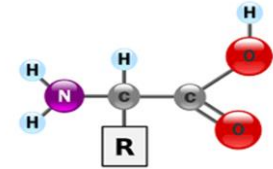


Amino Acids



- Amino Acids are the building units of proteins. Polymers of amino acids linked together by what is called “Peptide bond” (see latter).
- There are about 300 amino acids occur in nature. Only 20 of them occur in proteins.

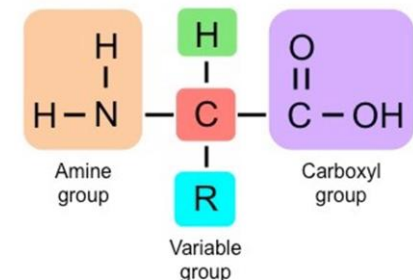
Structure of amino acids:

Each amino acid has 4 different groups attached to α - carbon (which is C-atom next to COOH). These 4 groups are : amino group, COOH gp,

Hydrogen atom and side

Chain (R)

Structure of a Generalised Amino Acid



- At physiological PH (7.4), -COOH gp is dissociated forming a negatively charged carboxylate ion (COO^-) and amino gp is protonated forming positively charged ion (NH_3^+) forming **Zwitter ion**
- N.B. Proline is an imino acid not amino acid (see latter)**

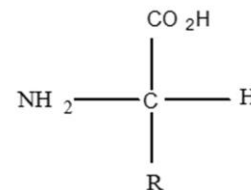
Classification of amino acids

I- Chemical classification: According to number of COOH and NH_2 groups i.e. according to net charge on amino acid.

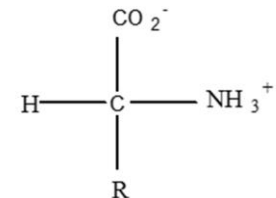
A- Monobasic, monocarboxylic amino acids i.e. neutral or uncharged:

The α -amino acids in peptides and proteins (excluding proline) consist of a carboxylic acid (-COOH) and an amino (-NH_2) functional group attached to the same tetrahedral carbon atom. This carbon is the α -carbon.

Distinct R-groups, that distinguish one amino acid from another, also are attached to the alpha-carbon (except in the case of glycine where the R-group is hydrogen). The fourth substitution on the tetrahedral α -carbon of amino acids is hydrogen.



Neutral formula

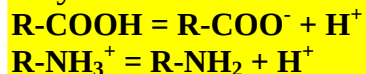


Zwitterion formula

General structure of amino acids. Neutral formula never found in the body.

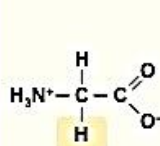
Acid-Base Properties of the Amino Acids

The α -COOH and α -NH₂ groups in amino acids are capable of ionizing (as are the acidic and basic R-groups of the amino acids). As a result of their ionizability the following ionic equilibrium reactions may be written:

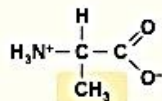


#-At physiological pH (around 7.4) the carboxyl group will be unprotonated and the amino group will be protonated. An amino acid with no ionizable R-group would be electrically neutral at this pH. This species is termed a **zwitterion**.

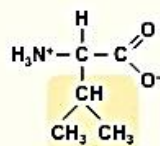
NON-POLAR



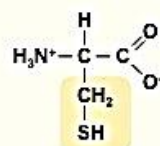
Glycine
(Gly / G)



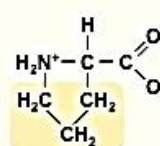
Alanine
(Ala / A)



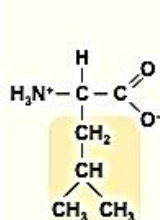
Valine
(Val / V)



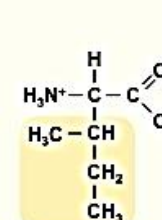
Cysteine
(Cys / C)



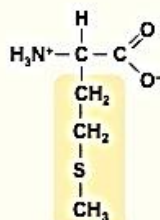
Proline
(Pro / P)



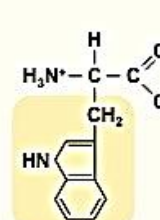
Leucine
(Leu / L)



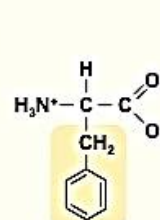
Isoleucine
(Ile / I)



Methionine
(Met / M)

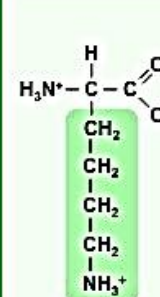


Tryptophan
(Trp / W)

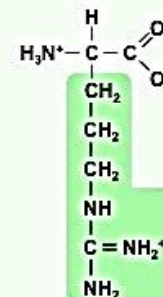


Phenylalanine
(Phe / F)

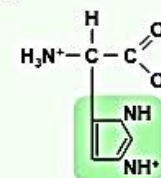
+ CHARGE



Lysine
(Lys / K)

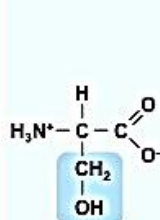


Arginine
(Arg / R)

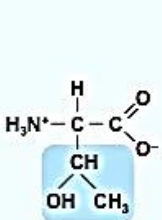


Histidine
(His / H)

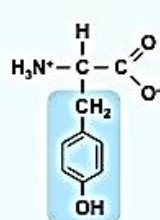
POLAR



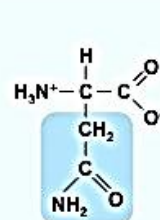
Serine
(Ser / S)



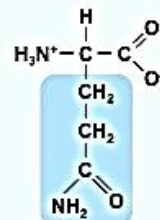
Threonine
(Thr / T)



Tyrosine
(Tyr / Y)

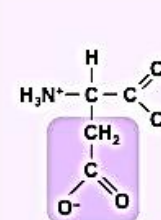


Asparagine
(Asn / N)

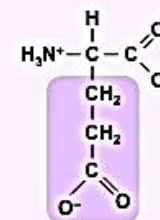


Glutamine
(Gln / Q)

- CHARGE



Aspartic Acid
(Asp / D)



Glutamic Acid
(Glu / E)

The 20 Universal Amino Acids

Subclassification of neutral amino acids:

All structures are required (See structures in hand out)

1- Glycine

R= H

2- Alanine

R= CH₃

3- Branched chain amino acids: R is branched such as in:

a- Valine R= isopropyl gp

b- Leucine R= isobutyl gp

c- Isoleucine R = is isobutyl

R is isobutyl in both leucine and isoleucine
but branching is different:

in leucine → branching occurs on γ carbon
in isoleucine → branching occurs on β- carbon

4- Neutral Sulfur containing amino acids:

e.g. Cysteine and Methionine. What is cystin?

5- Neutral, hydroxy amino acids:

e.g. Serine and Threonine

Optical Properties of the Amino Acids

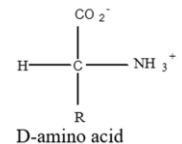
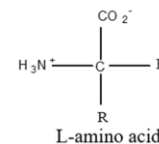
A tetrahedral carbon atom with 4 distinct constituents is said to be **chiral**. The one amino acid not exhibiting chirality is glycine.

&&-Chirality describes the handedness of a molecule that is observable by the ability of a molecule to rotate the plane of polarized light either to the right (**dextrorotatory**) or to the left (**levorotatory**).

All of the amino acids in proteins exhibit the same absolute steric configuration as **L-glyceraldehyde**. Therefore, they are all L-α-amino acids.

&&-D-amino acids are never found in proteins, although they exist in nature. D-amino acids are often found in polypeptide antibiotics.

The aromatic R-groups in amino acids absorb ultraviolet light with an absorbance maximum in the range of 280nm. The ability of proteins to absorb ultraviolet light is predominantly due to the presence of the tryptophan which strongly absorbs ultraviolet light.



6- Neutral aromatic amino acids:

a- Phenyl alanine : It's alanine in which one hydrogen of CH_3 is substituted with phenyl group. So it's called phenyl alanine

b- Tyrosine: - it is P- hydroxy phenyl alanine

- it is classified as **phenolic amino acid**

c-Tryptophan: as it contains indole ring so it is classified as **heterocyclic amino acid**

7- Neutral heterocyclic amino acids:

a- Tryptophan: contains indole ring

b- Proline: In proline, amino group enters in the ring formation being α -imino gp so proline is an α -imino acid rather than α -amino acid

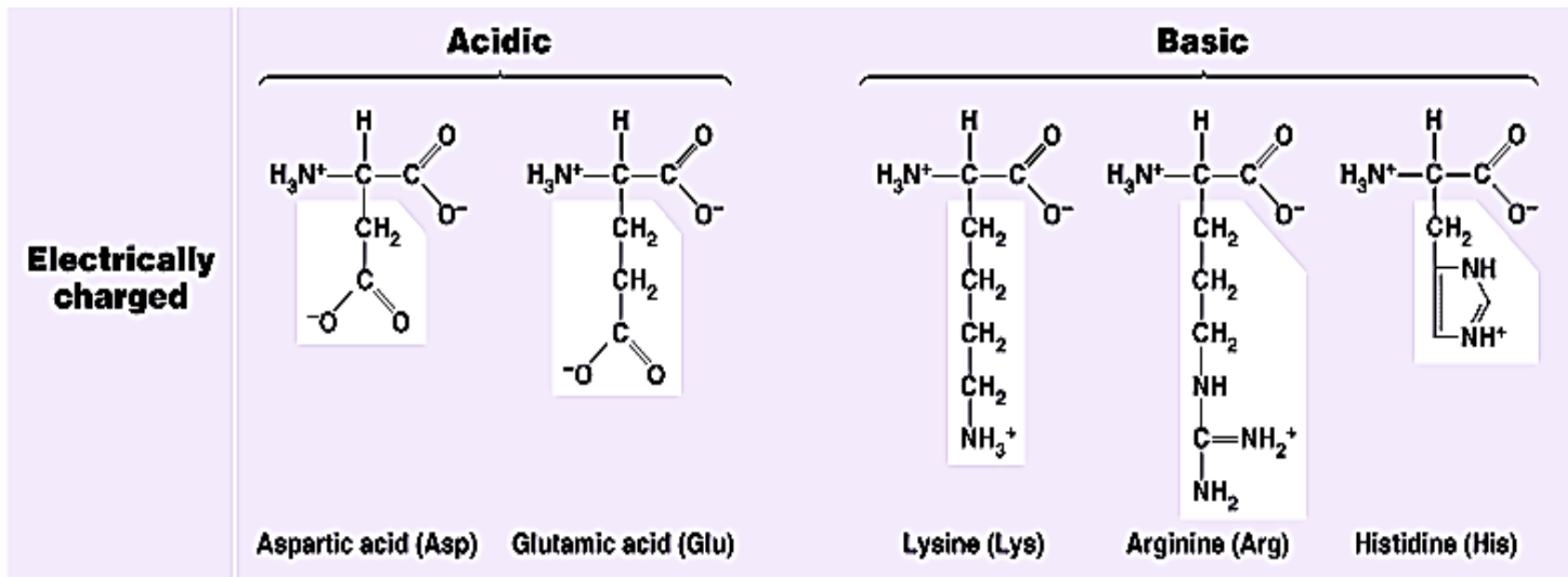
B- Basic amino acids: Contain two or more NH_2 groups or nitrogen atoms that act as base i.e. can bind proton.

At physiological pH, basic amino acids will be **positively charged** e.g.

a- Lysine

b-Arginine: contains guanido group

c-Histidine: is an example on basic heterocyclic amino acids



C- Acidic Amino acids: at physiological pH will carry negative charge.

e.g. Aspartic acid (aspartate) and Glutamic acid (glutamate). see structures in hand out.

Asparagine and Glutamine: They are amide forms of aspartate and glutamate in which side chain COOH groups are amidated. They are classified as neutral amino acids.

II- Classification according to polarity of side chain (R):

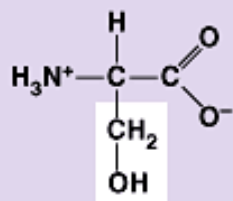
A- Polar amino acids: in which **R** contains polar **hydrophilic group** so can form hydrogen bond with H_2O . In those amino acids, **R** may contain:

- 1- OH group : as in serine, threonine and tyrosine
- 2- SH group : as in cysteine
- 3- amide group: as in glutamine and asparagine
- 4- NH_2 group or nitrogen act as a base (basic amino acids): as lysine, arginine and histidine
- 5- $COOH$ group (acidic amino acids): as aspartic and glutamic .

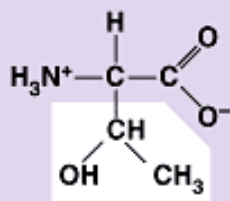
B- Non polar amino acids:

R is alkyl **hydrophobic group** which can't enter in hydrogen bond formation. **9 amino acids** are non polar (glycine, alanine, valine, leucine, isoleucine, phenyl alanine, tryptophan, proline and methionine)

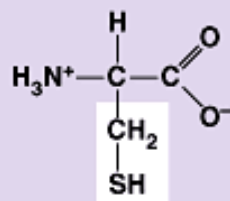
Polar



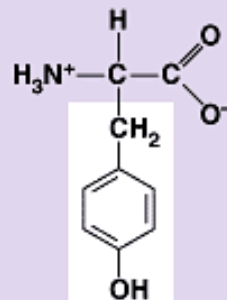
Serine (Ser)



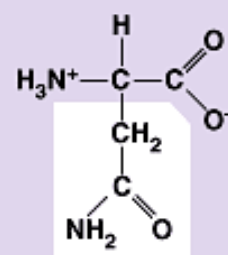
Threonine (Thr)



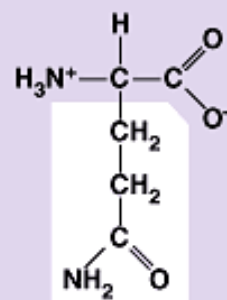
Cysteine (Cys)



Tyrosine (Tyr)

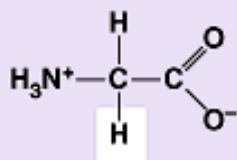


Asparagine (Asn)

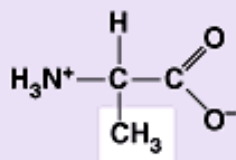


Glutamine (Gln)

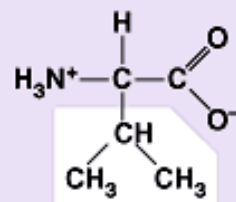
Nonpolar



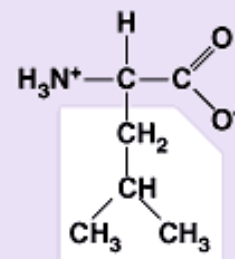
Glycine (Gly)



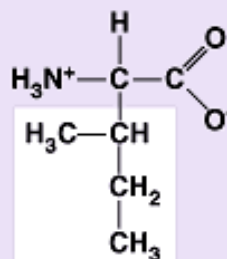
Alanine (Ala)



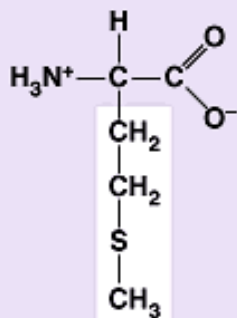
Valine (Val)



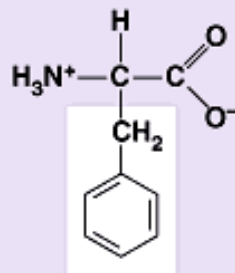
Leucine (Leu)



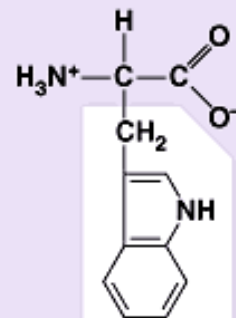
Isoleucine (Ile)



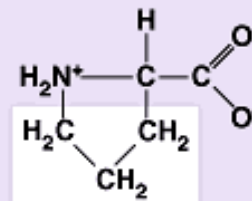
Methionine (Met)



Phenylalanine (Phe)



Tryptophan (Trp)



Proline (Pro)

III- Nutritional classification:

1-Essential amino acids: These amino acids can't be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.

2-Semiessential amino acids: These are formed in the body but not in sufficient amount for body requirements especially in children.

Summary of essential and semiessential amino acids:

V= valine i= isoleucine l= lysine l= leucine

A = arginine* H= histidine* M= methionine

T= tryptophan Th= threonine P= phenyl alanine

***= arginine and histidine are semiessential**

3-Non essential amino acids: These are the rest of amino acids that are formed in the body in amount enough for adults and children. They are the remaining 10 amino acids.

IV- Metabolic classification: according to metabolic or degradation products of amino acids they may be:

1- Ketogenic amino acids: which give ketone bodies. **Lysine** and **Leucine** are the only pure ketogenic amino acids.

2- Mixed ketogenic and glucogenic amino acids: which give both ketonbodies and glucose. These are: **isoleucine, phenyl alanine, tyrosine and tryptophan.**

3- Glucogenic amino acids: Which give **glucose**. They include the rest of amino acids. These amino acids by catabolism yields products that enter in **glycogen and glucose formation**.

Amphoteric properties of amino acids: that is they have both basic and acidic groups and so can act as base or acid.

Neutral amino acids (monobasic, monocarboxylic) exist in aqueous solution as “ Zwitter ion” i.e. contain both positive and negative charge. Zwitter ion is electrically neutral and can't migrate into electric field.

Isoelectric point (IEP) = is the pH at which the zwitter ion is formed.

e.g IEP of alanine is 6

Chemical properties of amino acids:

1- Reactions due to COOH group:

-Salt formation with alkalis, ester formation with alcohols, amide formation with amines and decarboxylation

2- Reactions due to NH₂ group:

deamination and reaction with ninhydrin reagent.

-Ninhydrin reagent reacts with amino group of amino acid yielding blue colored product. The intensity of blue color indicates quantity of amino acids present. Ninhydrine can react with imino acids as proline and hydroxy proline but gives **yellow color.**

3- Reactions due to side chain (R):

- 1- **Millon reaction:** for tyrosine gives red colored mass
- 2- **Rosenheim reaction:** for trptophan and gives violet ring.
- 3- **Pauly reaction:** for imidazole ring of histidine: gives yellow to reddish product
- 4- **Sakagushi test:** for guanido group of arginine and gives red color.
- 5- **Lead sulfide test (sulfur test):** for sulfur containing amino acids as cysteine give brown color.

Fate of α -amino group:

Q/ what is the fate of α -amino group?

A/ In times of dietary surplus, the potentially toxic nitrogen of amino acids is eliminated

1-Transamination to other α -keto acids. 2-Glutamate by oxidative demination releases free amino group to produce α -ketoglutarate (α -KG) 3- $(-\text{NH}_4^+)$ converted into urea by urea cycle.

Peptides and Proteins

20 amino acids are commonly found in protein.

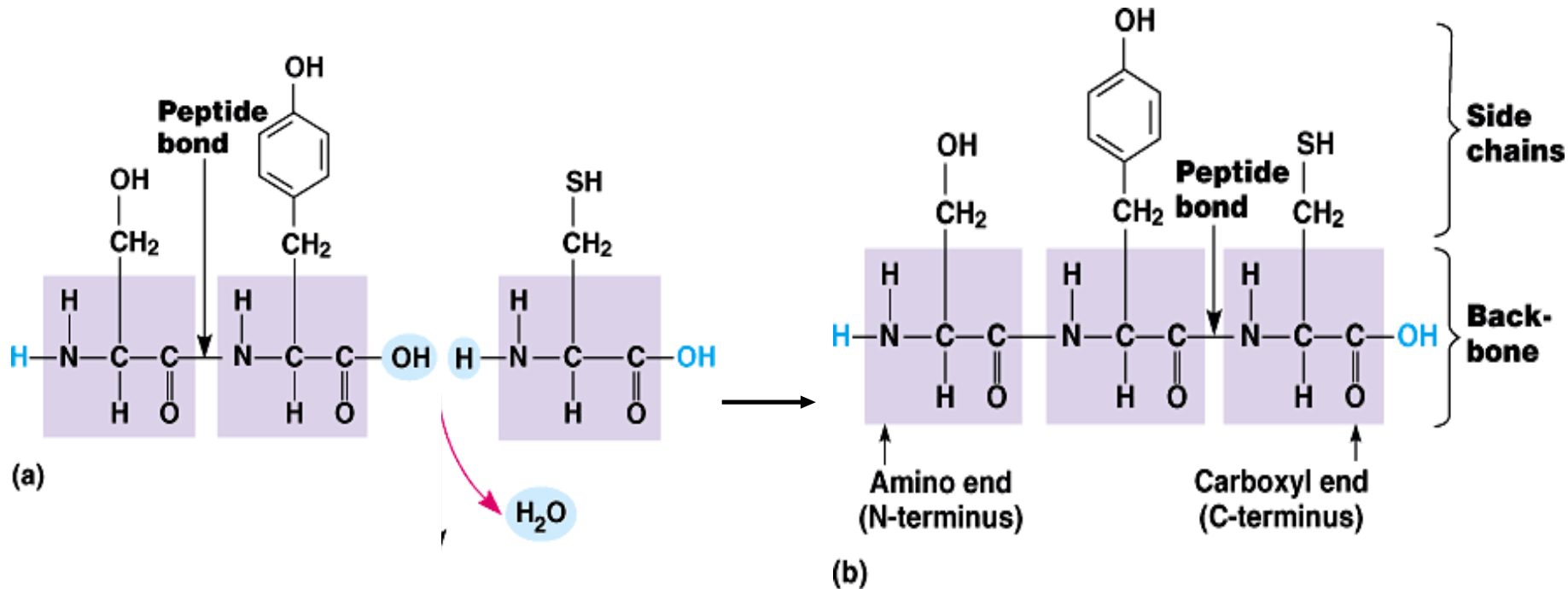
These 20 amino acids are linked together through “peptide bond forming peptides and proteins (what’s the difference?).

- The chains containing less than 50 amino acids are called “peptides”, while those containing greater than 50 amino acids are called “proteins”.

Peptide bond formation:

α -carboxyl group of one amino acid (with side chain R1) forms a covalent peptide bond with α -amino group of another amino acid (with the side chain R2) by removal of a molecule of water. The result is : **Dipeptide** (i.e. Two amino acids linked by one peptide bond). By the same way, the dipeptide can then forms a second peptide bond with a third amino acid (with side chain R3) to give **Tripeptide**. Repetition of this process generates a polypeptide or protein of specific amino acid sequence.

Peptide bond formation:



- Each polypeptide chain starts on the left side by free amino group of the first amino acid enter in chain formation . It is termed (N-terminus).
- Each polypeptide chain ends on the right side by free COOH group of the last amino acid and termed (C-terminus).

***Importance of Peptides:**

1. A number of hormones (e.g. Insulin) and some neurotransmitters are peptides.
2. Several antibiotics (e.g. Gramacidin and Valinomycin) are peptides.
3. Some antitumor agents are peptides (e.g. Bleomycin).

#-The presence of the carbonyl group in a peptide bond allows electron resonance stabilization to occur such that the peptide bond exhibits rigidity not unlike the typical $-C=C-$ double bond. The peptide bond is, therefore, said to have **partial**

Examples on Peptides:

1- Dipeptide (tow amino acids joined by one peptide bond):

Example: Aspartame which acts as **sweetening agent** being used in replacement of cane sugar. It is composed of **aspartic acid** and **phenyl alanine**.

2- Tripeptides (3 amino acids linked by two peptide bonds).

Example: GSH which is formed from 3 amino acids: **glutamic acid**, **cysteine** and **glycine**. It helps in absorption of amino acids, protects against hemolysis of RBC by breaking H_2O_2 which causes cell damage.

3- octapeptides: (8 amino acids)

Examples: Two hormones; oxytocine and vasopressin (ADH).

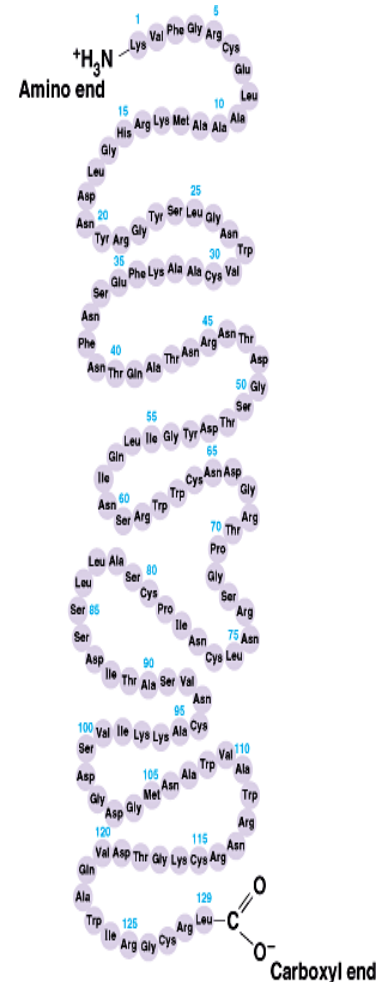
4- polypeptides: 10- 50 amino acids: e.g. Insulin hormone

Protein structure:

There are four levels of protein structure (primary, secondary, tertiary and quaternary), Protein is a polymer of more than 100 amino acids. Each of them is called residue. There are 4 basic levels of structure in protein architecture.

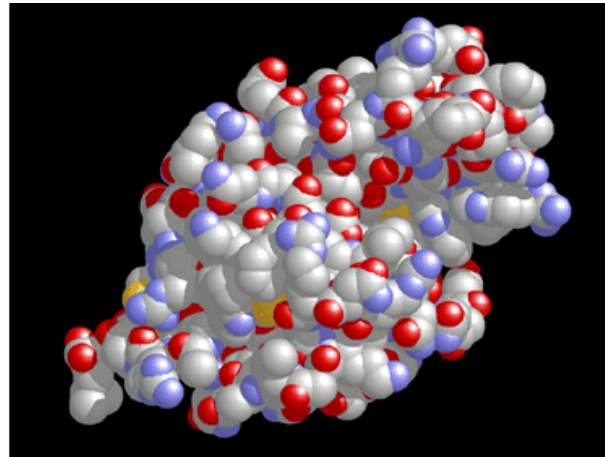
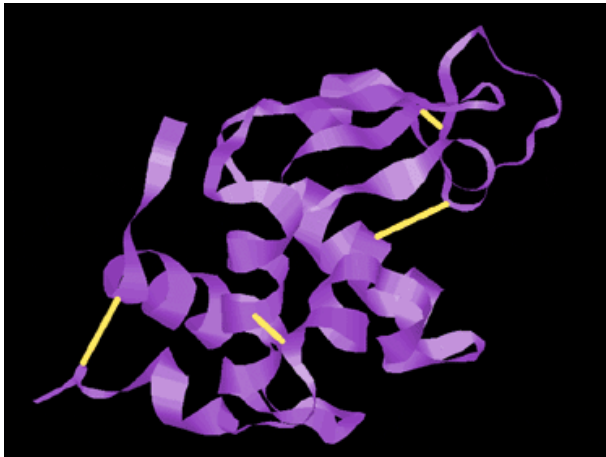
Primary structure:

- The **primary structure** of a protein is its unique sequence of amino acids.
 - Lysozyme, an enzyme that attacks bacteria, consists of a polypeptide chain of 129 amino acids.
 - The precise primary structure of a protein is determined by inherited genetic information.
 - At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group (the C-terminus).



High orders of Protein structure

- A **functional protein** is **not just** a polypeptide chain, but **one or more** polypeptides precisely **twisted, folded and coiled** into a molecule of unique shape (**conformation**). This conformation is essential for some protein function e.g. Enables a protein to recognize and bind specifically to another molecule e.g. hormone/receptor; enzyme/substrate and antibody/antigen.

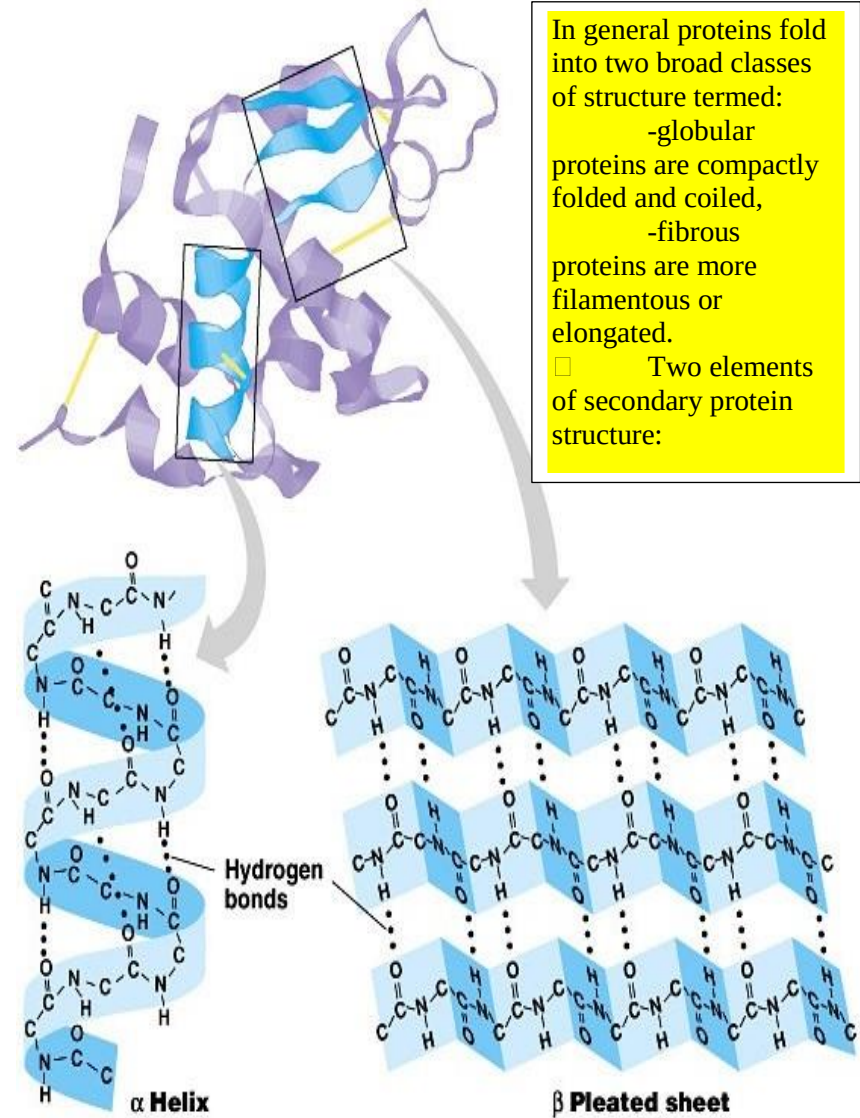


2- Secondary structure:

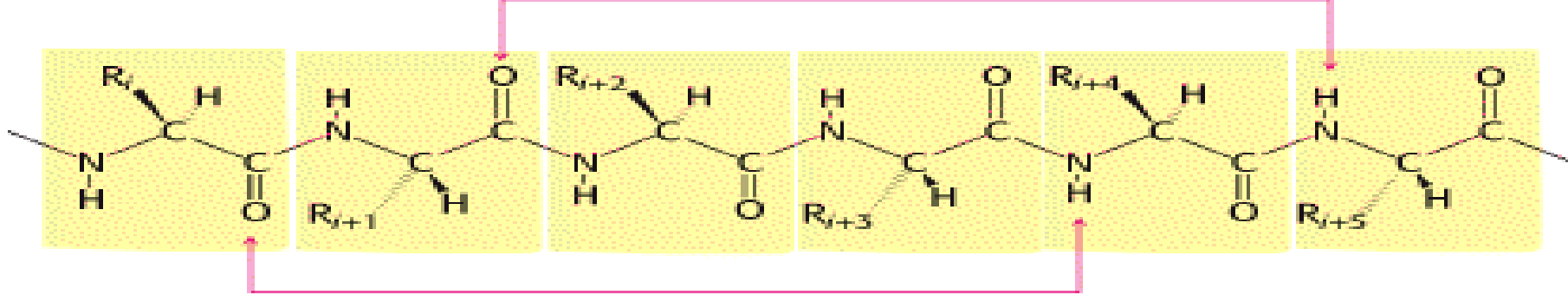
Results from hydrogen bond formation between hydrogen of -NH group of peptide bond and the carbonyl oxygen of another peptide bond. According to H-bonding there are two main forms of secondary structure:

α -helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one.

β -sheets: is another form of secondary structure in which two or more polypeptides (or segments of the same peptide chain) are linked together by hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain (or segment).



- α -Helix: Right-handed helix with 3.6 amino acid residues per turn. Hydrogen bonds are formed parallel to the helix axis.
- β -Sheet: A parallel or antiparallel arrangement of the polypeptide chain. Hydrogen bonds are formed between the two (or more) polypeptide strands.
- β -Turn: A structure in which the polypeptide backbone folds back on itself. Turns are useful for connecting helices and sheets.
- □ β -Sheets are either parallel or antiparallel.



Hydrogen bonding in α -helix: In the α -helix CO of the one amino acid residue forms H-bond with NH of the fourth one.

Supersecondary structure or Motifs :

occurs by combining secondary structure.

The combination may be: α -helix- turn- α -helix- turn.....etc

Or: β -sheet -turn- β -sheet-turn.....etc

Or: α -helix- turn- β -sheet-turn- α -helix

Turn (or bend): is short segment of polypeptides (3-4 amino acids) that connects successive secondary structures.

e.g. β -turn: is small polypeptide that connects successive strands of β - sheets.

- **Tertiary structure**

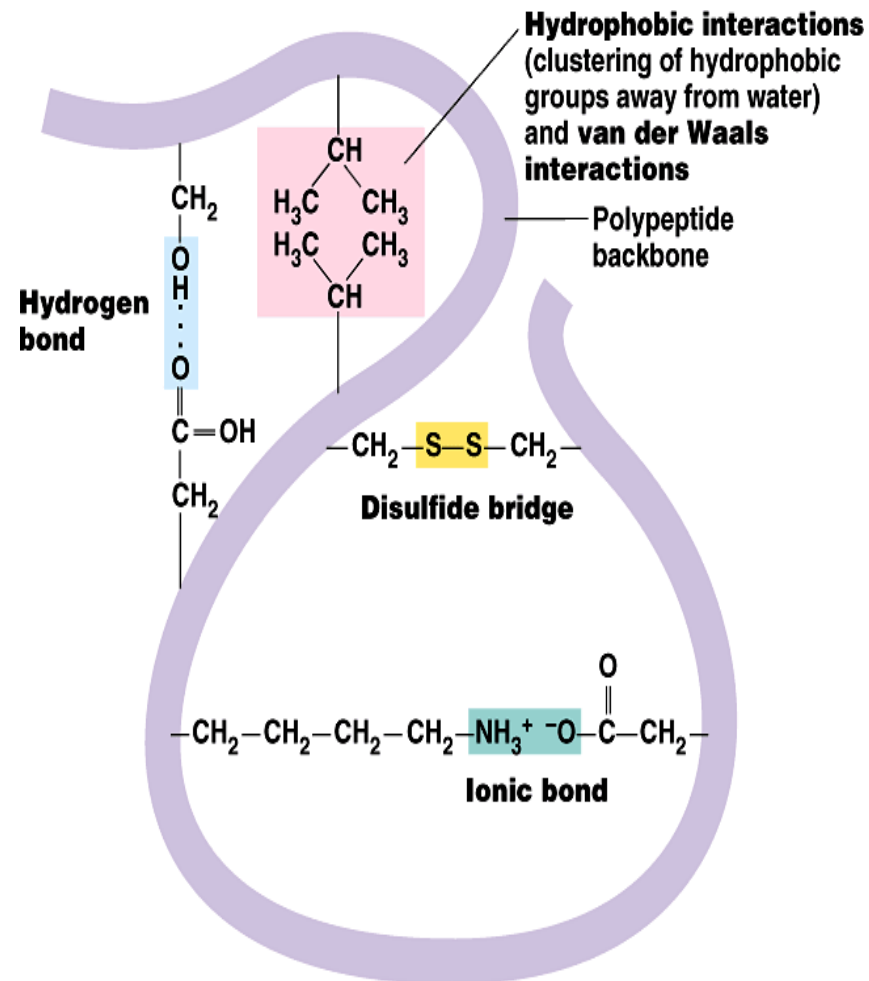
Is determined by a variety of interactions (bond formation) among R groups and between R groups and the polypeptide backbone.

a. **The weak interactions** include:

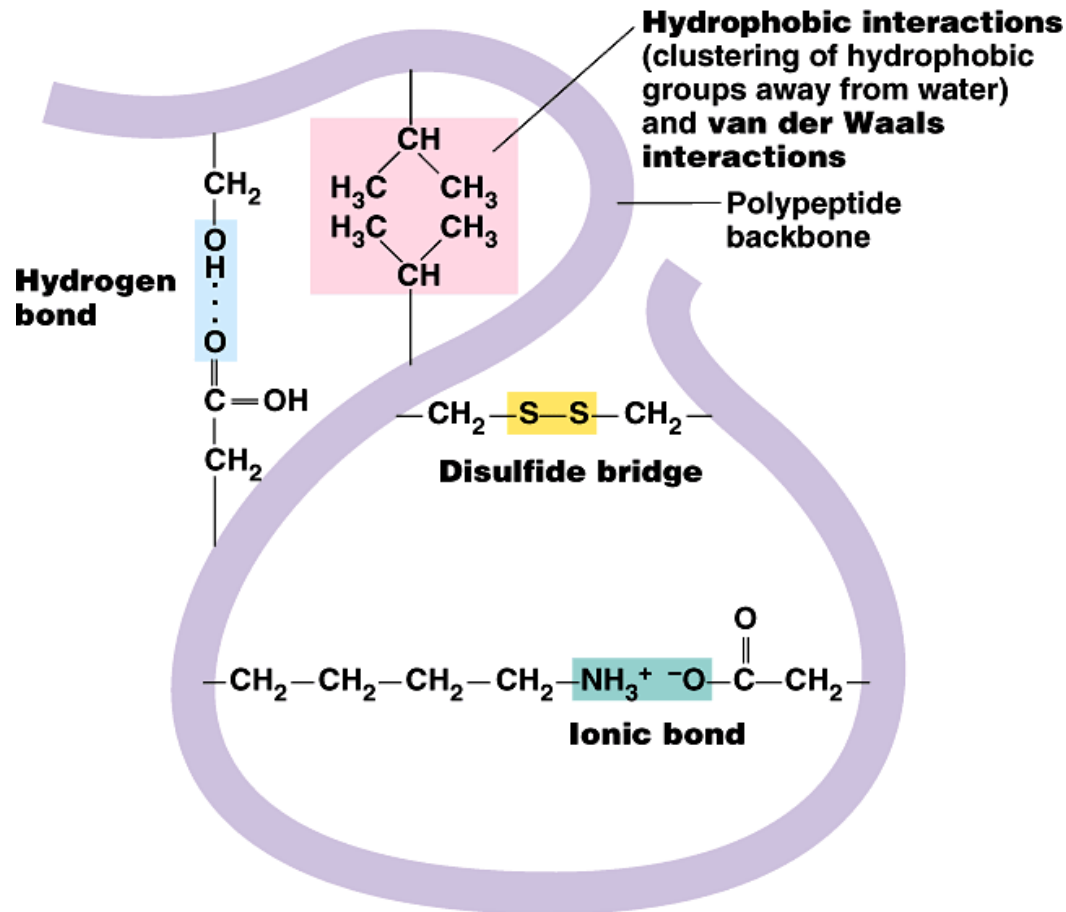
- **Hydrogen bonds** among polar side chains

- **Ionic bonds** between charged R groups (basic and acidic amino acids)

- **Hydrophobic interactions** among hydrophobic (non polar) R groups.

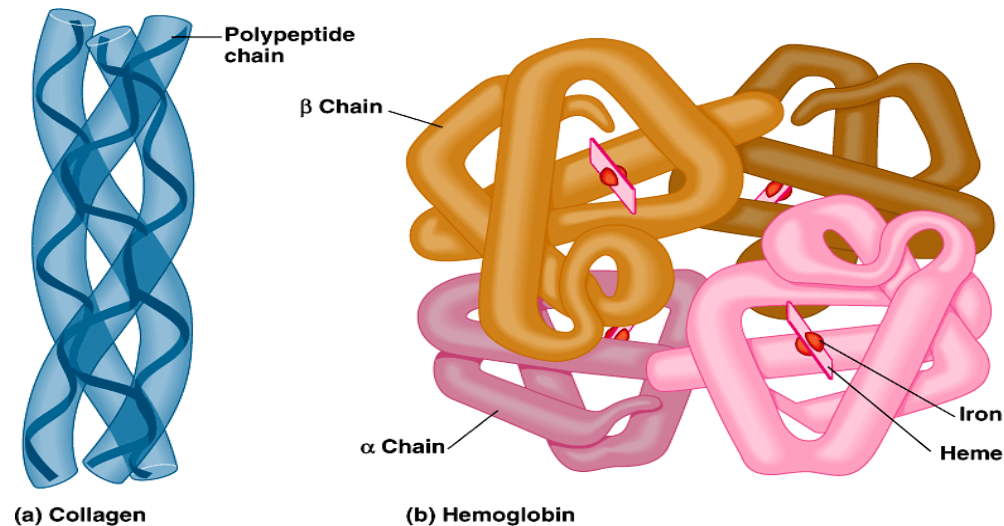


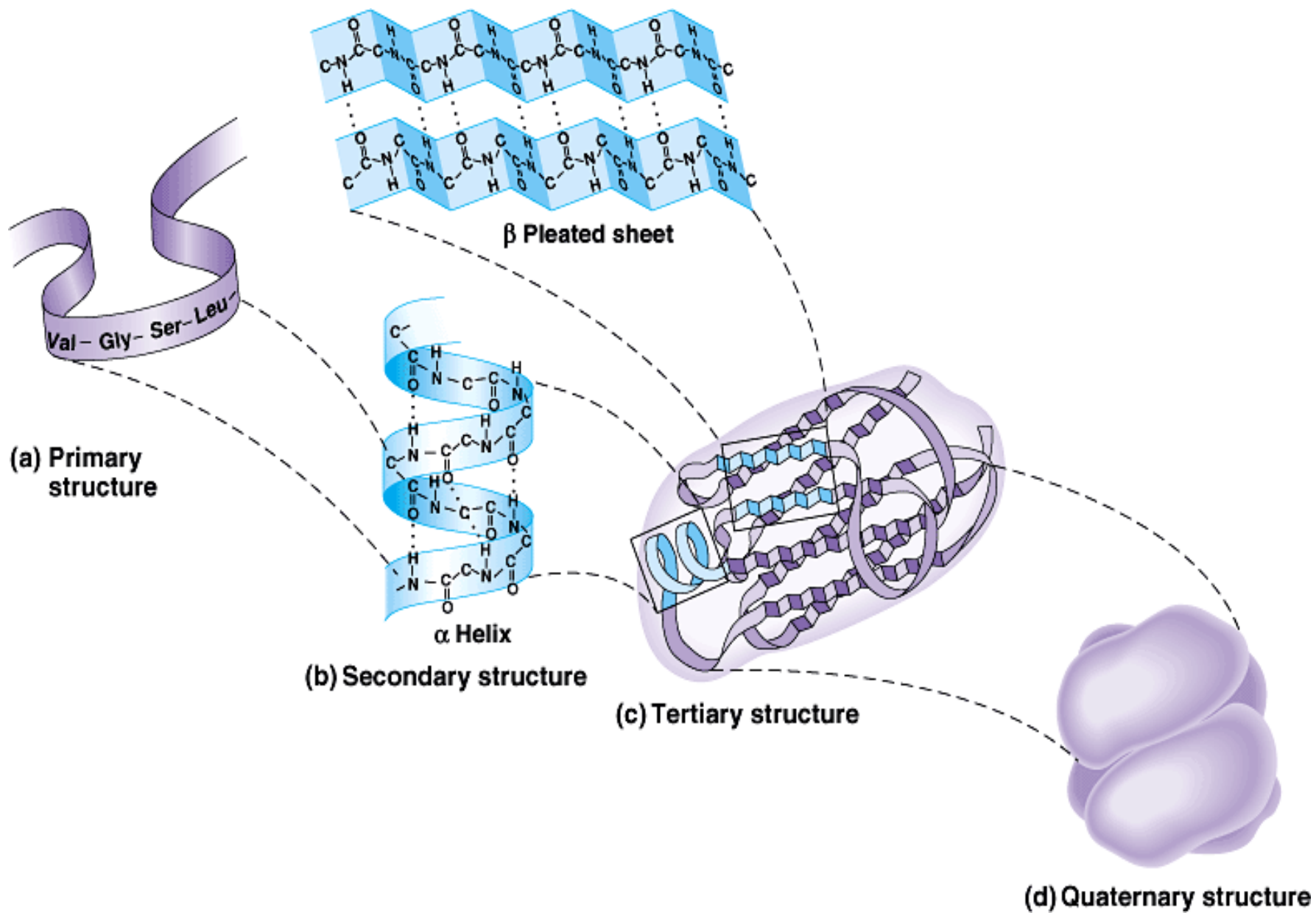
b. Strong covalent bonds include **disulfide bridges**, that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.



Quaternary structure: results from the aggregation (combination) of two or more polypeptide subunits held together by non-covalent interaction like H- bonds, ionic or hydrophobic interactions.

- Examples on protein having quaternary structure:
 - **Collagen** is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.
 - This provides the structural strength for their role in connective tissue.
 - **Hemoglobin** is a globular protein with four polypeptide chains (tetrameric)
 - **Insulin**: two polypeptide chains (dimeric)





Classification of proteins

I- Simple proteins:

i.e. on hydrolysis gives only amino acids **Examples:**

1- Albumin and globulins: present in egg, milk and blood

They are proteins of high biological value i.e. contain all essential amino acids and easily digested.

Types of globulins:

α 1 globulin: e.g. antitrypsin: see later

α 2 globulin: e.g. hepatoglobin: protein that binds hemoglobin to prevent its excretion by the kidney

β -globulin: e.g. transferrin: protein that transport iron

γ -globulins = **Immunoglobulins** (antibodies): responsible for immunity.

Protein Functions:

1. Enzyme catalysis: e.g. All enzymes that catalyze cell reactions are proteins.
2. Transport and storage: Hemoglobin transport oxygen, Ferritin store iron.
3. Coordinated motions: e.g. muscles contain two motion proteins (myosin and actin)
4. Mechanical support: e.g. collagen (a fibrous protein)
5. Immune and Protection: e.g. Antibodies (immunoglobulin-A,-G,-M, and-E)
6. Generation and transmission of nerve pulses: e.g. Rhodopsin (a light-sensitive protein in retinal rod cells).
7. Control of growth and differentiation: e.g. (Hormones: insulin, growth hormone...)

2- Globins (Histones): They are basic proteins rich in histidine amino acid.

They are present in : a - combined with DNA
 b - combined with heme to form hemoglobin of RBCs.

3-Gliadines are the proteins present in cereals.

4-Scleroproteins: They are structural proteins, not digested.
 include: keratin, collagen and elastin.

α -keratin: protein found in hair, nails, enamel
 of teeth and outer layer of skin.

a-It is α -helical polypeptide chain, rich in cysteine and hydrophobic (non polar) amino acids so it is water insoluble.

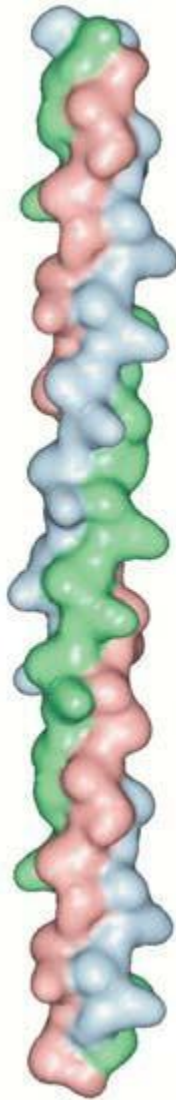


b- collagens: protein of connective tissues found in bone, teeth,
 cartilage, tendons, skin and blood vessels.

- Collagen may be present as gel e.g. in extracellular matrix or in vitreous humor of the eye.
- Collagens are the most important protein in mammals. They form about 30% of total body proteins.
- There are more than 20 types of collagens, the most common type is **collagen I** which constitutes about 90% of cell collagens.

- **Structure of collagen:** three helical polypeptide chains (trimeric) twisted around each other forming triplet-helix molecule.

- $\frac{1}{3}$ of structure is glycine, 10% proline, 10% hydroxyproline and 1% hydroxylysine. Glycine is found in every third position of the chain. The repeating sequence –Gly-X-Y–, where X is frequently proline and Y is often hydroxyproline and can be hydroxylysine.



Solubility: collagen is insoluble in all solvents and not digested.

- When collagen is heated with water or dil. HCl it will be converted into **gelatin** which is soluble , digestible and used as diet (as jelly). Gelatin is classified as derived protein.

Some collagen diseases:

1- Scurvy: disease due to deficiency of vitamin C which is important coenzyme for conversion of proline into hydroxyproline and lysine into hydroxylysine. Thus, synthesis of collagen is decreased leading to abnormal bone development, bleeding, loosening of teeth and swollen gum.

2- Osteogenesis Imperfecta (OI): Inherited disease resulting from genetic deficiency or mutation in gene that synthesizes collagen type I leading to abnormal bone formation in babies and frequent bone fracture in children. It may be lethal.

C- Elastin: present in walls of large blood vessels (such as aorta).

It is very important in lungs, elastic ligaments, skin, cartilage,
It is elastic fiber that can be stretched to several times as its normal length.

Structure: composed of 4 polypeptide chains (tetramer), similar to collagen being having 33% glycine and rich in proline but in that it has low hydroxyproline and absence of hydroxy lysine.

Emphysema: is a chronic obstructive lung disease (obstruction of air ways) resulting from deficiency of α 1-antitrypsin particularly in cigarette smokers.

Role of α 1-antitrypsin: Elastin is a lung protein. Smoke stimulate

enzyme called elastase to be secreted from neutrophils (in lung). Elastase cause destruction of elastin of lung.

α 1-antitrypsin is an enzyme (secreted from liver) and inhibit elastase and prevent destruction of elastin. So deficiency of α 1-antitrypsin especially in smokers leads to degradation of lung and destruction of lung (loss of elasticity of lung, a disease called emphysema).

Conjugated proteins

i.e. On hydrolysis, give protein part and non protein part and subclassified into:

1- Phosphoproteins: These are proteins conjugated with phosphate group. Phosphorus is attached to oh group of serine or threonine.
e.g. Casein of milk and vitellin of yolk.

2- Lipoproteins:

These are proteins conjugated with lipids.

Functions: a- help lipids to transport in blood
b- Enter in cell membrane structure helping lipid soluble substances to pass through cell membranes.

3- Glycoproteins:

proteins conjugated with sugar (carbohydrate)

e.g. – Mucin

- Some hormones such as erythropoietin
- present in cell membrane structure
- blood groups.

4- Nucleoproteins: These are basic proteins (e.g. histones) conjugated with nucleic acid (DNA or RNA).

e.g. a- chromosomes: are proteins conjugated with DNA

b- Ribosomes: are proteins conjugated with RNA

5- Metalloproteins: These are proteins conjugated with metal like iron, copper, zinc, ...

- a- Iron-containing proteins:** Iron may present in heme such as in
- hemoglobin (Hb)
 - myoglobin (protein of skeletal muscles and cardiac muscle),
 - cytochromes,
 - catalase, peroxidases (destroy H_2O_2)
 - tryptophan pyrrolase (destroy indole ring of tryptophan).

Iron may be present in free state (not in heme) as in:

- **Ferritin:** Main store of iron in the body. ferritin is present in liver, spleen and bone marrow.
- **Hemosidrin:** another iron store.
- **Transferrin:** is the iron carrier protein in plasma.

b- Copper containing proteins:

- e.g. - Ceruloplasmin which oxidizes ferrous ions into ferric ions.
- Oxidase enzymes such as cytochrome oxidase.

c- Zn containing proteins: e.g. Insulin and carbonic anhydrase

d- Mg containing proteins:e.g. Kinases and phosphatases.

Chromoproteins: These are proteins conjugated with pigment. e.g.

- All proteins containing heme (Hb, myoglobin, ...)
- - Melanoprotein:e.g proteins of hair or iris which contain melanin.

Derived proteins

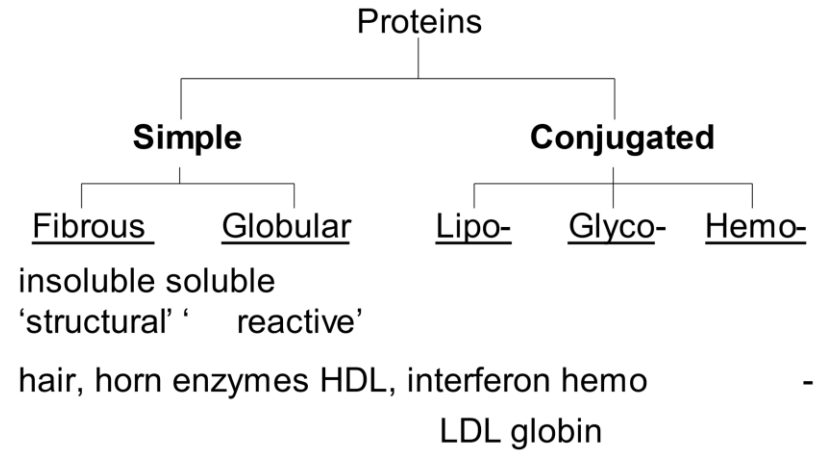
Produced from hydrolysis of simple proteins.

- e.g. - Gelatin: from hydrolysis of collagen
- Peptone: from hydrolysis of albumin

PROTEIN DENATURATION

- Heat
- Mechanical agitation
- pH change
- Inorganic salts
- polar organic solvents
- Soaps and detergents

Proteins by Structure



Proteins by Structure

Fibrous

Collagens

bones lungs hair/feathers muscles
tendons ligaments horn/nails
cartilage

Elastins

Keratins

Myosins

Proteins by Structure

Globular

Albumins

egg whites antibodies(γ

Globulins

enzymes -globulin)

Proteins by Function

Enzymes	- the biological catalysts
Contractile	- muscle
Hormones	- insulin, growth hormone
Neurotransmitters	- endorphins
Storage	- store nutrients, eg. seeds, casein in milk
Transport	- hemoglobin
Structural	- collagen, keratins
Protective	- antibodies
Toxins	- snake venom, botulinum

Role of protein in the: cornea, lens , retina The lenses in the eyes are built of long cells, this means crystalline cells are elongated. The cells are deprived of cell nuclei and mitochondria. This leaves the protein to be a smooth and transparent solution. The crystalline proteins are of three types: alpha, beta, and gamma. The crystalline solutions in the eyes are the mixture of all three. Crystalline is a water-soluble structural protein, found in the lens and the cornea of the eye accounting for the transparency of the structure. The crystallins are water-soluble structural proteins that occur in high concentration in

the cytoplasm of eye lens fiber cells. Four major groups of crystalline have been distinguished on the basis of size, charge and immunological properties: alpha-, beta- and gamma-crystalline occur in all vertebrate classes (though gamma-crystalline are low or absent in avian lenses); and delta-crystalline is found exclusively in reptiles and birds.

What are eye proteins called? a crystalline is a water-soluble structural protein found in the lens and the cornea of the eye accounting for the transparency of the structure. **What does the eye lens protein do?** Crystallins are the most prevalent proteins in the lens. Comprising of two families, α - and β and γ -crystallins, they make up 90% of water-soluble proteins of the mammalian lens. They are highly organized and provide a refractive index gradient, which allows for transparency of the lens.

A cataract occurs when there is a buildup of proteins in the lens, creating protein clumps. These clumps, or deposits, prevent light from passing clearly through the lens, thus disrupting normal vision. There are several reasons why a cataract may form including: Aging – The eyes mainly consist of water and protein Traumatic Cataract – Another common cause of cataracts is trauma Diabetes – People with diabetes are 60% more likely to develop cataracts. Congenital Cataract – While cataracts are normally associated with the aging process High Blood Pressure – High blood pressure (HBP) is known to cause elevated inflammation which may result in cataracts. Excessive Alcohol Consumption – Studies have shown that high alcohol consumption significantly increases the risk of cataracts.

Lipids & Lipoproteins

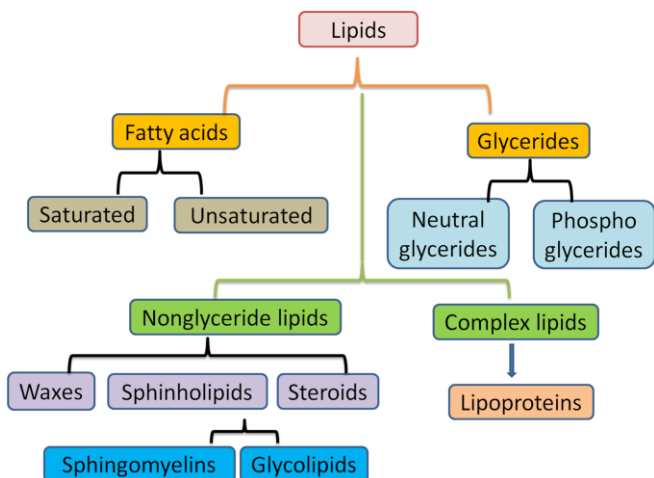
Lipids: Biological molecules that are insoluble in aqueous solutions and soluble in organic solvents are classified as lipids.

*-Neutral lipids(e.g. cholesterol esters, triglyceride..) are uncharged molecules.

Major Roles of Biological of Lipids:

1. They serve as structural components of biological membranes.
2. They provide energy reserves, predominantly in the form of triacylglycerols.
3. Both lipids and lipid derivatives serve as vitamins and hormones.
4. Lipophilic bile acids aid in lipid solubilization.
5. Serve as thermal and electrical insulator.

Classification of Lipids:



The types of lipids that we will look at include.

- Fatty Acids
 - In the carboxylic acid family
- Waxes
- Fatty Acids + Alcohols
- Triglycerides
- 3 Fatty acids + glycerol
- Phospholipids and glycolipids
- 2 fatty acids + glycerol + phosphate + X
- Steroids
- Derivatives of cholesterol
- Eicosanoids
- Derivatives of the Fatty acid arachidonic acid
- Membranes

- Formed from phospholipids and glycolipids

1-Fatty Acids:

Fatty acids are long-chain hydrocarbon molecules containing a carboxylic acid moiety at one end.

*Fatty acids fill two major roles in the body:

1. As the components of more complex membrane lipids.
2. As the major components of stored fat in the form of triacylglycerols.

* **Saturated fatty acids:** Fatty acids that contain no carbon-carbon double bonds.

* **Unsaturated fatty acids:** Fatty acids that contain double bonds.

Fatty acids may be further subdivided as follows:

(1) **Monounsaturated** (monoethenoid, monoenoic) acids, containing one double bond.

(2) **Polyunsaturated** (polyethenoid, polyenoic) acids, containing two or more double bonds.

(3) **Eicosanoids:** These compounds, derived from eicosa- (20-carbon) polyenoic fatty acids, comprise the **prostanoids**, **leukotrienes (LTs)**, and **lipoxins (LXs)**. Prostanoids include **prostaglandins (PGs)**, **prostacyclins (PGIs)**, and **thromboxanes (TXs)**.

#The site of unsaturation in a fatty acid is indicated by the symbol Δ and the number of the first carbon of the double bond (e.g. palmitoleic acid is a 16-carbon fatty acid with one site of **unsaturation** between **carbons 9** and 10, and is designated by 16:1 ^{Δ 9}).

@ Naturally occurred unsaturated FA occurs in cis-form.

@ Body can biosynthesize lipids and can supply the body with all the various fatty acid structures needed except the **essential FA**.

***Essential fatty acids;** must be provided in the diet (the highly unsaturated fatty acids: these are all **polyunsaturated fatty acids**: the **C20** fatty acid **arachidonic acid** (20:4;5,8,11,14), and the two **C18 acids** **linoleic acid** (18:2;9,12) and **linolenic acid** (18:3;9,12,15). **linoleic acid** and **linolenic acid**) because they containing unsaturation sites beyond carbons 9 and 10.

Physiologically Relevant Fatty Acids:

Numerical Symbol	Common Name	Structure	Comments
14:0	Myristic acid	$\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$	
16:0	Palmitic acid	$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$	End product of mammalian F.A. synthesis

16:1 ^{Δ₉}	Palmitoleic acid	CH ₃ (CH ₂) ₅ C=C(CH ₂) ₇ COOH	
18:0	Stearic acid	CH ₃ (CH ₂) ₁₆ COOH	
18:1 ^{Δ₉}	Oleic acid	CH ₃ (CH ₂) ₇ C=C(CH ₂) ₇ COOH Physiologically most important omega-9 monounsaturated fatty acid (MUFA)	Nonessential fatty acid
18:2 ^{Δ_{9,12}}	Linoleic acid	CH ₃ (CH ₂) ₄ C=CCH ₂ C=C(CH ₂) ₇ COOH Essential fatty acid, an omega-6 PUFA	Essential fatty acid
18:3 ^{Δ_{9,12,15}}	Linolenic acid	CH ₃ CH ₂ C=CCH ₂ C=CCH ₂ C=C(CH ₂) ₇ COOH Essential fatty acid, an omega-3 PUFA	Essential fatty acid
20:4 ^{Δ_{5,8,11,14}}	Arachidonic acid	CH ₃ (CH ₂) ₃ (CH ₂ C=C) ₄ (CH ₂) ₃ COOH An omega-6 PUFA, precursor for eicosanoid synthesis	Precursor for eicosanoid synthesis Essential fatty acid

&&Prostaglandines:

Synthesized *in vivo* by cyclation of the center of the (20C-atoms unsaturated FA that called Eicosanoic acid) to form

cyclopentane cycle. Examples of prostaglandins: thromboxane, prostaglandine 2 (PGE₂)



Figure : PEG2

2-Basic Structure of Triacylglycerides

Triacylglycerides (TG) are composed of a glycerol backbone to which 3 fatty acids are esterified. TG are the stored lipids in the **body tissues**.

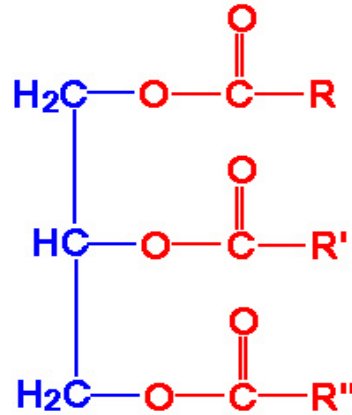


Figure: Basic composition of a triacylglyceride

3-Basic Structure of Phospholipids

The basic structure of phospholipids is very similar to that of the triacylglycerides except that C-3 of the glycerol backbone is esterified to **phosphoric acid**.

*The building block of the phospholipids is **phosphatidic acid** (X= hydrogen atom).

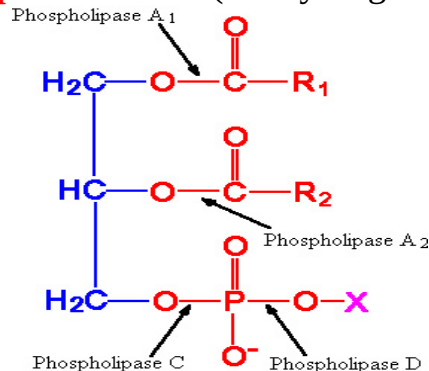
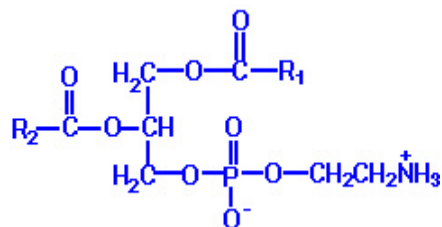
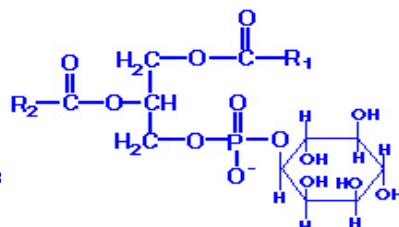


Figure: Basic composition of a phospholipid. X can be a number of different substituents.

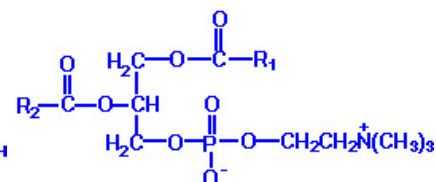
*Substitutions include ethanolamine (**phosphatidylethanolamine**), choline (**phosphatidylcholine**, also called **lecithins**), serine (**phosphatidylserine**), glycerol (**phosphatidylglycerol**), *myo*-inositol (**phosphatidylinositol**), and phosphatidylglycerol (**diphosphatidylglycerol** more commonly known as **cardiolipins**).



Phosphatidylethanolamine



Phosphatidylinositol



Phosphatidylcholine (lecithins)

4-Basic Structure of Plasmalogens

Plasmalogens are phospholipids substituted at C-1 (*sn*1) of glycerol contain either an *O*-alkyl or *O*-alkenyl ether species. One of the most potent biological molecules is **platelet activating factor**.

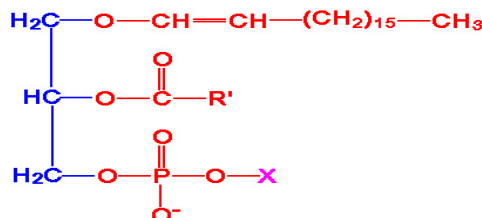


Figure: basic composition of *O*-alkenyl plasmalogens.

5-Basic Structure of Sphingolipids

*Sphingolipids are composed of a backbone of sphingosine which is derived itself from glycerol.

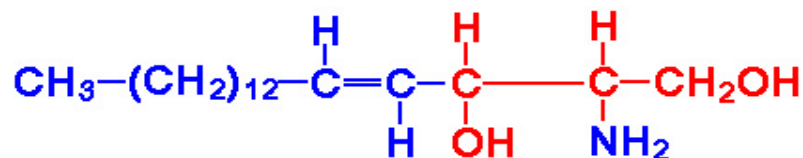
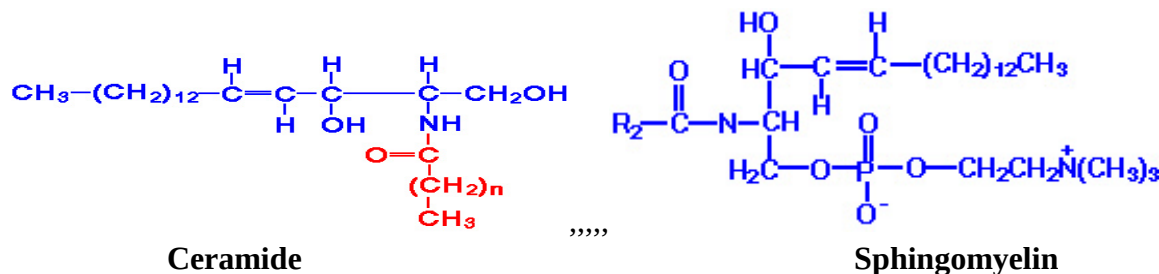


Figure: Sphingosine

* **Ceramides:** A family of molecules composed of sphingosine when N-acetylated by a variety of fatty acids. Sphingolipids predominate in the myelin sheath of **nerve fibers**.



* **Sphingomyelin** is an abundant sphingolipid generated by transfer of the phosphocholine moiety of phosphatidylcholine to a ceramide, thus sphingomyelin is a unique form of a phospholipid.

The other major class of sphingolipids (besides the sphingomyelins) are the **glycosphingolipids** generated by substitution of carbohydrates to the *sn1* carbon of the glycerol backbone of a ceramide. There are 4 major classes of glycosphingolipids:

Cerebrosides: contain a single moiety, principally galactose.

Sulfatides: sulfuric acid esters of galactocerebrosides.

Globosides: contain 2 or more sugars.

Gangliosides: similar to globosides except also contain sialic acid.

6- Steroids:

Steroids are lipids derived from the cyclopentanophenanthrene.

Cholesterol is an extremely important biological steroid: 1-Constituent of plasma membrane and lipoproteins 2-precursor for the synthesis of the **steroid hormones**, sex hormones, vitamin D, and bile acids.

- ❖ Both dietary cholesterol and that synthesized *de novo* are transported through the circulation in **lipoprotein particles**. The same is true of cholesteryl esters, the form in which cholesterol is stored in cells.

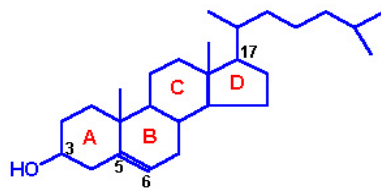


Figure: Cholesterol

Lipid Peroxidation:

It is a chain reaction providing continuous supply of free radicals ($\text{ROO}^\cdot$, $\text{RO}^\cdot$, and $\text{OH}^\cdot$) that initiates further peroxidation. This process causes **different disorders: rancidity** (auto oxidation of lipids by oxygen), **aging, cancer, atherosclerosis, inflammation, damage to tissue in vivo.**

Notes:

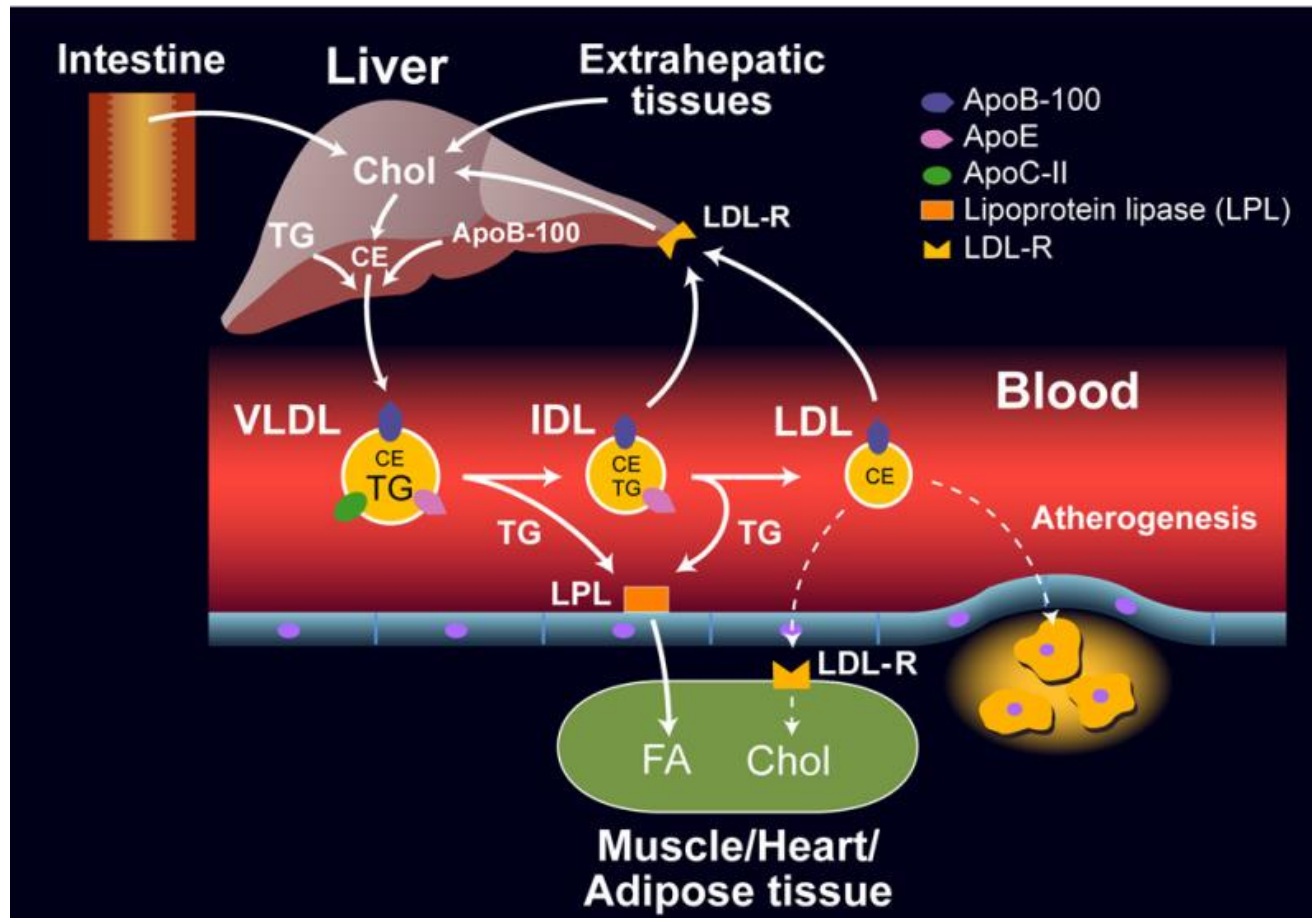
Amphipathic molecule: Part of the molecule is hydrophilic (polar) and the other is hydrophobic (non-polar). Polar group faces the water phase and the non-polar faces the hydrophobic phases (oil); this is the main feature of **plasma membrane.**

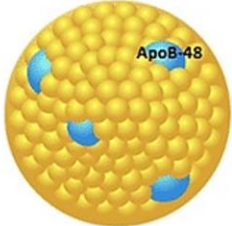
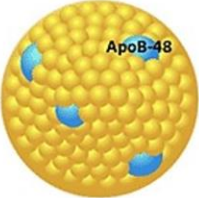
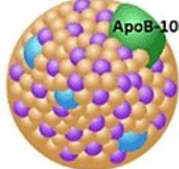
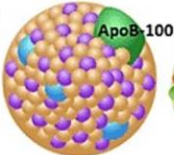
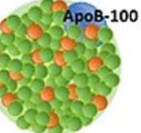
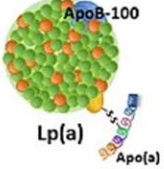
- **Micelles:** Critical concentration of polar lipids in aqueous medium.
- **Liposome:** Consist of spheres of lipid layers that enclose part of water.
- **Emulsion:** Larger particles formed by non-polar lipids in an aqueous medium.

#-Aggregation of bile salts into micelles and liposomes with the product of fat digestion are important in facilitating absorption of lipids from intestine.

Lipoproteins: Macromolecular complex of lipids and proteins. They are the transport vehicles for lipids in the circulation. There are five types of lipoproteins.

1. **Chylomicrons:** transport primarily triglycerides from the digestive track to liver.
2. **VLDL:** (Very Low-Density Lipoprotein) transport triglycerides from liver to other tissues. transport the lipids (endogenously synthesized) mainly TG from liver to peripheral tissues).
3. **IDL:** Intermediate density lipoproteins, are formed from the degradation of **very low-density lipoproteins** as well as **high-density lipoproteins**, that enable fats and cholesterol to move within the water-based solution of the bloodstream.
4. **LDLs:** (low density lipoproteins) transport cholesterol, triglycerides and phospholipids from the liver to other tissues ("**bad**" cholesterol).
5. **HDLs:** (high density lipoproteins "**good**" cholesterol) transport cholesterol and phospholipids back carry from peripheral tissues to the liver.

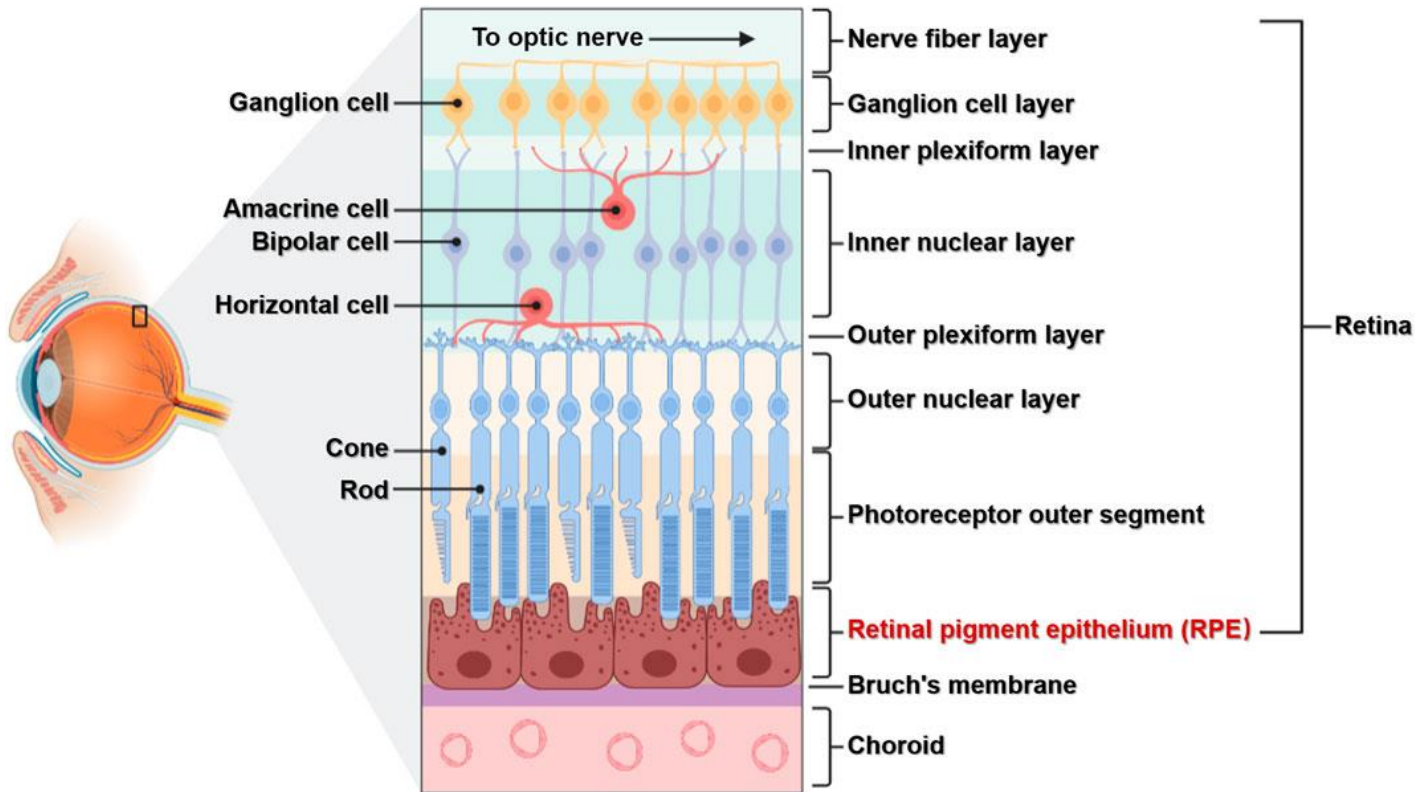


	ApoB-48		ApoB-100			Apo(a)
	- MW: 264,000 daltons - Metabolic function: assembly and secretion of CMs from the small intestine; structural protein of CMs and CM remnants		- MW: 540,000 daltons - Metabolic function: assembly and secretion of VLDL from the liver; structural protein of VLDL, IDL, LDL and Lp(a); ligand for LDL receptor			- MW: 250,000-800,000 daltons - Metabolic function: not completely defined, but it is an independent predictor of coronary artery disease
						
	CM	CM remnant	VLDL	IDL	LDL	Lp(a)
	CM	CM remnant	VLDL	IDL	LDL	Lp(a)
Source	intestine	CM	liver (intestine)	VLDL	VLDL	liver
Density (g/dl)	< 0.95	< 1.006	0.95-1.006	1.006-1.019	1.019-1.063	1.05-1.12
Diameter (nm)	75-1200	45-150	30-80	25-35	18-25	about 25
Molecular weight (daltons)	400 x10 ⁶	unknown	10-80 x10 ⁶	5-10 x10 ⁶	2.3 x10 ⁶	about 4 x10 ⁶
Structural components	99-98% total lipid and 1-2% total protein	94-92% total lipid and 6-8% total protein	93% total lipid and 7% total protein	85% total lipid and 15% total protein	80% total lipid and 20% total protein	80% total lipid and 20% total protein
Apolipoprotein composition	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E	B-48, E	B-100, C-I, C-II, C-III, E	B-100, C-I, C-II, C-III, E	B-100	B-100, Apo(a)

- Lipids are key components of the retina, and are closely associated with the aging processes.
- Omega-3 fatty acids show protective properties against inflammation and neurodegeneration in retinal aging and the development of Age-related macular degeneration (AMD).

- The eye retina is a part of the central nervous system, together with the brain and the spinal cord and as such is also naturally rich in lipids

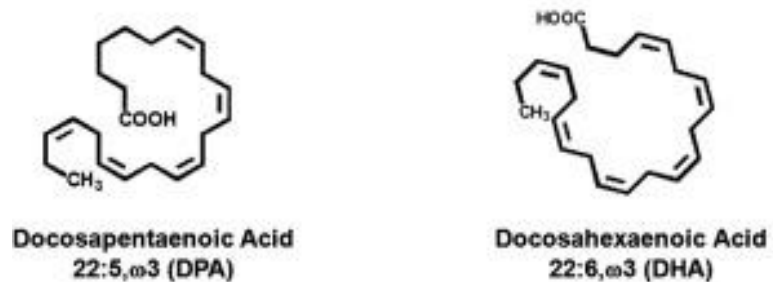
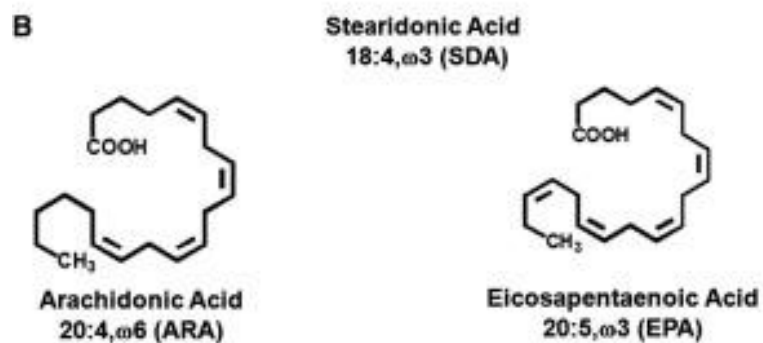
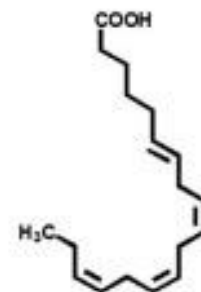
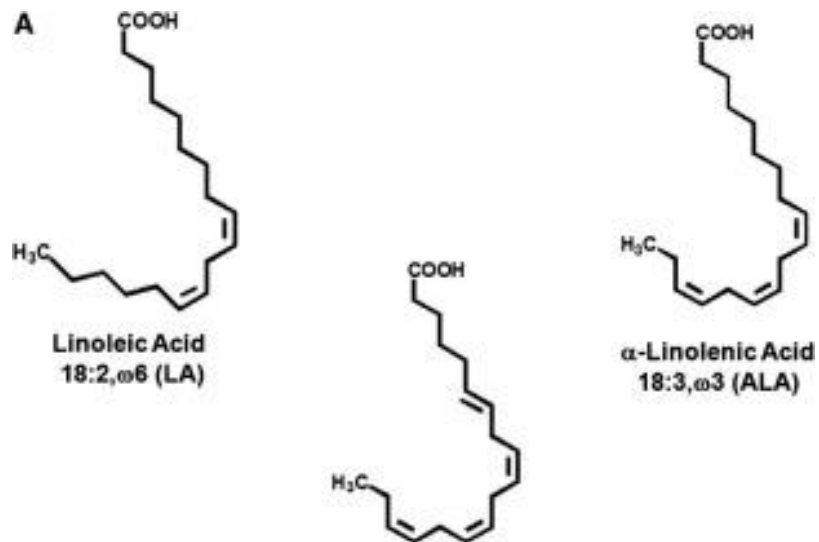
Lipids in eyes



Lipids as crucial components of the retina

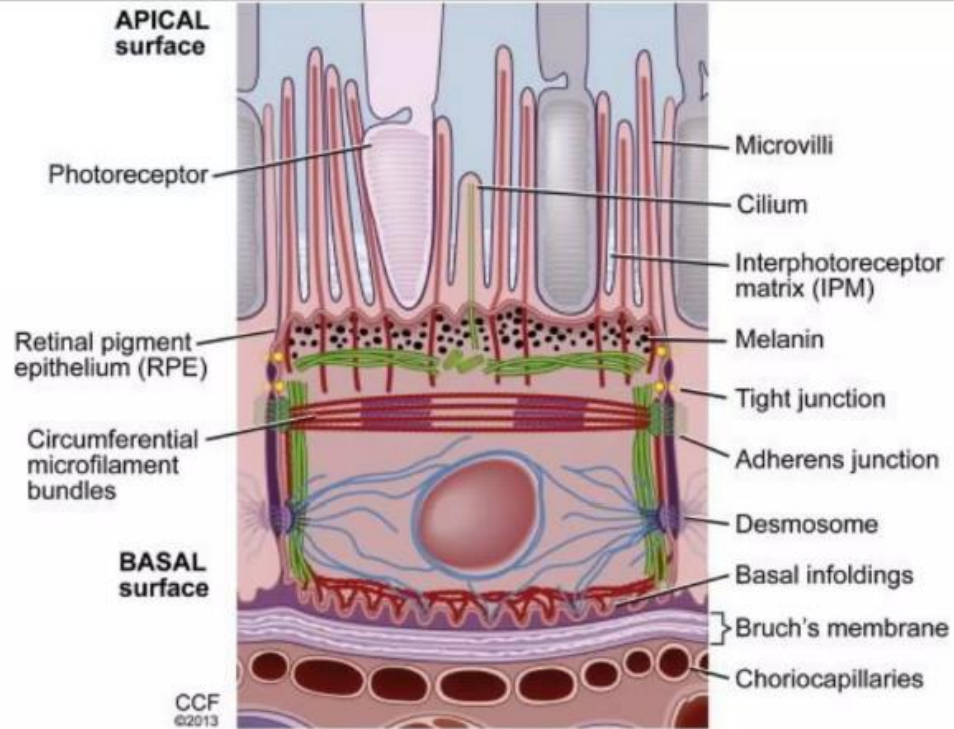
- The retina covers the internal side of the posterior chamber of the eye
- The retina is composed of
 - neurosensory tissue: neuroretina,
 - a pigment epithelium: retinal pigment epithelium (RPE)
- The main function of the neuroretina is to convert the light stimulus into an electrical signal that can be decoded by the brain.
- The RPE creates a physical and metabolic barrier between the neuroretina and the choriocapillary is that limits the entry of exogenous compounds in the neuroretina.
- One of the primary function of the RPE is to eliminate the metabolic debris generated by photoreceptors.
- The RPE exhibits an endogenous capacity to synthesize and secrete lipoprotein-like particles
- Low density lipoprotein particles (LDL) participate significantly in retinal lipid supply.
- Lipids account for about 25% of the dry matter in the neuroretina.
- Phospholipids are the prominent lipids therein (more than 85%), while cholesterol is present as free cholesterol (10%), and to a lesser extent as cholesteryl esters (less than 2%)

- Phospholipids are present in great quantity in the outer segment of rods and cones.
- Docosahexaenoic acid (DHA) is the main long-chain polyunsaturated fatty acid in the phospholipids of the neuroretina: 12–20% of the fatty acids in human and more than 30% in rodent
- The potential of a diet enriched in DHA and EPA (eicosapentaenoic acid) to increase the level of the longer chain omega-3 fatty acids (EPA; DPA, docosapentaenoic acid; and DHA) in the retina has clearly been demonstrated
- Intervention trials have been conducted in pregnant and lactating women and premature and at-term babies in order to evaluate the efficacy of dietary long chain omega-3 fatty acids to improve vision performance in infants.
- The positive effect of omega-3 fatty acids was obvious only in studies where the intake of DHA was higher than 1g daily.



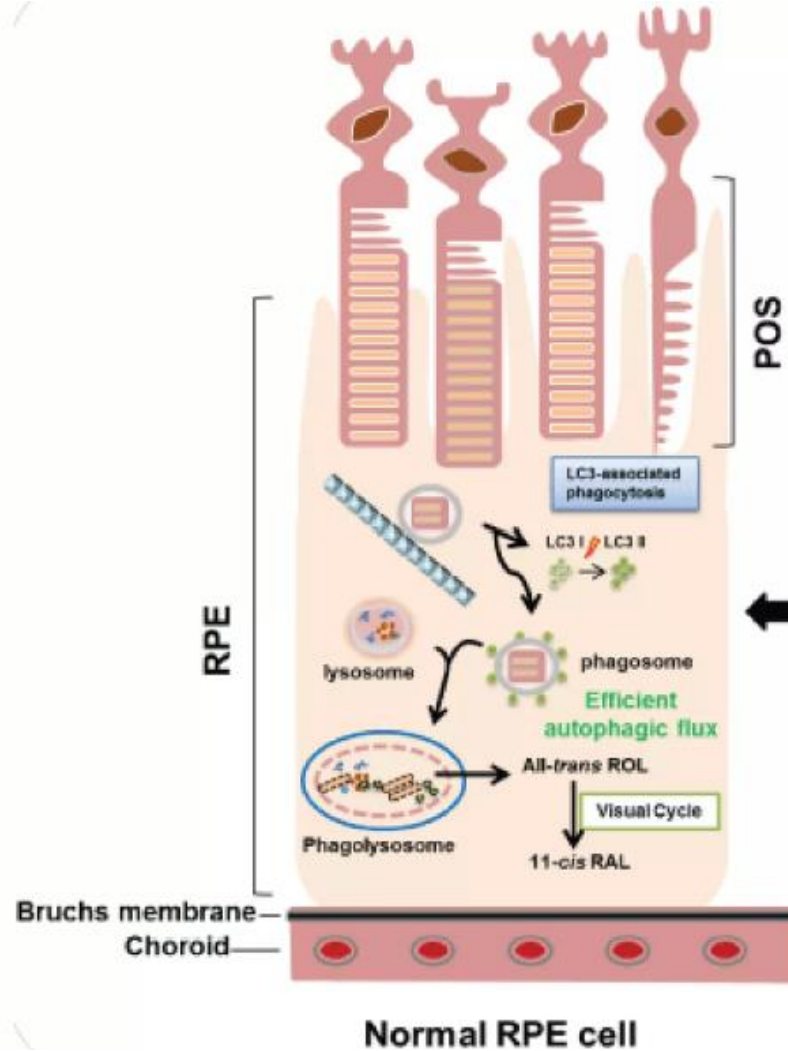
Aging of the retina & Lipids

- The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina.
- AMD targets a specific area of the retina: the macula.
- High fat intake has been associated with higher risk for AMD.
- Smoking and light exposure are, for instance, recognized as promoting factors.



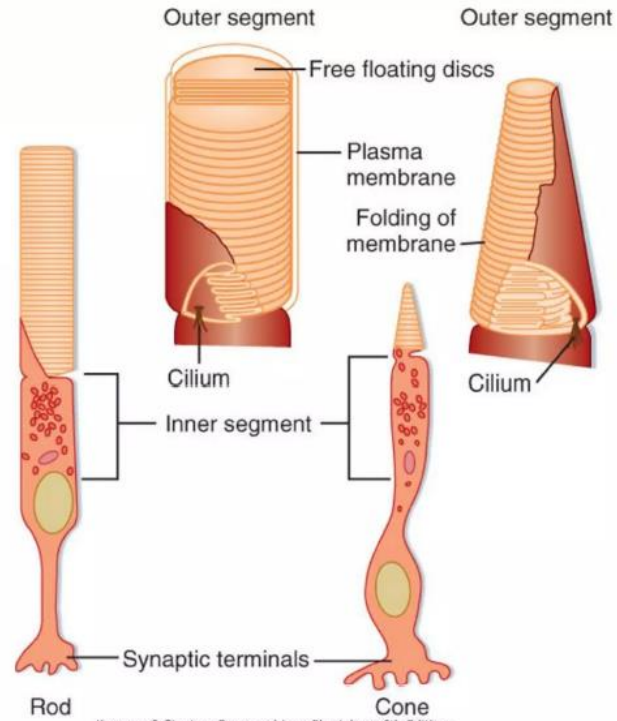
- **choriocapillaries supply** the nutrients to the **retinal pigment epithelial (RPE)** cells, which delivers them to the interphotoreceptor matrix.
- **Low density lipoprotein (LDL)** is the main carrier of DHA, and since the RPE cells contain LDL receptors
- it is likely that the **uptake and delivery of DHA to the photoreceptor cells are receptor mediated** with subsequent release of DHA phospholipids, or free DHA, into the interphotoreceptor matrix.
- **Fatty acid-binding proteins (FABPs)** present in the interphotoreceptor matrix bind DHA, and are believed to be involved in the transport of DHA to the photoreceptor cells.

Disc Shedding in retina



- Disc membranes are assembled at the inner segment, and form discs at the base of the outer segment
- These membranes have a short lifetime, and are replaced every 9–14 days
- The discs move outward toward the tip apical region where they are shed into the adjacent RPE, phagocytosed and digested by the lysosomal system.
- However, the retina conserves its DHA by retrieving it from the phagosomal membranes within the RPE and recycling it for incorporation into newly forming disc membranes

DHA accumulation in the retina



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.
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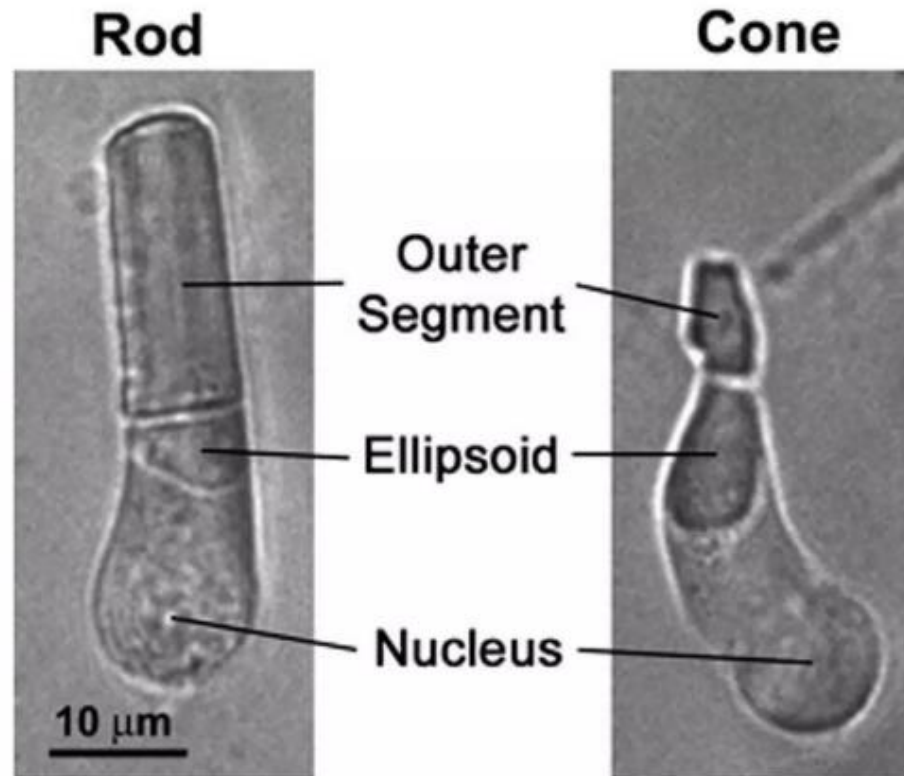
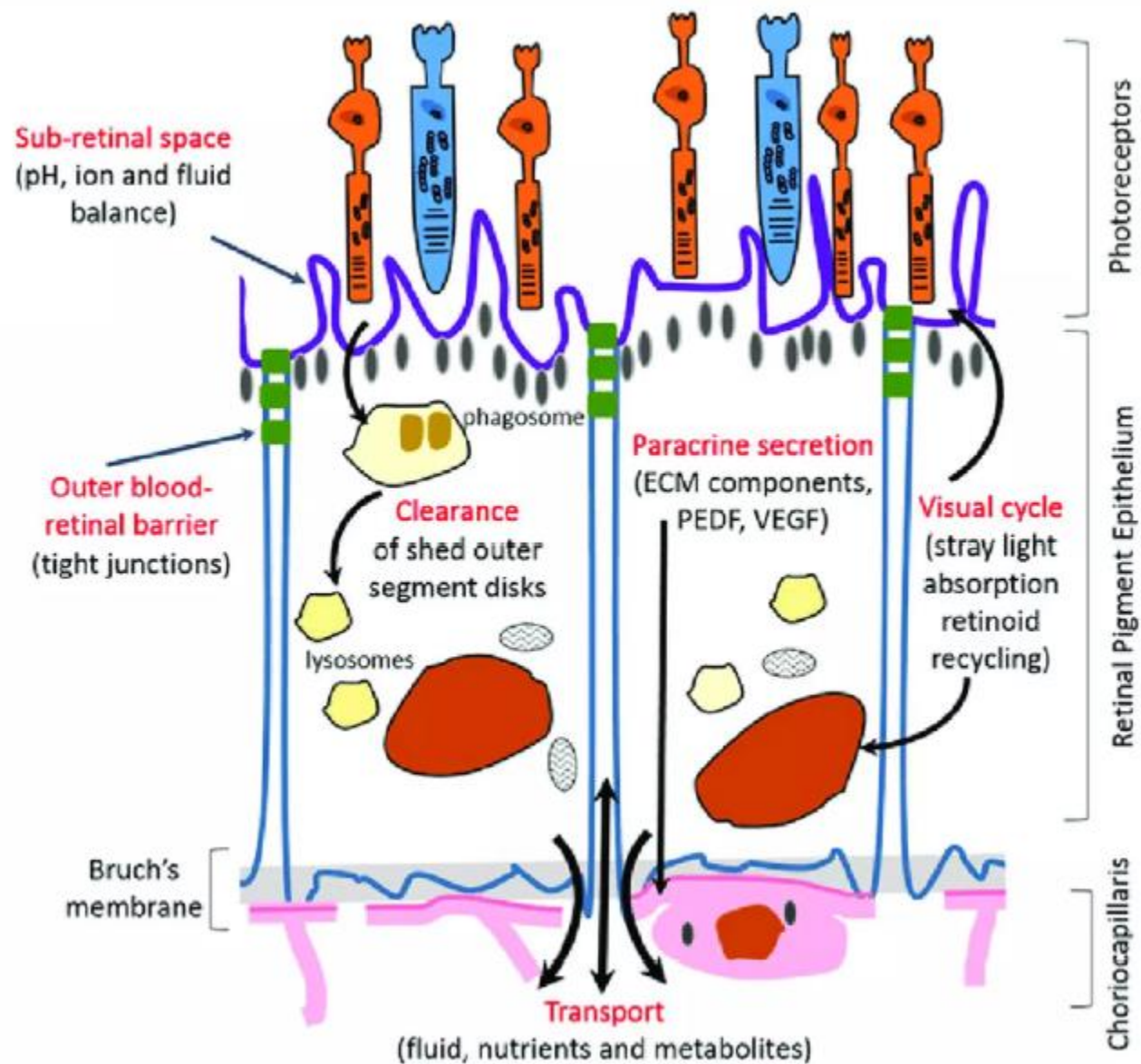


Figure 1. Brightfield images of living rod and cone photoreceptors isolated from a salamander retina. Phototransduction takes place in the outer segment, while the ellipsoid is densely packed with mitochondria. Rods are responsible for dim light vision, cones for bright light vision. Courtesy of Yiannis Koutalos.



- The recycling mechanism is not fully understood, but it has been postulated to occur via one of the two following mechanisms:
- (1) by **returning the DHA** from the RPE back to the photoreceptors (short-loop)
- (2) by **entry of DHA into the systemic circulation**, where it follows a similar pathway to cellular and dietary DHA via the liver, and reuptake by the RPE cells, with delivery to photoreceptor cells for new disc formation (long-loop)
- This selective retention of lipid is unique to the photoreceptor cells.



Role of DHA

1. **DHA affects the membrane structure** by altering its **permeability, fluidity, thickness and lipid-phase properties** while increasing the rate of rhodopsin activation
2. **DHA surrounds rhodopsin** (approximately 60 molecules of phospholipid for each rhodopsin), excluding cholesterol from **creating a fluid microenvironment** within the rod outer-segment membranes
3. **membrane fluidity is an important biophysical factor** of the disc membranes, and this fluidity is brought about by the presence of DHA and other PUFAs on the constituent phospholipids

4. The membrane's fluid state allows Brownian movement of the protein components within the plane of the disc membrane, enabling transduction and amplification of the signal
5. *membranes containing DHA have higher MII formation, MII-transducing interaction and activation and, finally, PDE activation.*

DHA and retinal oxidative stress

- DHA has high degree of unsaturation
- It is **susceptible to oxidation** within the photoreceptor disc membranes
- the membrane stabilising substances, vitamin E and taurine, along with the retinal antioxidants, vitamin C, carotenoids, superoxide dismutase and glutathione (and its associated enzymes) helps in fighting against oxidative damage of eye
- However a constant cellular and dietary supply is required to maintain the disc membranes.
- studies have demonstrated that depletion of DHA from the developing retina leads to **abnormalities in electroretinogram (ERG) and visual evoked potential (VEP), resulting in reduced visual function**

Dietary deficiency of DHA and visual function

- diets low in Omega-3 fatty acids led **to impaired visual acuity**
- The retinal dysfunction occurs due to **inadequate disc membrane DHA phospholipids to support rhodopsin in light capture**, and hence MII formation
- Cells compensate this lack of DHA by converting omega-6 EFA linoleic acid to decosapentanoic acid, which is not efficient in supporting rhodopsin.
- The retinal abnormalities due to DHA deficiency are reversible
- but the **responsiveness of the visual cortex, and the higher cortical centres involved in visual function**, appear long-lasting and irreversible
- In infants: supplementation should be approached with caution as these infants have low retinal levels of vitamin E and **increased retinal DHA concentration could increase susceptibility to retinal oxidative damage**

Aging of the retina & Lipids

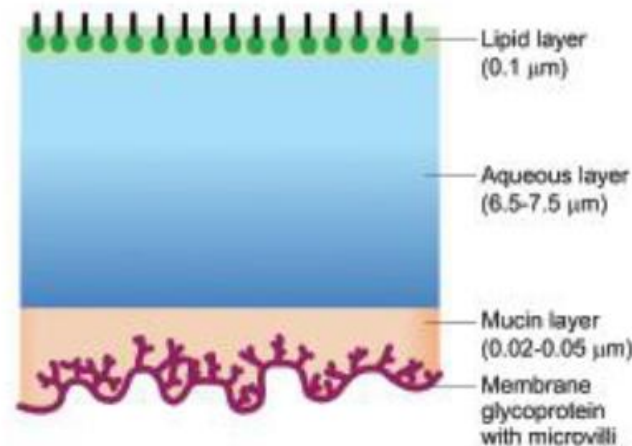
- The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina
- AMD targets a specific area of the retina: the macula.

- High fat intake has been associated with higher risk for AMD.
- Smoking and light exposure are, for instance, recognized as promoting factors
- In a study it was observed that participants who have the highest omega-3 long-chain polyunsaturated fatty acid (EPA and DHA) intake (0.11% of total energy intake) were 30% less likely to develop Geographic atrophy and neovascular AMD than low consumers (0.01% of total energy intake).

Lipids in tears

- Tear film is actually composed of three basic layers: **mucin, water and lipids** from posterior to anterior.
- **Lipid or oily layer** is the outermost layer of tear film formed at air-tear interface from the secretions of Meibomian, Zeis, and Moll glands.
- This layer prevents the overflow of tears, retards their evaporation and lubricates the eyelids as they slide over the surface of the globe.
- Lipids within tears help prevent water evaporation from the ocular surface and protect the eye against infection.
- Prolonged dry eyes leads to cloudy cornea, inhibiting self repair of the damaged cornea.

Structure of tear film



Eye Diseases linked to lipids

Arcus senilis refers to an annular lipid infiltration of corneal periphery. This is an age-related change occurring bilaterally in 60 percent of patients between 40 and 60 years of age and in nearly all patients over the age of 80.

Fatty degeneration (Lipoid keratopathy) of cornea is characterized by whitish or yellowish deposits. The fat deposits mostly consist of cholesterol and fatty acids

Diabetic retinopathy: hyperlipidemia is a risk factor.

Seborrhoeic or squamous blepharitis: glands of Zeis secrete abnormal excessive neutral lipids which are split by *Corynebacterium acne* into irritating free fatty acids

Xanthelasma:

- These are creamy-yellow plaque-like lesions which frequently involve the skin of upper and lower lids near the inner canthus.
- Xanthelasma represents lipid deposits in histiocytes in the dermis of the lid.
- These may be associated with diabetes mellitus or high cholesterol levels.

THE DRY EYE:

- Lipid deficiency is extremely rare.
- It has only been described in some cases of congenital anhidrotic ectodermal dysplasia along with absence of meibomian glands.
- However, lipid abnormalities are quite common in patients with chronic blepharitis and chronic meibomitis
- Lipid soluble drugs have better permeability in eyes.

Asteroid hyalosis.

- It is characterised by small, white rounded bodies suspended in the vitreous gel.
- These are formed due to accumulation of calcium containing lipids.

- Asteroid hyalosis is a unilateral, asymptomatic condition usually seen in old patients with healthy vitreous.
- There is a genetic relationship between this condition, diabetes and hypercholesterolaemia.
- The genesis is unknown and there is no effective treatment

Lipodermoids.

- These are solid tumours usually seen beneath the conjunctiva.
- These are mostly located adjacent to the superior temporal quadrant of the globe.
- These do not require any surgical intervention unless they enlarge significantly.



Vitamins

Biochemistry

Hayder K. Khattar Al thalme

2023

Definition of vitamins

- Group of organic compounds that are essential for normal growth and nutrition and are required in small quantities in diet as they cannot be synthesized by the body.
- The term vitamin is derived from the words vital and amine, because vitamins are required for life and were originally thought to be amines

Properties of vitamins

- **Vital** to life; are essential
- Organic compounds
- **Individual units**; not linked in chains
- Do not provide energy
- Assist with release of energy (coenzymes)
- **Needed in small amounts**: micro/milli grams
- Fruits and vegetables are a primary source

Importance of vitamins

Vitamins	Functions
All B groups, c and K	Co enzymes
B1-B7	Metabolism of energy
B6, B9, B12	Red blood cell synthesis and amino acid metabolism
B3, B5, B7	Fatty acid synthesis
B1, B6, B12	Nerve transmission
C and E	Antioxidants
A and D	Gene expression

Classifications of vitamins

Water Soluble

- Vitamin C
- B Vitamins
 - Thiamine (B₁)
 - Riboflavin (B₂)
 - Niacin
 - Pantothenic Acid
 - Biotin
 - Pyridoxine (B₆)
 - Folic Acid
 - Vitamin B₁₂
(cyanocobalamin)

- Cannot be stored in the body,
- Provided by the dietary intake.

Lipid Soluble

- Vitamin A
- Vitamin D
- Vitamin E
- Vitamin K

- Can be stored in the body,
- Excess is not secreted out of the body,
- Provided by the dietary intake, except Vit D (increased by exposure to the sun).

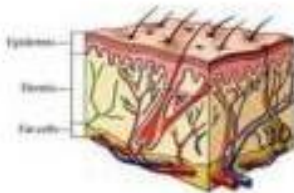
Fat Soluble Vitamins

A, D, E and K

+ Vitamin A

- Helps vision

- Keeps skin healthy



- Deficiency:
 - Night blindness
 - Xerophthalmia

Sources of vitamin A and beta-carotene:



Vitamin A comes from animal sources such as eggs, meat and dairy products

Beta-carotene, a precursor of vitamin A, comes from green, leafy vegetables and intensely colored fruits and vegetables



ADAM.

The daily amount: 900 mcg/ day for adult males and 700 mcg/ day for adult females.

+ Vitamin D cholecalciferol

- Needed for strong teeth and bones
- Regulates calcium and phosphorus metabolism

The daily amount :800 International unit/day especially for adults over 50. Exposure to sunlight for 10-15 min without sunscreen, twice a week, is sufficient to absorb Vitamin D.

The body itself makes vitamin D when it is exposed to the sun

Cheese, butter, margarine, fortified milk, fish, and fortified cereals are food sources of vitamin D



Deficiency:

- Rickets
- Bone deformity





Vitamin E Tocopherol

- Antioxidant role (prevents destruction of Vit. A & C)
- Protects cell membranes from damage
- Protects red blood cells (rbc)



- Deficiency:
 - Reduced # of RBC
 - Nerve tissue damage in infants



Vitamin E is found in corn, nuts, olives, green, leafy vegetables, vegetable oils and wheat germ, but food alone cannot provide a beneficial amount of vitamin E, and supplements may be helpful

The daily amount= 15 mcg of alpha-tocopherol/day



Vitamin K

Food sources of vitamin K include cabbage, cauliflower, spinach and other green, leafy vegetables, as well as cereals

- Helps in clotting blood



- Found in green leafy vegetables

Deficiency –

Bleeding caused by prolonged clotting time

The daily amount= for age 14 – 18 Y= 75 mcg/day;
age 19 and older= 90 mcg/day

Water Soluble Vitamins

C and B-groups

Vitamin C

■ **Helps keep gums, teeth, bones healthy**

■ **Needed for wound healing**

Citrus fruits, green peppers, strawberries, tomatoes, broccoli and sweet and white potatoes are all excellent food sources of vitamin C (ascorbic acid)



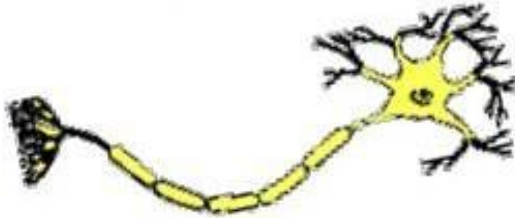
Deficiency: Scurvy –

- **swollen and bleeding gums**
- **loose teeth**
- **slow-healing wounds**

The daily amount= 90 mg/day for males and 75 mg/day for females.
For smokers= it should increase by 35 mg/day to reduce the effect of nicotine.

B₁ Thiamin

- Needed for healthy nerves



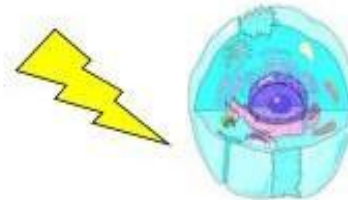
Vitamin B1 (Thiamine) is found in fortified breads and cereals, fish, lean meats and milk

ADAM

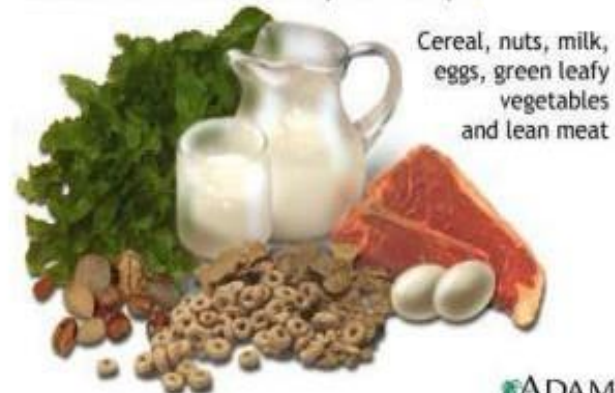
The amount of Thiamin/day = 1.1- 1.2 mg/day. Its presence in adequate amount helps to release energy from foods, promotes normal appetite, and is important in maintaining proper nervous system function

B₂ Riboflavin

- Helps cells use energy in foods



Food sources of Riboflavin (vitamin B2):



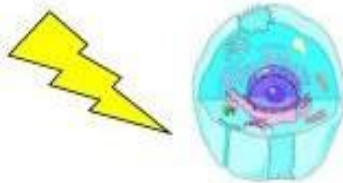
Cereal, nuts, milk, eggs, green leafy vegetables and lean meat

ADAM

The daily amount : 1.3 mg/day and Females: 1.1 mg/day

B₃ Niacin

- Helps cells use energy in foods



Vitamin B₃



Food sources of Niacin (vitamin B₃) include dairy, poultry, fish, lean meat, nuts and eggs

ADAM.

The daily amount of Vit B₃ is 16 mg/day for male and ; 14 mg/day for female.

B₆ Pyridoxine

- Needed for red blood cells
- Keeps nerves healthy



Vitamin B₆

Food sources of vitamin B₆ (pyridoxine) include beans, legumes, nuts, eggs, meats, fish breads and cereals



ADAM.

The daily amount is 1.43 mg/day

Biotin: B7

Biotin is liver, kidney, egg yolk, milk, most fresh vegetables, yeast breads and cereals. Biotin is also made by intestinal bacteria.

What does Biotin do ?

It helps release energy from carbohydrates and aids in the metabolism of fats, proteins and carbohydrates from food.

Biotin Deficiency

Biotin deficiency is uncommon under normal circumstances, but symptoms include fatigue, loss of appetite, nausea, vomiting, depression, muscle pains, heart abnormalities and anemia.



Tomatoes



Carrots



Almonds



Onions



Romaine Lettuce



Eggs



Salmon



Walnuts



Sweet Potato



Cauliflower

The daily amount: 30 mcg/day for adult males and females

Folic Acid, Folate : B9

Folic acid is found in liver, kidney, dark green leafy vegetables, meats, fish, whole grains, fortified grains and cereals, legumes, and citrus fruits

What does Folic acid do?

It aids in:

1. protein metabolism,
2. promoting red blood cell formation.
3. Folate may also play a role in reducing the risk for coronary heart disease.

Folate Deficiency

Folate deficiency affects:

1. cell growth and protein production, which can lead to overall impaired growth.
2. anemia and diarrhea.



The daily amount: is 400 mcg/day for adult males and females. For pregnancy =600 mcg/day.

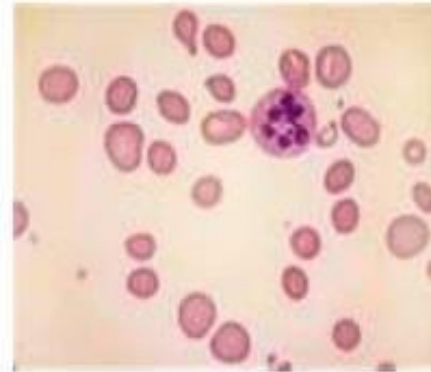
+ **B₁₂ Cobalamine**

- Helps cells use energy in foods
- Needed for formation of RBC



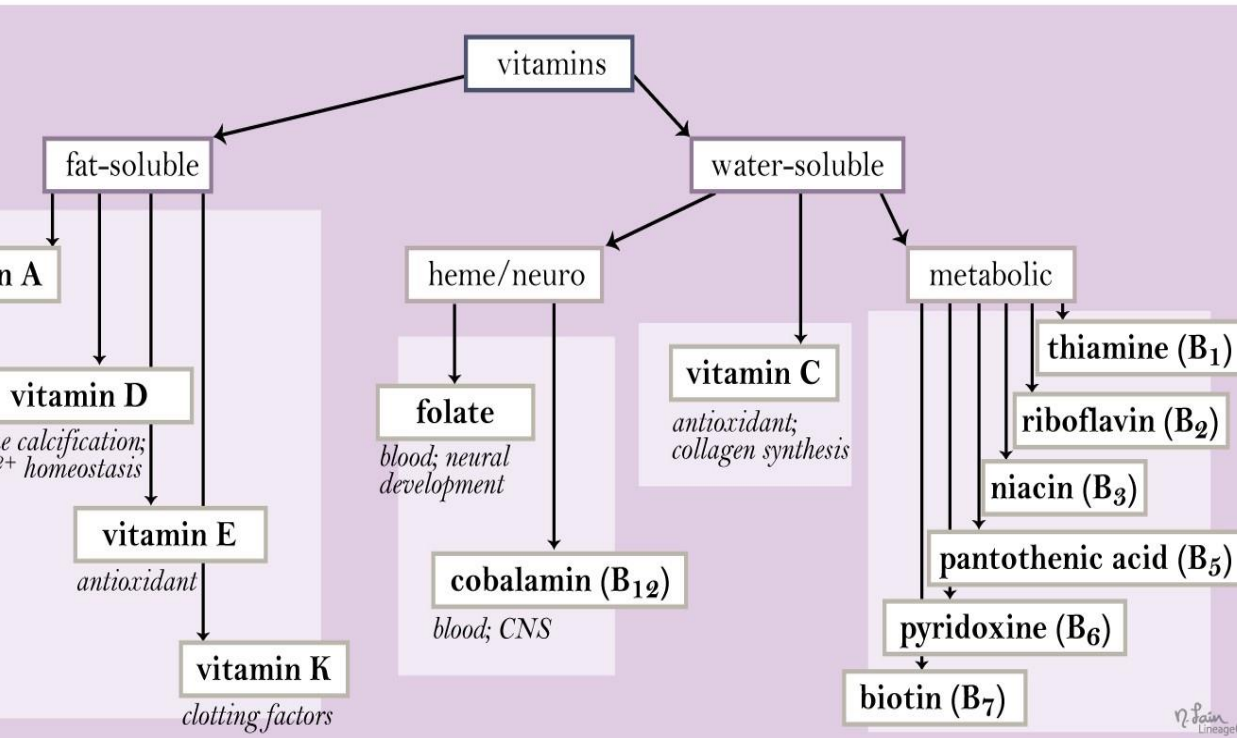
Food sources of Niacin (vitamin B3) include dairy, poultry, fish, lean meat, nuts and eggs

Deficiency – pernicious anemia

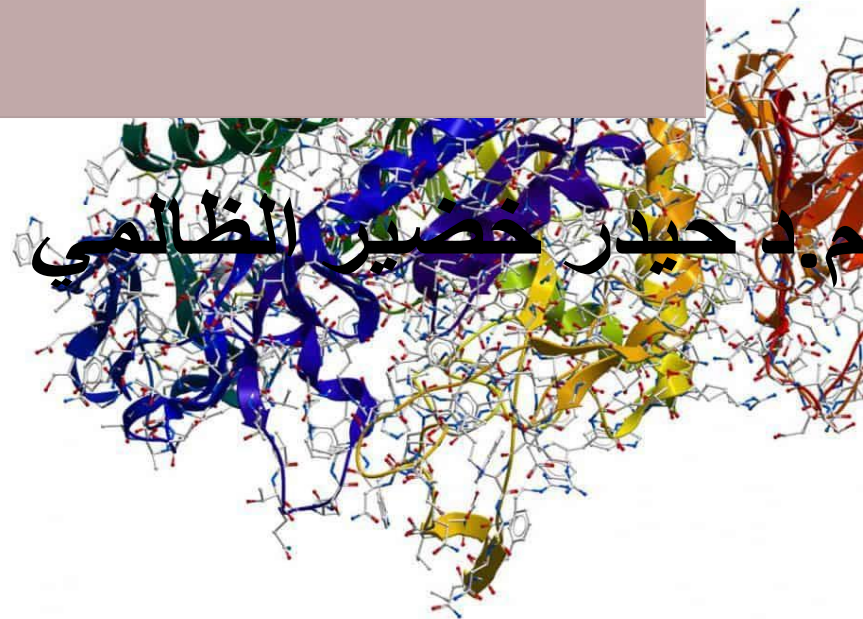
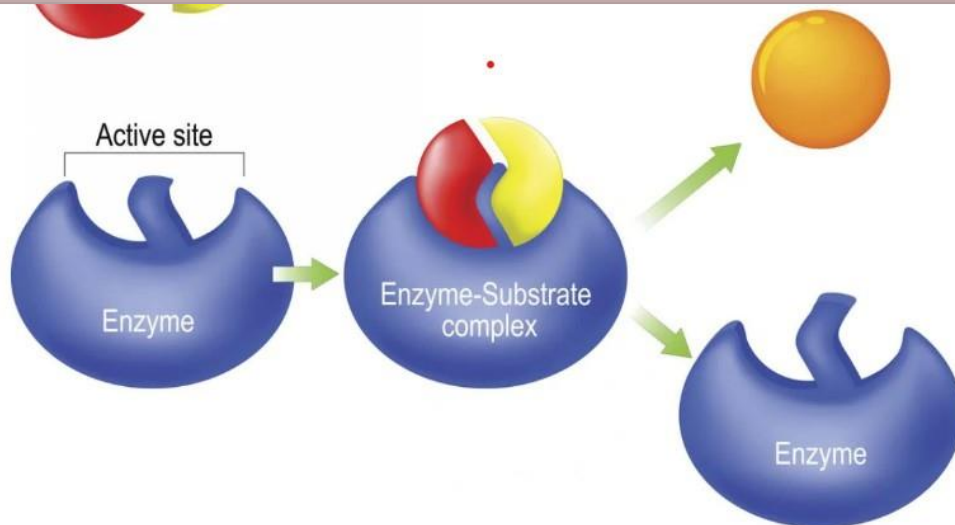


The daily amount of B12 is 2.4 mcg/day for adult males and females.

Vitamin Algorithm



Enzyme Structure, classification and mechanism of action



Definition : enzymes are biological catalysts which bring about chemical reaction in the living cell.

- . produced by the living organism in small amounts.
- . Functions: digestion, breathing, synthesis and break down of CHOS, proteins, fats
- . enzymes acts upon substance called substrate.
- . enzymes convert substrate into product. Ex: lactose $\xrightarrow{\text{lactase}}$ galactose + glucose
- . 16% of weight is nitrogen.

physical properties:

1. Heat labile
2. Soluble in water
3. Precipitate by precipitating agent (ammonium sulphate or trichloroacetic acid).

General properties of enzymes:

1. all enzymes are proteins.
2. enzymes accelerate the reaction but:
 - a. do not alter the reaction equilibrium
 - b. not consumed in overall reaction
 - c. required in very small quantities.
3. enzymes are highly specific for their substrate.
4. enzymes possess active site, at which interaction with substrate take place.

Sources of enzymes:

Endoenzymes: enzymes that function within the cells, most of enzymes are these types.

Ex: metabolic oxidase.

Exoenzymes: enzymes that are liberated by cells and catalyze reactions outside the cell.

Ex: digestive enzymes (amylase, lipase, protease).

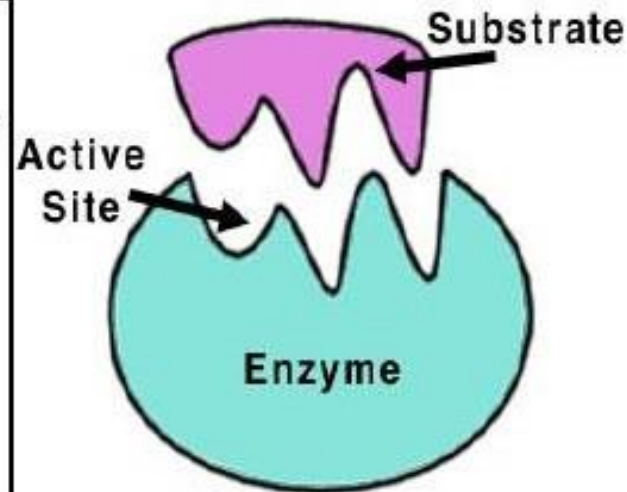
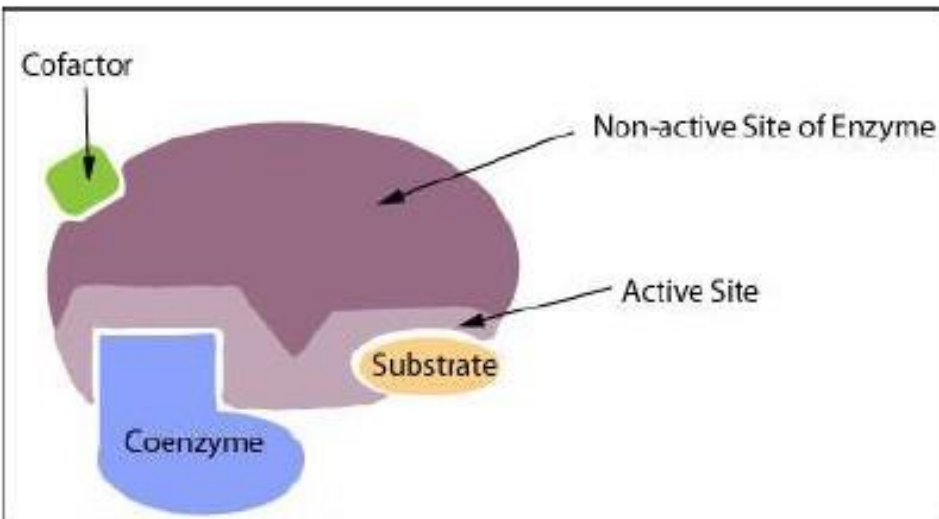
Chemical composition of enzymes:

Enzymes classified according to their chemical composition into.

1. Enzyme consist of only protein.

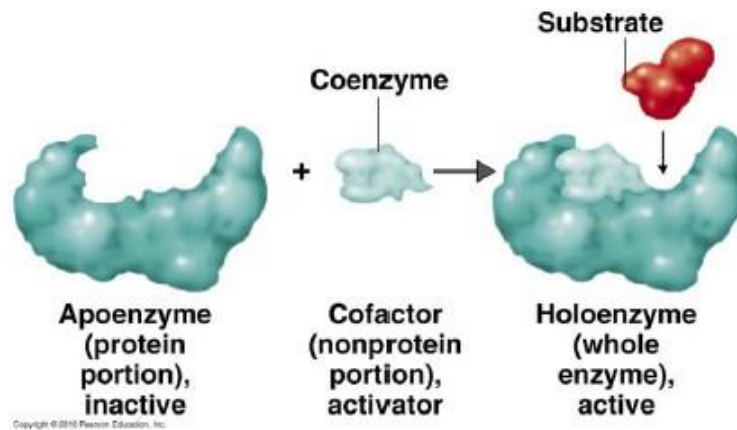
Ex: pepsin, trypsin (amino acids binding peptide bonds).

2. Enzyme consist of : protein (enzyme) + Co - Enzyme = Holoenzyme (apoenzyme)



3. Enzyme consist of:

Protein (enzyme) + prosthetic group (Co – factor) = **Holoenzyme**



Coenzymes : are typically organic molecules, used by enzymes to help catalyse reactions, contain functionalities not found in proteins,

cofactors : are catalytically essential molecules or ions that are covalently bound to the enzyme

Holoenzyme : enzyme consist of Apoenzyme + prosthetic group

Apoenzyme : term refers to the protein part of enzyme.

Active site of enzyme: the point in the enzyme which interaction with substrate, co-enzyme, inhibitor take place.

Zymogen: the active form of enzyme.

Ex: pepsinogen $\xrightarrow{\text{Hcl}}$ pepsin (active)

Ex: trypsinogen $\xrightarrow{\text{enterokinase}}$ trypsin (active)

The difference between Co-enzymes and Co- factors:

Co-enzymes

1. binds loosely and can easily separated from enzyme by dialysis.
2. organic compounds (ex: water soluble vitamins such as Vit C and B
4. non protein.
5. heat resistance.
6. their function as co-substrate.

Co - factors

- 1.conjugated with protein(enzyme)
2. metallic ions (Fe, Mn, Cu,Mg)
3. has low molecular weight

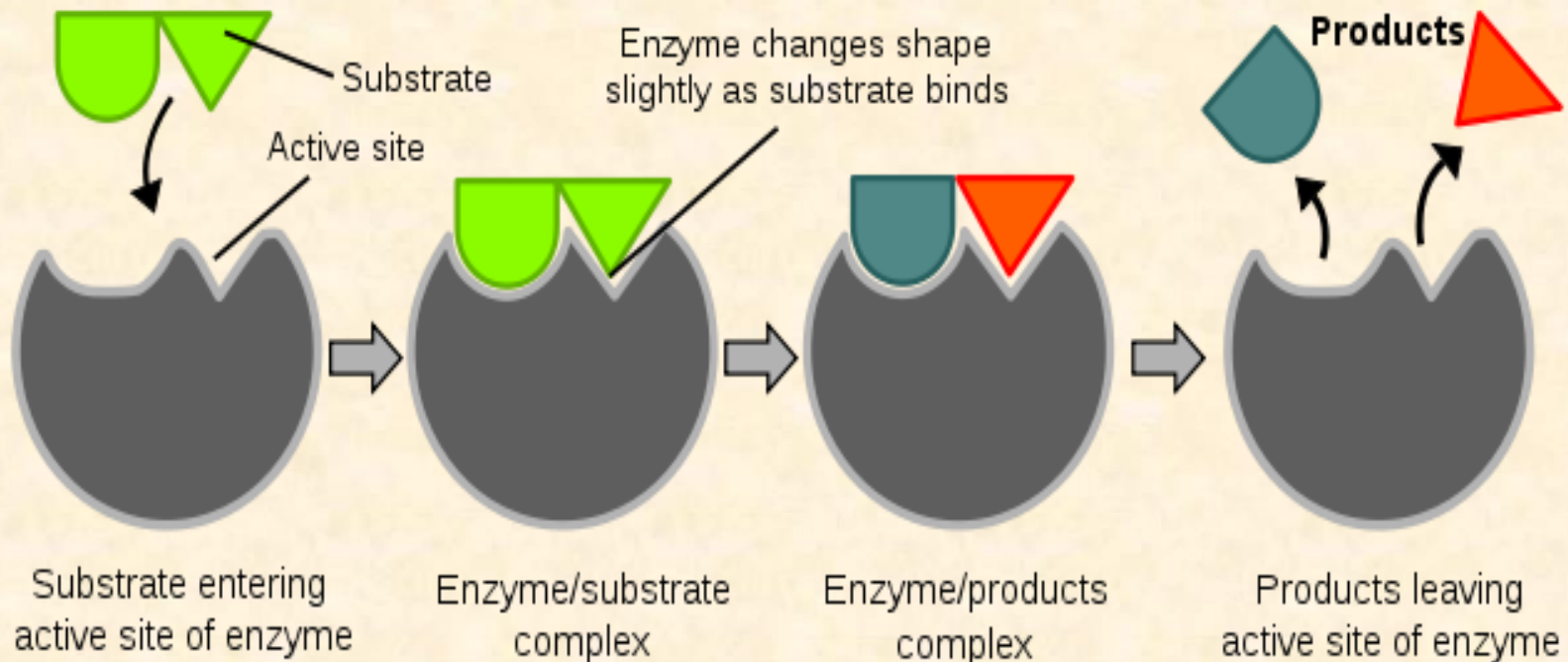
(Enzymes as Biological Catalysts)

- **Enzymes** are proteins that increase the rate of reaction by lowering the energy of activation
- They catalyze nearly all the chemical reactions taking place in the cells of the body.
- Not altered or consumed during reaction.
- Reusable

- 
- Enzymes play an important role in Metabolism, Diagnosis, and Therapeutics.
 - All biochemical reactions are enzyme catalyzed in the living organism.
 - Level of enzyme in blood are of diagnostic importance e.g. it is a good indicator in disease such as myocardial infarction.
 - Enzyme can be used therapeutically such as digestive enzymes.

ACTIVE SITES

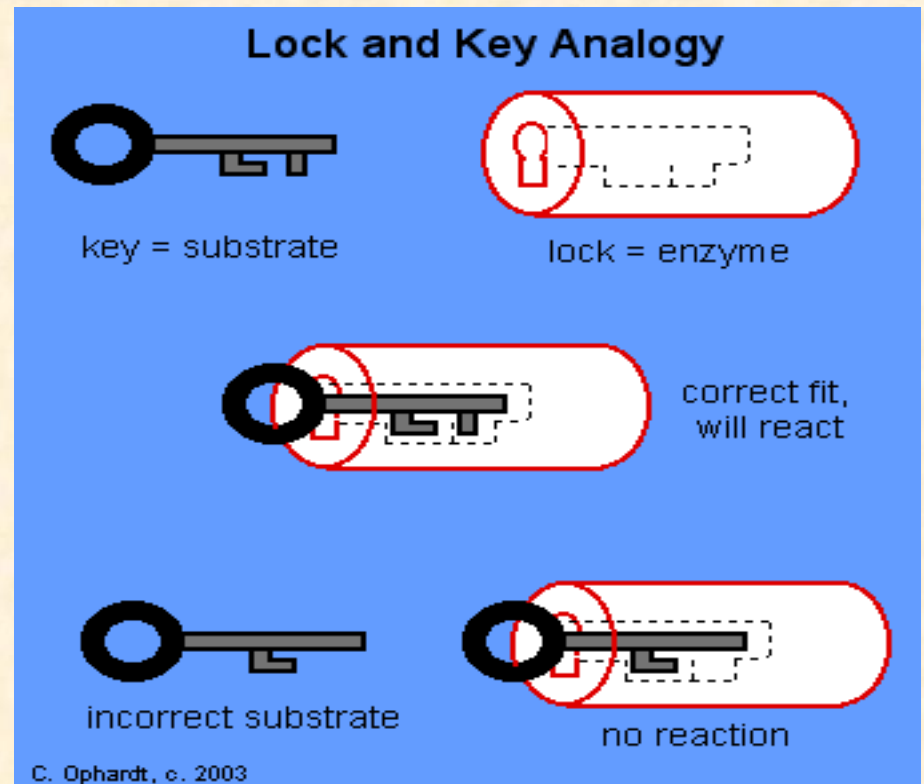
- Enzyme molecules contain a special pocket or cleft called the active sites.



Lock-and-Key Model

- In the lock-and-key model of enzyme action:
 - the active site has a rigid shape
 - only substrates with the matching shape can fit
 - the substrate is a key that fits the lock of the active site

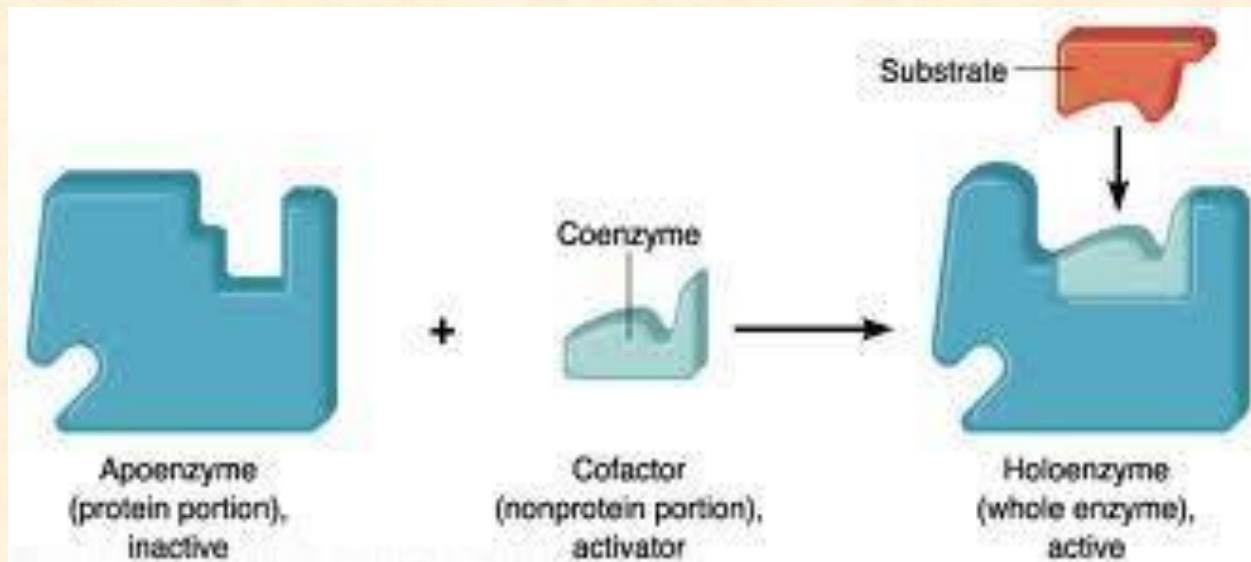
This explains enzyme specificity
This explains the loss of activity when enzymes denature



APOENZYME and HOLOENZYME

Apoenzyme or apoprotein is an enzymatically inactive protein part of an enzyme, which requires a cofactor for its activity. Apart from catalytic RNA, most of the enzymes are proteins. Not all the enzymes require a cofactor. Enzymes that do not require any cofactor are known as simple enzymes, e.g. pepsin, trypsin, etc

Holoenzyme is a complete, functional enzyme, which is catalytically active. Holoenzyme consists of an apoenzyme together with its cofactors. Holoenzyme contains all the subunits required for the functioning of an enzyme, e.g. DNA polymerase III, RNA polymerase .



Important Terms to Understand Biochemical Nature And Activity of Enzymes

- **Cofactor:**
 - A cofactor is a non-protein chemical compound that is bound (either tightly or loosely) to an enzyme and is required for catalysis.
 - Types of Cofactors:
 - Coenzymes.
 - Prosthetic groups.

Types of Cofactors

- Coenzyme:

The non-protein component, loosely bound to apoenzyme by non-covalent bond.

- **Examples :** vitamins or compound derived from vitamins.

Coenzymes are a specific type of helper or partner that are organic molecules required for enzyme function that bind loosely to an enzyme. They are often, though not always, derived from vitamins. Prosthetic groups are enzyme partner molecules that bind tightly to an enzyme.

- Prosthetic group

The non-protein component, tightly bound to the apoenzyme by covalent bonds is called a Prosthetic group.

This is a component of a conjugated protein that is required for the protein's biological activity, The prosthetic group may be organic (such as a vitamin, sugar, RNA, phosphate or lipid) or inorganic (such as a metal ion). Prosthetic groups are bound tightly to proteins and may even be attached through a covalent bond.

Enzyme Specificity

- Enzymes have varying degrees of **specificity** for substrates
- Enzymes may recognize and catalyze:
 - a single substrate
 - a group of similar substrates
 - a particular type of bond

Important Terms to Understand Biochemical Nature And Activity of Enzymes

Activation energy or Energy of Activation:

- All chemical reactions require some amount of energy to get them started.

OR

- It is First push to start reaction.

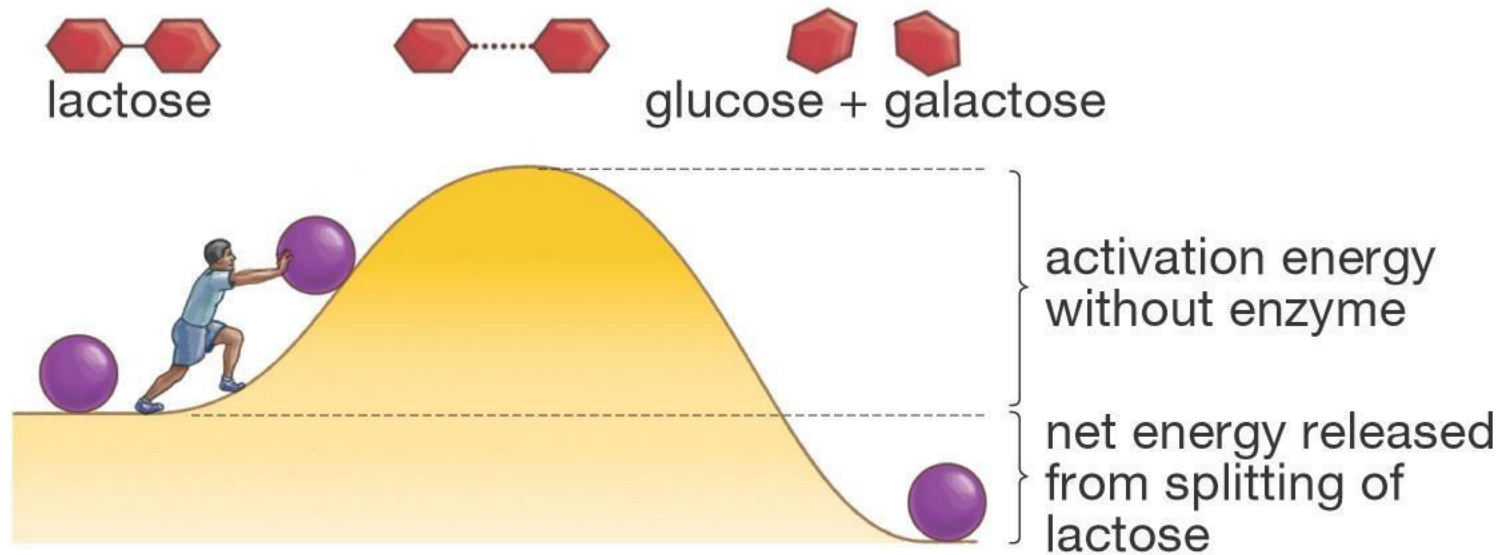
This energy is called activation energy.

Mechanism of Action of Enzymes

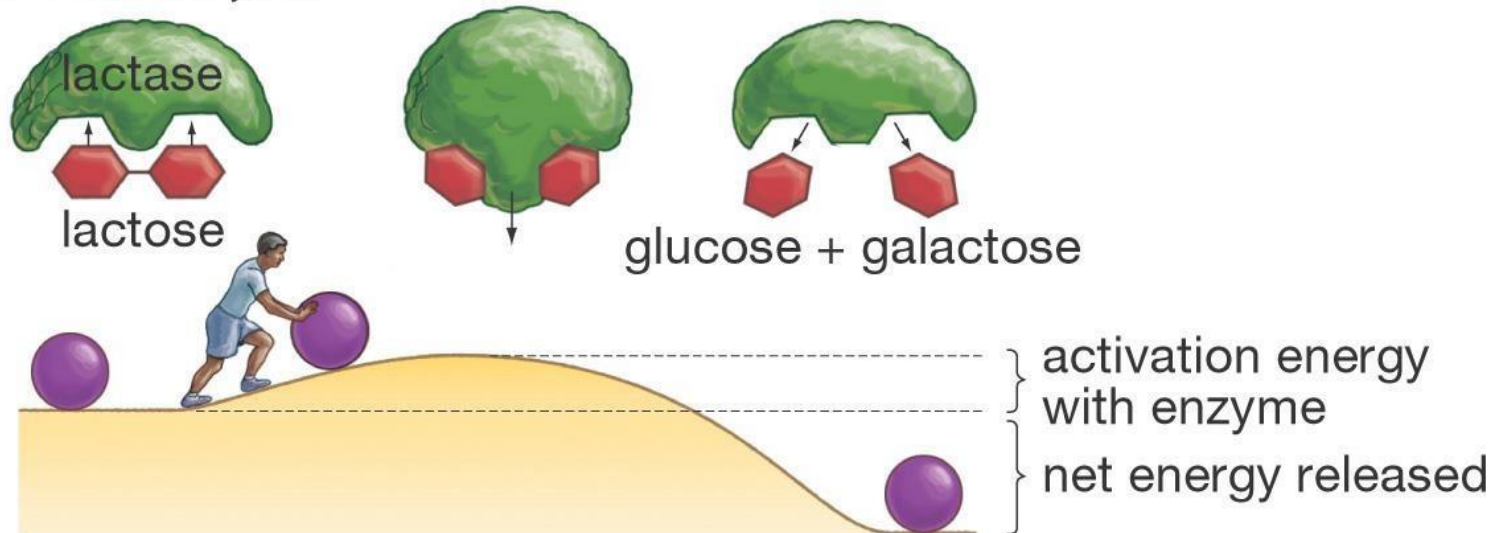
- Enzymes increase reaction rates by decreasing the Activation energy:
- **Enzyme-Substrate Interactions:**
 - **Formation of Enzyme substrate complex by:**
 - Lock-and-Key Model
 - Induced Fit Model

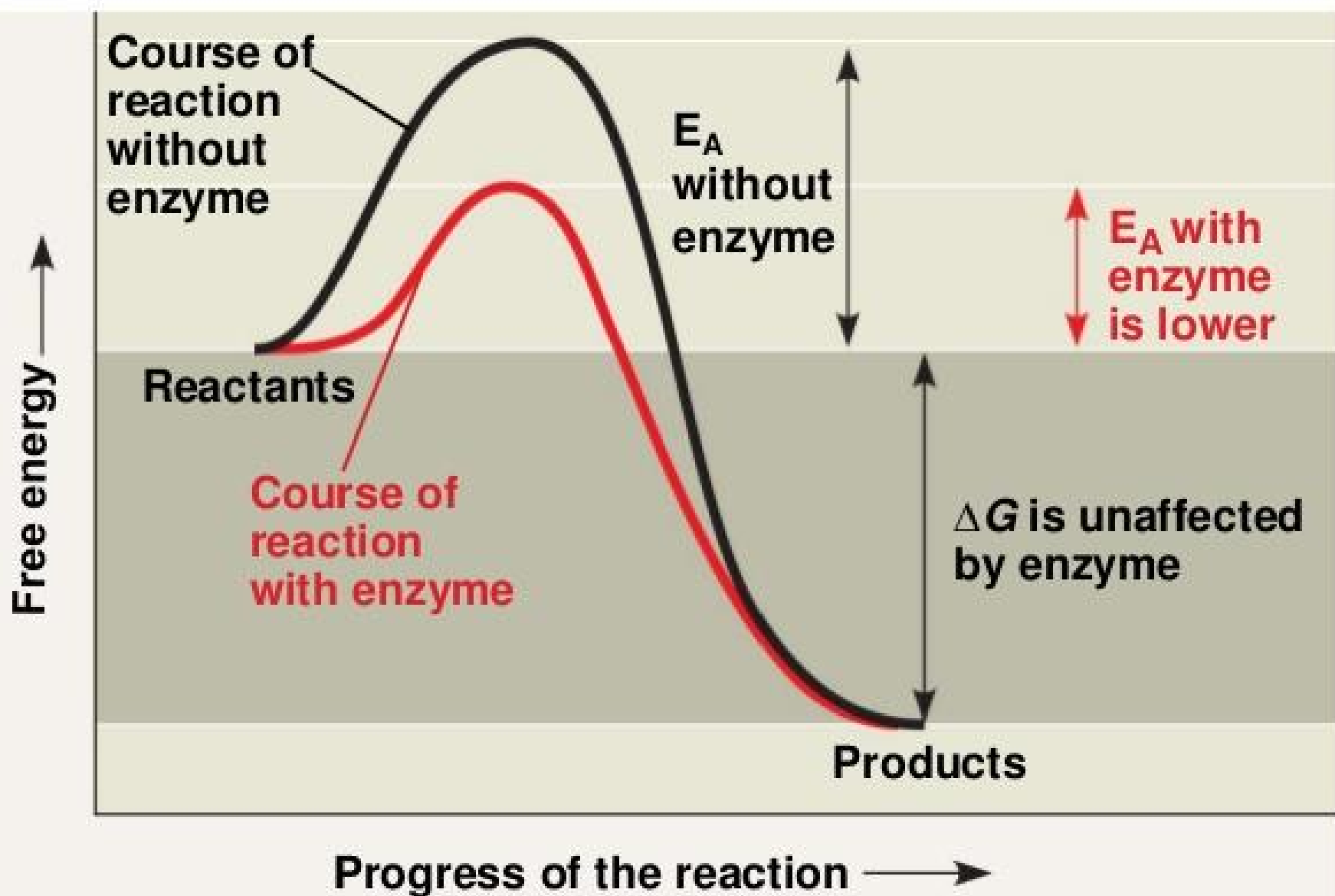
Enzymes Lower a Reaction's Activation Energy

(a) Without enzyme



(b) With enzyme



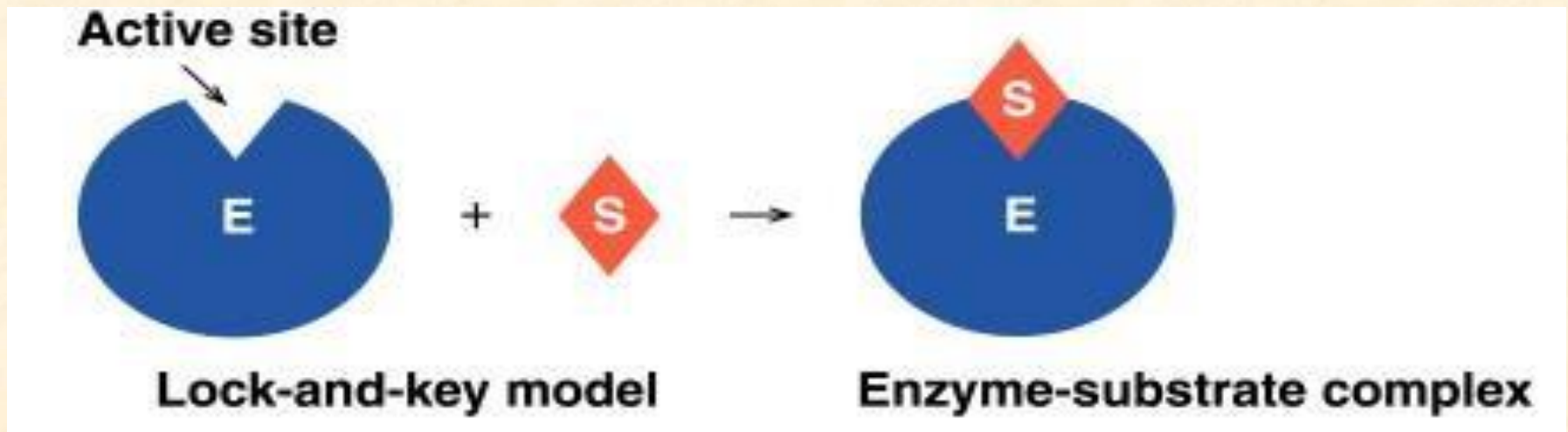


MECHANISM OF ACTION OF ENZYMES

1- Lock: Key model of enzyme action: implies that the active site of the enzyme is complementary in shape to that of its substrate, i.e. the shape of the enzyme molecule and the substrate molecule should fit each other like a lock and Key. In 1958, Daniel Koshland, postulated another model; which implies that the shapes & the active sites of enzymes are complementary to that of the substrate only after the substrate is bound.

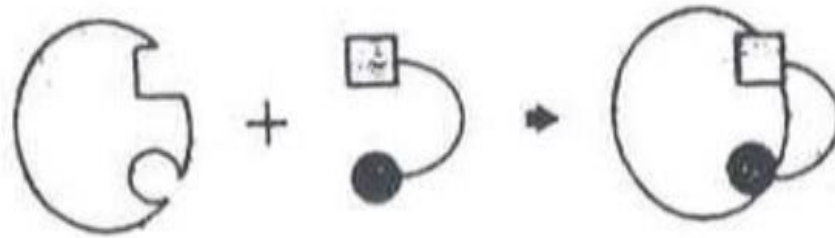
Lock-and-Key Model

- In the lock-and-key model of enzyme action:
 - the active site has a rigid shape
 - only substrates with the matching shape can fit
 - the substrate is a key that fits the lock of the active site
- This is an older model, however, and does not work for all enzymes

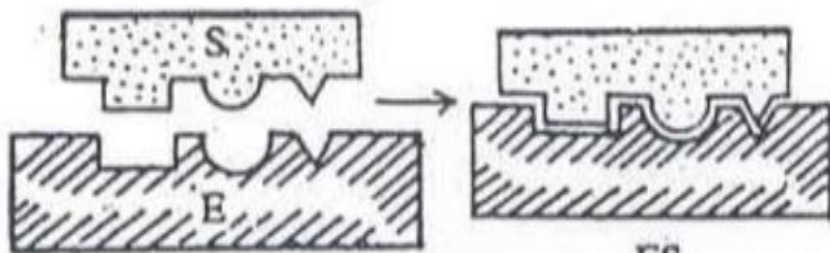


2-Induced fit Model :

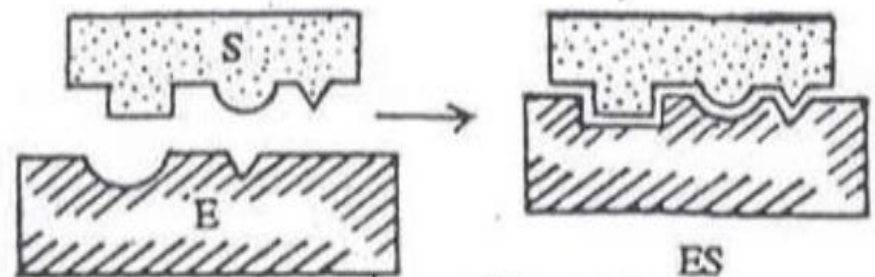
is a model that implies the shapes & the active sites of enzymes are complementary to that of the substrate only after the substrate is bound.



Template or lock-and-key model



Template model



Induced fit model

Induced Fit Model

- In the **induced-fit model** of enzyme action:
 - the active site is flexible, not rigid
 - the shapes of the enzyme, active site, and substrate adjust to maximize the fit, which improves catalysis
 - there is a greater range of substrate specificity
- This model is more consistent with a wider range of enzymes

Active site



+

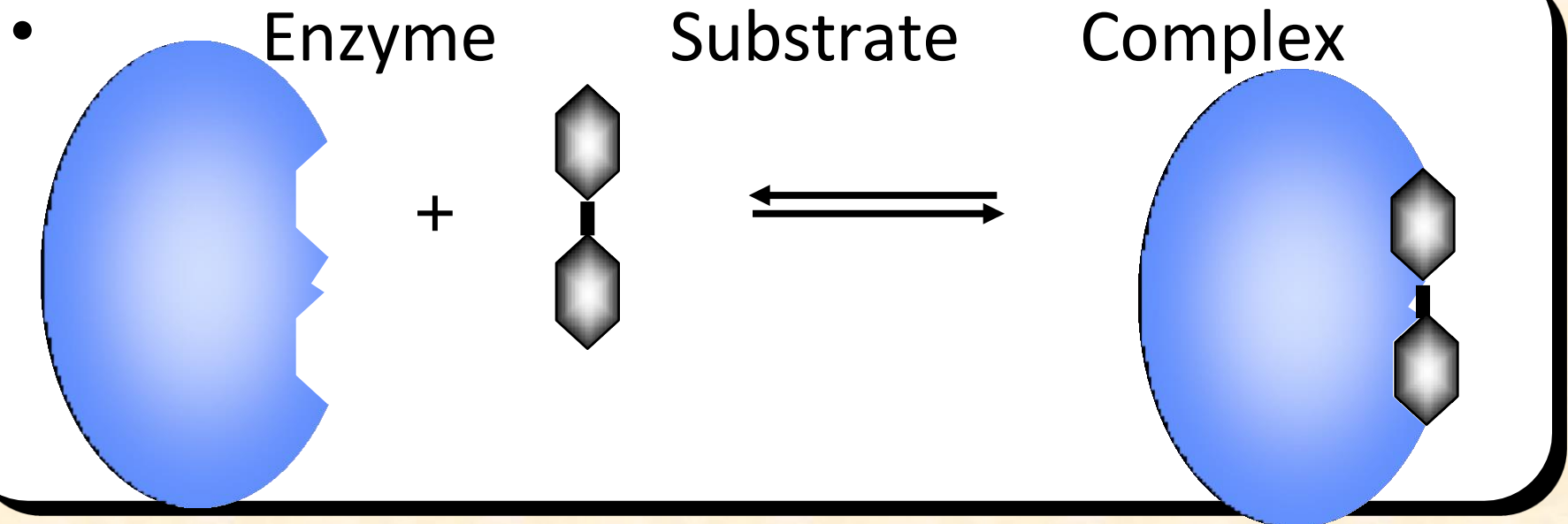
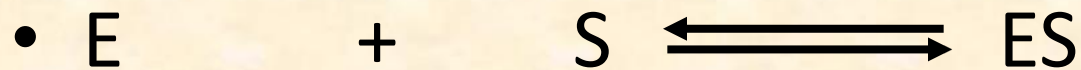


Induced fit model

Enzyme-substrate complex

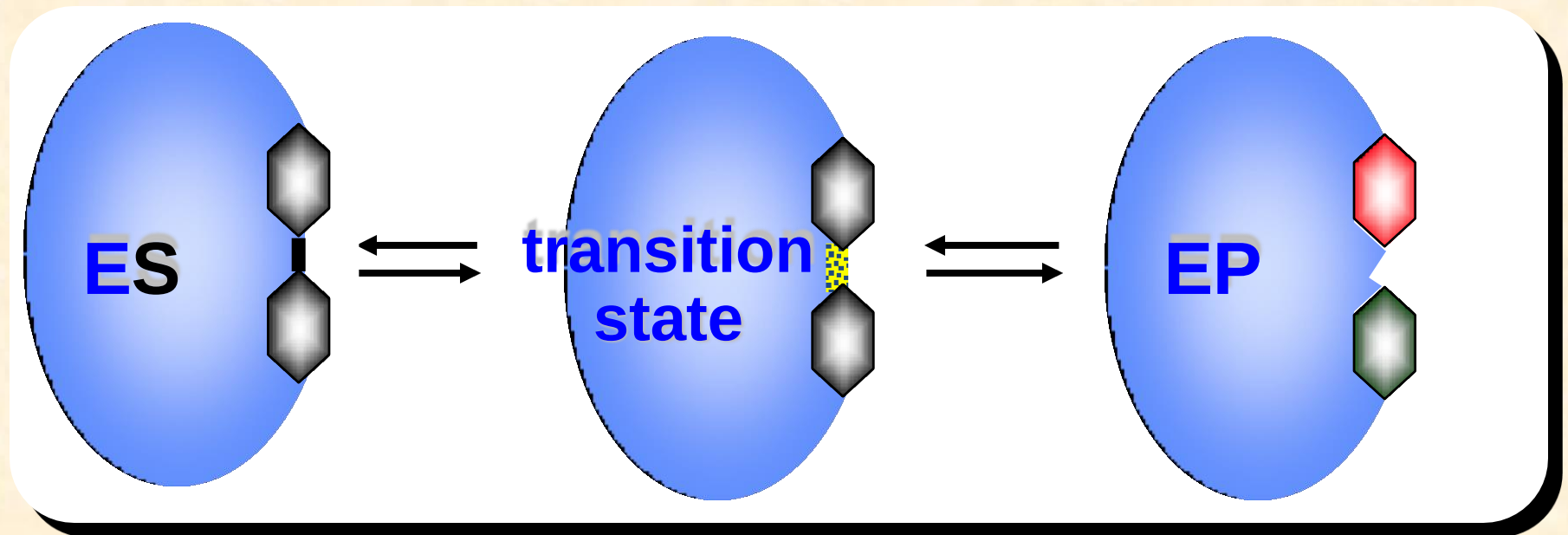
Enzyme-substrate complex

- Step 1:
- Enzyme and substrate combine to form complex



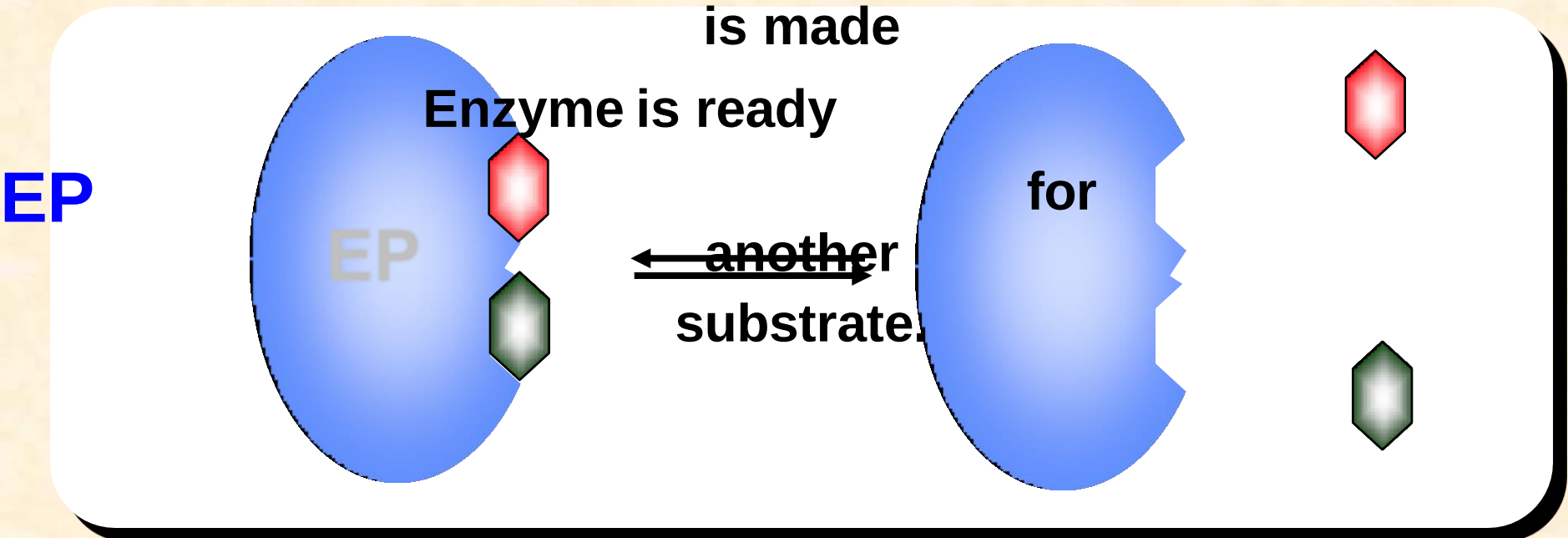
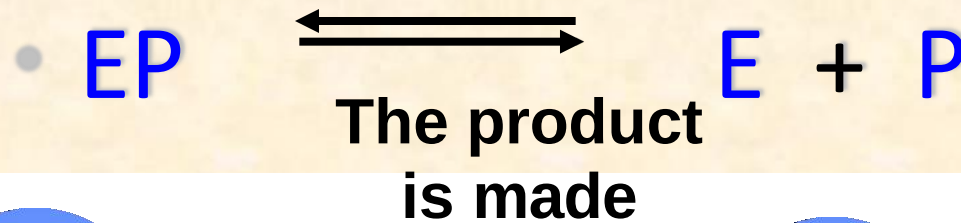
Enzyme-product complex

- Step 2:
- An enzyme-product complex is formed.



Product

- The enzyme and product separate



What Affects Enzyme Activity?

- **Three factors:**

1. Environmental Conditions

2. Cofactors and Coenzymes

3. Enzyme Inhibitors

1. Environmental Conditions

1. Extreme Temperature are the most dangerous

- high temps may denature (unfold) the enzyme.

2. pH (most like 6 - 8 pH near neutral)

3. substrate concentration .

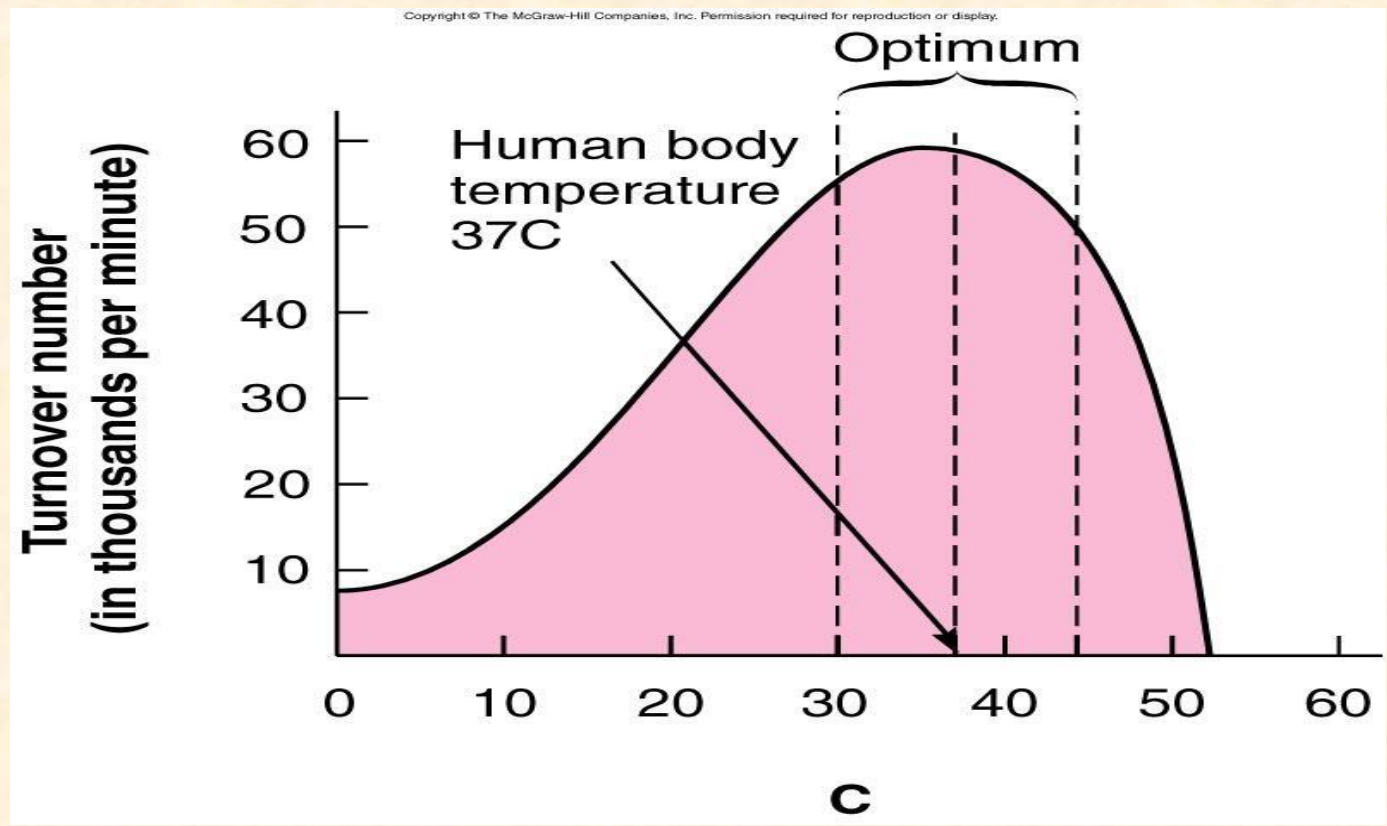
2. Cofactors and Coenzymes

- Inorganic substances (zinc, iron) and vitamins (respectively) are sometimes needed for proper enzymatic activity.
- Example:

Iron must be present in the quaternary structure - hemoglobin in order for it to pick up oxygen.

Environmental factors

- ***Optimum temperature*** The temp at which enzymatic reaction occur fastest.

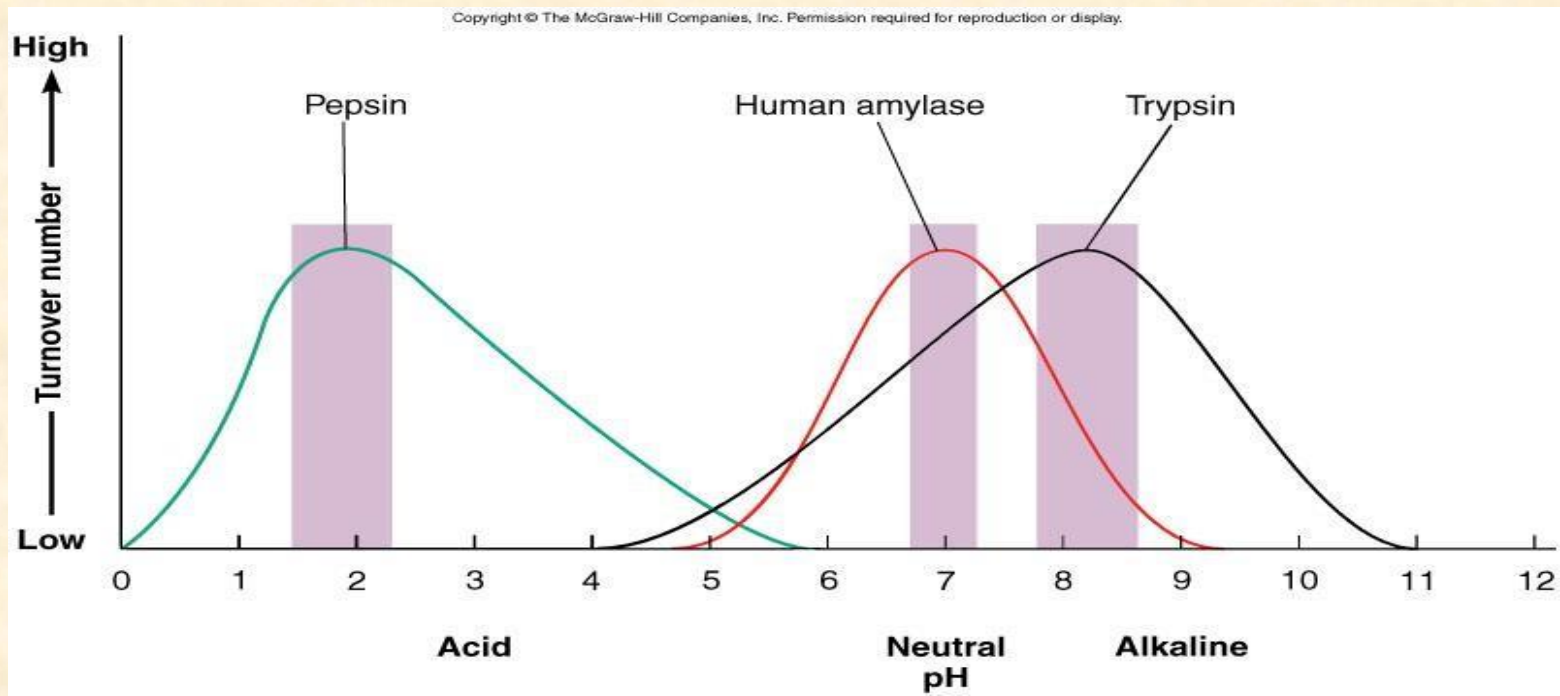


Environmental factors

- pH also affects the rate of enzyme-substrate complexes

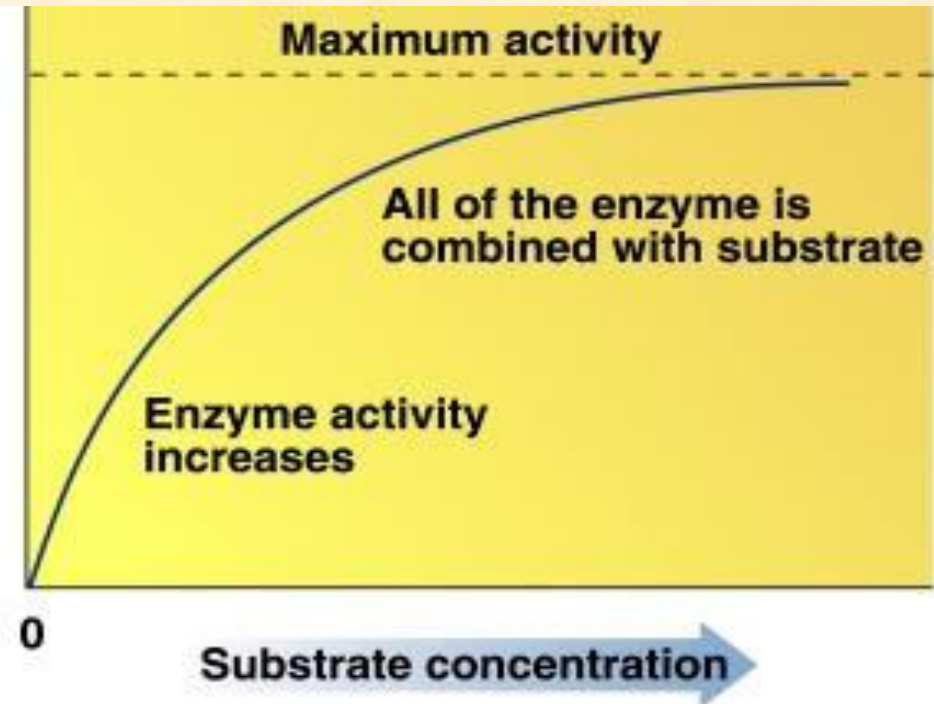
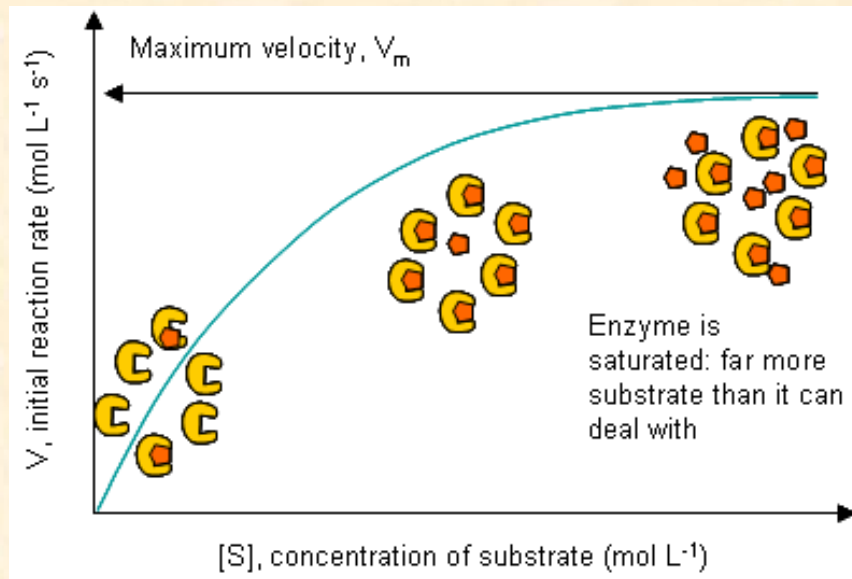
— Most enzymes have an optimum pH of around 7 (neutral)

- However, some prefer acidic or basic conditions



Substrate Concentration and Reaction Rate

- The rate of reaction increases as substrate concentration increases (at constant enzyme concentration)
- Maximum activity occurs when the enzyme is saturated (when all enzymes are binding substrate)



Enzyme Inhibition

Any substance that can diminish the velocity of an enzyme-catalyzed reaction is called an inhibitor and the process is known as inhibition. There are two major types of enzyme inhibition, Irreversible and Reversible.

1- Irreversible Inhibition

The type of inhibition that can not be reversed by increasing substrate concentration or removing the remaining free inhibitor is called Irreversible inhibition. Example: Acetyl cholinesterase catalyzes the hydrolysis of Acetylcholin (to acetic acid and choline) a neurotransmitter substance functioning in certain portions of the nervous system

2-REVERSIBLE INHIBITION

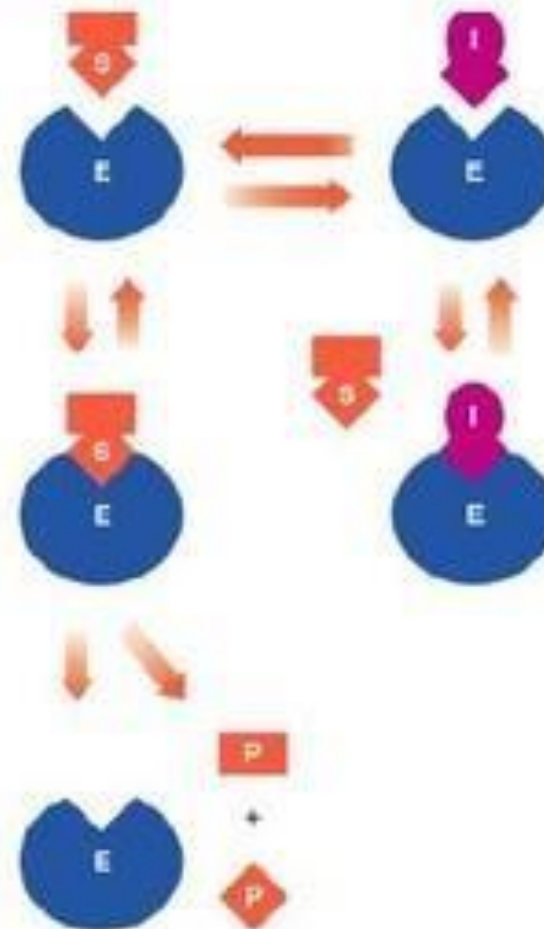
This type of inhibition can be Competitive, Non- competitive and uncompetitive Competitive Inhibition: This type of inhibition occurs when the inhibitor binds reversibly to the same site that the substrate would normally occupy, therefore, competes with the substrate for that site.

In competitive inhibition the inhibitor and substrate compete for the same active site on the enzyme as a result of similarity in structure. The enzyme substrate complex will be broken down to products ($E+S \rightarrow ES \rightarrow E+P$) where as enzyme inhibitor complex; (EI) will not be broken down to products.

Reversible Competitive Inhibition

A **competitive inhibitor**:

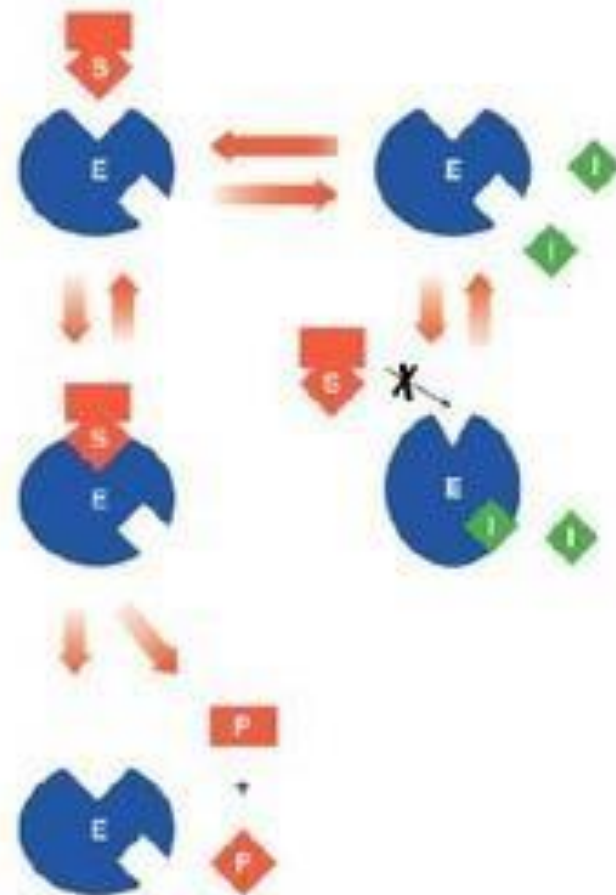
- Has a structure like the substrate.
- Competes with the substrate for the active site.
- Has its effect reversed by increasing substrate concentration.



Noncompetitive Inhibition

A **noncompetitive inhibitor**:

- Has a structure different than the substrate.
- Distorts the shape of the enzyme, which alters the shape of the active site.
- Prevents the binding of the substrate.
- Cannot have its effect reversed by adding more substrate.



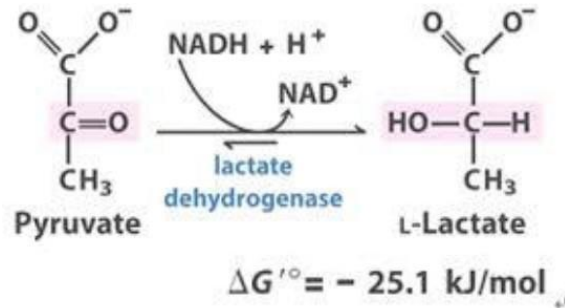
Naming Enzymes

- The name of an enzyme in many cases end in *–ase*
- For example, *sucrase* catalyzes the hydrolysis of sucrose
- The name describes the function of the enzyme
For example, *oxidases* catalyze *oxidation reactions*
- Sometimes common names are used, particularly for the digestion enzymes such as *pepsin* and *trypsin*
- Some names describe both the substrate and the function
- For example, *alcohol dehydrogenase* oxidizes ethanol

**Enzymes Are Classified into six functional
Classes (EC number Classification) by the
International Union of Biochemists (I.U.B.). on the
Basis of the Types of
Reactions That They Catalyze**

- **EC 1. Oxidoreductases**
- **EC 2. Transferases**
- **EC 3. Hydrolases**
- **EC 4. Lyases**
- **EC 5. Isomerases**
- **EC 6. Ligases**

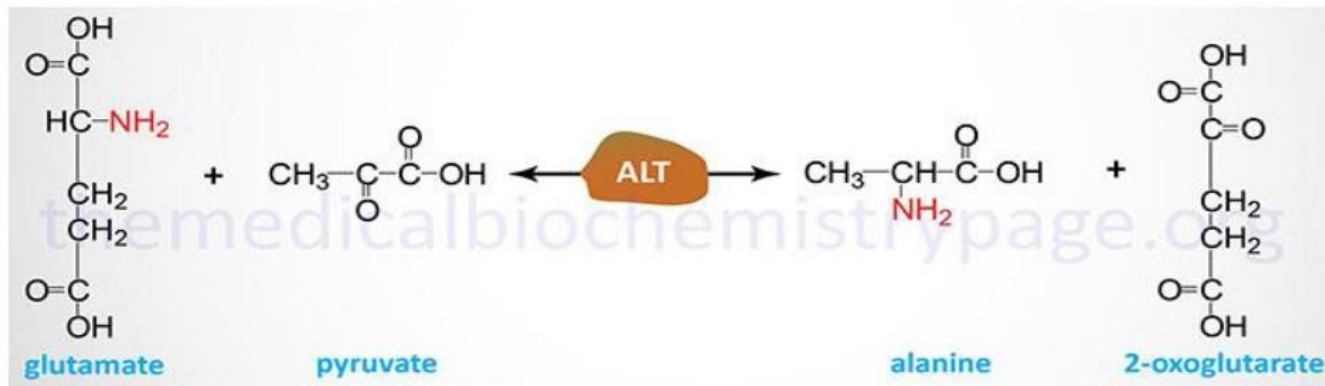
1. Oxidoreductases: one compound oxidized, another reduced. Ex: lactate dehydrogenase, tyrosinase,



2. Transferase:

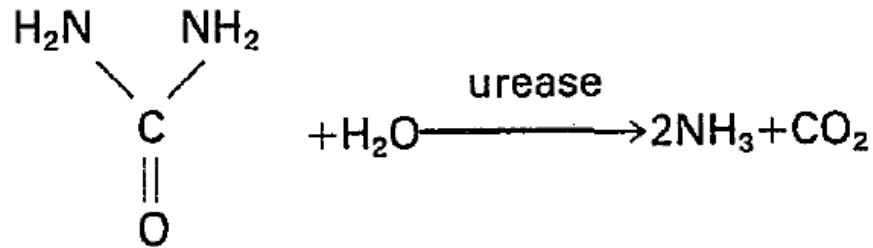
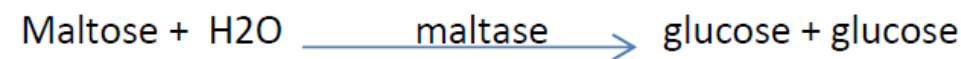
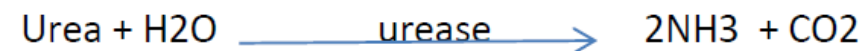
Enzyme transfer group containing C, N or S, from one substrate to another substrate.

Ex: Transaminase (glutamate oxaloacetate transaminase(**GOT**) or Aspartate transaminase (**AST**). and glutamate pyruvate transaminase(**GPT**), alanine transaminase(**ALT**) (transfer of amine group)



3. Hydrolyase:

Catalyse hydrolysis of ester, peptide or glycoside bound by addition of H₂O across the bond.

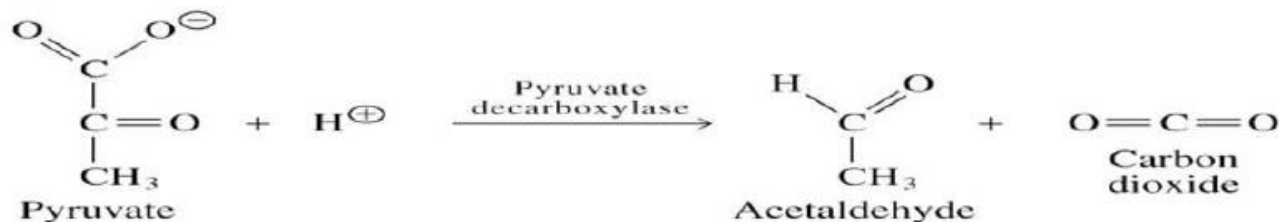


4. Lyasis:

Additional or removal of group without hydrolysis, oxidation, reduction producing double Bond.

4. Lyases

- Catalyze **lysis of a substrate**, generating a **double bond** in a nonhydrolytic, nonoxidative elimination



5. Isomerase:

Produce optical, geometric or position isomer of substrates by intermolecular rearrangement.

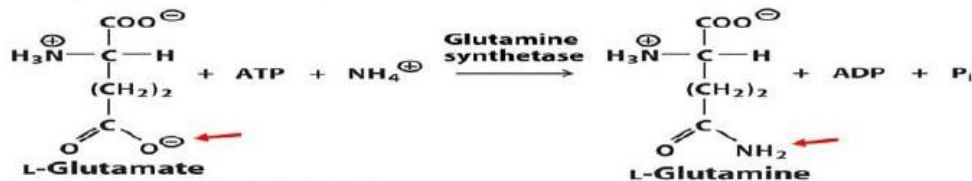


6. Ligases or synthetase:

link two substrate together usually by pyrophosphate bound.

6. Ligases (aka **synthetases**)

Example: L-glutamine synthetase
(EC 6.3.1.2)



Unnumbered figure pg 132s, Principles of Biochemistry, 4/e
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- L-glutamate / NH₄⁺ = substrates
- L-glutamine = product
- ATP = co-factor

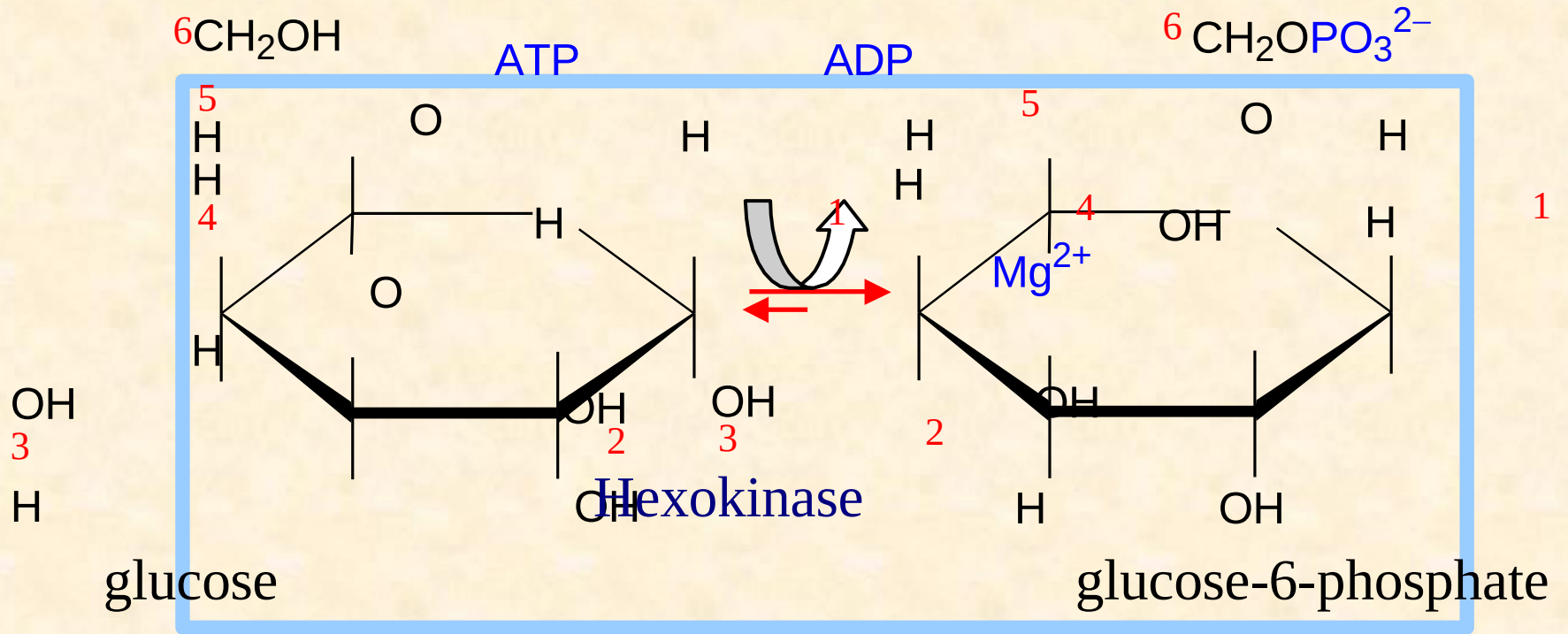
Principle of the international classification

Each enzyme has **classification number** consisting of four digits:

Example, **EC:** **(2.7.1.1)** HEXOKINASE

- **EC: (2.7.1.1)** these components indicate the following groups of enzymes:
- **2. IS CLASS (TRANSFERASE)**
- **7. IS SUBCLASS (TRANSFER OF PHOSPHATE)**
- **1. IS SUB-SUB CLASS (ALCOHOL IS PHOSPHATE ACCEPTOR)**
- **1. SPECIFIC NAME**

ATP,D-HEXOSE-6-PHOSPHOTRANSFERASE (Hexokinase)



1. Hexokinase catalyzes:



ENZYMES IN CLINICAL DIAGNOSIS:

Plasma enzymes can be classified into two major groups

1. Those relatively, small group of enzymes secreted into the plasma by certain organs (i.e. Enzymes those have function in plasma) For example: - the liver secretes zymogens of the enzymes involved in blood coagulation.
2. Those large enzyme species released from cells during normal cell turnover. These enzymes are normally intracellular and have no physiologic function in the plasma. In healthy individuals the levels of these enzymes are fairly constant and represent steady state in which the rate of release from cells into the plasma is balanced by an equal rate or removal from the plasma.

Many diseases that cause tissue damage result in an increased release of intracellular enzymes into the plasma. The activities of many of these enzymes are routinely determined for diagnostic purposes in diseases of the heart, liver, skeletal muscle, and other tissues.

The level of specific enzyme activity in the plasma frequently correlates with the extent of tissue damage. Thus, the degree of elevation of a particular enzyme activity in plasma is often useful in evaluating the diagnosis and prognosis for the patient.

Measurement of enzymes concentration of mostly the latter type in plasma gives valuable information about disease involving tissues of their origin.

1. Lipase:

It is an enzyme catalyzing the hydrolysis of fats. It is secreted by pancreas and Liver. The plasma lipase level may be low in liver disease, Vitamin A deficiency, some malignancies, and diabetes mellitus. It may be elevated in acute pancreatitis and pancreatic carcinoma.

2. α - Amylase

α - amylase is the enzyme concerned with the break down of dietary starch and glycogen to maltose. It is present in pancreatic juice and saliva as well as in liver, fallopian tubes and muscles. The enzyme is excreted in the Urine. The main use of amylase estimations is in the diagnosis of acute pancreatitis. The plasma amylase level may be low in liver disease and increased in high intestinal obstruction, mumps, acute pancreatitis and diabetes.

3. Trypsin: Trypsin is secreted by pancreas. Elevated levels of trypsin in plasma occur during acute pancreatic disease.

4. Alkaline phosphates (ALP)

The alkaline phosphates are a group of enzymes, which hydrolyze phosphate esters at an alkaline pH. They are found in bone, liver, kidney, intestinal wall, lactating mammary gland and placenta. In bone the enzyme is found in osteoblasts and is probably important for normal bone function. The level of these enzymes may be increased in rickets and osteomalacia, hyperparathyroidism, obstructive jaundice, and metastatic carcinoma. Serum alkaline phosphatase levels may be increase in congestive heart failure result of injury to the liver.

5. Acid Phosphatase (ACP)

Acid phosphatases catalyzing the hydrolysis of various phosphate esters at acidic pH is found in the prostate, liver, red cells, platelets and bone. It may be elevated in metastatic prostatic carcinoma.

6. Transaminases:

Two transaminases are of clinical interest.

A- Aspartate Transaminase, AST or (Glutamate oxaloacetate transaminase, GOT):

catalyzes the transfer of the amino group of aspartic acid to α - ketoglutarate forming glutamate and oxaloacetate.

AST or GOT is widely distributed, with high concentration, in the heart, liver, skeletal muscle, kidney and erythrocytes, and damage to any of these tissues may cause raised levels.

B. Alanine transaminase, ALT (Glutamate pyruvate transaminase, GPT):

Transfer the amino group of alanine to α - ketoglutarate, forming glutamate and pyruvate. It is present in high concentration in liver and to a lesser extent in skeletal muscle, kidney and heart.

- Serum levels of glutamate- pyruvate transaminase (SGOT) and Glutamateoxaloacetate- transaminase (SGOT) are useful in the diagnosis of liver parenchymal damage and myocardial damage respectively. In liver damage, both enzymes are increased, but SGPT increases more. In myocardial infarction SGOT is increased

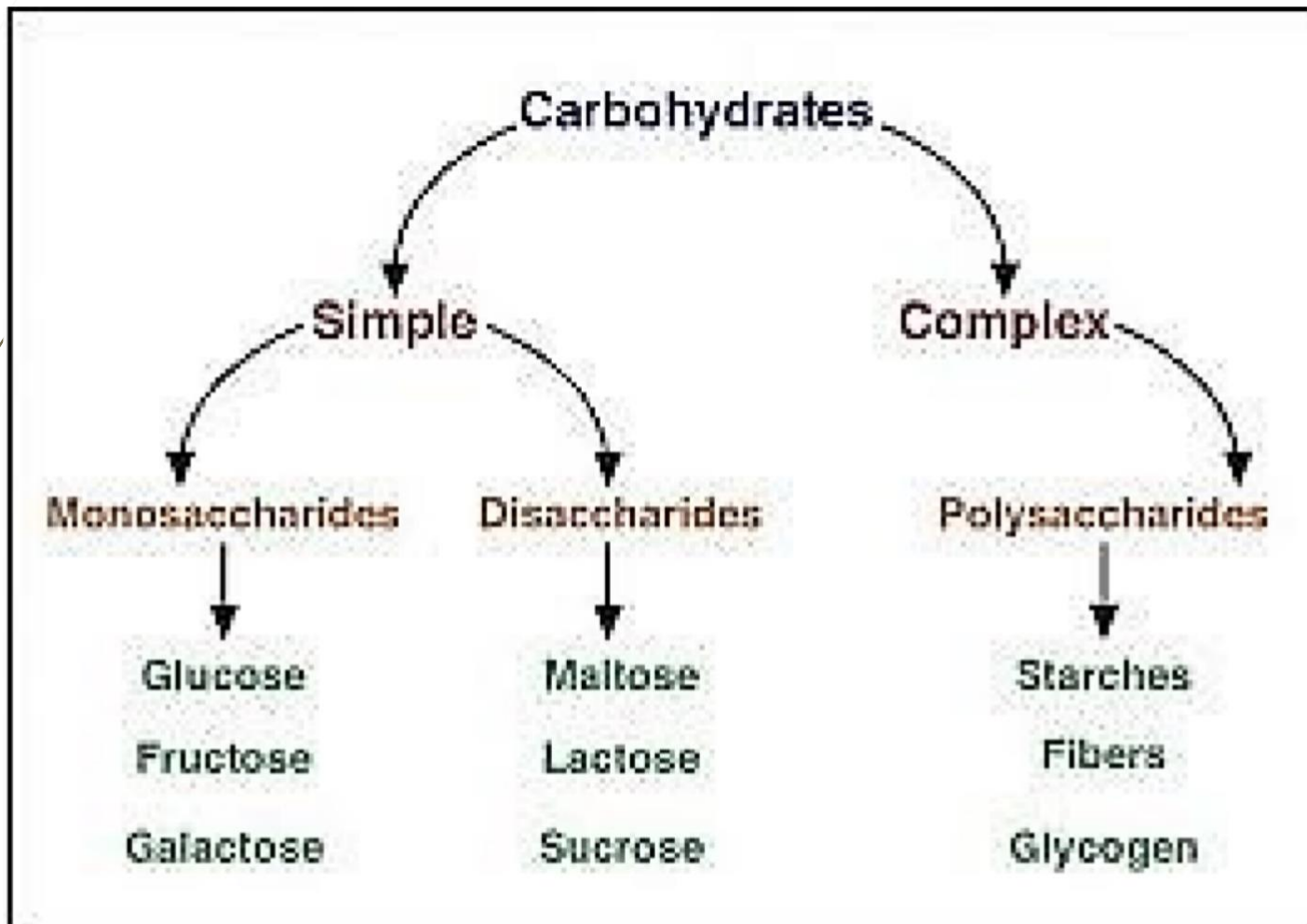
7. Lactate Dehydrogenase (LDH)

It catalyzes the reversible interconversion of lactate and pyruvate. It is widely distributed with high concentrations in the heart, skeletal muscle, liver, kidney, brain and erythrocytes. The enzyme is increased in plasma in myocardial infarction, acute leukemias, generalized carcinomatosis and in acute hepatitis. Estimation of its isoenzymes is more useful in clinical diagnosis to differentiate hepatic disease and myocardial infarction.

8. Creatine kinase (CK) or creatine phosphokinase (CPK):

CK (CPK) is found in heart muscle, brain and skeletal muscle. Measurement of serum creatine phosphokinase activity is of value in the diagnosis of disorders affecting skeletal and cardiac muscle. The level of CPK in plasma highly increased in myocardial infarction.

Carbohydrates



Carbohydrates

Definition:-

Carbohydrates may be defined as organic compounds occurring in foods and living tissues and including sugars, starch, and cellulose, composed of the elements C, H, and O.

Carbohydrates are

- A major source of energy from our diet.
- Also called saccharides, which means “sugars.”

The importance Of carbohydrates

Functions of Carbohydrates:

1 - Source of energy for living beings, e.g. glucose

2 - Storage form of energy, e.g. glycogen

3 - Serve as structural component, e.g. glycosaminoglycans in humans

4 - Non-digestible carbohydrates like cellulose, serve as dietary fibers

5 - Constituent of nucleic acids RNA and DNA, e.g. ribose and deoxyribose sugar

6 - Play a role in immunity and also involved in detoxification, e.g. glucuronic acid

Classification of Carbohydrates

Classification:

According to no. of sugar units

Monosaccharides: 1 sugar unit : glucose, fructose, galactose, *which present mainly in fruits*

Disaccharides: 2 sugar units: **lactose** *which known as sugar milk* (galactose + glucose), **maltose** (glucose + glucose), **Sucrose** (glucose + fructose).

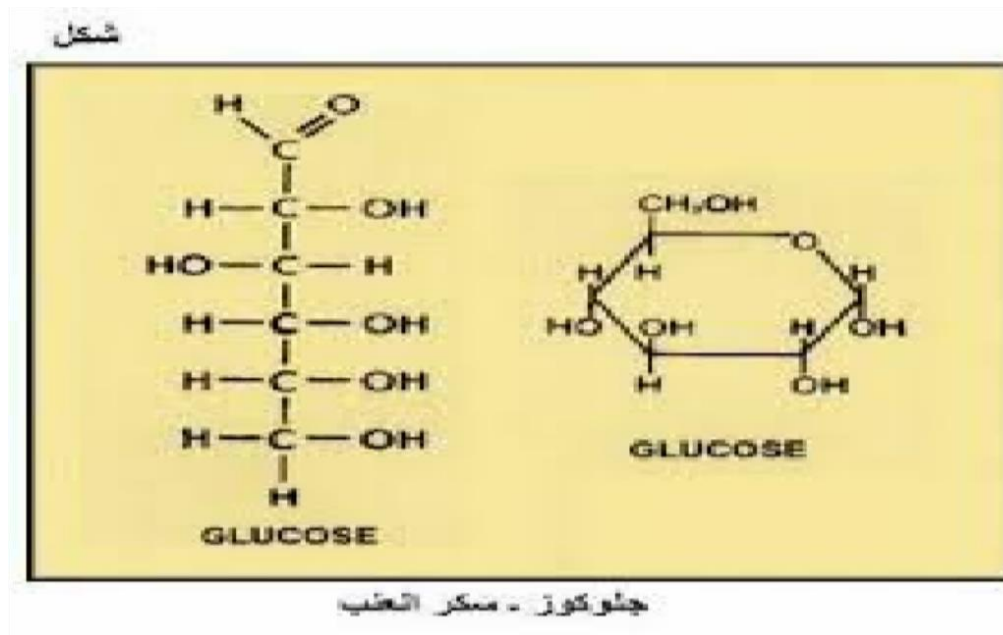
Oligosaccharides: 3-9 units

Polysaccharides: 10 or more units

The suffix *ose* indicates that a molecule is a carbohydrate

GLUCOSE

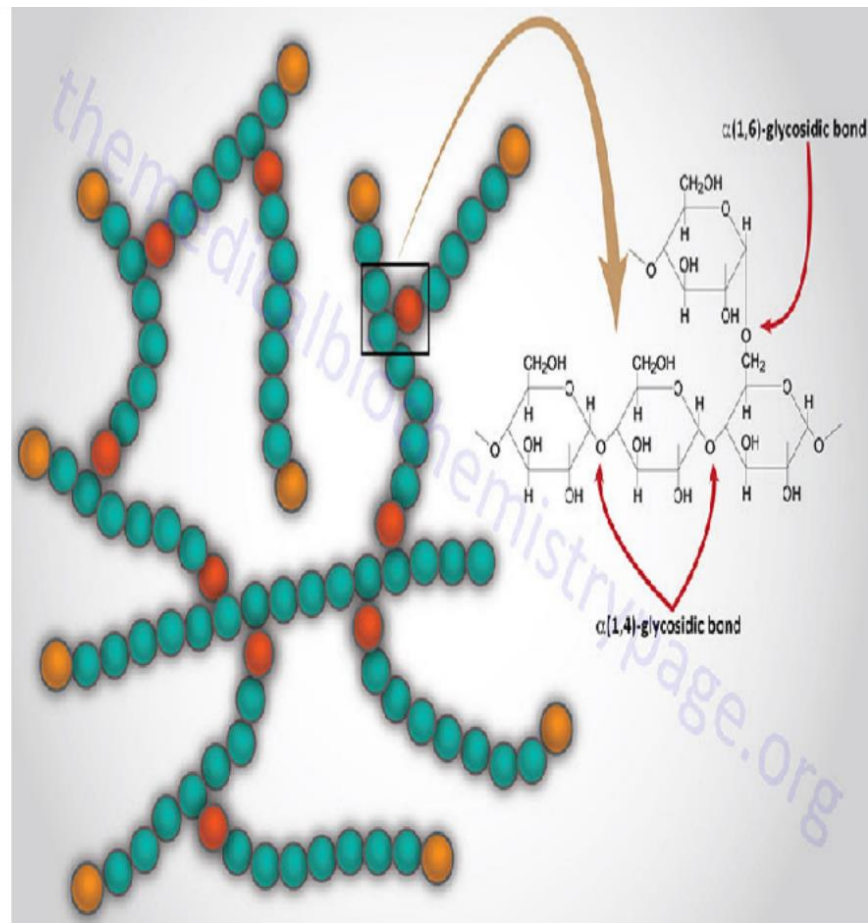
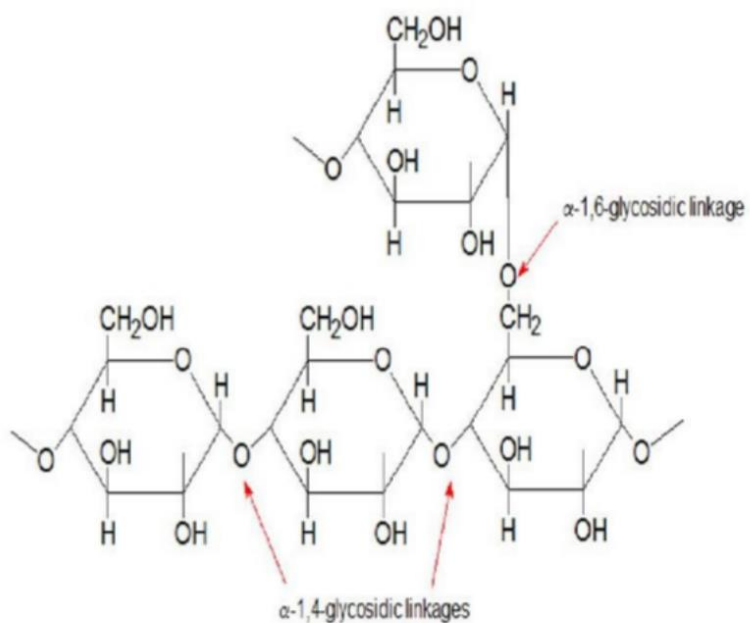
- Physiologically and biomedically , glucose is the most important **monosaccharide**
- It is called blood sugar
 - $C_6H_{12}O_6$
- It is source of energy
- It is can be stored in our body in form of glycogen



GLYCOGEN METABOLISM

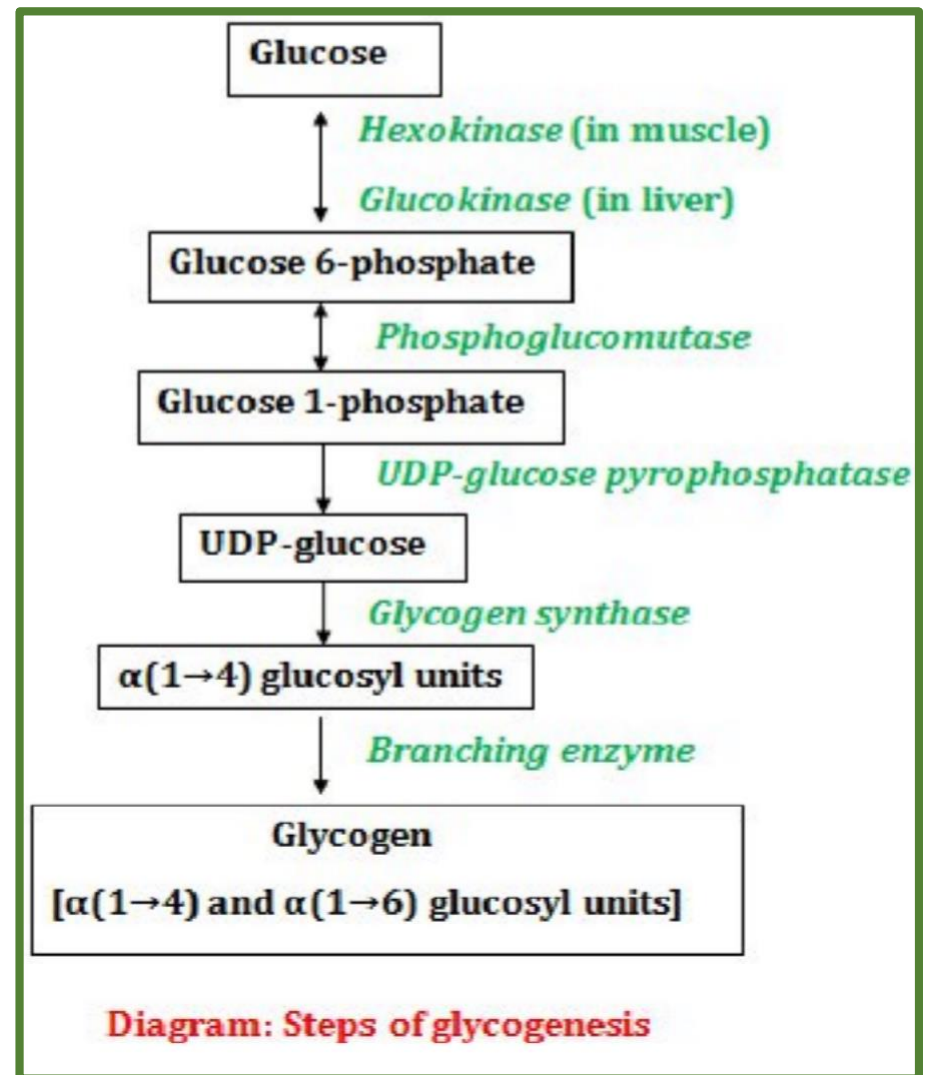
- Glycogen is the major storage form of glucose mainly in the liver and muscle.
- The concentration of liver glycogen (up to 6%) is greater than in muscle tissues (1%).
- The synthesis(glycogenesis) and degradation(glycogenolysis) occur via different pathways. Glycogenesis and glycogenolysis are both cytosolic processes

Glycogen structure



Glycogenesis

Glycogenesis is the pathway for the formation of glycogen from glucose. This process requires energy, supplied by ATP and uridine triphosphate (UTP). It occurs in muscle and liver.



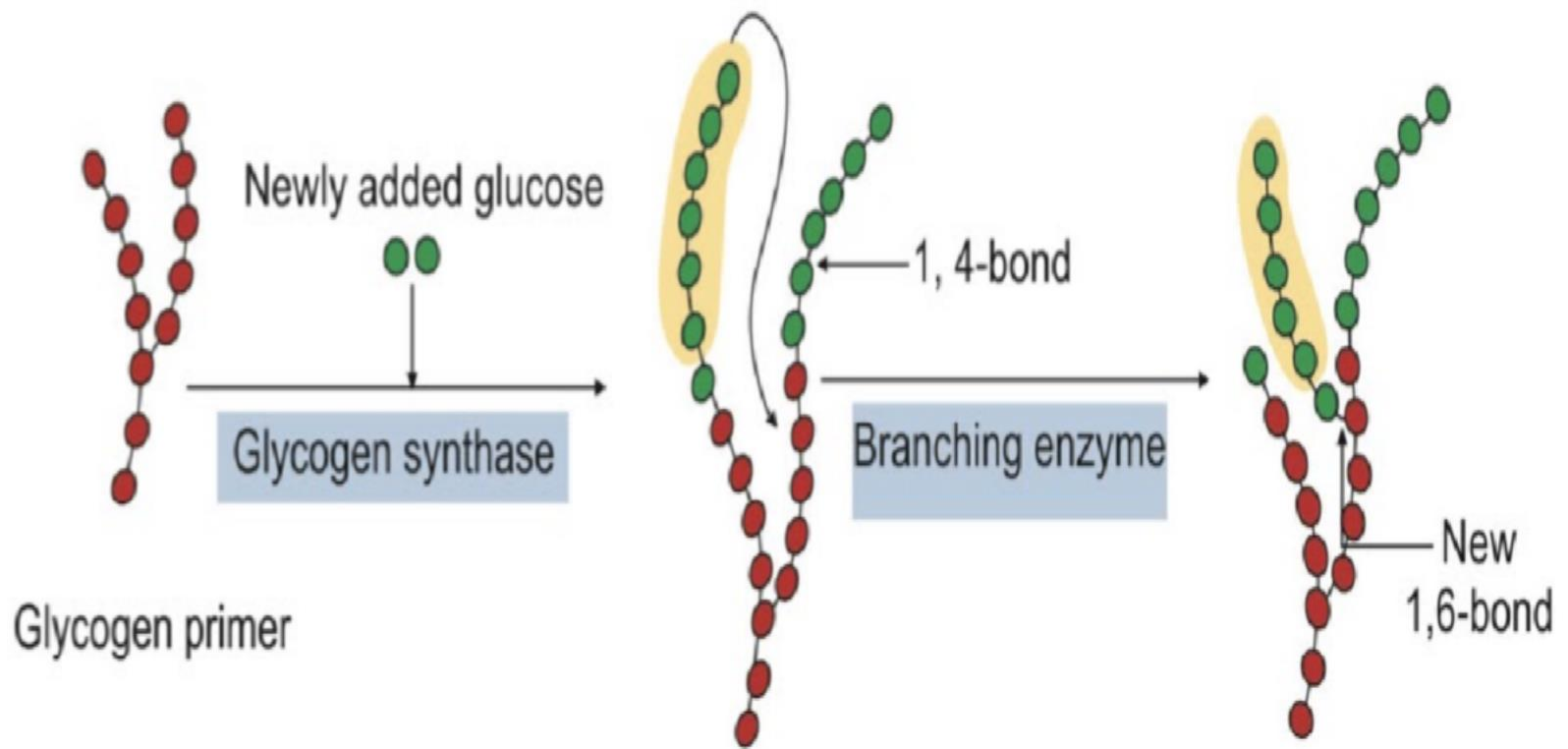
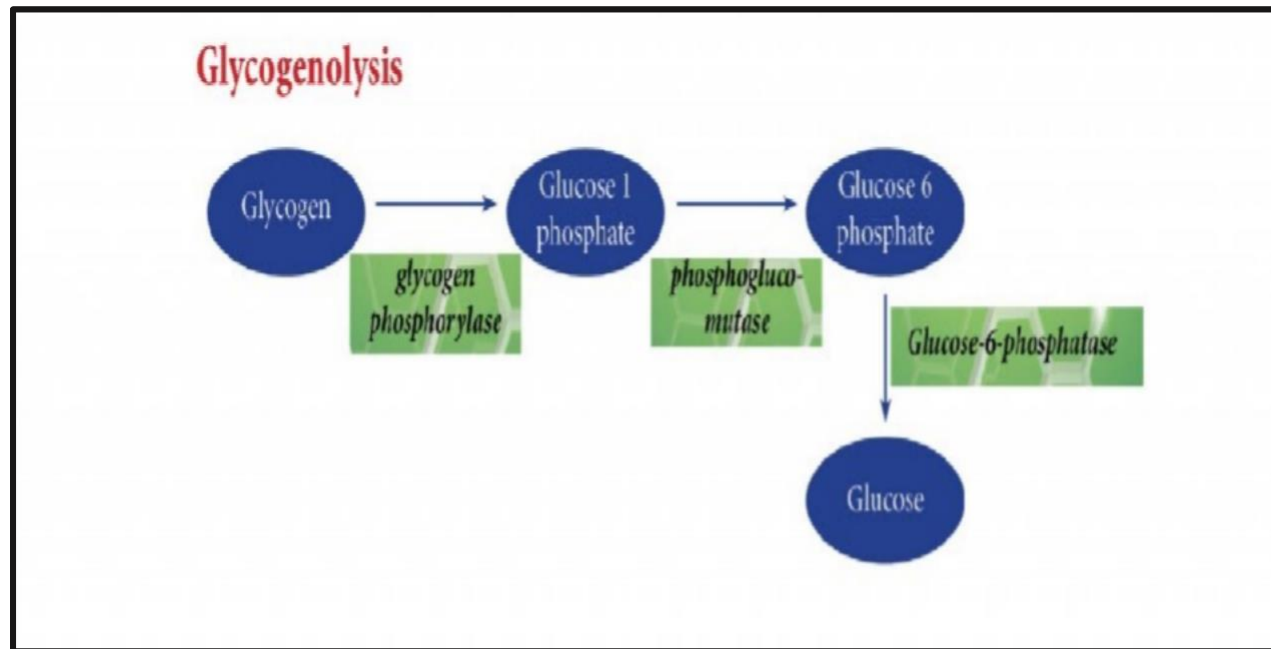


Figure 12.11: Schematic representation of glycogenesis (mechanism of branching)

Glycogenolysis

Glycogenolysis is the degradation of glycogen to glucose-6-phosphate and glucose in muscle and liver respectively. Glycogenolysis is not the reverse of glycogenesis but is a separate pathway.



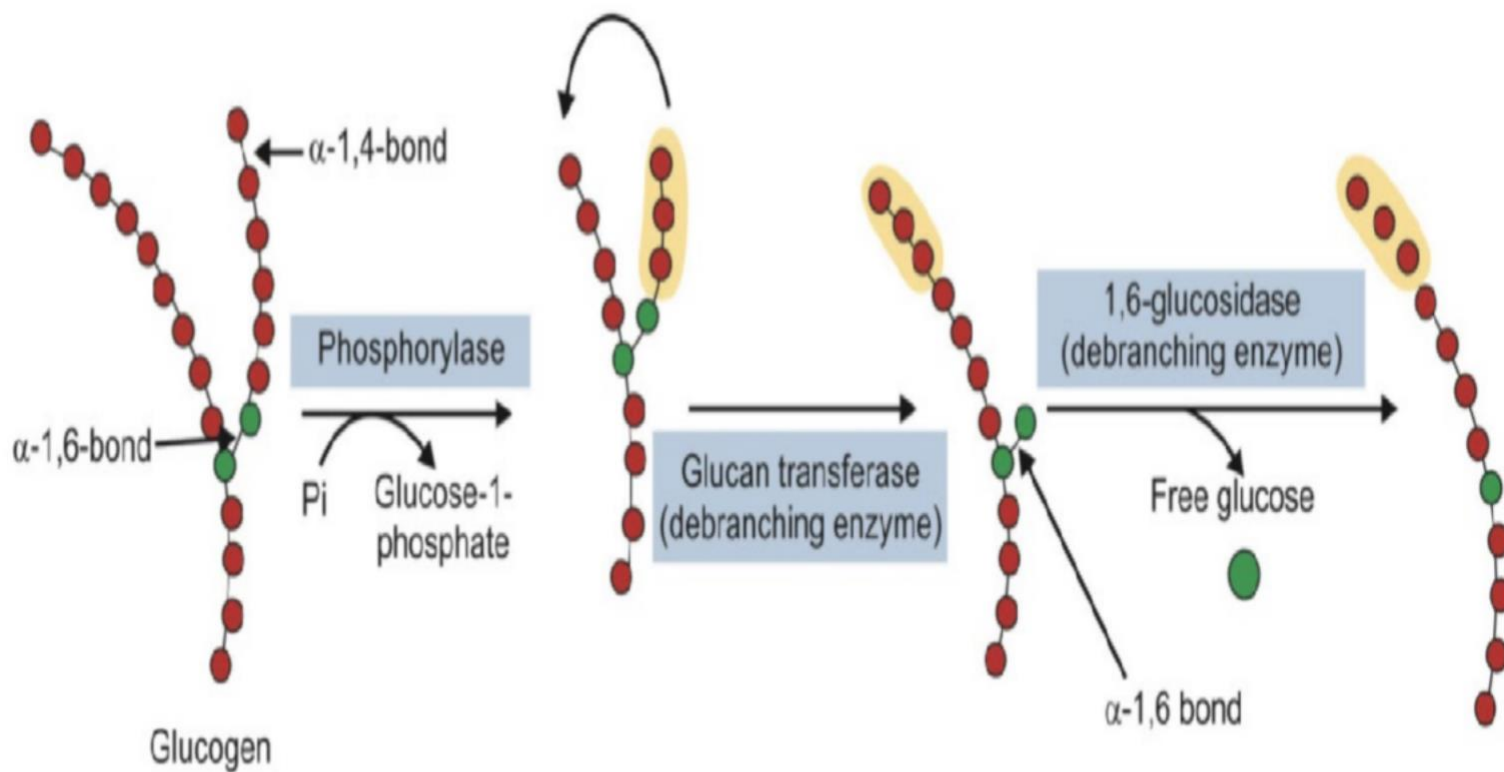


Figure 12.12: Schematic representation of glycogenolysis (mechanism of debranching)

Significance of Glycogenolysis and Glycogenesis

In liver

Following a meal, excess glucose is removed from the portal circulation and stored as glycogen by glycogenesis. Conversely, during fasting, blood glucose levels are maintained within the normal range by release of glucose from liver glycogen by glycogenolysis.

In muscle

The function of muscle glycogen is to act as a readily available source of glucose within the muscle itself during muscle contraction. The muscle cannot release glucose into the blood, because of the absence of glucose-6-phosphatase that hydrolyzes glucose 6-phosphate to glucose. Therefore, muscle glycogen stores are used exclusively by muscle.

Glucose metabolism

Glycolysis

is the sequence of reactions that converts glucose into pyruvate in the presence of oxygen (aerobic) or lactate in the absence of oxygen (anaerobic) with the production of ATP.

It is a unique pathway since it can utilize oxygen if available, or it can function in the total absence of oxygen

Location

Glycolysis is the major pathway for the utilization of glucose and is found in cytosol of all cells.

- **Under aerobic condition**

pyruvate is taken up into mitochondria and after conversion to acetyl-CoA is oxidized to CO_2 and H_2O by citric acid cycle with production of ATP.

- **Anaerobic Glycolysis**

- Tissues that function under hypoxic conditions produce lactate, e.g. exercising skeletal muscle and erythrocytes.

- In erythrocytes even under aerobic conditions, glycolysis produce lactate because of absence of mitochondria.

Gluconeogenesis

The synthesis of glucose from noncarbohydrate precursors is called gluconeogenesis

Precursors for gluconeogenesis include:

- Lactate
- Glycerol
- Glucogenic amino acids

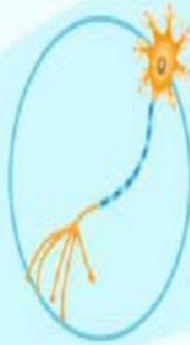
Location of Gluconeogenesis

Gluconeogenesis occurs mainly in the cytosol. Liver is the major tissue for gluconeogenesis. During starvation, the kidney is also capable of making glucose by gluconeogenesis.

Diabetes mellitus

- Diabetes mellitus is a group of diseases in which blood glucose levels are elevated. Diabetes is the most common disorder of carbohydrate metabolism
- Diabetes is the leading cause of many **complications** as:
 - end-stage renal disease
 - non traumatic amputations,
 - blindness.
 - atherosclerotic disease.
 - deaths

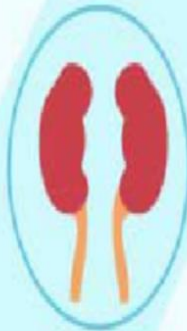
Diabetic
neuropathy



Cardiovascular
disease



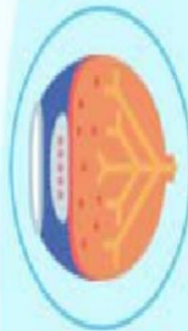
Diabetic
nephropathy



Diabetic
foot ulcers



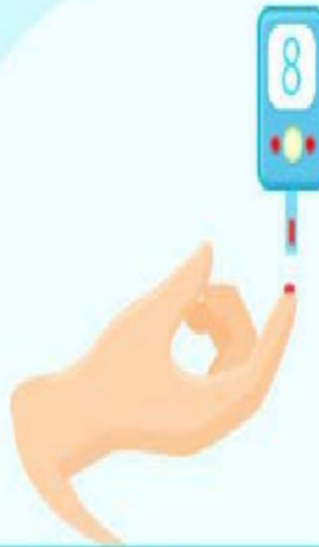
Diabetic
retinopathy



Cognitive
deficit



Diabetes Complications



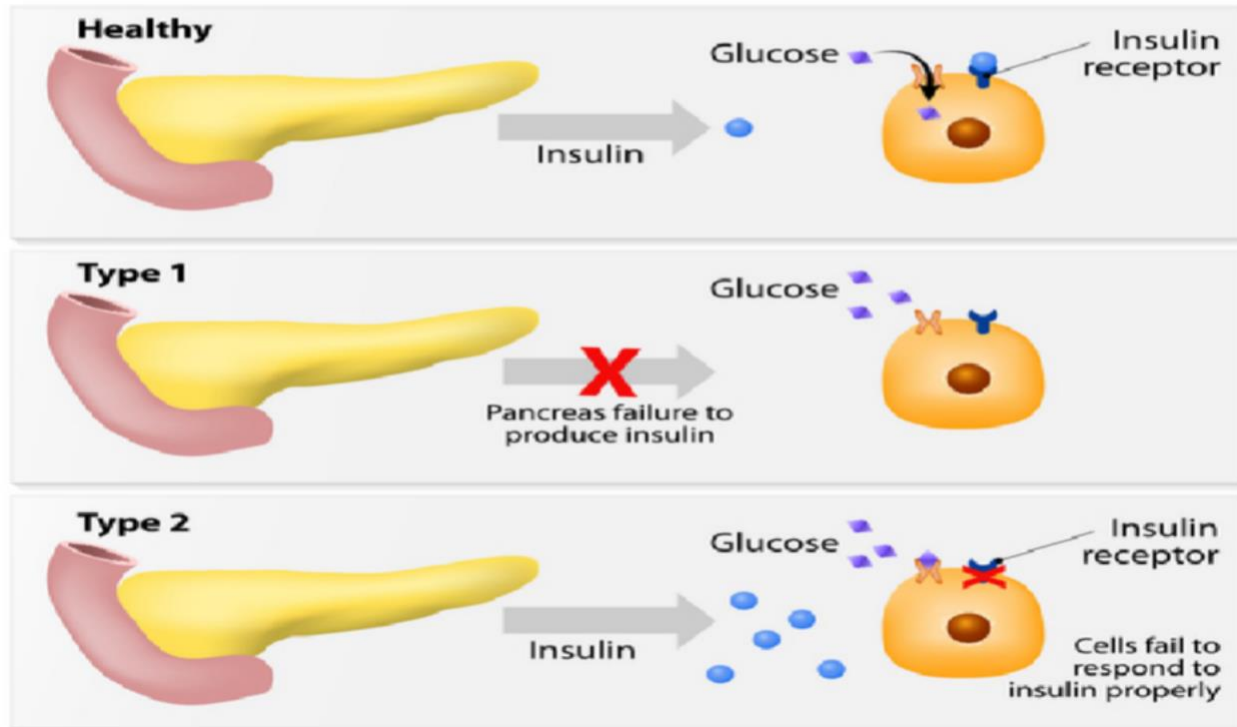
Pathophysiology

- After carbohydrates digestion and absorption the blood glucose is elevated which stimulates the pancreas to release insulin that facilitates glucose entry inside the cells to use it as a source of energy or in other metabolic processes
- In diabetes mellitus, metabolism of all the main foodstuffs is altered. The basic effect on glucose metabolism is insulin deficiency or insulin resistance

Classification

- **type 1 diabetes mellitus**, which is caused by an absolute or near **absolute deficiency of insulin**,
- represents approximately **10% of all cases** of diabetes.
- There usually is an **autoimmune destruction** of insulin-producing beta cells in the islets of the pancreas
- **type 2 diabetes mellitus**, which is characterized by the presence of **insulin resistance** with an inadequate compensatory increase in insulin secretion which usually end with relative or absolute deficiency in insulin secretion.
- Type 2 diabetes is the most common type of diabetes, affecting approximately **90% of cases**. Many of them are **obese**

DIABETES MELLITUS



In addition, women who develop diabetes during their pregnancy are classified as having **gestational diabetes**.



Other specific types of diabetes.

Diagnosis of Diabetes

Any of the followings tests is diagnostic to DM:

- Fasting blood glucose ≥ 126
- Random blood glucose or 2 Hrs. post prandial blood glucose ≥ 200 mg/dl
- HbA1c $\geq 6.5\%$

To confirm the diagnosis repeat the same test in different day

Glycated hemoglobin

- **Glycated hemoglobin (HbA1c)** is the term used to describe the formation of a hemoglobin compound produced when glucose reacts with the globin part of hemoglobin.
- HbA1c testing provides an index of average blood glucose levels over the past 2 to 4 months (depending on RBC life span)
- Conditions associated with shortened red blood cell survival such as hemolysis and pregnancy will lower the HbA1c level .

**Thank you for
your listening**