place in the enzyme that include arrangement of certain (a.a)s both to the substrate binding site and at catalytic site.

These changes are called ***(conformational changes)*** and the site in which these changes take place are called ***Allosteric site*** being important for the enzyme catalytic reaction. This type is more flexible than the lock and key type and it has wide application in explainin



Catalytic efficiency

Most enzyme-catalyzed reactions are highly efficient, proceeding from 103 to 108 times faster than uncatalyzed reactions.

Factors affecting Enz. Activity

1.Enzyme concentration.

2.Temperature.

3.PH

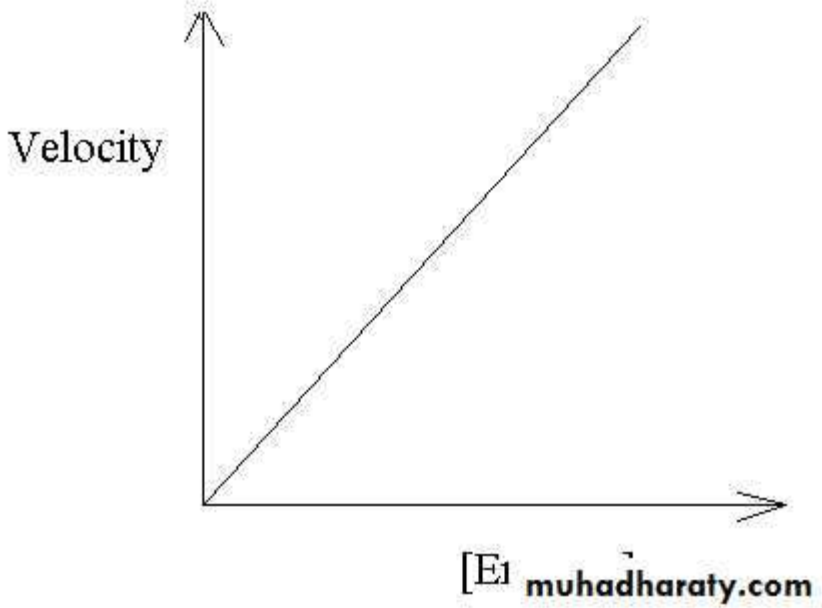
4.Substrate concentration.

5. Inhibiters

6. Activators

Enzyme concentration:

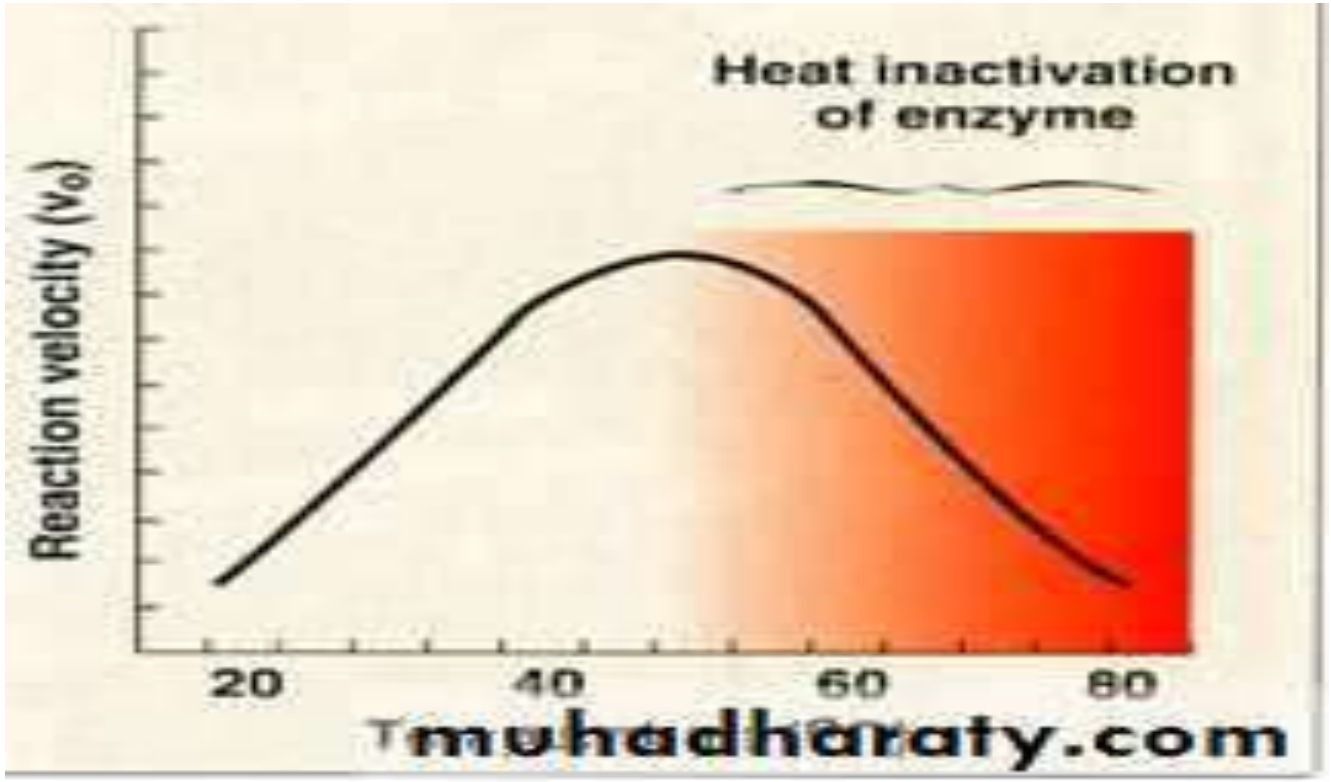
The rate of the reaction is directly proportional to [enzyme]



Temperature

The rate of the reaction increases with the temperature increasing until reaching the (Maximal velocity) at the (Optimal temperature) . Increasing of the temperature after the optimal temperature decreasing in the reaction velocity.

The velocity decreases due to (enzyme denaturation)

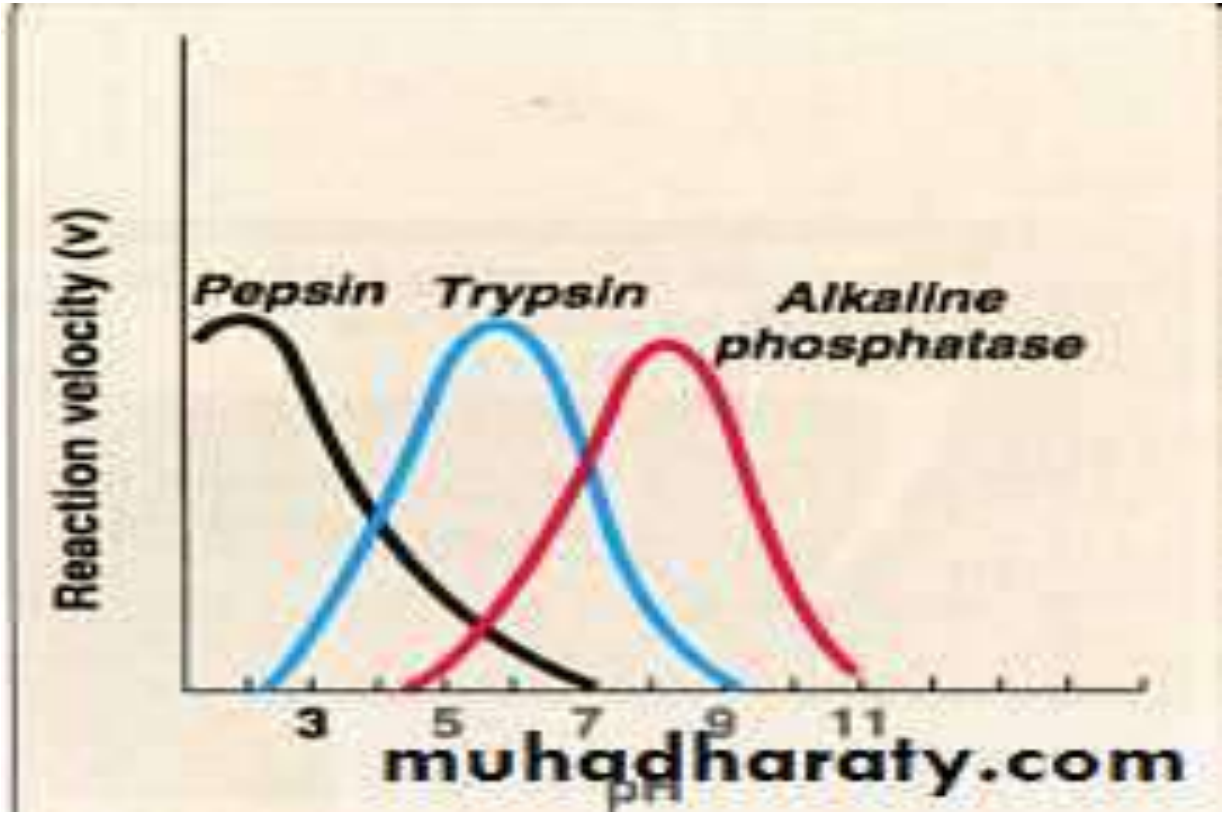


Effect of PH

Each enzyme has its own (Optimal PH).

Any change in the PH decreasing in the reaction velocity due to change in the ionization of the active site A.A.

This ionization inactivation of the active site decrease in enzyme activity.



Substrate concentration

Rate of the catalytic enzyme increases rapidly constant.

1-low [S] active sites are not saturated rapid reaction .

2-High [S] Saturated active sites slow reaction.

Substrate concentration

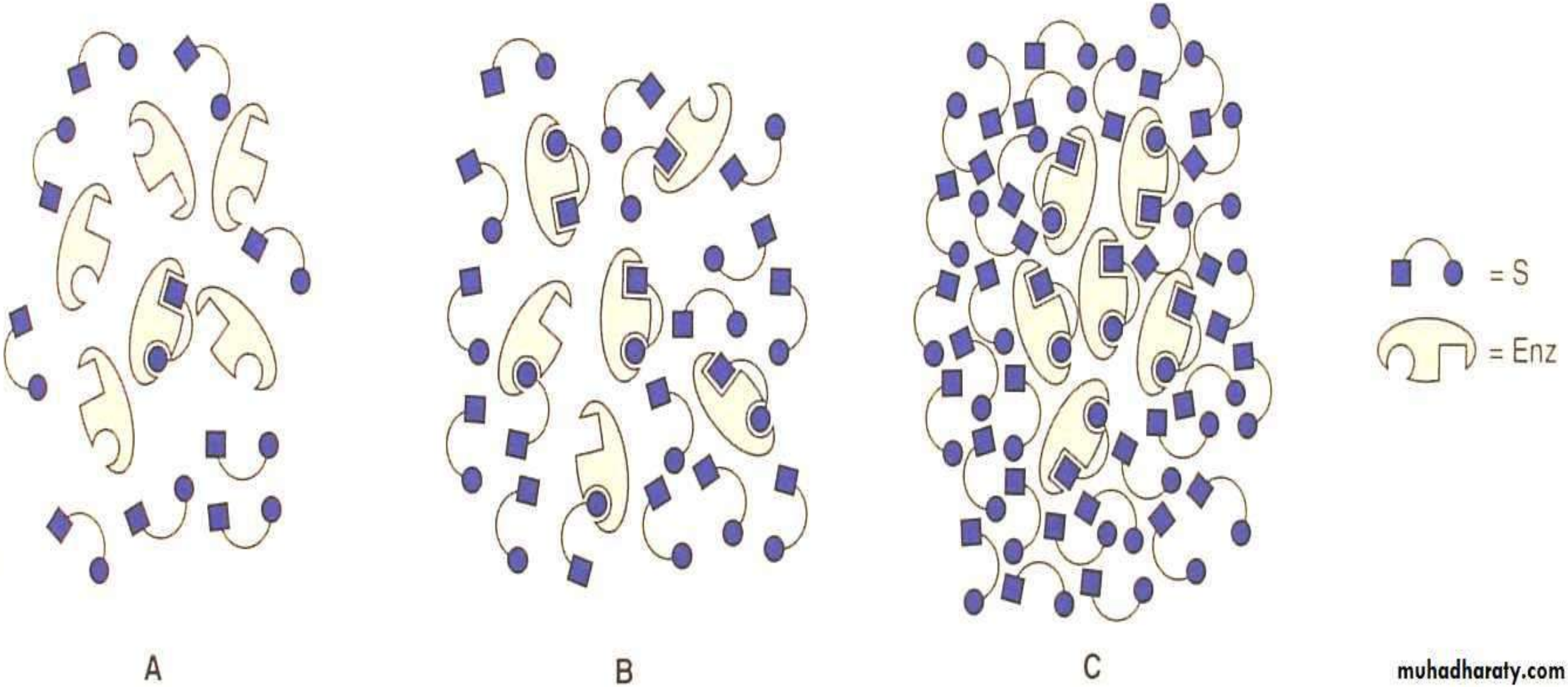
The rate or velocity of a reaction (v) is the number of substrate molecules converted to product per unit time and is usually expressed as µmoles product formed per minute.

The rate of an enzyme-catalyzed reaction increases with substrate concentration until a maximal velocity (Vmax) is reached.

A. Low [S]

B. 50% [S] or Km

C. High, saturating [S]



The Michaela's- menten constant (Km).

The quantitative relationship between substrate concentration and Vmax. For different enzymes, it is defined as that substrate conc. at which a given enzyme give one – half it maximum velocity . In many cases the Km is an inverse measure of the affinity of the enzyme for its substrate : the lower the Km the higher the affinity .

$$v_o = \frac{[V_{max}][S]}{Km + [S]}$$

v_o = initial reaction velocity

V_{max} = maximal velocity

[S] = substrate concentration

Characteristics of Km

The Michaelis constant is characteristic of an enzyme and a particular substrate, and reflects the affinity of the enzyme for that substrate.

Km does not vary with the concentration of enzyme. A numerically small (low) Km reflects a high affinity of the enzyme for substrate because a low concentration of substrate is needed to half-saturate the enzyme.

Large Km:

A numerically large (high) Km reflects a low affinity of enzyme for substrate because a high concentration of, substrate is needed to half-saturate the enzyme.

The rate of the reaction is directly proportional to the enzyme concentration at all substrate concentrations.

When [S] is much less than Km, the velocity of the reaction is proportional to the substrate concentration.

Uses of Km

Experimentally, Km is a useful parameter for characterizing the number and/or types of substrates that a particular enzyme will utilize. It is also useful for comparing similar enzymes from different tissues or different organisms. Also, it is the Km of the rate-limiting enzyme in many of the biochemical metabolic pathways that determines the amount of product and overall regulation of a given pathway. Clinically, Km comparisons are useful for evaluating the effects mutations have on protein function for some inherited genetic diseases

Introduction to Biochemistry

MACROMOLECULES

Building Blocks

All large molecules (macromolecules) in our bodies are created from monomers. The building and deconstruction of these macromolecules are done by two processes.

Dehydration Synthesis

Simply put, we take small things and make one big thing.

Dehydration = removing water

Synthesis = put together

Hydrolysis

Simply put, we use water to break a big thing apart.

Hydro = water

lysis = break apart

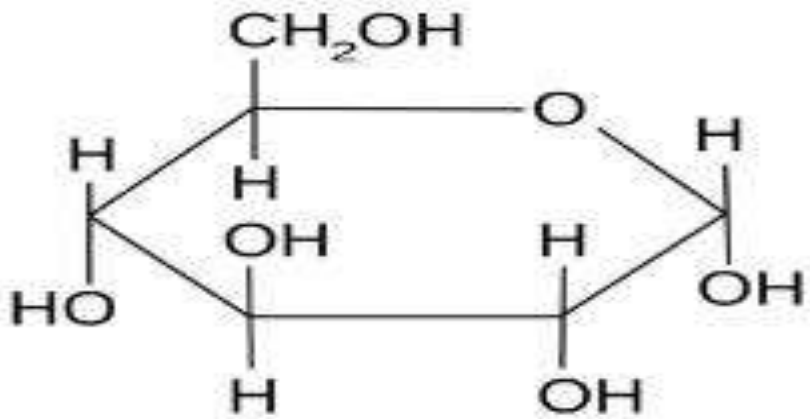
CARBOHYDRATES

Structure

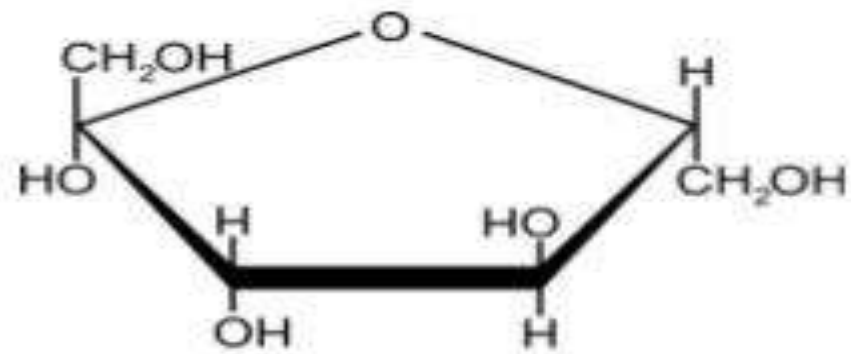
The building blocks of carbohydrates are **monosaccharides**.

All carbohydrates follow the generic formula of $C_nH_{2n}O_n$

Examples of monosaccharides include:



Glucose ($C_6H_{12}O_6$)

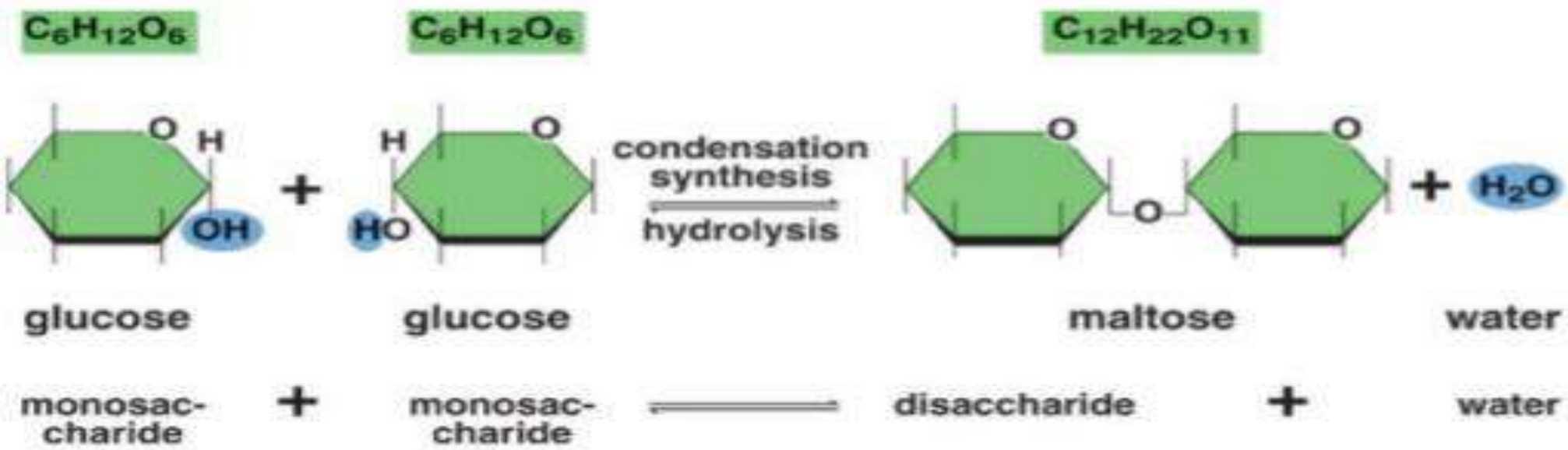


Fructose ($C_6H_{12}O_6$)

CARBOHYDRATES

Polymers

Disaccharides: When two monosaccharides are joined together in a dehydration synthesis reaction they form a disaccharide.



CARBOHYDRATES

Polymers

Examples of Disaccharides:

Maltose = Glucose + Glucose

Sucrose = Glucose + Fructose

Lactose = Glucose + Galactose

CARBOHYDRATES

Polymers

Polysaccharide: When very long chains of monosaccharides are arranged into a complex molecule we call this a polysaccharide.

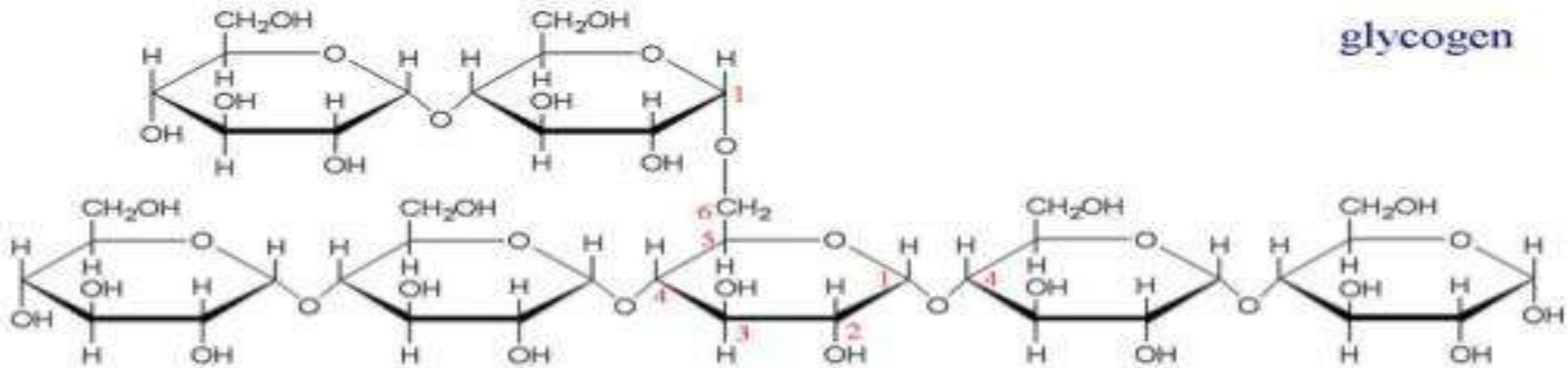
Polysaccharides have different structures and functions depending on the monomers that produce them.

CARBOHYDRATES

Polymers

Glycogen: Produced when very long chains of the monomer glucose are bonded together.

Function: Long term energy storage in animals.



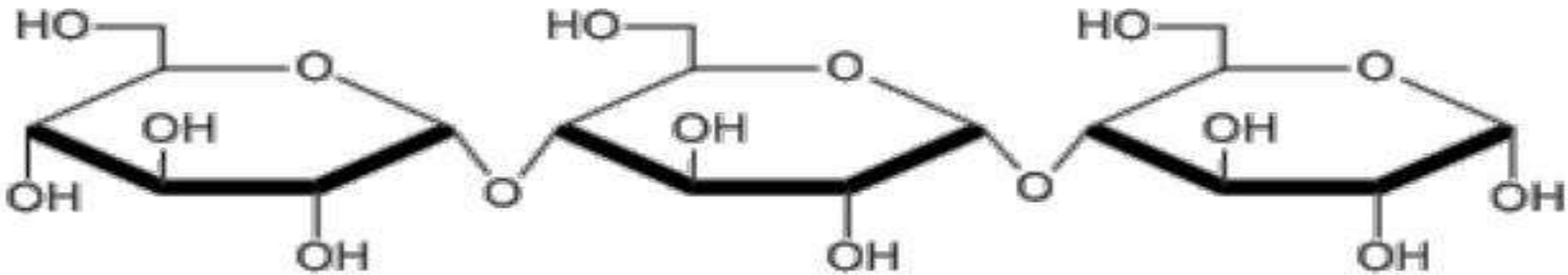
glycogen

CARBOHYDRATES

Polymers

Starch: Produced when very long chains of the monomer glucose are bonded together.

Function: Long term energy storage in plants.

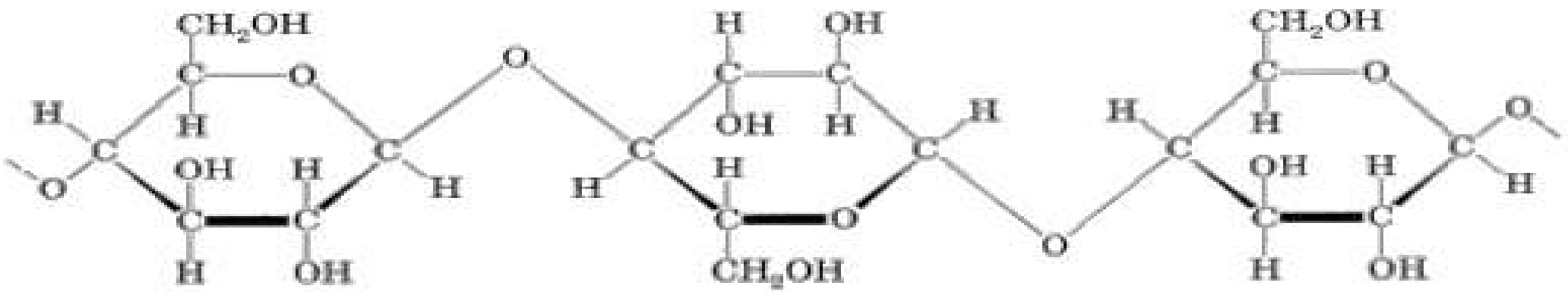


CARBOHYDRATES

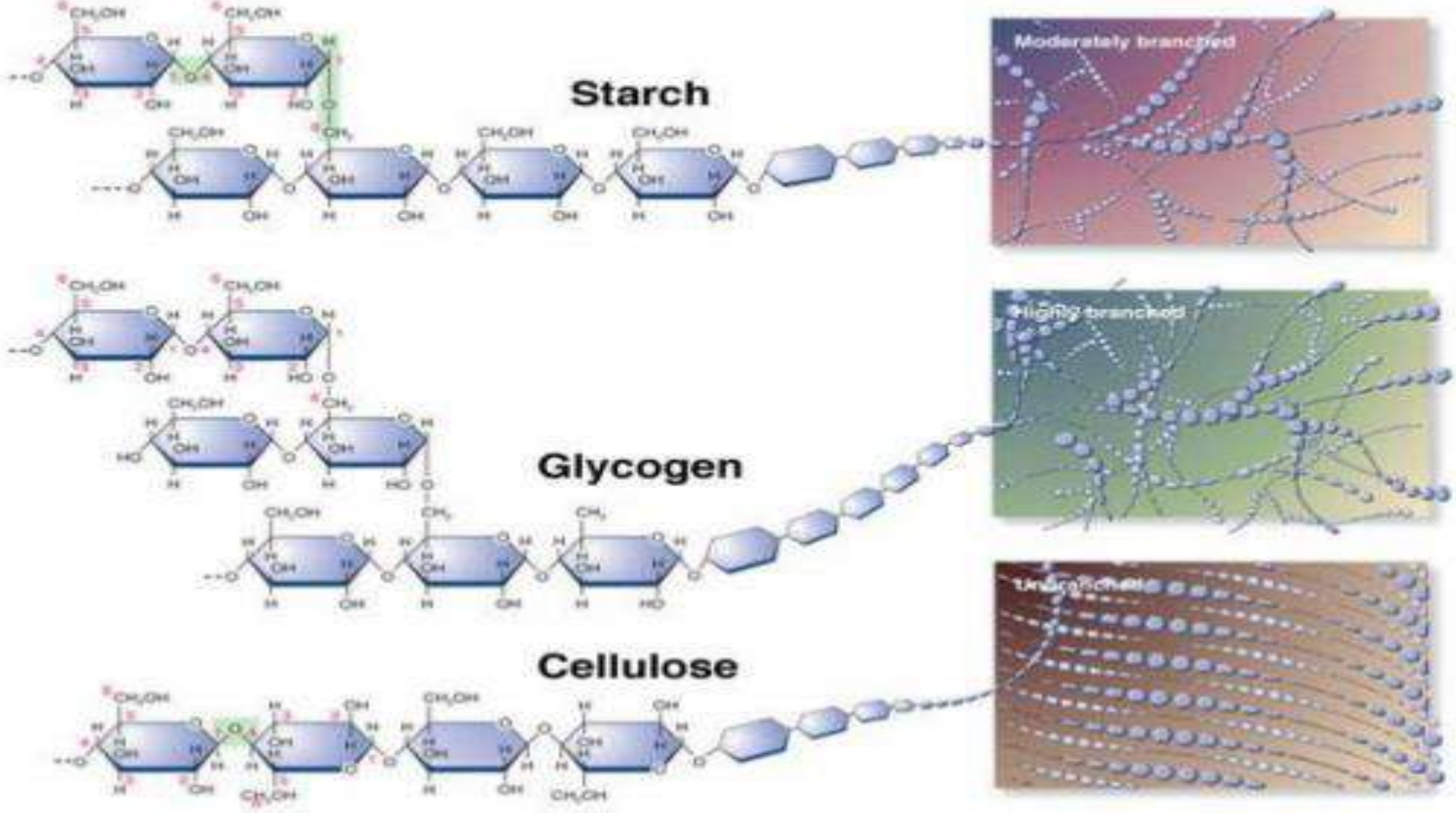
Polymers

Cellulose: Produced when very long chains of the monomer glucose are bonded together. The difference between starch and cellulose is the monomer glucose is reversed 180 degrees each time in cellulose.

Function: Structural compound found in plants.



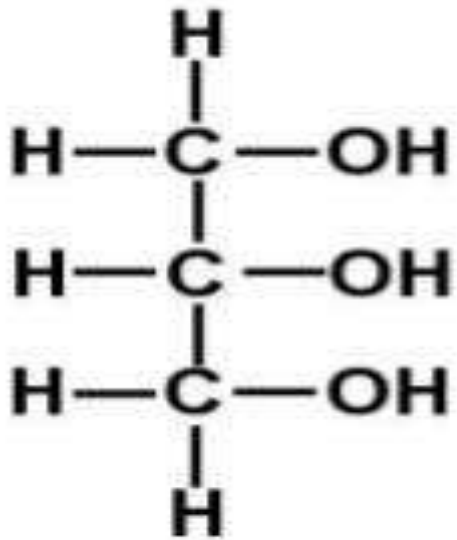
CARBOHYDRATES



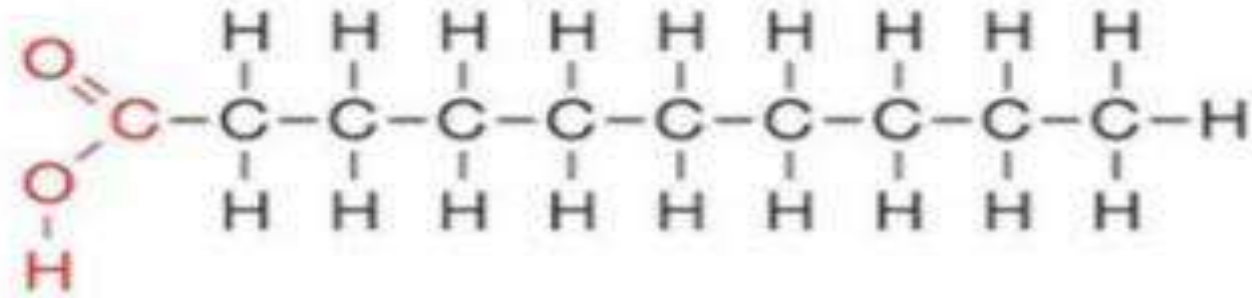
LIPIDS

Structure

All lipids are insoluble in water. The building blocks of lipids are **glycerol and fatty acids.**



Glycerol



fatty acid (saturated)

LIPIDS

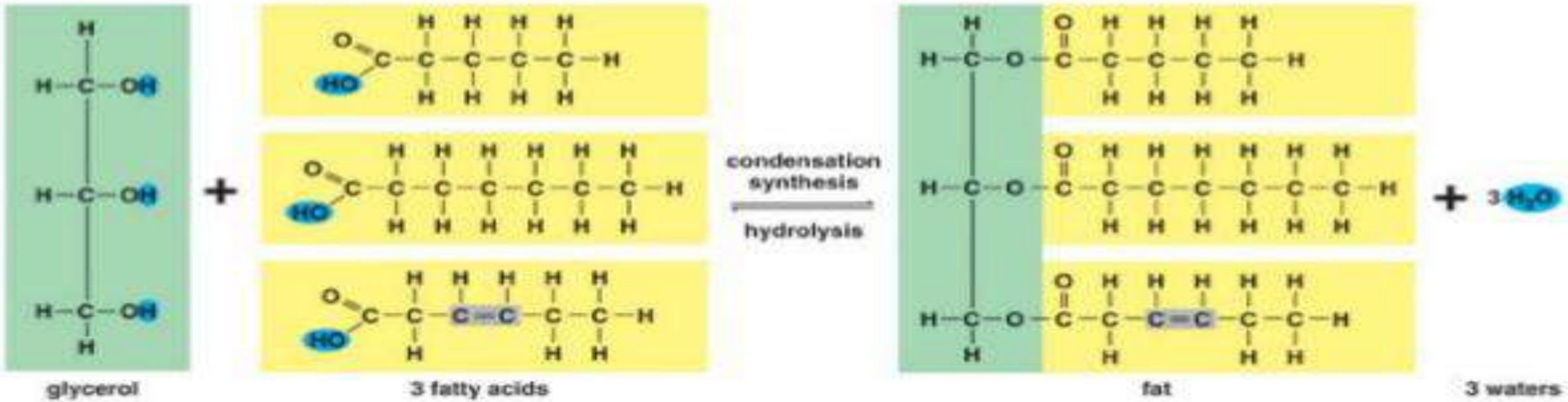
Function

- Long term energy stores
- Membrane formation
- Serve as hormones
- Provide insulation
- Protection of internal organs

LIPIDS

Polymers

Triglycerides: fats and oils that are formed by synthesizing a glycerol molecule with 3 fatty acids.



LIPIDS

Polymers

Triglycerides: the fatty acids (10-30 carbon chains) are what provide the variability in fats and oils.

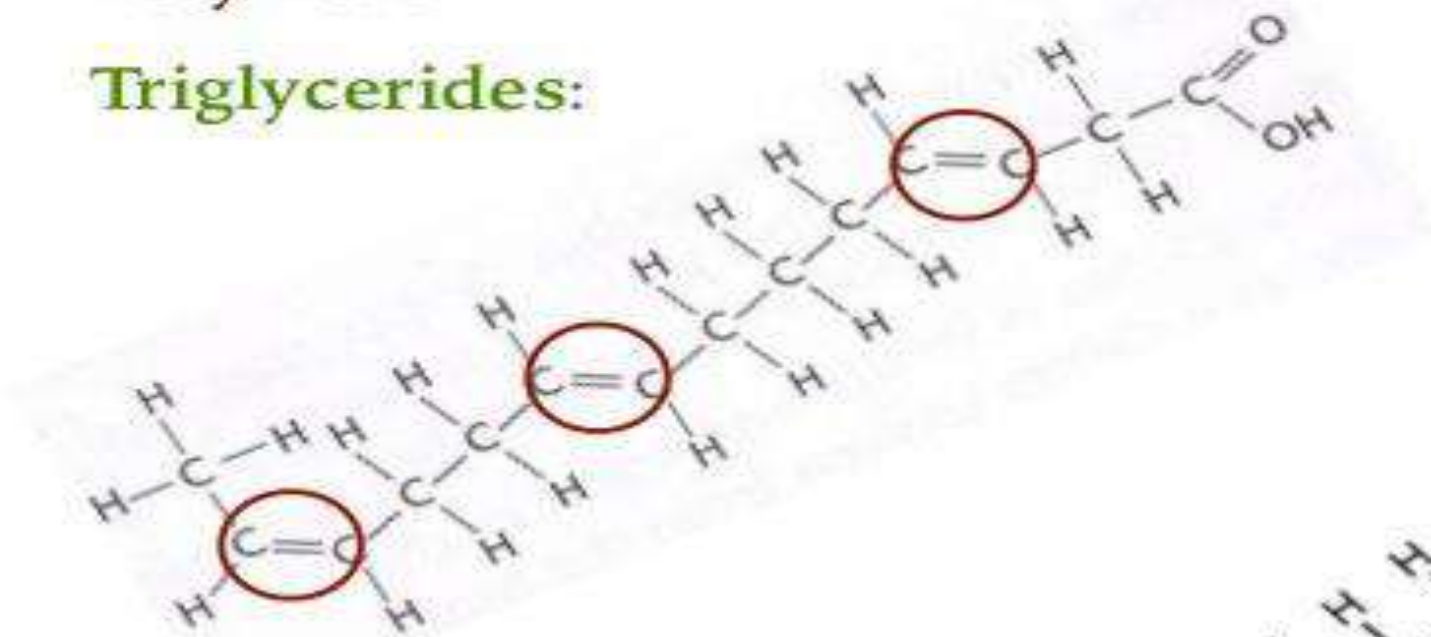
Saturated fatty acids: all the carbon atoms in the chain contain the maximum number of hydrogen atoms. Usually solid at room temperature

Unsaturated fatty acids: one or more double bonds between carbon atoms in the chain. Usually liquid at room temperature.

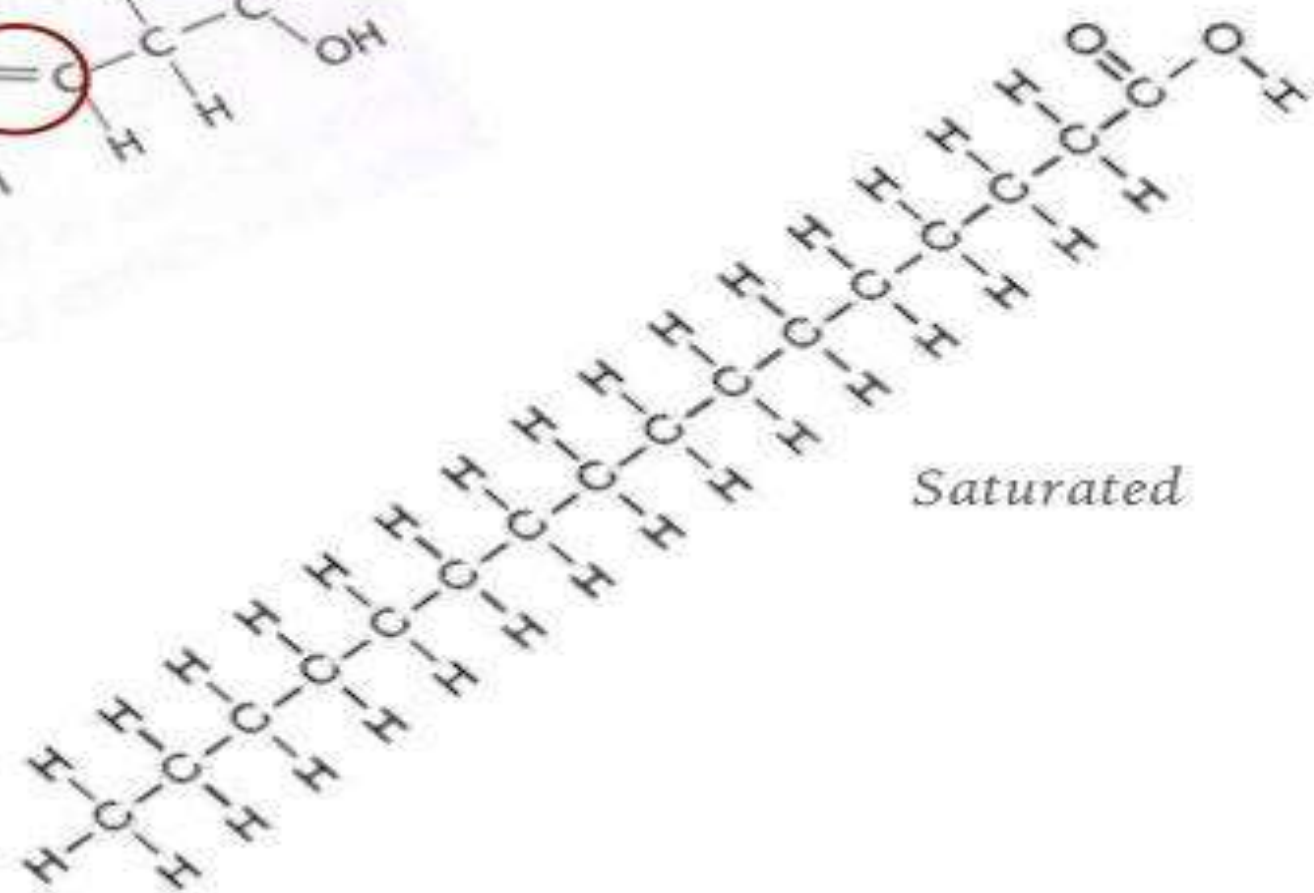
LIPIDS

Polymers

Triglycerides:



Unsaturated

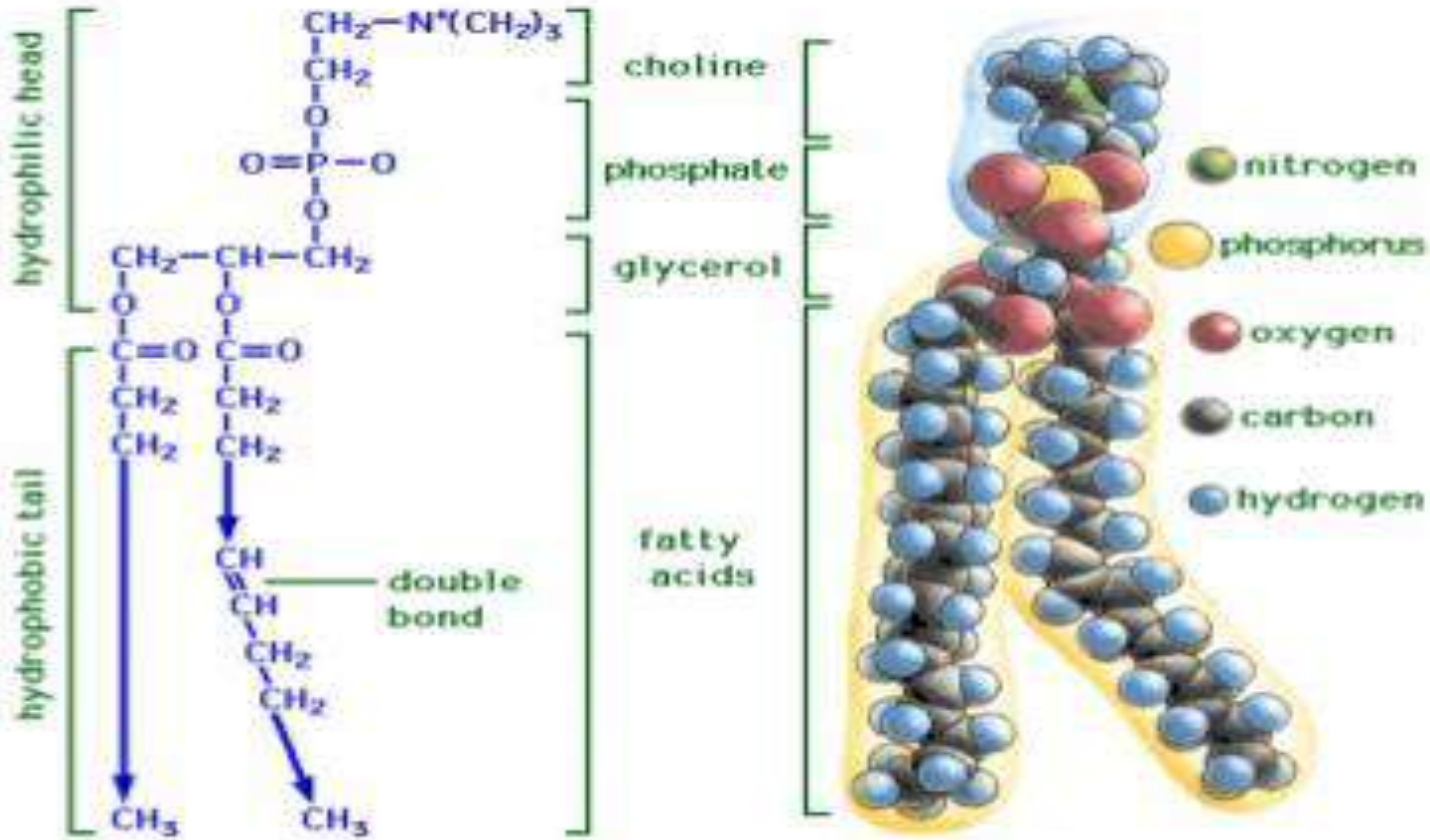


Saturated

LIPIDS

Polymers

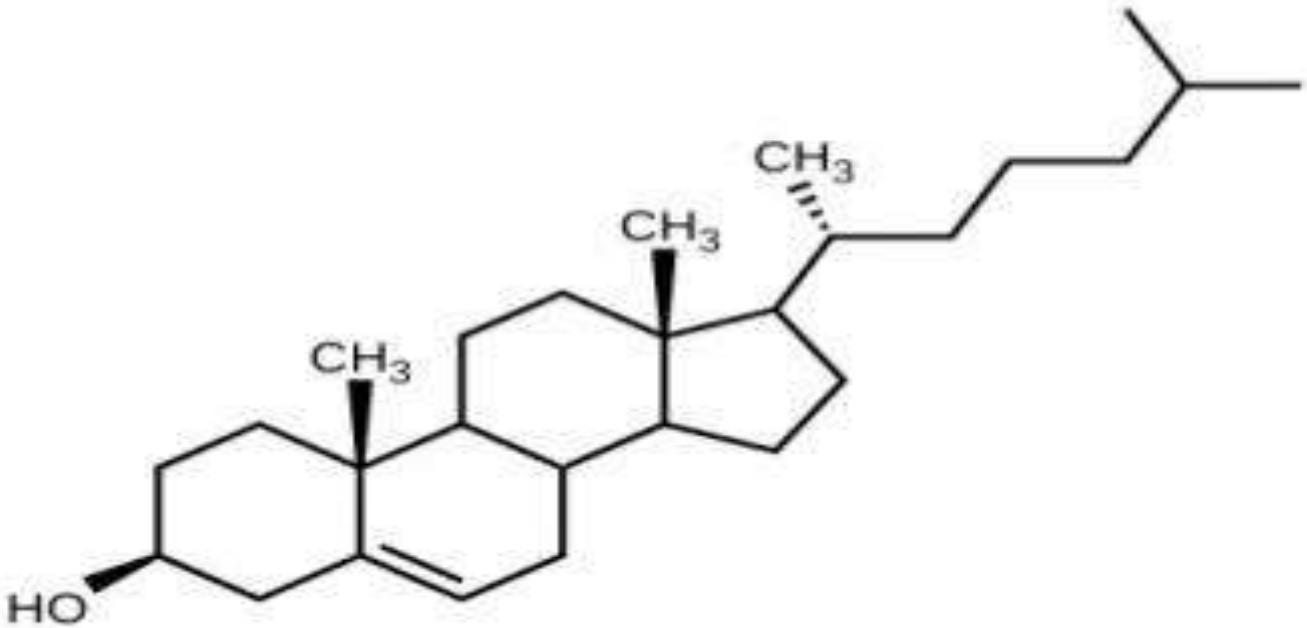
Phospholipids: A modified triglyceride. One fatty acid is removed and replaced with a phosphate group. This creates a polar molecule. One end hydrophilic (water loving) and the other is hydrophobic (water hating)



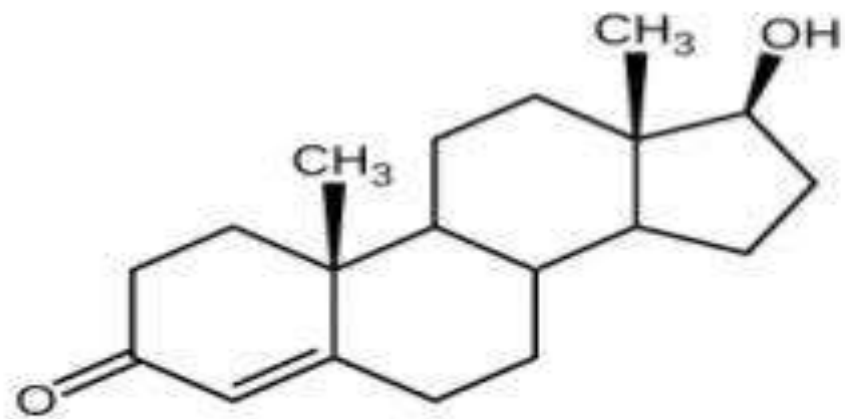
LIPIDS

Polymers

Cholesterol and Derivatives: found in many areas of the body such as cell membranes. Also include steroids and bile acid.



(a) Cholesterol



(b) Testosterone

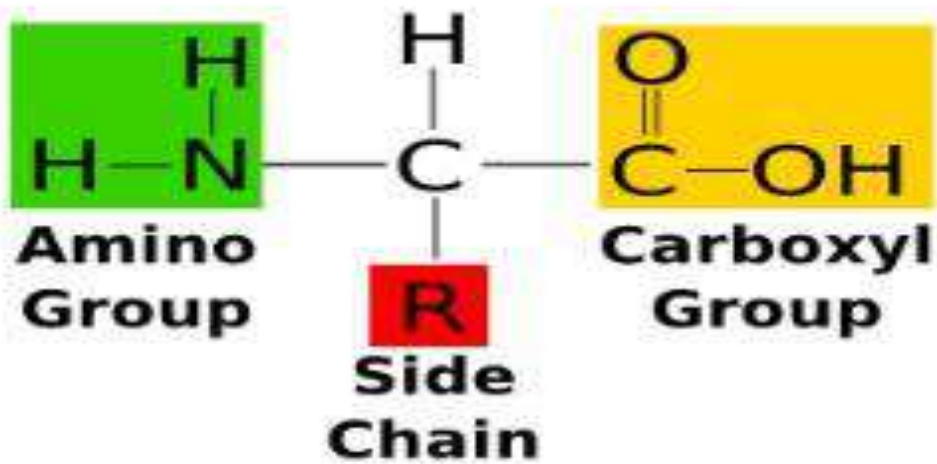
PROTEINS

Structure

The building blocks of proteins are **amino acids**. One end contains an amine group and one end contains a carboxyl group.

There are 20 amino acids, of which 9 can not be produced by your body.

The generic amino acid molecule looked like this:



PROTEINS

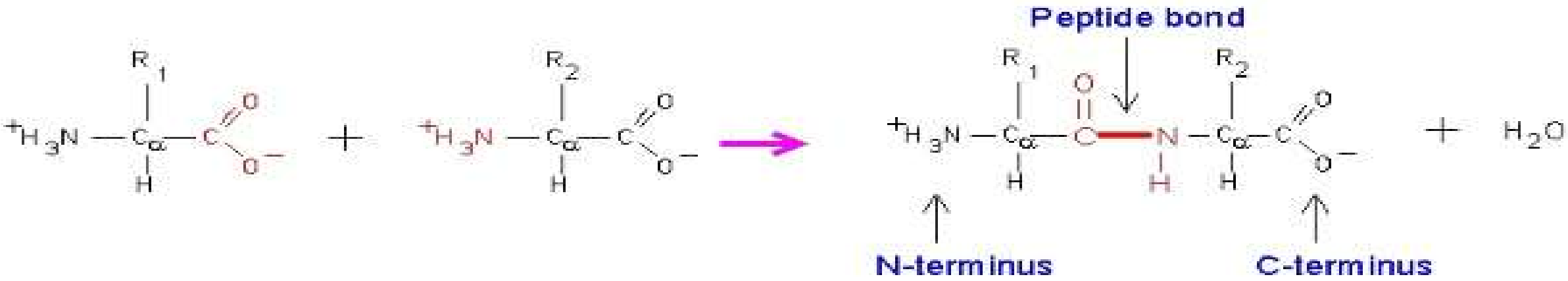
Function

- Structural Proteins
- Enzymes - speed reactions (end in ase)
- Antibodies
- Transport carriers
- Allow materials to cross cell membrane

PROTEINS

Polymers

Peptide chains: amino acids are bonded together via dehydration synthesis. The bond formed between amino acids are called peptide bonds.



PROTEINS

Polymers

Levels of Organization: The more amino acids that are added to the structure, the more complex it becomes. We group proteins structures into 4 classifications.

Primary: polypeptide chain.

Secondary: α helix and β sheets

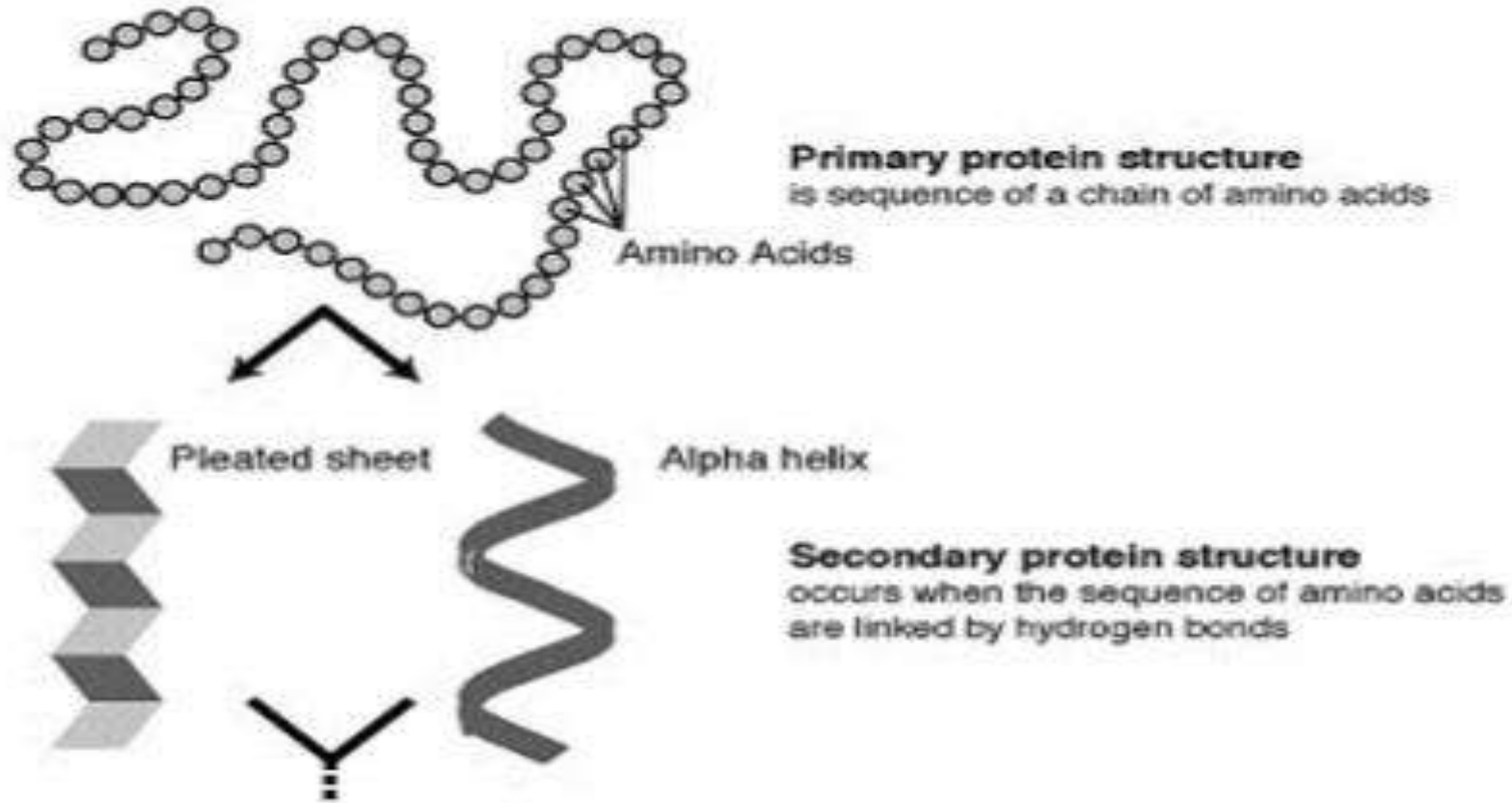
Tertiary: Globular Structures

Quaternary: Multiple polypeptide chains.

PROTEINS

Polymers

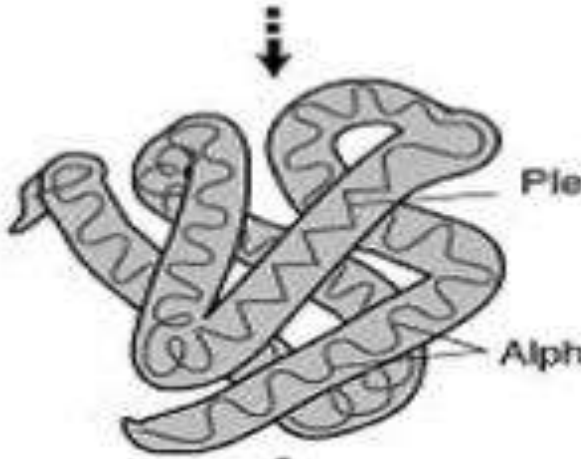
Levels of Organization:



PROTEINS

Polymers

Levels of Organization:



Tertiary protein structure
occurs when certain attractions are present between alpha helices and pleated sheets.

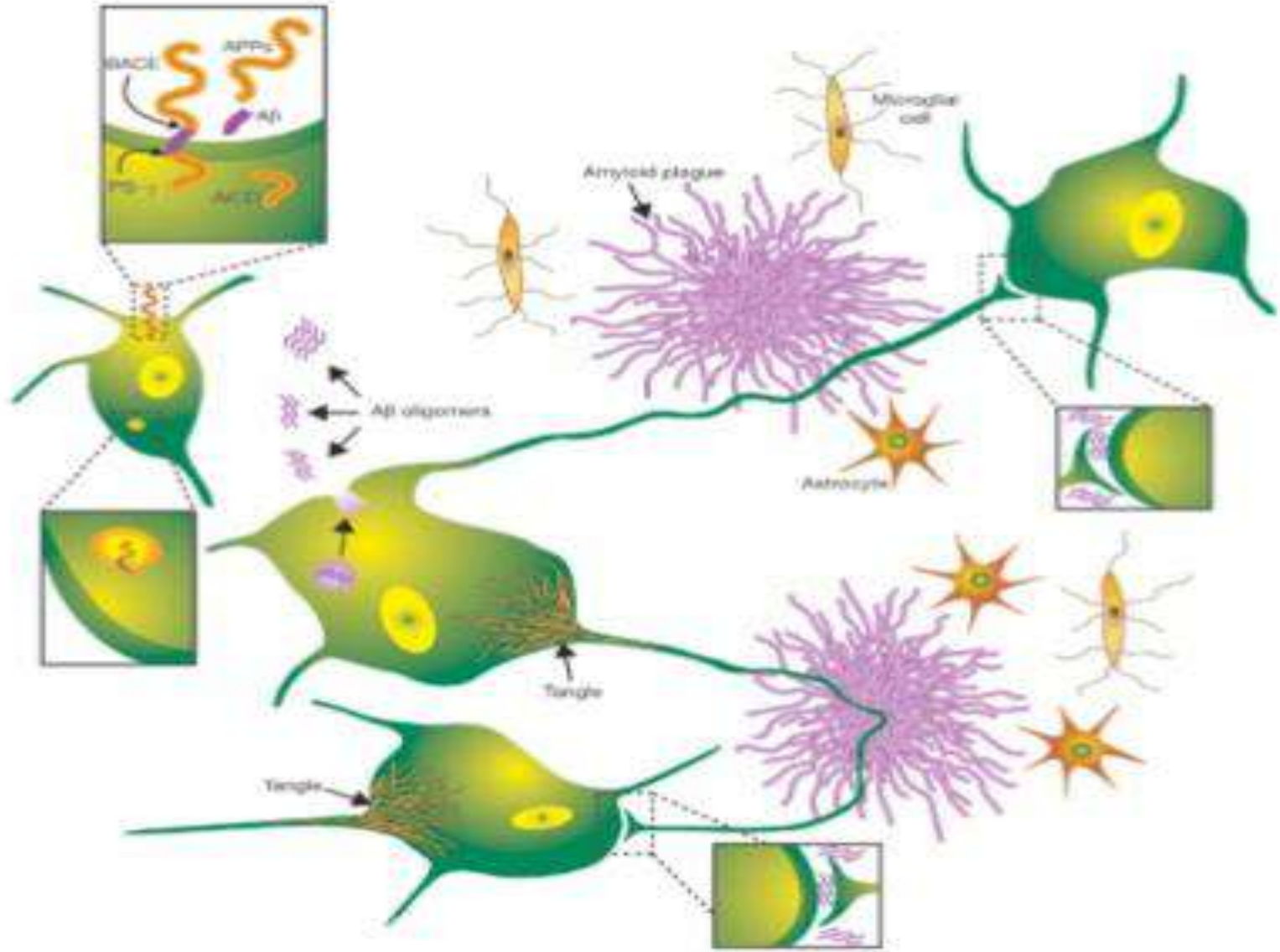
Quaternary protein structure
is a protein consisting of more than one amino acid chain.

PROTEINS – DISEASE

Alzheimer's

Amyloid plaque made of protein envelops axons

Tau changes shape and stick together causing tangles inside cell bodies.



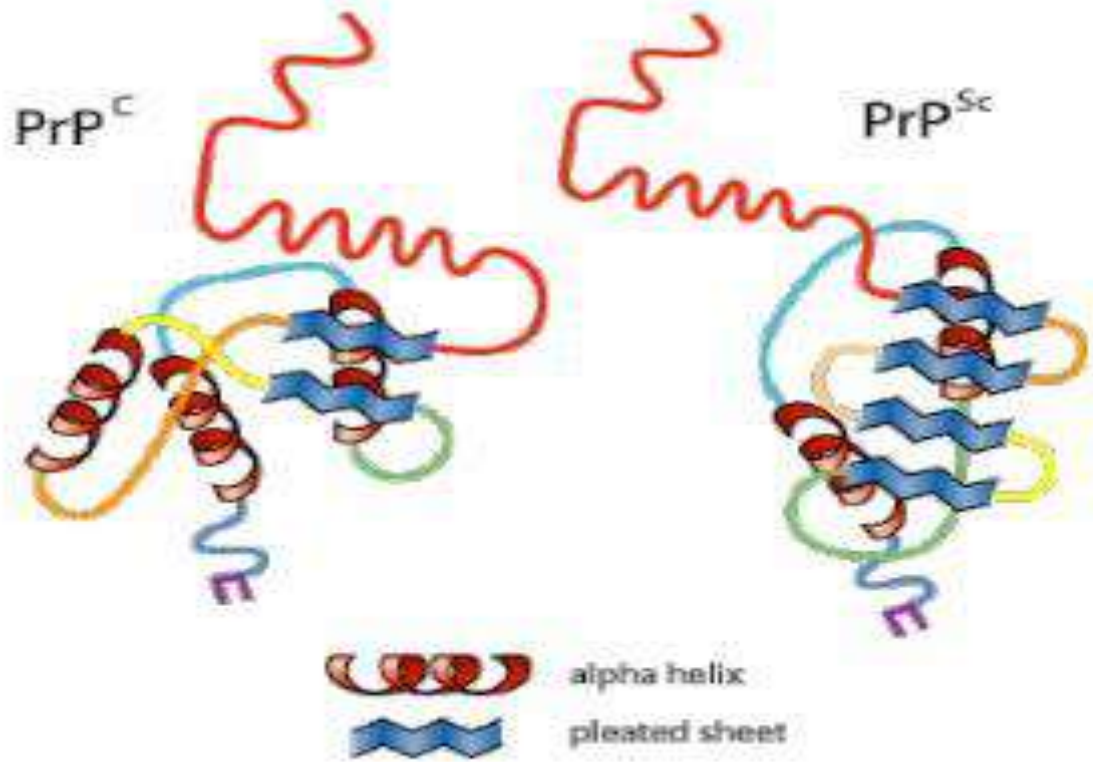
PROTEINS – DISEASE

Creutzfeld-Jacobs disease

Normally soluble prion proteins become insoluble

These proteins become insoluble in the presence of other insoluble prions

Insoluble prions damage brain tissue causing disease



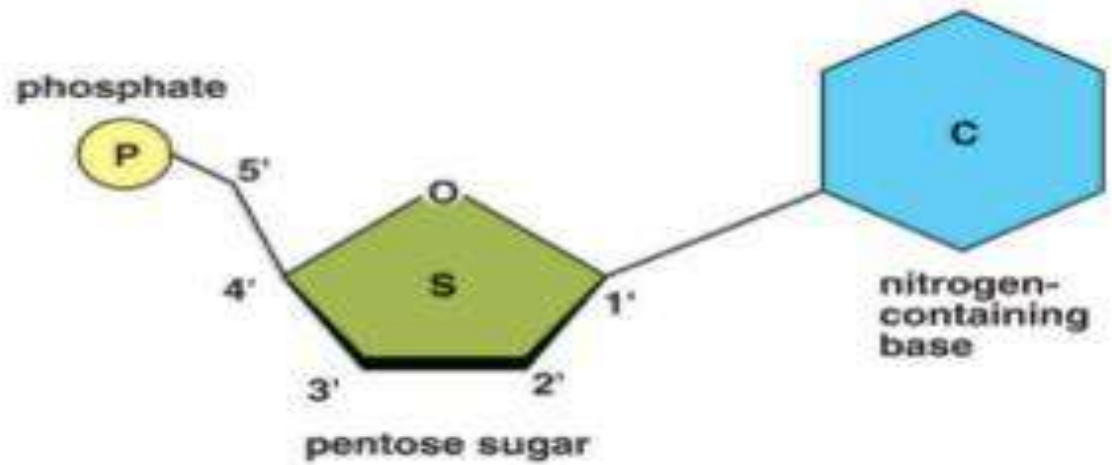
NUCLEIC ACIDS

Structure

The building blocks of nucleic acids are **nucleotides**.

Nucleotides consist of a phosphate group, a 5 sided sugar, and a nitrogenous base.

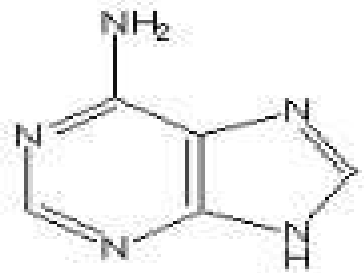
The generic nucleotide molecule looked like this:



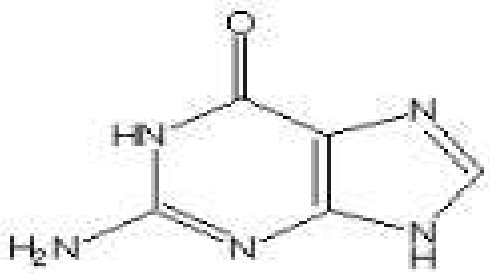
NUCLEIC ACIDS

Structure

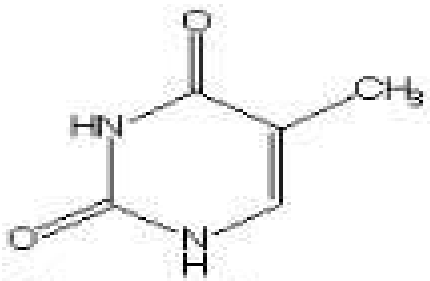
There are 5 nitrogenous bases that are used to create the polymers DNA and RNA.



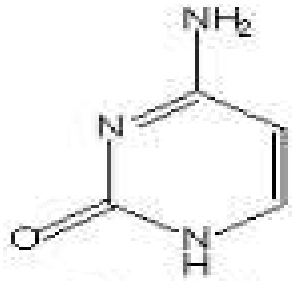
adenine



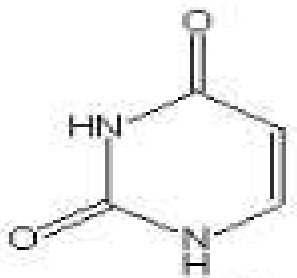
guanine



thymine



cytosine



uracil

NUCLEIC ACIDS

Function

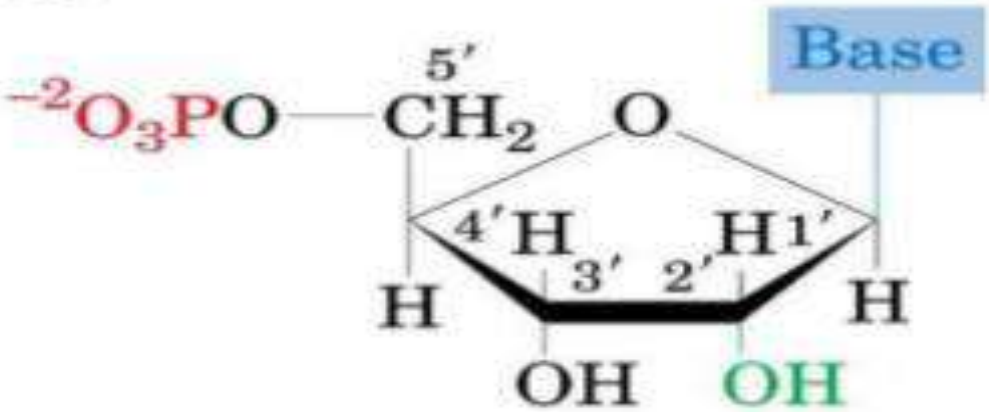
- Energy
- Storage and transfer of genetic information

NUCLEIC ACIDS

Polymers

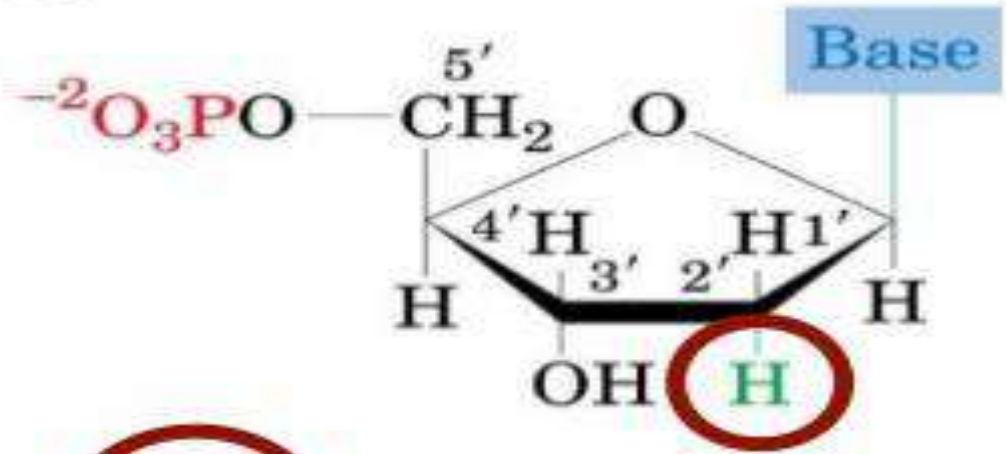
DNA and RNA:

(a)



Ribonucleotides

(b)



Deoxyribonucleotides

NUCLEIC ACIDS

Polymers

DNA and RNA:

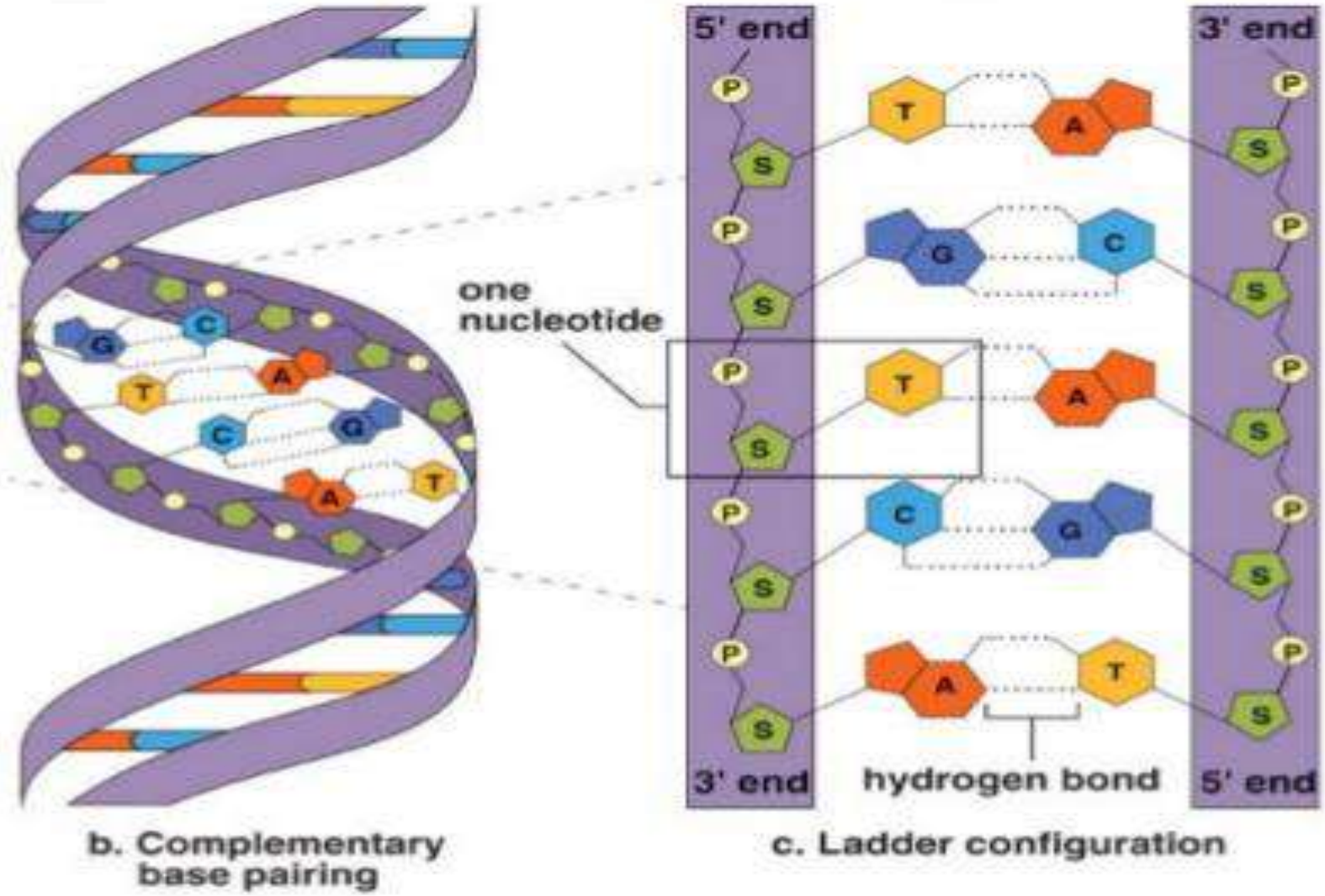
Table 2.3 DNA Structure Compared to RNA Structure

	DNA	RNA
Sugar	Deoxyribose	Ribose
Bases	Adenine, guanine, thymine, cytosine	Adenine, guanine, uracil, cytosine
Strands	Double stranded with base pairing	Single stranded
Helix	Yes	No

NUCLEIC ACIDS

Polymers

DNA:



NUCLEIC ACIDS

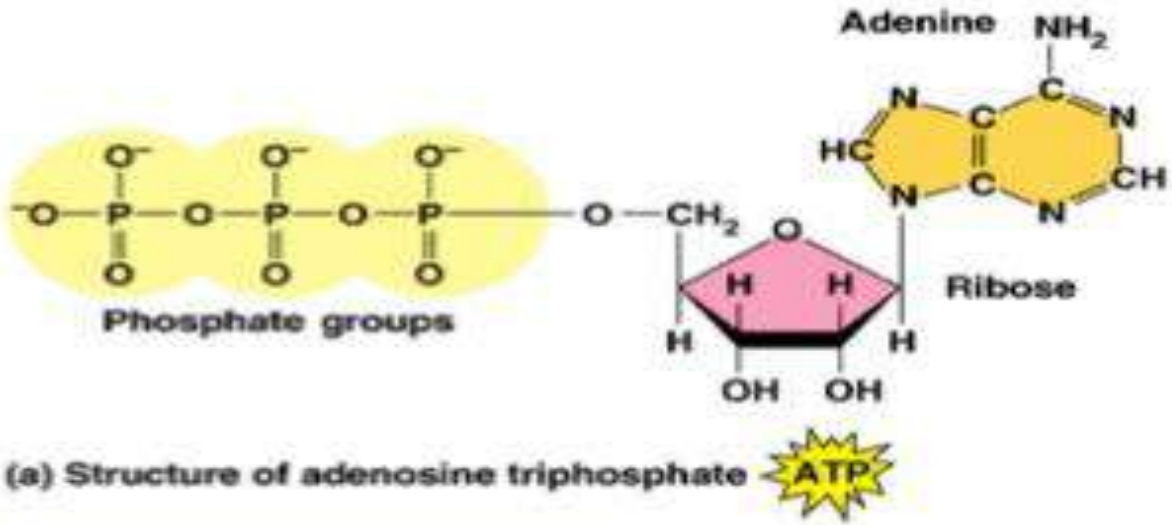
Special Nucleotide: ATP

Adenosine triphosphate (ATP) contains the nucleic acid adenine. It has 3 high energy phosphates attached.

ATP is the energy currency for the cell. When phosphates are removed, energy is released that allow for reactions to occur in the cell.

NUCLEIC ACIDS

Special Nucleotide: ATP



(a) Structure of adenosine triphosphate

Adenosine triphosphate (ATP)

Inorganic phosphate

Adenosine diphosphate (ADP)

(b) Hydrolysis of ATP