1-Biochemistry

Is the science concerned with study of chemical processes occurring in living tissues (change in material & energy).

Clinical biochemistry : Is the application part of biochemistry for diagnosis of the clinical condition by determining various constituents in different body fluids.

Determination can be qualitative or quantitative different body fluid used for diagnosis include

a) blood
b) plasma
c) serum
d) urine
e) Cerebral spinal fluid (CSF)
f) sputum
g) stools
h) semen

Introduction:

- The human body is mainly water plus a wide variety of biologically active chemicals which sub serve all the functions of the body .
- Biochemistry describes how these molecules are made and the interactions between them at molecular level .
- Cell biology then goes on to describe how the biochemical sare organized into cells and cellular components, which then form the tissues of the body .
- Normal processes within the body are called physiological whereas processes that cause disease are called **pathological.**

Metabolism:

- All the processes of replication, growth, repair and so on that are vital to the survival of a cell require energy.
- Much of the economy of any cell is taken over by the chemistry require firstly, to generate that energy, and secondly, to harness it to drive crucial processes or to build molecules needed by the cell to maintain itself.
- All this chemistry is termed metabolism .
-

Chemical machines :

At any time a cell may have many thousands of individual chemical reactions going on simultaneously, each a part of a metabolic pathway that may result in the breakdown of larger molecules, or the assembly of large molecules from smaller ones, or simply the conversion of one molecule into another. All of these pathways need to be controlled so that molecules are produced in the right place in the right amounts.

***Catabolism and anabolism* :**

- In general, metabolism that involves degrading complex molecules to simpler ones called catabolism is the route by which chemical energy is generated.
- By contrast, the metabolism that results in the synthesis of more complex molecules from simpler components anabolism has a net requirement for chemical energy.
- It is these synthetic metabolic pathways that produce the components needed for cell growth, repair and replication.

Basic chemistry :

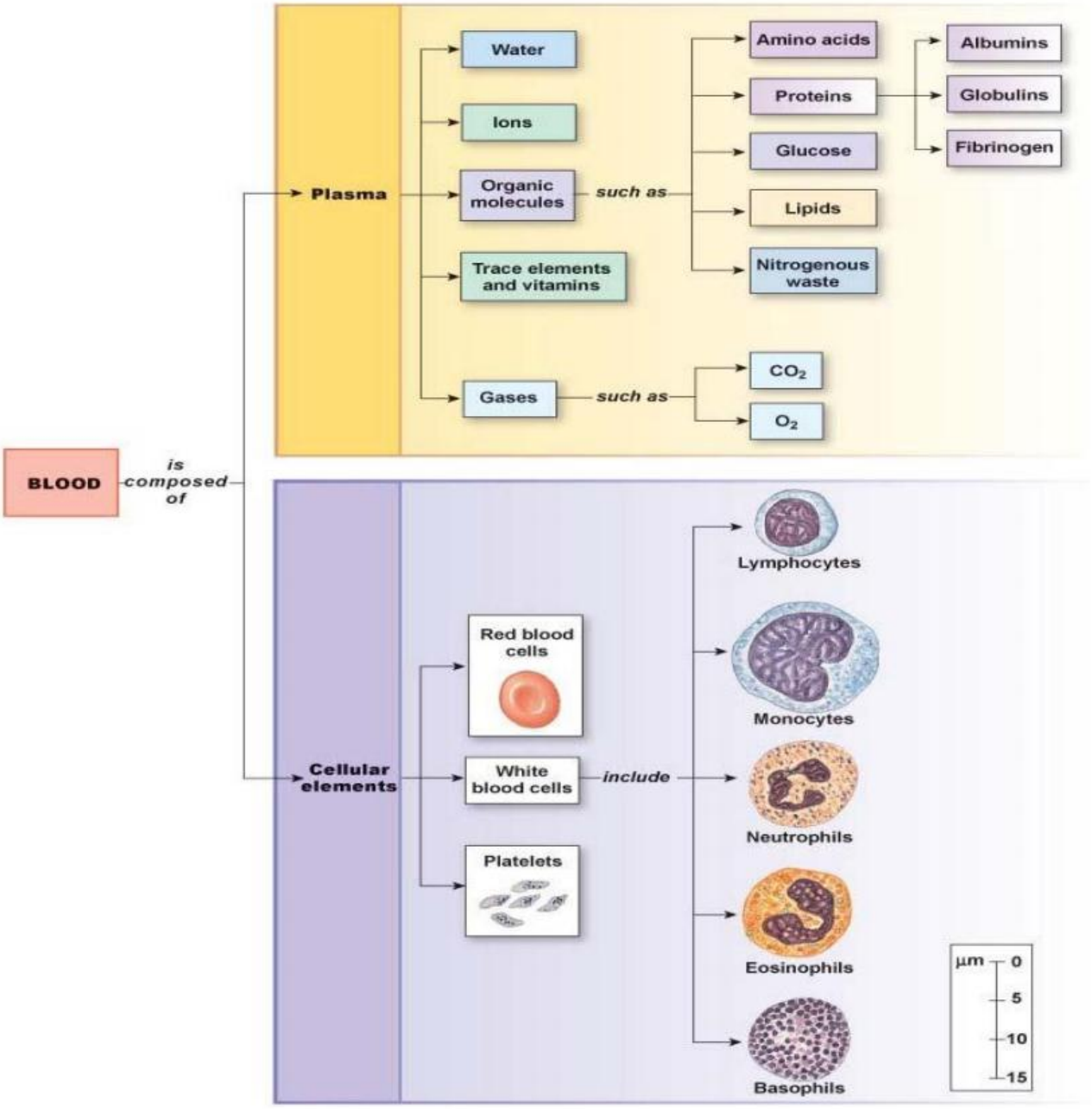
Chemical composition of the human body

1) The chemical which make up the human body are mainly compounds consisting of combinations of carbon, hydrogen and oxygen atoms with small quantities of other elements.
2) These are known as organic compounds because they contain carbon. Together with nitrogen, carbon, hydrogen, and oxygen make up 96.3% of the body weight.
3) The remaining 3.7% is made up of seven minor elements.
4) As well as these major and minor elements there are a number of trace elements which are required in very small amount (less than 0.01%).
5) Many of these are needed as special components of proteins called enzymes and are required for their activation.

The Blood

- Blood is a tissue which circulates in a closed system of blood vessels.
- It consist of cellular protein (red & white blood cells and the platelets) form (45%) of blood volume and suspended in extra cellular liquid medium: the plasma (55%) of blood volume blood represent 8% of body weight, it's approximately 5-6 litter and it consist of :

1. **Plasma.**
2. **Blood cells** : those consist of :
    1) Red blood cell. 2) White blood cell 2)Platelets.



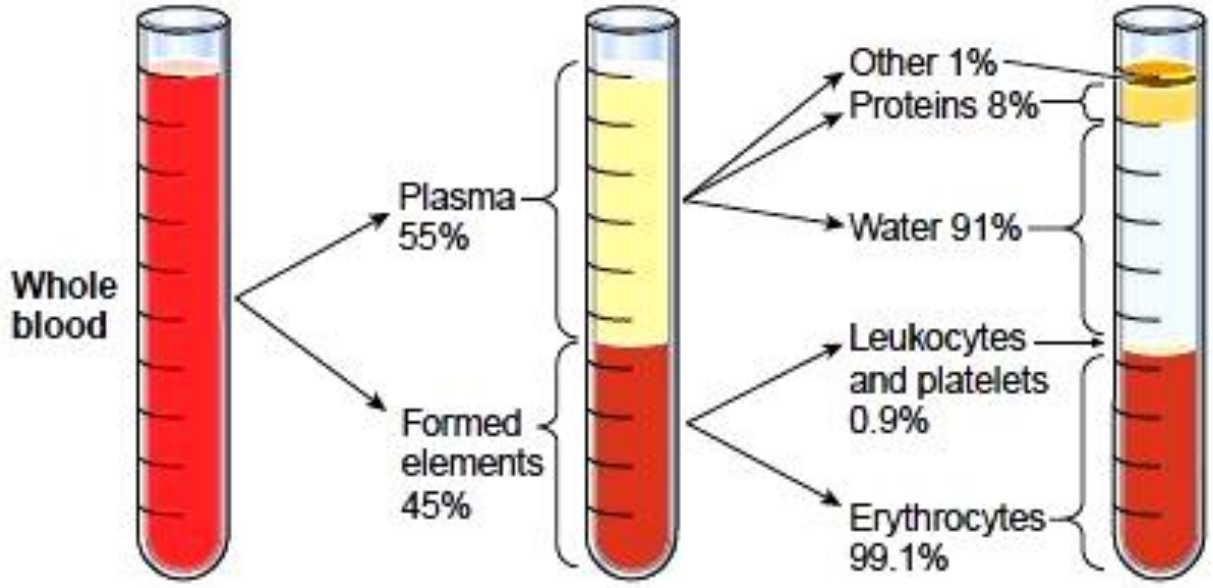
The figure show the composition of Blood

Plasma

- Water 90%
- dissolved solutes 10%
- blood gases O_2 and Co_2

dissolved solutes 10%:

- organic substances 9.1 %
  - Plasma proteins 7.1
  - Others 2 %: Lipids, enzymes, Hormones, nutrients, Waste products
- In-organic substances 0.9 %: Various electrolytes as Na^+, K^+, Hco_3^-, Ca^{++}, Po_4^{--}



Blood is divided into four major products:

1. ***Red balls:***

- Constitute about 45% of the blood and oxygen transport function of the lungs to other parts of the body and the transfer of carbon dioxide from various parts of the body to the lungs, and contain hemoglobin which gives blood its red color. There are 5 million cubic millimeter in the globule of blood and lives of each period of 120 days and then break down to the bone marrow to produce another ball again.

2. ***white balls:***

- Defend the body against diseases and fight germs, and it has many kinds can be differentiated by shape and range in number between 4-10 in thousands of cubic millimeter of blood.

3. ***Platelets:***

- It is the smallest blood cells that help the blood clot that stops bleeding if injured man, God forbid, by bridging the wound, and number between 150-450 thousand cubic millimeter in and incompleteness lead to bleeding may lead to death .

4. ***Plasma***

- Is a yellow liquid protein consists mainly of water. And plasma constitute more than half the size of the blood, and contains all the clotting factors and other proteins as diverse as albumin and Alomeonocalopulin (antibodies) and the plasma transfer of digested food to all parts of the body, as bearing waste metabolism to the kidneys and lungs in order to remove them out of the body, and swim in plasma blood cells.
- Plasma consists of water ,electrolytes, metabolites, nutrients ,proteins and hormones. The water and electrolytes composition of plasma is practically the same as that of all extra cellular fluids.
- Blood proteins (Hemoglobin, albumin, globulins, fibrinogen) these proteins is very importance because the change in the amounts of various plasma proteins occur in many diseases.
- The analysis of clinical biochemistry required whole blood, serum or plasma. When blood is drawn and allowed to clot, a clear liquid (serum) exuded from the clotted blood. Plasma on the other hand ,separates from the cells only when blood is prevented from clotting (uncoagulated).

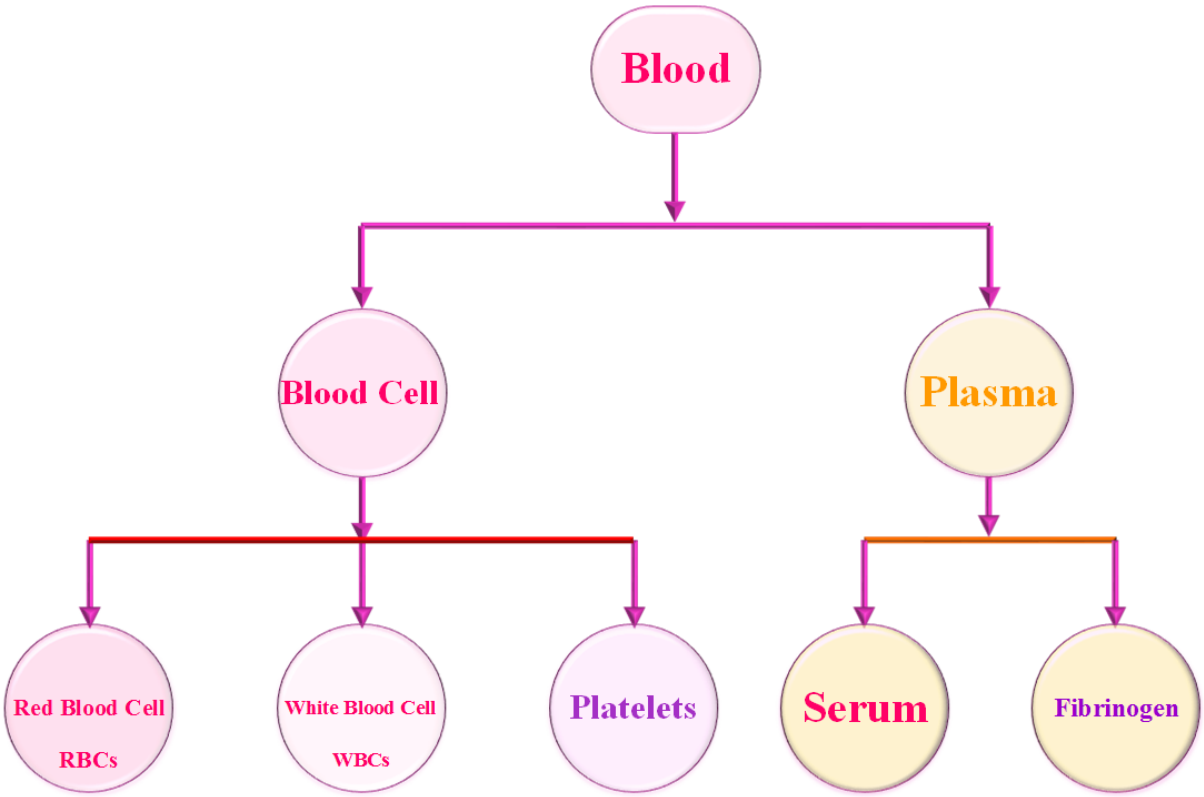


Diagram show the percent of the most important contents in Blood

Blood composition	Per 100 mil/ litter
hemoglobin	12-16 gm
Plasma protein	6-8 gm
glucose	60-90 mg
Total cholesterol	150 – 250 mg
Free cholesterol	50 – 70 mg
Uric acid	3-5 mg
Urea	12 – 40 mg
Creatinine	0.7 – 1.5 mg
sodium	320 –340 mg
Potassium	16-22 mg
Calcium	9-11 mg
Bilirubin	0.2-0.8 mg

Function of blood

- The function of blood all except specific cellular one's such as oxygen transport and cell-mediated immunologic defense are carried out by plasma and its constituents they are as follows: -

1. Transport of oxygen from the lungs to the tissues and of CO_2 from the tissues to the lungs.
2. Nutrition transport of absorbed food materials.
3. Excretion transport of metabolic wastes the kidneys, lunges, skin and intestines for removal.
4. Maintenance of normal acid-base balance in the body.
5. Regulation of water balance through the effects of blood an the exchange of water between the circulating fluid and the tissue fluid .
6. Regulation of body temperature by the distribution of body heat.
7. Defense against infection by the leukocytes (white blood cell) and the circulating antibodies.
8. Transport of hormones and regulation of metabolism.
9. Transport of metabolism.

Collection of blood specimens:-

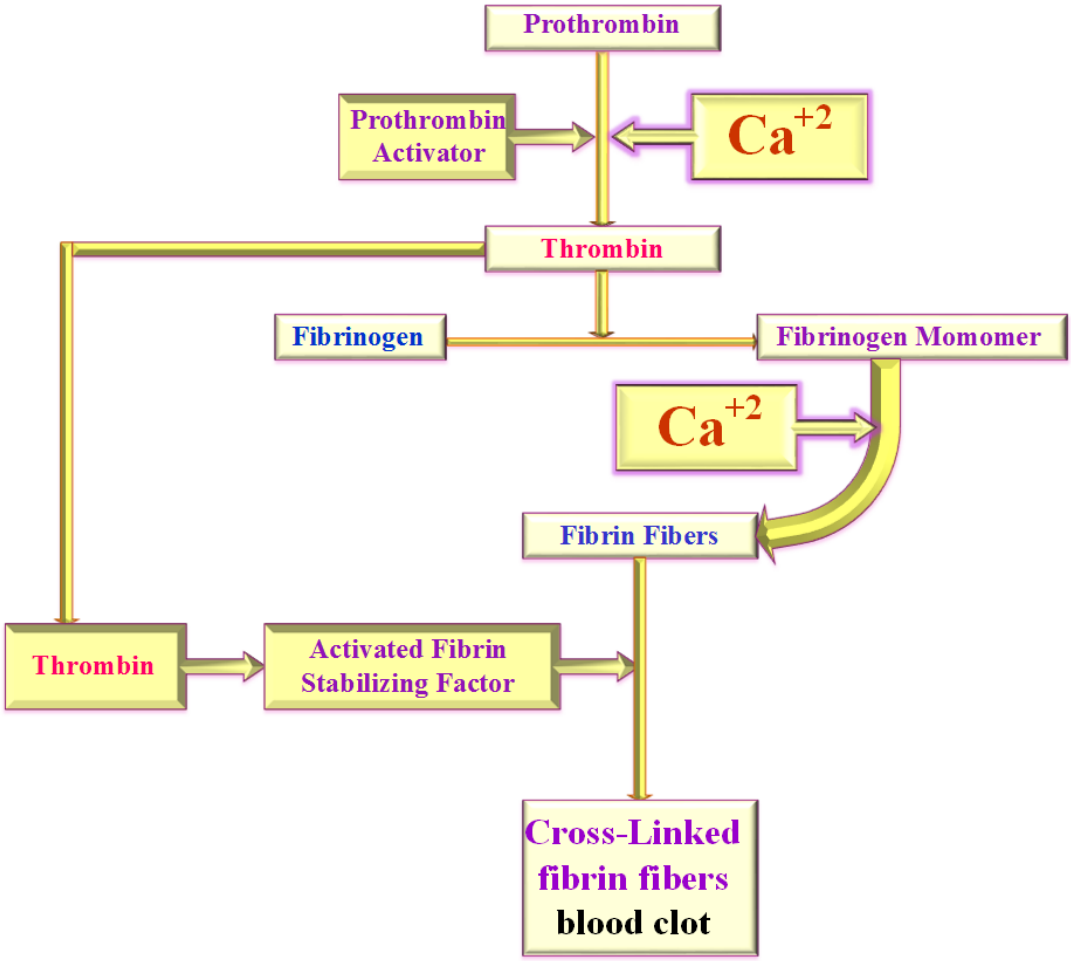
1. Blood may be obtained from veins or arteries most tests in the clinical chemistry laboratory are performed on venous blood, While arterial blood is used for blood gas deamination.
2. Whole blood ,Serum and plasma
   A. **Composition** : The great majority of analyses performed in a clinical chemistry laboratory require Whole blood ,Serum and plasma.
   B. **Collection** : Four general considerations of chemical analysis are :
      1) The use of tourniquet should be used for minimum period of time sine prolonged stays may result hemolysis of blood.
      2) blood should not be taken while intravenous solution since these solution may influence the chemical assay.
      3) Syringes or tubes used to obtain blood by clean and dry to avoid contamination or hemolysis .
      4) Some test require blood collection in to tubes which contain anticoagulants blood should be collected in container appropriate is used through (but gentle) mixing is necessary to avoid clotting.

3. **Venous blood serum or plasma: when used to prepared the serum have in many steps:**

1) The blood is drawn from the patient by using a syringe it is transferred to clean and dry tube after the needle removed .
2) The blood is allowed to clot for at least 10 to 15 min , at room temp
3) Making a gentle sweep around the inside walls of the tube with wooden stick should performed before centrifugation. Excessive ringing is unnecessary and produce hemolysis.
4) Then centrifuged the blood to separated serum.

- ***The clotting process:-***

- The blood clot is formed by protein fibrinogen which is present in soluble form in the plasma and which is transformed an insoluble network or fibrous material (fibrin) .
- The change of fibrinogen to fibrin is caused by thrombin, which in blood fluid exists as prothrombin. The conversion of prothrombin to thrombin depends on the action of thromboplastin and Ca^{+2} . These stages may be diagrammed as follows:



Conversion of Prothrombin to Thrombin and Polymerization of Fibrinogen to form Fibrin Fibers

- ***Anticoacoagulants:-***

✓ When whole blood or plasma is required an anticoagulants must be used. The most commonly used are:

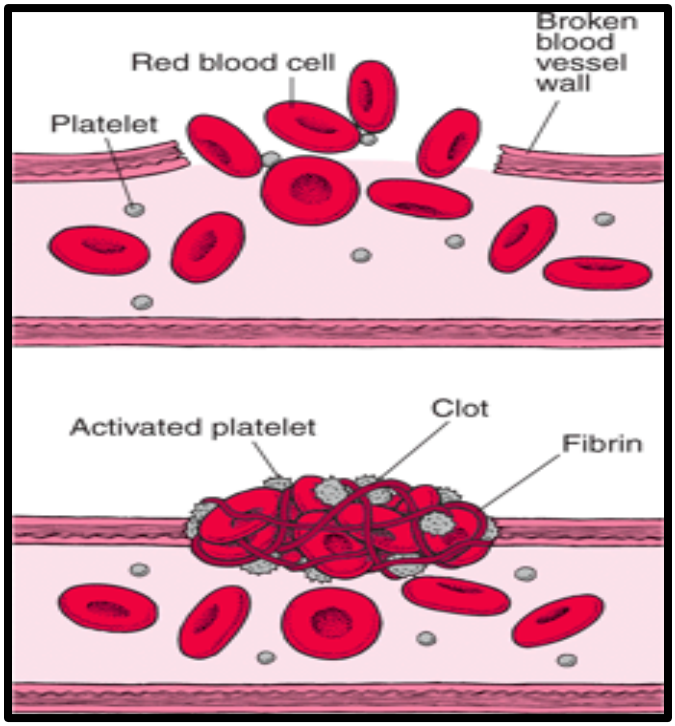
1) ***Heparin:-*** Is a normal blood constituent, but its physiological concentration is not high enough to prevent clotting in freshly blood. It is a polysaccharide derivative and apparently functions by inhibiting thrombin formation (antithrombin).

2) ***Oxalate:-*** Act by precipitating Ca^{+2} from the blood, this prevents clotting. Potassium oxalate are used most commonly, also Li, Na and ammonium salts are used.

3) ***EDTA:-*** Acts similarly to oxalates, except that it renders the Ca^{+2} unavailable for the clotting enzymes by chelating it rather than precipitating it.

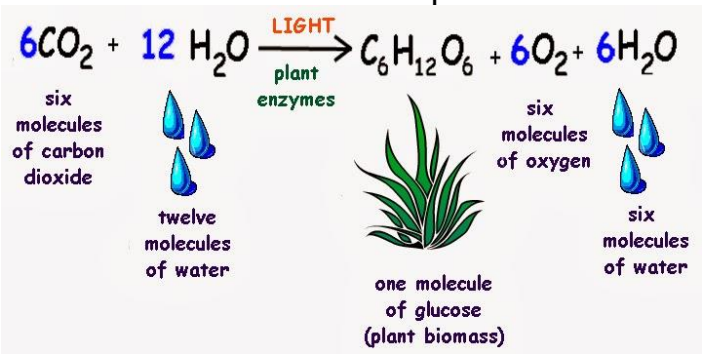
Avoiding hemolysis: The hemolysis of blood avoid by using:

A. Taking the blood slowly in to the syringe and expel it slowly in to the tube after removing the needle .
B. Avoid the used of an excessive amount of anticoacogulent and mix with this by gentle rotation .
C. The centrifuge used for separated at low and moderate speeds .
D. When need loosen to clot do this as gently as possible with a clean dry than glass rode or wooden stick .
E. Used dry and clean tubes .
F. Used tourniquet for short time as possible).



Carbohydrate

- ☒ ***Carbohydrate*** can be defined chemically as aldehyde or ketone derivatives of poly-hydroxyl (more than one OH group) alcohols are as compound that yield these derivatives an hydrolysis.
- ☒ ***Carbohydrates*** are the body's primary fuel source. Its compounds have carbon, hydrogen and oxygen.
- ☒ All the carbohydrates broken down to glucose.
- ☒ Glucose stored in the liver and a muscle until it is used for energy.
- ☒ ***Carbohydrates*** spare protein so that protein can concentrate on building, repairing, and maintaining body tissues instead of being used up as an energy source. Carbohydrate importance source of energy to the body energy storage as glycogen in animals and as starch in plants, it has a structural function in the plant like cellulose



- ☒ For fat to be metabolized properly, carbohydrates must be present. If there are not enough carbohydrates, then large amounts of fat are used for energy.

Carbohydrates turn to fat

- ✓ The digestion of carbohydrates actually starts in the mouth where an enzyme called salivary amylase starts the breakdown. The rest of the digestion process occurs mainly in the small intestine where enzymes break down large carbohydrate molecules into a simpler form called glucose. Glucose is absorbed into the blood stream and is used in several different ways:

A. Much of the glucose is used for immediate energy needs by the cells.
B. If there is more glucose than the cells need, then part of the glucose is stored as glycogen in the liver and muscle tissue. If blood glucose levels drop too low, the body can use this stored glycogen to replenish the supply. If levels are too high, the excess continues to be stored as glycogen.
C. After energy needs are met and the glycogen stores are filled, any excess glucose can be converted to fatty acids and stored as fat tissue. The fat tissue has unlimited storage capabilities

Blood Glucose Targets:

1. Pre-meal blood glucose: 80 – 120 mg/dL.
2. 2 hour post-meal blood glucose: 90 –less than 180 mg/dL.

increase in glucose level more than 180mg/ dL in blood called glycosuria

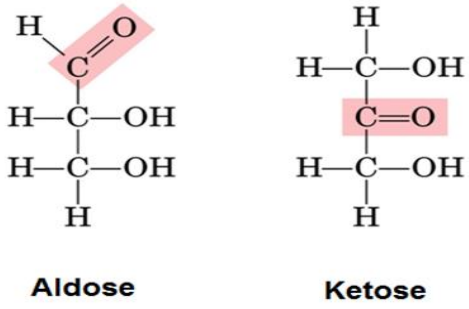
Type of Carbohydrates:

✓ Carbohydrate are classified depending up on the number of carbon atoms they may be classified to (aldoses or ketoses) depending up on the aldehyde or ketone group is present.

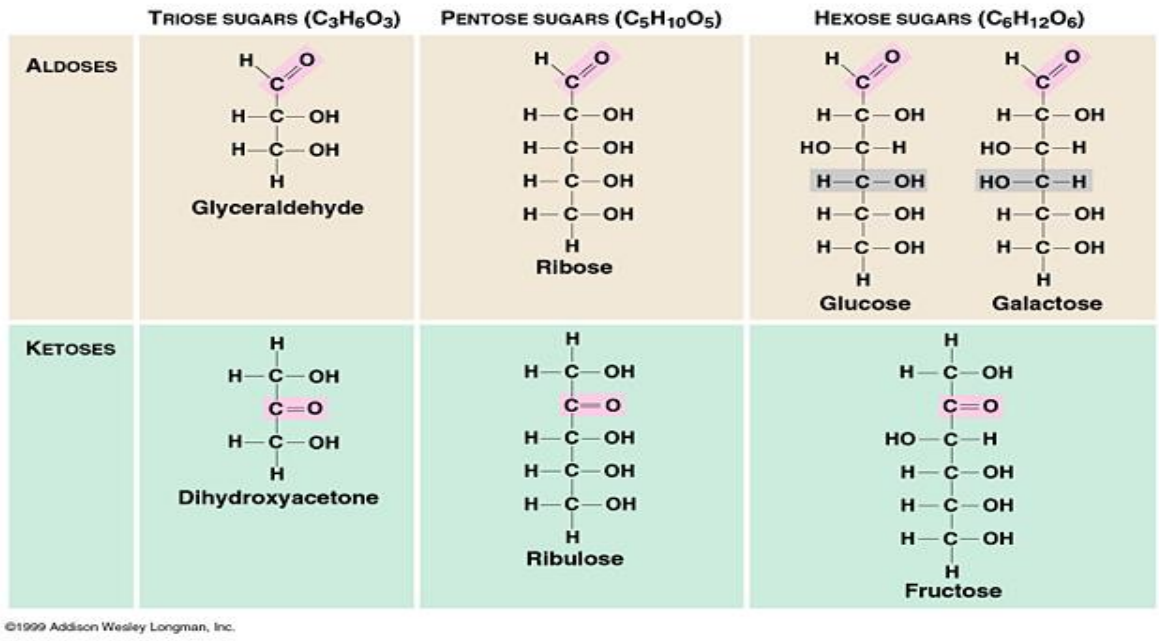
1. ***Monosaccharide :*** this is called simple sugar, cannot be hydrolyzed in to simpler from . they may be subdivided in to :-
   A. Tiroses C3
   B. Tetroses C4
   C. Pentoses C5
   D. Hexoses C6
   E. Heptoses C7

☒ ***Divided in to two functional group***

1) Aldoses
2) Ketoses



Aldose Ketose

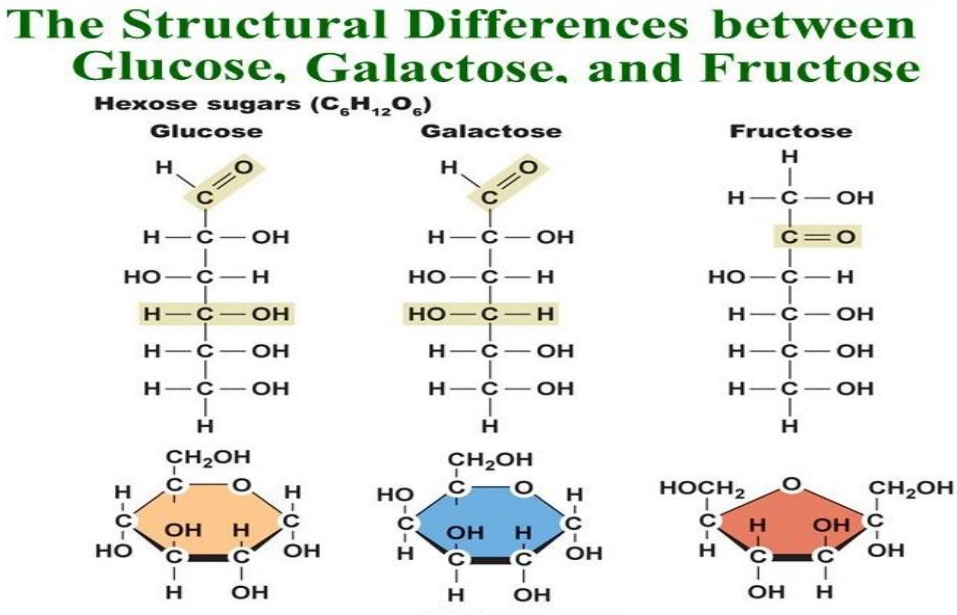


- ***Hexoses :This include***

1) **Glucose :** Glucose is a main source of energy of human body, therefore, an increase glucose levels caused carbohydrate disorders. The formula of glucose is $C_6H_{12}O_6$ which have the chemical structure
   - ✓ Found naturally in fruits, sweet corn and honey .Glucose is the form of sugar normally found in the blood stream and used by the body for energy.
   - ✓ Increase in glucose level in the body lead to convert the glucose to fate which storage in adipose tissue. Also cause diabetes diseases. This called Hyperglycemia .
   - ✓ Decrease the glucose in body lead to malfunctioning of all the process in living cells and organs, like hepatic disease and adrenal, pituitary gland disorder. It called Hypoglycemia.

2) **Fructose :** Fructose have the chemical structure
   Found in fruits and honey. Increase the activity of seminal (sperms) in males. Increase in fructose cause diabetes diseases.

3) **Galactose:**
   - ➢ Does not occur freely in nature but is produced from the breakdown of milk sugar (lactose). Its breakdown to glucose specifically in liver by liver cell, It used to determine liver function. Increase in galactose cause diabetes diseases.

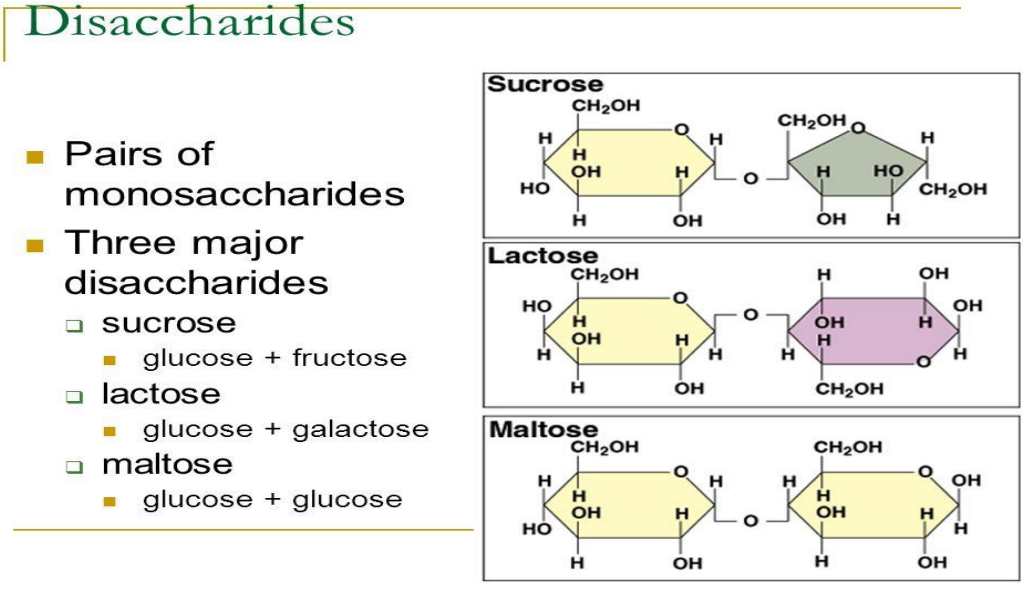


2. ***Disaccharides:***

- ✓ Which is in hydrolysis give two simple sugar (Consist of two monosaccharide different units). Disaccharide joined covalently by an O-glycosidic bond. ***The common disaccharide :***

A. ***Sucrose*** fructose + glucose
B. ***Maltose*** glucose + glucose
C. ***Lactose*** glucose + galactose

- ✓ The figure show how O-glycosdic bond form



A. Sucrose :

Ordinary table sugar. It is found mainly in sugar cane, sugar beets, maple syrup, and maple sugar . Sucrose is formed when glucose and fructose bond together .Breakdown the sucrose occurs in small intestine. The increase of sucrose due to the absent of sucrase enzyme, make it pass from the small intestine to the big intestine, hence used by some bacteria which produce toxic products that lead to diarrhea. Also cause diabetes.

B. Maltose :

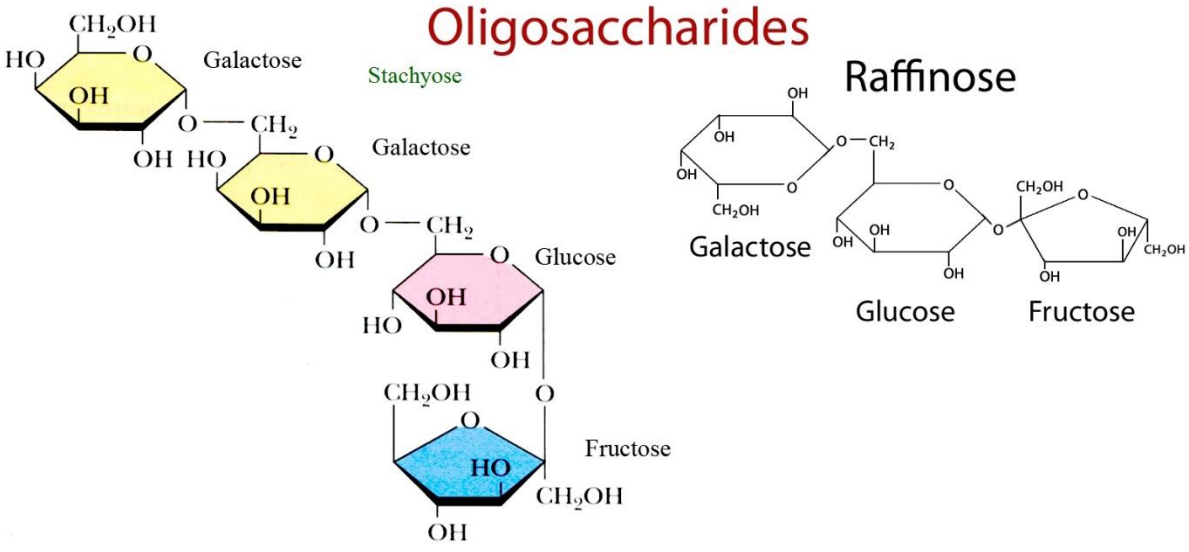
Appears when starch is broken down by the body and also occurs in germinating seeds. It is formed when two units of glucose bond together. Increase in maltose cause diabetes.

C. Lactose :

The sugar found in milk.It is made by the combination of glucose and galactose. Its breakdown in small intestine. The increase of lactose due to the absent of lactase enzyme, make it pass from the small intestine to the big intestine, hence used by some bacteria which produce toxic products that lead to diarrhea. Also cause diabetes .

3. Oligosaccharide :

- ✓ Which is (3-6) monosaccharide units on hydrolysis like :
  - A. ***Raffinose*** galactose + glucose + fructose
  - B. ***Stachyose*** galactose + galactose + glucose + fructose



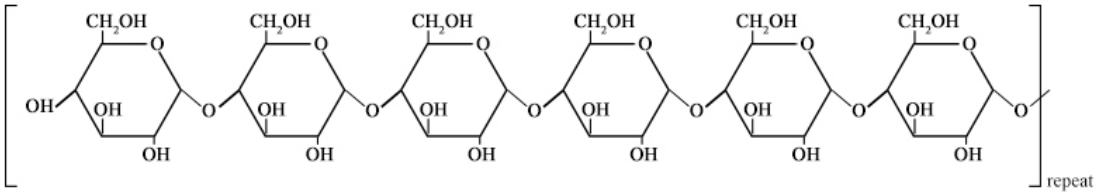
4. ***Polysaccharides :***

Are sugar polymers containing more than 20 or more monosaccharide units, and some have hundreds or thousands of units. And this include :

1) Starch

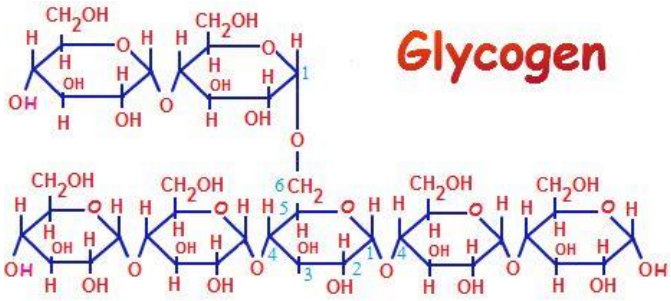
- ✓ Found in grains, roots, vegetables and legumes. It is made up of many (up to 1000) glucose units . Its breakdown by digestion process. Breakdown by salivary amylase, pancreatic excretions and after that in small intestine . Increase cause diabetes diseases .

STARCH



2) Glycogen:

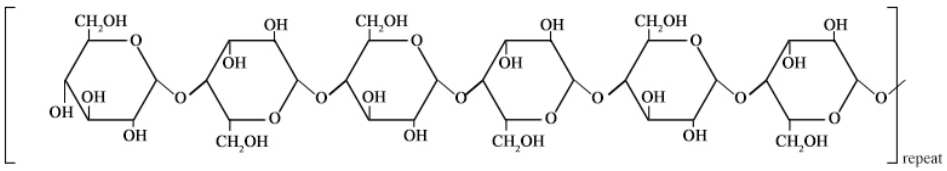
- ✓ The storage form of carbohydrates in humans and animals. Also is the primary source of glucose and energy. Muscle glycogen is used directly as energy. Liver glycogen may be converted to glucose and carried by the blood to the tissues for their use.



3) Cellulose :

- ✓ Made up of many glucose molecules and is the supportive framework of plants. Cellulose cannot be digested by humans. Therefore, it provides bulk to the stool. Cellulose is a type of fiber . Increase in cellulose in high levels may lead to some intestinal malfunctioning muscle.

CELLULOSE



Digestion and absorption of carbohydrate

In the mouth the saliva is capable of hydrolysis starch and glycogen to maltose ,this of little significance in the body because of short time it can act on the food. Salivary amylase is readily activated at pH = 4 or less so digestion action on food in the mouth in acidic environment. The pancreas completed the digestion by action of pancreatic α-amylase ,it is similar in action to salivary amylase that hydrolyzing starch and glycogen to malt triose and a mixture of branched (1,6) oligosaccharides α-limit dextrin and some glucose . The PH of pancreatic secretion is alkaline (7.5-8) or higher ,the product of carbohydrate digestion are absorbed to blood stream through intestine in the form of monosaccharide (glucose, fructose, mannose and galactose) the pentose sugar is also absorbed.

- ***Normal values :***
  A. Fasting blood suger F.B.S = 80 – 120 mg/100ml
  B. Random blood sugar R.B.S = 120 -180 mg/100ml

Carbohydrate Metabolism

-***Metabolism*** : Is the process of anabolism (synthesis of compounds) and catabolism (breakdown of larger molecules).

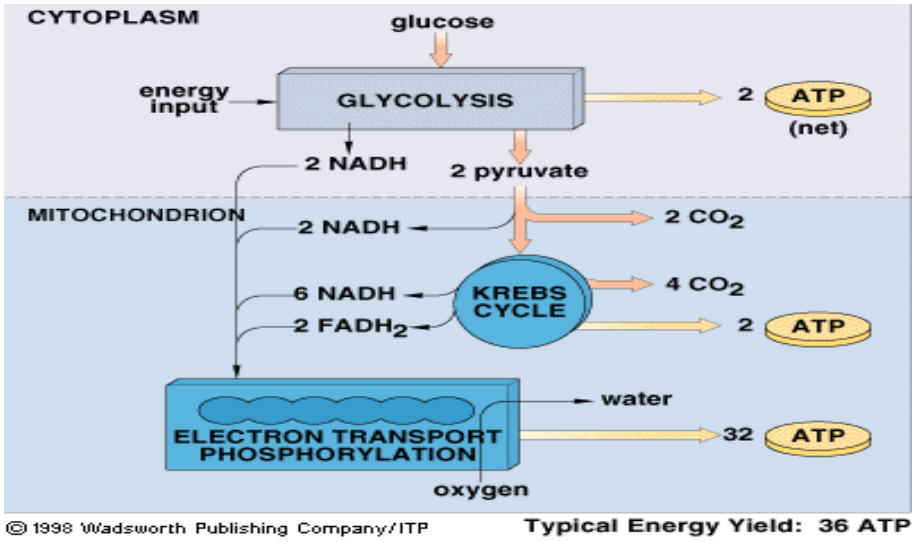
-Metabolic pathways fall into three categories:

1) Anabolic pathways are those involved in the synthesis of compounds .
2) Catabolic pathways are involved in the breakdown of larger molecules, commonly involving oxidative reactions.
3) Amphibolic pathways acting as links between the anabolic and catabolic pathways, e.g., the citric acid cycle.

- ***Metabolism of glucose***
  - The absorption of glucose occur in small intestine the glucose after absorption transferred to blood stream than to liver to stored as glycogen or metabolized to CO_2 and energy, or converted to fat keto acid , amino acid protein or converted to fat and strode in adipose tissue .

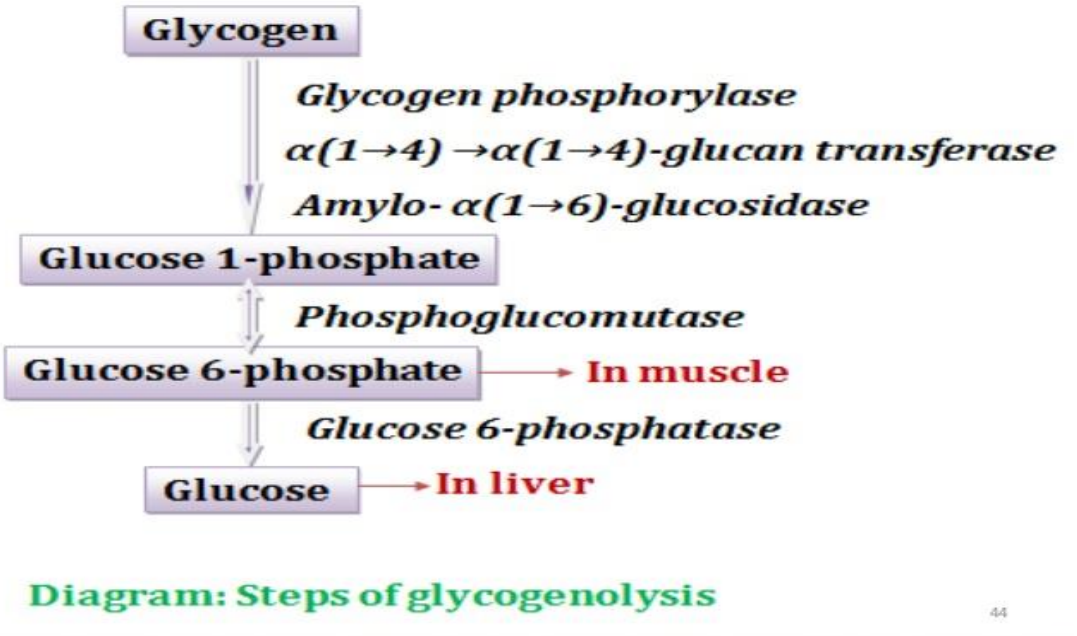
Glycolysis :

- ✓ The process by which glucose molecules degraded and yield 2Pyrovate and 2ATP.



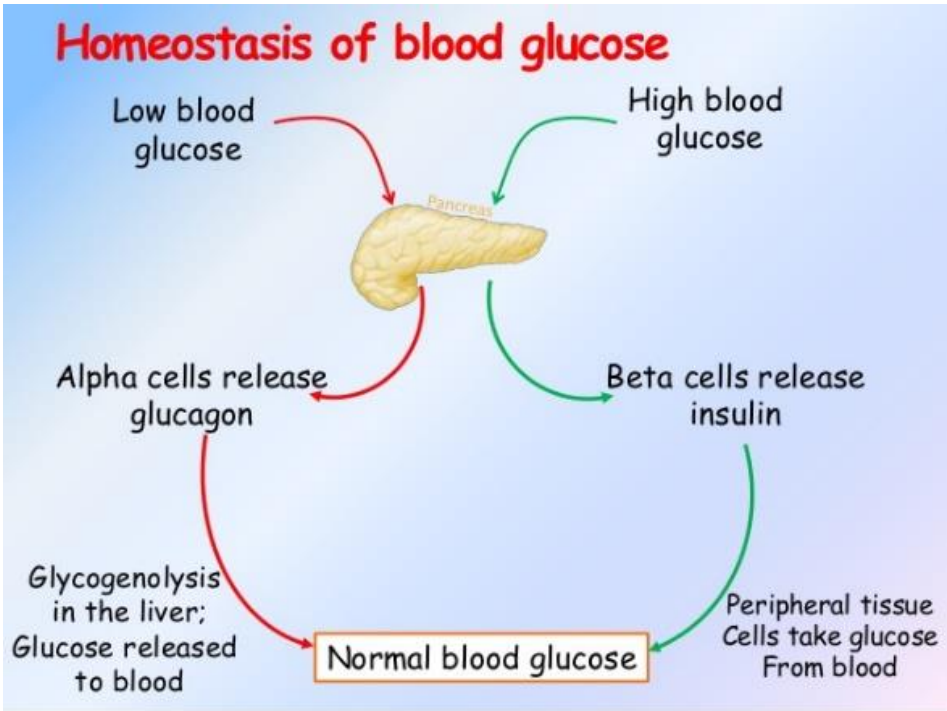
- ✓ ***Gluconeogenesis:*** The process of synthesizing glucose from non-carbohydrate precursors.

- ✓ ***<u>Glycogenolysis :</u>*** The process breakdown of glycogen to glucose.
- ✓



Regulation of blood glucose concentration

- ✓ The blood glucose level constant in fasting for (8h) the body taking amount of glycogen stored and converted to glucose six phosphate then the enzyme glucose six phosphatase found in liver and kidney converted to glucose .
- ✓ When the blood glucose level increased as result of creasing the absorption from the converted to glycogen and stored in liver .



Hormone effected the concentration of glucose in blood

1. ***Insulin :*** this hormone excreted from β- cells of pancreas help for the formation of glycogenesis and lipogenesis and blood glucose level decreased when insulin lack glucose level increased and caused hyperglycemia .

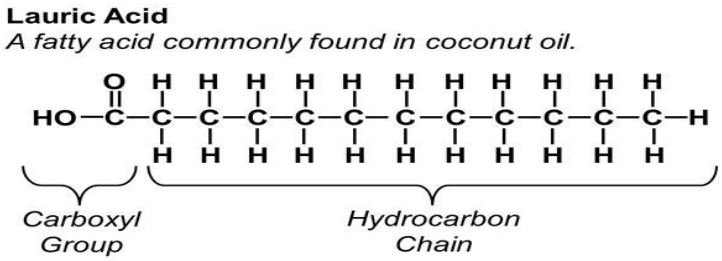
2. ***Growth hormone :*** This hormone excreted form anterior pituitary gland ,the action of this hormone against the insulin hormone formation increasing of glucose level.
3. ***Hydrocortisone :*** This hormone excreted from the adrenal cortex promote the glyconeogensis pathway.
4. ***Epinephrine :*** This hormone promote the glycogenolysis pathway and formation of glucose .
5. ***Thyroxin :*** This hormone excreted from thyroid gland help glycogenolysis and increase the glucose level and increase the percent of operation of glucose in small intestine.
6. ***Glucagon :*** This hormone excreted from α-cell of pancreas help the glycogenolysis pathway and increasing the glucose level .

Lipids

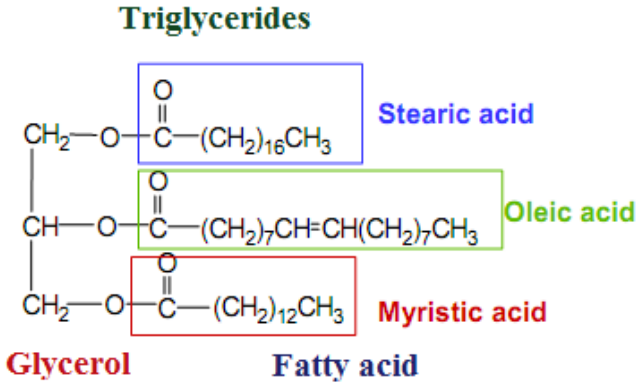
1. lipids are a large and diverse group of naturally occurring organic compounds that are related by their solubility in nonpolar organic solvents
   The (e.g .ether, chloroform, acetone and benzene) and general insolubility in water .
2. lipids are important dietary constituents not only because of their high energy value but also because of the fat-soluble vitamins and the essential fatty acids contained in the fat of natural foods ,there are great structural verity among the lipids.
3. The essential fatty acids is unsaturated [linoleic acid, and arachidonic acid
4. Lipids have to be transported in plasma from one tissue to another, from the intestine or the liver to other tissues to the liver ,there are complex mechanism that control the release of lipids from the tissues from plasma and the uptake of lipids by the tissues from plasma , abnormalities of these mechanism may be associated with the development of disease.
5. Lipid are transported in the blood stream in the form of multi molecular complexes called lipoproteins.

Classification of lipid

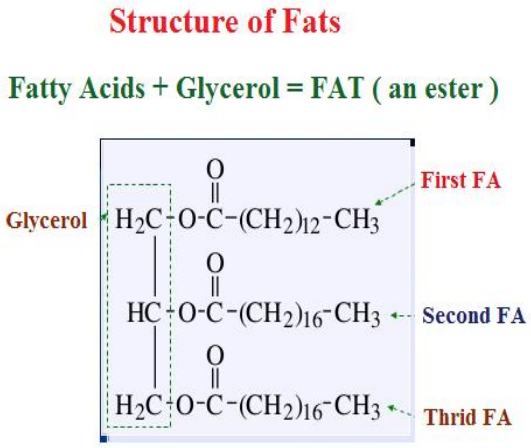
1. ***Fatty Acids*** **–** most lipids contain fatty acids (the simplest type of lipids) in their structures. They are carboxylic acids with an even number of carbon atoms, usually between 10 and 20 (memorize their common names).



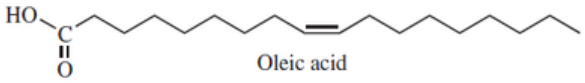
2. ***Fats and Oils :***
   A. Triglycerides (triacylglycerols or TAG's) are triesters of glycerol and fatty acids. They are the major form of energy storage in animals.



B. Fats are solids at room temperature and most come from animal sources.



C. Oils are liquids at room temperature and the most commonly used oils come from plant sources.



D. Saturated fatty acids have higher melting point than unsaturated fatty acids because they can pack together more tightly.

3. ***Phospholipids:*** are a family of lipids similar to TAG's except that one hydroxyl group of glycerol is replaced by the ester of phosphoric acid and an amino alcohol, bonded through a phosphodiester bond. Depending on the amino alcohol, these can be Lecithins (containing choline) or Cephalines (containing ethanolamine or serine). These are the most abundant lipids in cell membranes.

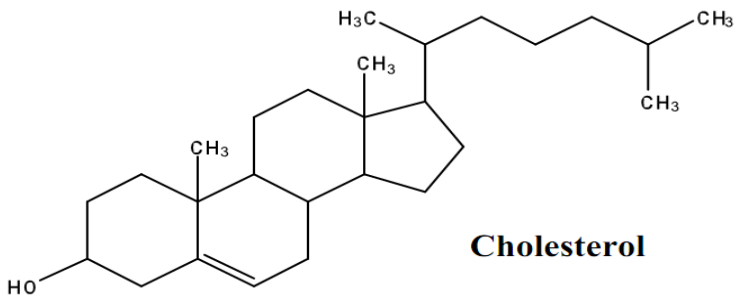
4. ***Sphingolipids :*** This is another group of phosphoslipids. They are esters of an 18 carbon alcohol called sphingosine (instead of glycerol). We find them in the biological membranes of the brain and nerve tissues. Some sphingolipids contain a carbohydrate such as galactose or glucose

5. ***Steroids*** : are compounds containing the steroid nucleus, which consists of three cyclohexane rings and one cyclopentane ring fused together.
6. ***Waxes*** :
   are esters of fatty acids with long chain primary alcohols. The leaves and fruits of many plants have waxy coatings .

7. ***Vitamins –*** Some vitamins (A, D2, E and K1) are fat soluble, therefore, considered lipids. They have important roles in vision, bone growth, and blood clotting.

Cholesterol

- Definition:- Cholesterol is a derivative lipid, has a chemical formula ($C_{27}H_{46}OH$) .The molecular weight of cholesterol is (386.66). and structure formula as shown:



Cholesterol

- It is formed from steroid unit, which consist of 4 rings. Cholesterol means (bile solid alcohol) choli bile & sterol solid .
- Cholesterol is essential for the formation of bile acids, which allow you to be able to digest fats.
- Cholesterol is also utilized by the body to produce cell membranes.
- Everybody needs to have some cholesterol in order to be healthy
- However it is when you have too much cholesterol that problems occur.
- When you have too much cholesterol medical professionals will say you are hypercholesterolemic, meaning that you have hypercholesterolemia, or too high of blood cholesterol.
- High blood cholesterol is a major risk factor for coronary heart disease and for stroke.

Found and synthesis:-

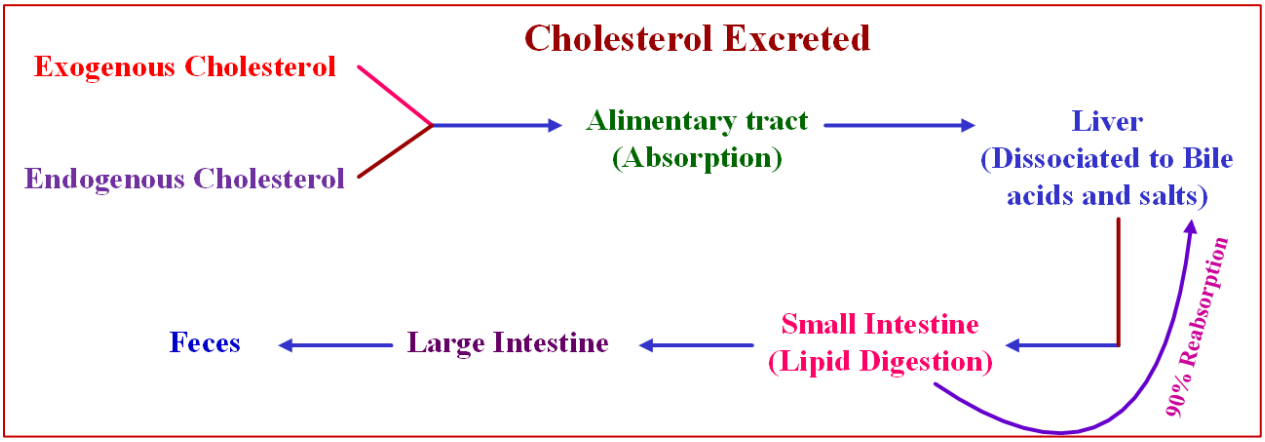
1. Cholesterol is found in all cells of body.
2. The *brain* and spinal cord contain large amount of cholesterol, which is form part of lipid "insulation".
3. It is a precursor of the *adrenal & sex hormones*.
4. Cholesterol may be synthesized from 2 carbon units (acetyl COA) in many body tissues, particularly liver, intestine and skin.

Sources:-

- ✓ The liver is the main endogenous source cholesterol .
- ✓ It is synthesized about 1 gm of cholesterol daily while the other tissues synthesized about ½ gm of it.
- ✓ The exogenous sources of cholesterol are egg yolk, meat, animals fats, milk, chess and butters.

Excretion :-

A. Cholesterol is absorbed by alimentary tract, reaches the liver through blood stream.
B. Liver cells oxidize the molecule by adding hydroxyl and carboxyl group to form cholic acid. These are excreted in the bile.(90%) of bile salts will reabsorbed to the liver via enterohepatic circulation, the remaining
C. Cholesterol is excreted with feces. These steps could be summarized as the following:-



Clinical significant:-

1. ***Normal case:-***

The normal range of Serum cholesterol is 140-240 mg/dL. This value is vary in adults with age, sex and diet.

2. ***Abnormal case:-***

A. ***Hypercholesterolemia:-*** It is involve an increase of serum cholesterol levels more than 280 mg/dL .

1-Atherosclerosis 2-***Heart diseases*** ***3- Nephrotic syndrome***.
4-Diabetes mellitus ***5- Obstructive jaundice*** ***6-Hypothyroidism.***

B. ***Hypocholesterolemia :-*** It is involve a decrease of serum cholesterol levels less than 140mg/dL .

Cholesterol Transporters:

**Cholesterol is transported through your blood stream by lipoproteins. There are two different types of lipoproteins:

1) LDL (low-density lipoproteins) ,is known as your "bad" cholesterol. When you have too much LDL circulating in your blood it can build up the inner walls of your heart

arteries. Over time this forms plaque. Plaque narrows your arteries and puts you at an increased risk for having a heart attack or a stroke.

2) HDL (high density lipoprotein) , is known as the "good" cholesterol. High levels of HDL have been shown to protect against heart attack. Low levels of HDL, however, can increase the risk of heart attack or stroke.

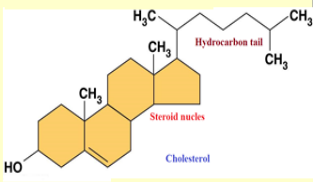
Total Cholesterol :

An HDL of ≥60 mg/dL gives some protection against heart disease.

Analyte	Reference Range
Total cholesterol	140–200 mg/dL (3.6–5.2 mmol/L)
HDL-C	40–75 mg/dL (1.0–2.0 mmol/L)
LDL-C	50–130 mg/dL (1.3–3.4 mmol/L)
Triglycerides	60–150 mg/dL (0.7–1.7 mmol/L)

Sources: dietary cholesterol (~ 25% of a daily turnover) - 0,3g/day

synthesis in tissues (~ 75 %) - 1 g/day



liver

(reproductive tissues -adrenal cortex, ovaries, testes, placenta)

enzymes of biosynthesis present in virtually all tissues

Transport:

as a component of lipoproteins, most as cholesteryl esters

chylomicrons: intestine → liver

VLDL: liver → plasma

LDL: plasma → extrahepatic tissues

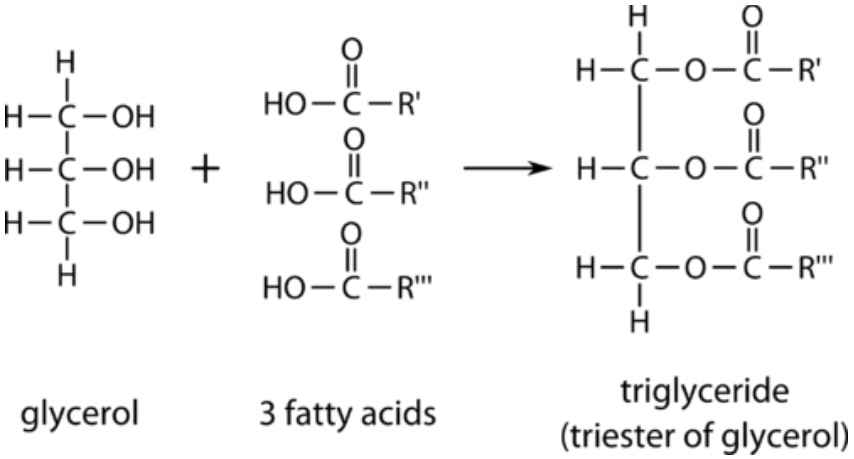
HDL: plasma → liver

(extrahepatic tissues)

Triglycerides

Triglycerides are formed when ***condensation reactions*** occur between one glycerol and three fatty acids. The hydroxyl groups of glycerol combine with the carboxyl groups of the fatty acids to form an ester linkage .This condensation reaction results in the formation of <u>three</u> molecules of water . Triglycerides can be either saturated or unsaturated, depending on the composition of the fatty acid chains.

Triglycerides are lipids, a type of fat. They are found in foods that come from both plants and animals. The triglycerides in plants come from vegetable oils, such as sunflower and peanut, which remain liquid at room temperature. Meat and dairy products contain triglycerides in animal fats, which remain solid at room temperature. Triglycerides are necessary for certain bodily functions, but high levels of them can lead to health problems. triglyceride, an ester derived from glycerol combined with three fatty acid molecules.



Glycerol is a triol, an alcohol which contains three hydroxyl functional groups. A fatty acid is a long carbon chain, generally from 12 to 24 carbons in length, with an attached carboxyl group. Each of the three fatty acid molecules undergoes an esterification with one of the hydroxyl groups of the glycerol molecule. The result is a large triester molecule referred to as a triglyceride. triglycerides are completely hydrophobic, meaning they cannot mix with water, so they cannot integrate into membranes. Because they can't mix with water, triglycerides bind to specialized proteins called lipoproteins to enable them to travel through the blood.

<u>Functions of triglycerides :</u>

1. Stores and transfers genetic information
2. Long term energy storage
3. Control the rate of reactions
4. Help to fight disease.

Triglycerides provide your body with energy, but their main function is to store energy for later use. The food you eat contains calories in the form of carbohydrates, protein and fat. When you consume more calories than your body can use, it stores those calories in the form

of triglycerides. Fat cells hold the triglyceride molecules until your body needs energy, such as between meals. Hormones signal the fat cells to release the triglycerides for your body to use.

Triglycerides function as a long-term storage form of energy in the human bods. Because of the long carbon chains, triglycerides are nearly nonpolar molecules and thus do not dissolve readily in polar solvents such as water. Instead, oils and fats are soluble in nonpolar organic solvents .

What is the normal range?

A simple blood test can reveal whether your triglycerides are healthy or not:

1- Normal - less than 150 milligrams per deciliter (mg / dL
2- Border height 150 to 199 mg / dL
3- High - 200 to 499 mg / dL
4- Very high - 500 mg / dL or higher

Your doctor usually examines high triglycerides as part of a cholesterol test, which is sometimes called a fat profile. You must fast before drawing blood to accurately measure triglycerides.

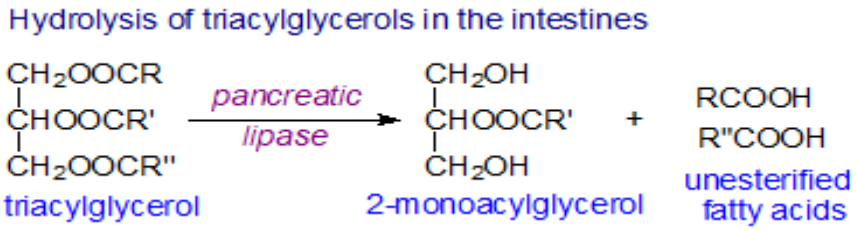
Clinical Hypertriglyceridaemia

Condition	Features
Secondary	Relatively common (obesity, diabetes, renal impairment, liver disease, drugs)
Polygenic	Accounts for the majority of cases
Familial HTG	TG predominates. CVD risk varies Predisposes to massive HTG
Familial Combined H/L	Overproduction of apo B lipoproteins TG and TC vary with age and weight
Massive HTG	Lipoprotein Lipase deficiency or saturation. Risk of pancreatitis

Triacylglycerol Metabolism in the Intestines and Liver

The process of fat digestion is begun in the stomach by acid-stable gastric or lingual lipases, the extent of which depending on species but may be important for efficient emulsification. However, this is insignificant in quantitative terms in comparison to the reaction with pancreatic lipase, which occurs in the duodenum. Entry of triacylglycerol degradation products into the

duodenum stimulates synthesis of the hormone cholecystokinin and causes the gall bladder to release bile acids,. Pancreatic lipase, co-lipase, bile salts and calcium ions act together in a complex at the surface of the emulsified fat droplets to hydrolyse triacylglycerols,and results in the release of the fatty acids from the 1 and 3 positions with formation of 2-monoacyl-*sn*-glycerols. Isomerization of the latter to 1(3)-monoacyl-*sn*-glycerols occurs to some extent, and these can be degraded completely by the enzyme to glycerol and free fatty acids.



What is difference between triglyceride and cholesterol?

Triglycerides and cholesterol are different types of lipids that circulate in your blood: Triglyceridesstore unused calories and provide your body with energy. Cholesterol is used to build cells and certain hormones.

Why is high triglycerides so important?

High triglycerides can contribute to atherosclerosis or increase the thickness of artery walls (atherosclerosis), which increases the risk of stroke, heart attack and heart disease , including obesity and metabolic syndrome - a group of conditions that include a very large amount of fat around the waist, high blood pressure, high triglycerides, and high Blood sugar and abnormal cholesterol levels. Extremely high triglycerides can lead to acute pancreatitis (pancreatitis).

High triglycerides can be a sign of:

1- Type 2 diabetes or prediabetes
2- Metabolic syndrome is a condition in which high blood pressure, obesity and high blood sugar are combined, which increases the risk of heart disease.
3- Low levels of thyroid hormones (hypothyroidism)
4- Some rare genetic conditions that affect how the body converts fats into energy

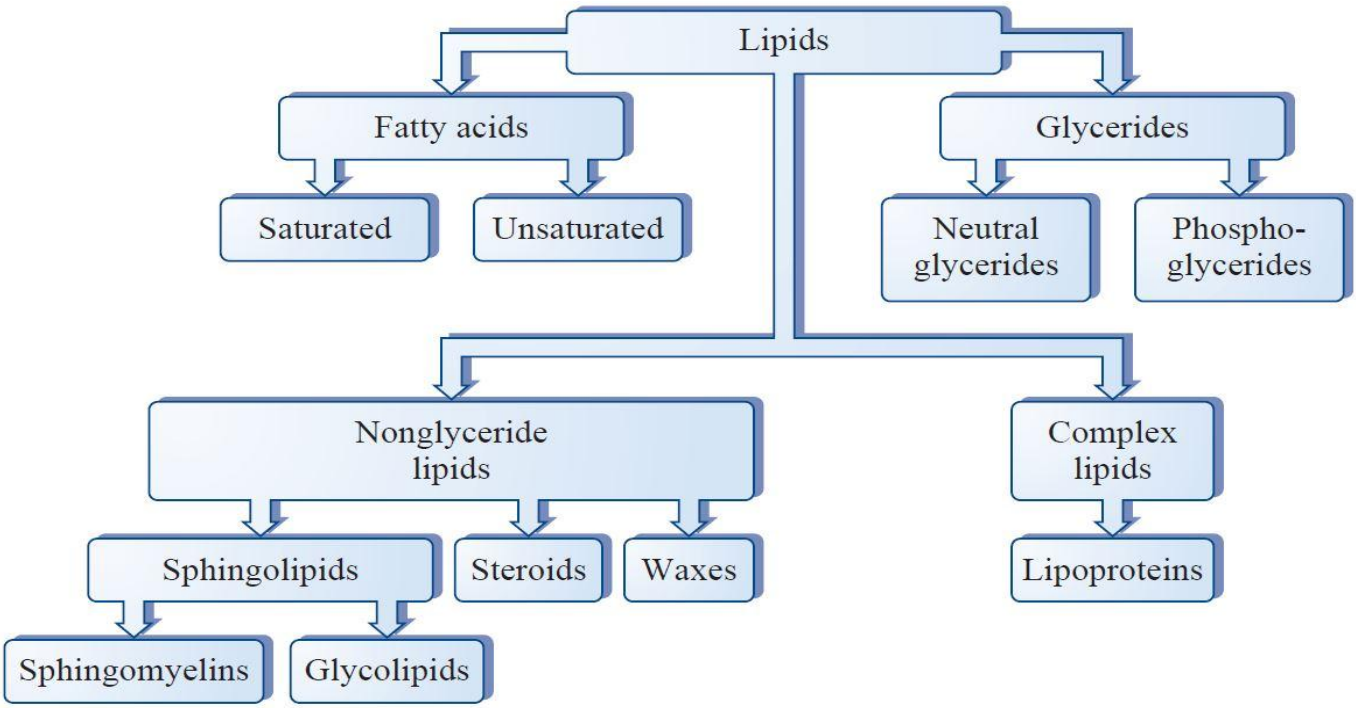
Sometimes high triglycerides are a side effect of taking some medications, such as:

1- Diuretics
2- Estrogen and progestin
3- Steroids
4- Beta blockers
5- Some immune suppressants

What is the best way to reduce triglycerides?

1-Exercise regularly. 2-Weight loss. 3-Choose healthy fats.
4-Avoid sugary and refined foods. Simple carbohydrates.
5-Limit your consumption of alcoholic beverages.

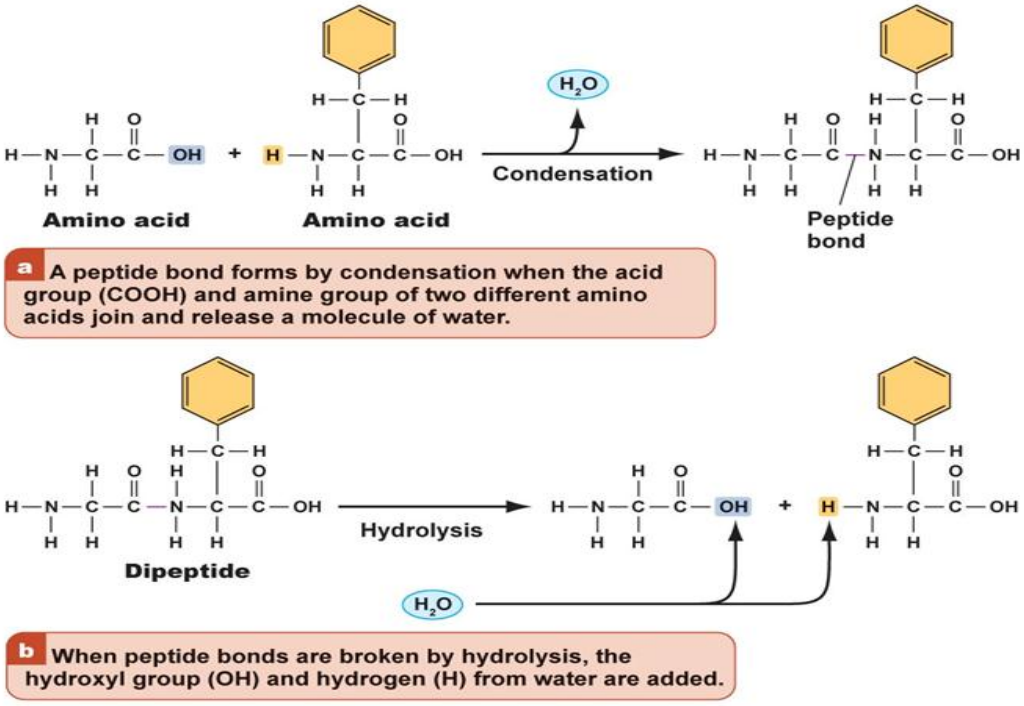
is associated with fatty liver, insulin resistance and type 2 diabetes.

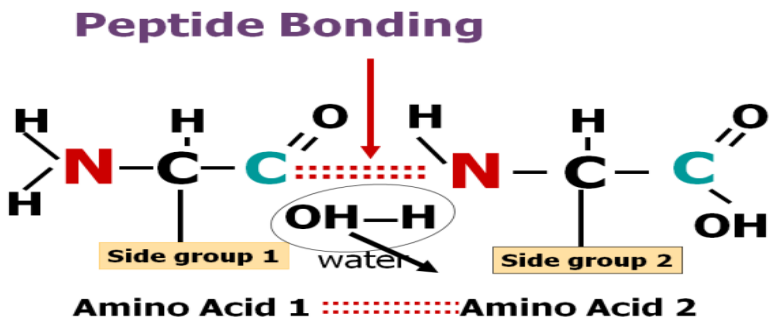

Lipids
Fatty acids
Glycerides
Saturated
Unsaturated
Neutral glycerides
Phospho-glycerides
Nonglyceride lipids
Complex lipids
Sphingolipids
Steroids
Waxes
Lipoproteins
Sphingomyelins
Glycolipids

PROTEINS

- **Proteins:** They are complex nitrogenous compounds of higher molecular weight built up by the chemical union of a large number of amino acid molecules through peptide bond, The protein found in plasma and urine, 90- 97% of digested protein absorbed by the cells of the intestine.
-
- **Peptides bond:** can defined when the amino group and carboxyl group in amino acid one and amino acid two combine by loss water molecule.

Condensation and Hydrolytic Reaction



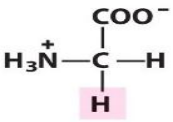


❖ **Every function in the living cell depends on proteins:**

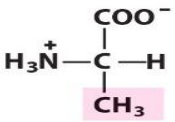
1. Motion and locomotion of cells organisms depends on protein.
2. The catalysis of all biochemical reactions is done by enzymes which contain protein .
3. The transport of materials in body fluids depends of proteins.
4. The receptors for hormones and other signaling molecules are proteins
5. The transcription factors that turn genes on and off it are proteins.
6. Many more-proteins are truly the physical basis of life.

Examples of amino acid

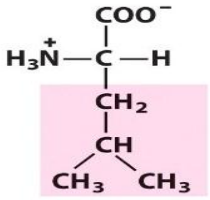
Aliphatic R groups



Glycine

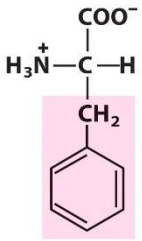


Alanine

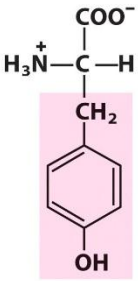


Leucine

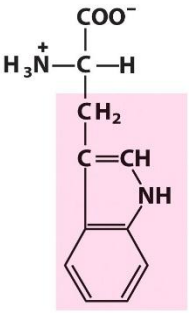
Aromatic R groups



Phenylalanine



Tyrosine



Tryptophan

Classification of proteins :

The first : The proteins classified in to

A. Simple protein : this protein have amino acid bind with peptide bond.
B. Complex protein : this have amino acid and additional materials like
   1) glycoproteins containing carbohydrates,
   2) lipoprotein containing lipid
   3) metalloprotein containing iron , copper and zinc.

The second : There are two types of protein in the body soluble and insoluble types . Only tests for the soluble proteins presently are performed on a routine basis in clinical chemistry laboratory because of the emphasis on fluid rather than solid-tissue samples

- The three common fluids that submitted for this analysis are serum, urine and cerebrospinal fluid (CSF)
- Serum (as contrasted with plasma) is deficient in those coagulation proteins, which are consumed during the process of blood coagulation.

Serum protein classified in to:

→ The type of proteins in serum include:

1- Albumin
2- Globulins
3- Fibrinogen

Properties of protein:

1. Sensitive to heat (denaturation :- a change in composition of protein so that physical, chemical and biological properties to be changed)
2. The solubility of protein depended on:
   a) Ionic concentration.
   b) PH.
   c) Temperature.
   d) Charge of the solvent
3. 90- 97% of digested protein absorbed by the cells of the intestine.

T.protein = 6.5 - 8 g/dL [65 - 80 g/L]
Albumin = 3.6 - 5 g/ dL [36 - 50 g/L]
Globulin = 2.5 - 3.5 g/ dL [24 - 37 g/L]

Digestion of protein

- ✓ Digestion of protein begins in the stomach by the enzyme pepsin.
- ✓ pepsin is endopeptidase; its specific for peptide bonds formed by aromatic or dicarboxylic amino acid .
- ✓ *The secretion of stomach is acid medium because the gastric secreted hydrochloric acid.*
- ✓ The protein digested in the pancreatic secretion by the enzyme trypsin and chymotrypsin , this enzyme acts in alkaline medium(7.5-8).
- ✓ Trypsin is specific for (basic amino acid ,whereas chymotrypsin is specific for protein aromatic amino acid .
- ✓ The intestinal juice secreted the enzyme need for the *digestive of proteins*, some enzyme found in intestine is dipeptide enzyme which digestive dipeptide to free amino acid .

- ✓ The end product of digested are absorbed from the intestine and transferred to the blood .

** The degradation of amino acids occurs in the liver as the following :
A. Glycogenic types of amino acids which convert to glucose
B. Ketogenic type of amino acids which convert to acetyl COA.

Clinical significances

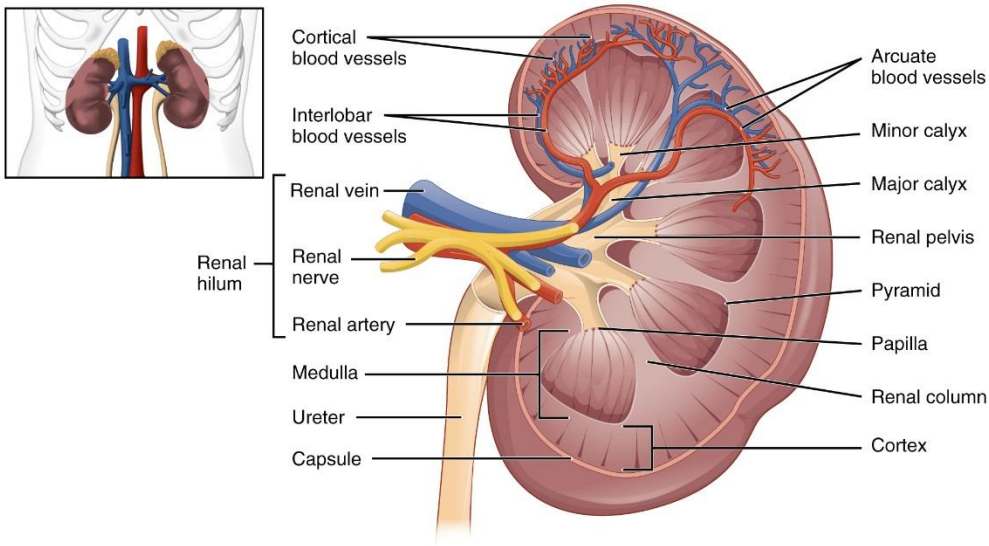
1. Normal case:- The normal range of S.total protein is 6.5-8 g/dL.
2. Abnormal cases-:

1) Hypoproteinemia:- It is involve a decrease of serum total protein levels less than 6.5 g/dL.
   a) Over hydration: the concentration of all fractions protein is proportionately decreased due to relative water excess.
   b) Kidney diseases as in the nephritic syndrome.
   c) Sever burns, bleeding, fever and necrosis where increased breakdown of protein,
   d) Sever malabsorption
   e) Increased requirement, as in growth, pregnancy and hyperthyroidism.
   f) Drugs: like estrogen .
2) Hyperproteinemia :- It is involve an increase of serum total protein levels more than 8 g/dl..
   a) Dehydration:-The total protein is increased and the rise being reflected proportionately in all protein fractions, dehydration may result from a decrease in water intake, as occurs in frank water depletion or from excessive water loss. as occurs in: vomiting. severe diarrhea and diabetic acidosis.

   b) Cirrhosis of the liver
   c) Drugs like, digitalis. epinephrine, steroids, progestin, insulin and thyroxin.
   d) Exercise:- An increase of (6-12%) occurs with vigorous exercise of short duration.

Kidney Function tests- Urea, Formation and destination

- The kidneys are the primary organs involved in the excretion of waste products , the other organs involved being the lungs, skin and intestines in the urinary system there are two kidneys which form and secrete urine by peristalsis; it is conveyed from each kidney through a ureter to the urinary bladder.
- The bladder provides temporary storage for about 300ml urine, which is eventually voided through the urethra to the exterior.
- The kidneys are situated at the posterior of the abdomen, one on either side of the vertebral column, the right kidney a little lower than the left, due to the space occupied by the liver .
- Each kidney, which is, bean- shaped, is enclosed in a capsule of fibrous tissue, which is easily stripped off.



Underneath the capsule lies the cortex, followed by the medulla, which is made up of renal pyramids, than the hilum, where the renal arteries and nerves enter and the renal vein and ureter leave the kidney.

Kidney function test

→ Kidney function tests are specialized tests and are advised when medical history, examination and routine tests like urine analysis are suggestive of some renal disease.

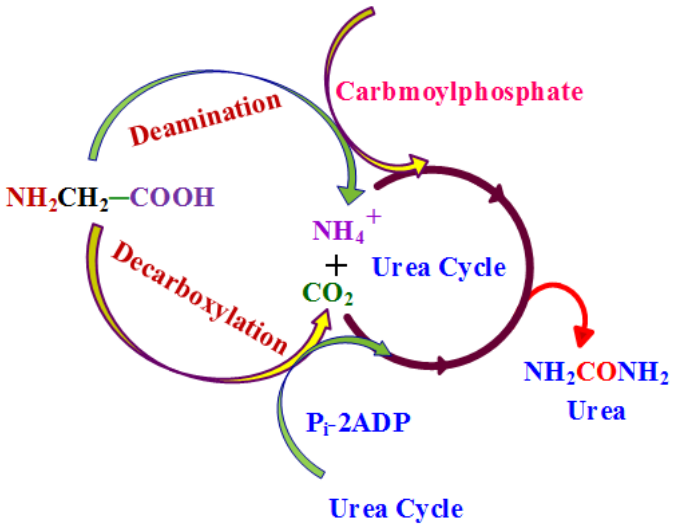
→ Estimation of kidney function is important in a number of clinical situations, including assessing renal damage and monitoring the progression of kidney disease.

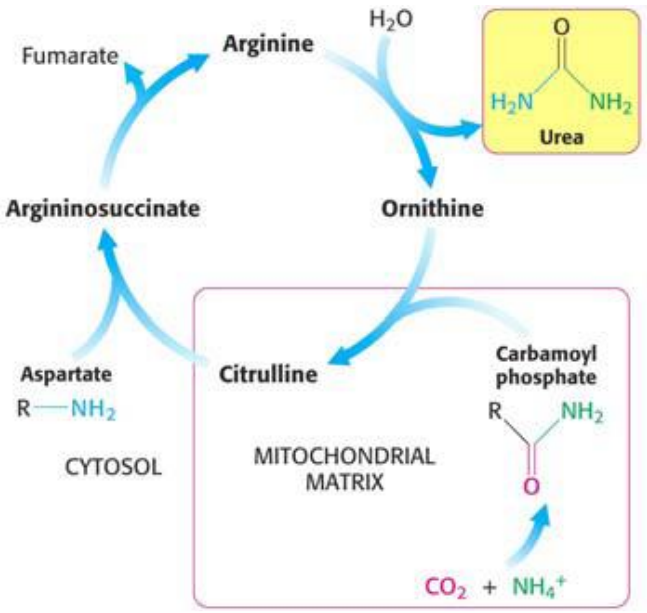
Kidney (Renal) functions tests

This test include determination the non-protein nitrogen compound such as urea, creatinine and uric acid.

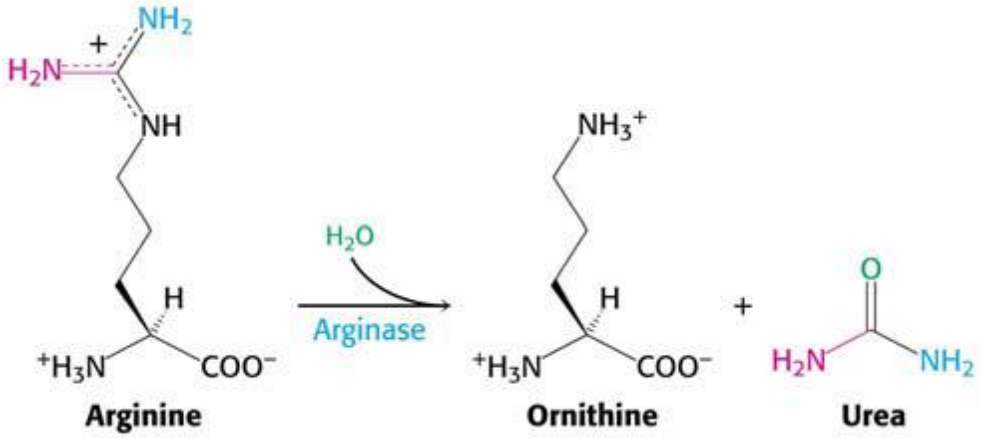
Determination of serum urea

- ✓ Definition; It is the most end, product of protein catabolism or it is detoxification product of ammonia.
- ✓ Synthesis; Urea is synthesis from ammonia in the liver. It is from deamination of amino acid or decarboxylation of amino acid.





- ✓ The molecular weight of urea is (60)
- ✓ Synthesis and Excreted :- Urea is synthesis from ammonia occurs in liver and it is excreted by kidney.



Clinical significant

1) Normal case

- ✓ The normal range of s.urea is 15-45 mg/dL. However the concentration of urea inside red cells is slightly less than in plasma due to the presence of large amounts of Hb inside the cells.

2) **Abnormal cases**

A. **Hypoureamia**: It is involving a decrease of serum urea levels less than 15 mg/dL.

1- Lever diseases
2- Pregnancy
3- Protein malnutrition
4- Acute rehydration

a- **Hyperureamia:**- It is involve an increase of serum urea levels more than 45 mg/dL .

a) Per-renal uraemia cases:- cardiac failure, vomiting and haemorrhage.
b) Renal-uraemia cases:- renal diseases, (renal failure and nephritis
c) Post- renal uraemia cases:- urinary track obstructive, tumor and stone.

Kidney Function tests- Creatinine, Formation and destination

Function of the kidney:

1. Maintenance of water and electrolyte balance of the body.
2. Maintenance of PH of the blood.
3. Excretion of drugs and toxins.

Notes:

1) The kidney removes waste products reabsorbs essential compounds and regulates water, electrolyte and acid base homeostasis.
2) The kidney produces two hormones l,25- dihydroxyl cholecalciferol and erythropoietin.
3) The kidney contains many millions of nephrons that act by filtering the blood and producing urine, the functional unit of the kidney is the nephron
4) Loss of kidney function can be, classified according to the cause pre-renal condition, renal disease or post-renal pathology.
5) Blood concentrations of urea and creatinine are indicators of renal disease.
6) Glomerular function can be assessed by measuring creatinine clearance.
7) Tubular function can be assessed by measuring the urinary concentration of compounds normally absorbed or excreted by the kidney , amino acids or hydrogen ions .
8) Proteinuria is the presence of abnormal amounts of protein in the urine (> 150mg /day).

Kidney function test

→ Kidney function tests are specialized tests and are advised when medical history, examination and routine tests like urine analysis are suggestive of some renal disease.

Estimation of kidney function is important in a number of clinical situations, including assessing renal damage and monitoring the progression of kidney disease.

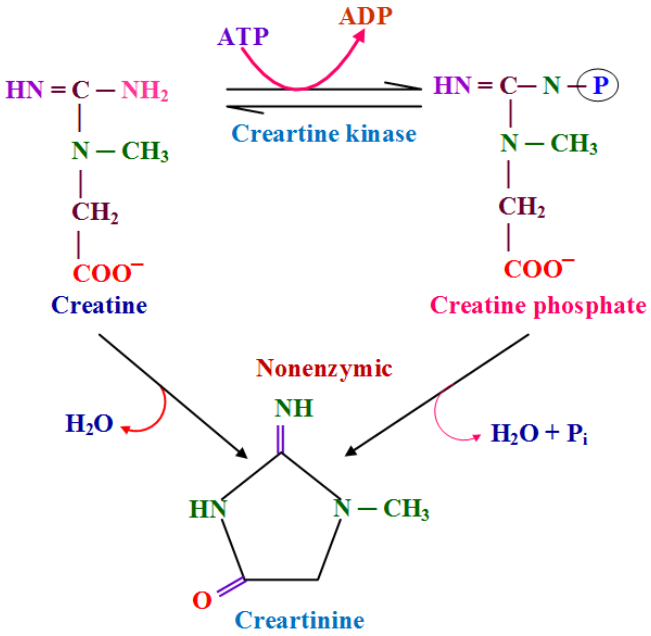
Kidney (Renal) functions tests:

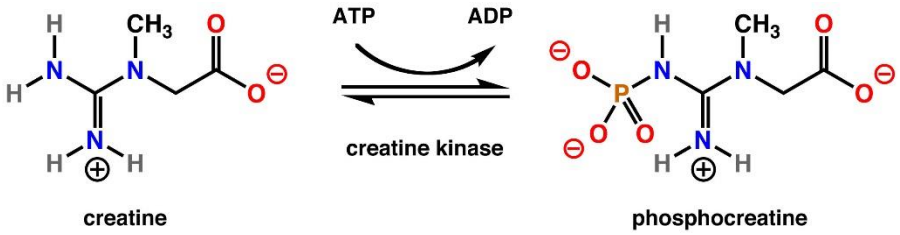
This test include determination the non-protein nitrogen compound such as urea, creatinine and uric acid.

i. Determination of serum creatinine:

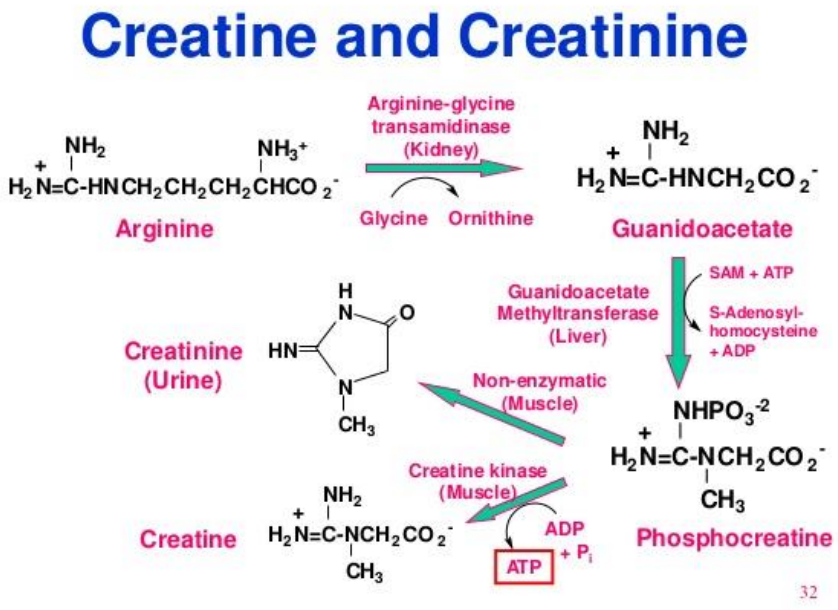
→ **Definition:** Creatinine is a waste product of creatine and metabolized in the kidneys, pancreas structurally, creatine is acid which makes up to 98% of total muscle mass and plays a crucial role in muscle contraction. Creatine is excreted in the form of anhydride, i.e. creatinine. Serum creatine concentration is increased in muscular atrophy and muscular dystrophy.

→ **Synthesis:** Creatinine is synthesized in liver, pancreas and kidneys from the amino acids arginine, glycine and methionine. Creatine is transported through the circulatory system to muscle, brain and other organs, where it is converted to phosphocreatine and acts as an energy reservoir much like ATP. Creatinine is produced as a waste product creatine and phosphocreatine, because much of the creatinine is produced in muscle, the amount of creatinine that is measured in blood is proportional to the patient's lean muscle mass.





→ The molecular weight of creatinine is (113).



→ The diagram which the flowing illustrates formed creatinine from creatine and phosphocreateatine

➢ Excreted: Creatinine enters the blood supply, where it is removed through the kidney.

☒ Clinical significant:

1. Normal case:

The normal range of s.creatinine is (male 0.3-1.3 mg/dl, female 0.2-1.1 mg/dl and children 0.3-0.7 mg/dl)

2. Abnormal cases:

1) **Hypo** (It is involved of decrease serum creatinine levels (male 0.3, female 0.2 and children 0.3) mg/dl).
   a) Muscular dystrophy
   b) Muscular atrophy

2) **Hyper** (It is involved increase of serum creatinine levels (male 1.3, female 1.1 & children 0.7) mg/dl-).
    a) Acromegaly
    b) Renal failure
    c) Nephritis
    d) Uremia
    e) Congestive heart failure.

Creatinine Clearance CCr:

- Renal clearance is a measure of kidney functional capacity. Clearance is the number of milliliters of plasma purified' from a substance per second.
- The substances meeting the following conditions are used to test the functional capacity of the kidneys:

A. They should be freely filtered through the glomerulus,
B. They should not bind to plasma proteins.
C. Plasma concentration and distribution should be constant.

- The substances that are filtered through the glomerulus but are neither reabsorbed nor excreted in tubules are used to test glomerular function
    a. inulin,
    b. mannitol
    c. creatinine
- The glomerular function of the kidneys is usually assessed by determination of endogenous creatinine clearance.
- Creatinine is filtered through glomeruli, only some being reabsorbed in tubules and some being secreted in tubules. With minor deviations, the endogenous creatinine clearance corresponds to glomerular filtration.
- The values of creatinine clearance slightly exceed glomerular filtration, because of some creatinine secretion that occurs in the tubules.

- Creatinine clearance (CCr) is calculated from the creatinine concentration in the collected urine sample (UCr), urine flow rate (V), and the plasma concentration (PCr).
- Since the product of urine concentration and urine flow rate yields creatinine excretion rate, which is the rate of removal from the blood, creatinine clearance is calculated as rate per min (UCr × V) divided by the plasma creatinine concentration. This is commonly represented mathematically as:

$$C_{cr} = \frac{U_{cr} \times V}{P_{cr}}$$

- Example: A person has a plasma creatinine concentration of 0.01 mg/ml and in 1 hour produces 60ml of urine with a creatinine concentration 1.25 mg/ml.

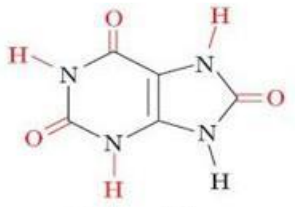
$$C_{cr} = \frac{1.25mg/ml \times \frac{60ml}{60min}}{0.01mg/ml} = \frac{1.25mg/ml \times 1ml/min}{0.01mg/ml} = \frac{1.25mg/min}{0.01mg/ml}$$
$$= 125ml/min$$

- An unexpectedly low or high 24-hour creatinine excretion rate voids the test Nevertheless, in cases where estimates of creatinine clearance from serum creatinine are unreliable, creatinine clearance remains a useful test. These cases include "estimation of GFR in individuals with variation in dietary intake (vegetarian diet, creatine supplements) or muscle mass (amputation, malnutrition, muscle wasting), since these factors are notspecifically taken into account in prediction equations.

Uric acid

Definition

Uric acid is the ultimate catabolite of purine metabolism in humans and higher primates. It is a weak organic acid that under physiologic conditions exists mainly as a monosodium salt. At a pH less than 5.75, as may occur in the urine, the predominant form is nonionized uric acid. The solubility of monosodium urate is about 18 times greater than uric acid in aqueous solutions. This solubility differential provides the therapeutic rationale for alkalinization of the urine pH to greater than 6.0 in patients forming uric acid stones.



Uric acid

The physiochemical definition of hyperuricemia may be considered 7.0 mg/dl measured by the specific uricase method. This represents the solubility limit of urate in plasma at 37°C. Levels beyond 7.0 result in supersaturated solutions that are prone to crystal formation.

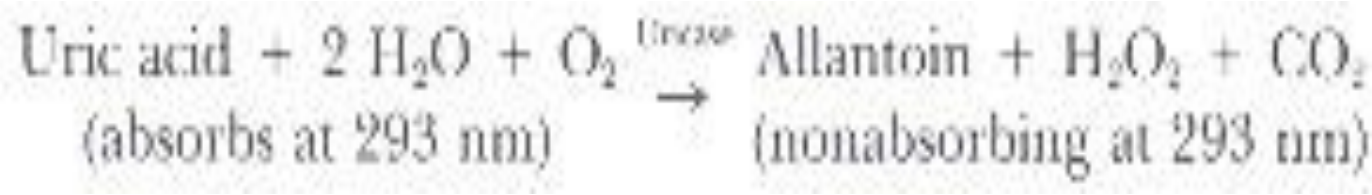
Uric acid levels are influenced by age and sex. Prior to puberty, the average serum uric acid is 3.6 mg/dl for males and females. Following puberty, values rise to adult levels with women typically 1 mg/dl less than men. This lower level in women apparently reflects estrogen-related enhancement of renal urate clearance and disappears at the menopause. Many additional factors, including exercise, diet, drugs, and state of hydration, may result in transient fluctuations of uric acid levels.

Technique

Currently, two methods are widely utilized to quantify uric acid. A colorimetric method depends on the reduction of a chromogen such as sodium tungstate by uric acid to produce a measurable color change. This technique has been commonly employed in automated hospital screening (SMA systems). The method measures materials other than urate, such as ascorbic acid.

Colorimetric determinations are generally considered an overestimation of true uric acid levels, and the normal range is usually 1 mg/dl higher than the more specific enzymatic techniques.

Enzymatic determination of uric acid results from the specific oxidation of uric acid by uricase, which converts its substrate to allantoin. The differential absorbance of these substances at 293 nm allows quantification.



Although traditionally a more expensive technique, uricase methods are currently available for SMA systems at comparable costs and are gradually replacing the less specific colorimetric method.

Go to:

Basic Science

Serum uric acid reflects the interactions of four major processes:

1- dietary purine intake,
2- endogenous purine metabolism,
3- urinary urate excretion,
4- intestinal uricolysis.

Dietary manipulation was once the mainstay of antihyperuricemic therapy. Nevertheless, even rigid purine-free diets result in only modest reductions of serum uric acid, generally in the range of 1 mg/dl. The advent of potent antihyperuricemic drugs has resulted in diminished emphasis on the therapeutic role of diet. Nonetheless, certain foods, such as organ meats, are rich in purines and can cause a significant flux in serum uric acid if ingested in sufficient quantities.

Endogenous purines are derived from de novo biosynthesis and breakdown of tissue nucleic acids. Measurement of the true rate of endogenous purine turnover requires isotopic dilution techniques carried out on patients severely restricted in dietary purines. A more practical approach in patients with normal renal function who are not taking uricosuric agents involves the measurement of a 24-hour urine collection for uric acid. This provides a crude estimate of the rate of purine production. On purine-restricted diets, a commonly accepted upper limit of uric acid excretion is 600 mg/24 hr. On an unrestricted diet, the limit is raised to 800 mg/24 hr.

A minority of patients with primary hyperuricemia excrete excessive amounts of uric acid. In only a small fraction of these patients has a specific regulatory enzyme defect been identified. Hyperuricemia secondary to hematologic diseases characterized by increased cellular turnover, such as hemolytic and myeloproliferative disorders, are associated with increased urinary excretion of uric acid. The accelerated turnover of nucleic acids in these disorders results in a compensatory increase in the rate of purine biosynthesis. Finally, certain exogenous substances, such as methylene blue and fructose, may stimulate purine biosynthesis.

The kidney is the major site for removal of uric acid and accounts for two-thirds to three-fourths of the daily losses. Urate excretion is believed to depend on a system that includes four components: glomerular filtration, proximal tubular reabsorption, secretion, and postsecretory reabsorption. In primary hyperuricemia and gout, most patients demonstrate a defect in the renal handling of uric acid. In theory, failure of any of the model's components could be involved in the development of hyperuricemia in these patients. At present, the exact site of the defect remains unresolved.

Diminished glomerular filtration rate and renal failure can lead to secondary hyperuricemia. Diuretics increase serum uric acid by multiple mechanisms including an increase in tubular reabsorption. The secretory mechanism for uric acid may be inhibited by a number of organic acids including lactate, betahydroxybutyrate, and acetoacetate. This accounts, in part, for the hyperuricemia seen in diabetic ketoacidosis and lactic acidosis. Salicylates in low dose (less than 2.5 gm/day) impair the secretory mechanism and raise serum uric acid levels. Higher doses inhibit urate absorption, producing a urate diuresis and reduction in serum uric acid.

About one-quarter to one-third of uric acid is normally disposed of by intestinal uricolysis carried out by enzymes of the gut bacterial flora. Uric acid reaches the intestines through alimentary secretions including saliva, bile, gastric, pancreatic, and intestinal juices. Hyperuricemia secondary to failure of intestinal uricolysis has not been recognized. The role of intestinal degradation expands in patients with renal insufficiency and may account for as much as 80% of urate elimination.

Clinical Significance

Hyperuricemia

Hyperuricemia may be conveniently divided into two major categories. *Symptomatic hyperuricemia* is manifested by gout, nephrolithiasis, and uric acid nephropathy. A larger group of patients have *asymptomatic hyperuricemia*. Some of these patients will eventually become symptomatic.

The risk of acute gouty arthritis increases with the level of serum uric acid and the duration of hyperuricemia. Acute fluctuations in serum uric acid may be associated with the precipitation of acute gouty arthritis. Sudden reductions in serum uric acid may accompany the introduction of antihyperuricemic therapy; hence, these patients often simultaneously begin prophylactic doses of colchicine.

Nephrolithiasis may accompany gouty arthropathy or occur as an independent problem. Uric acid forms radiolucent stones or may contribute to the formation of calcium stones. In patients with gout, the risk of stone formation rises with the level of serum uric acid. A better correlation exists between stone formation and urinary uric acid excretion. One study found the prevalence of stones to be 50% in gouty patients excreting greater than 1100 mg of uric acid per 24 hours.

Acute uric acid nephropathy results from the precipitation of uric acid crystals within the collecting tubules and ureters. It is a severe form of acute renal failure and is classically associated with the chemotherapy of leukemias and lymphomas. It may also occur following strenuous exercise and epileptic seizures. Hyperuricosuria, aciduria, and urine concentration seem to act in concert to produce this syndrome. The diagnosis can be made by the demonstration of a uric acid to creatinine ratio greater than 1 in the setting of acute renal failure.

Routine screening of hospitalized patients will identify a substantial number with elevated serum uric acid and no related symptoms. Most of these patients will remain asymptomatic throughout their lives. A complete discussion of the management of asymptomatic hyperuricemia is beyond the scope of this chapter. Suffice it to say that the weight of current evidence speaks against the normalization of uric acid in asymptomatic patients. Regardless of the level of uric acid, little seems to be lost by awaiting the onset of the first bout of arthritis or kidney stone.

Hypouricemia

Hypouricemia is commonly defined as a serum urate concentration of 2 mg/dl or less. A low serum urate concentration may result from decreased production or increased excretion. Quantification of urinary uric acid can facilitate a distinction between these two mechanisms. Patients with hypouricemia secondary to impaired production will have little or no urinary uric acid.

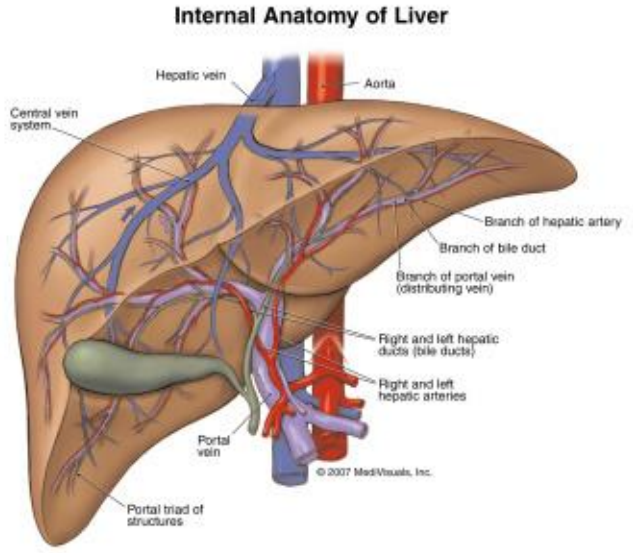
Hypouricemia can be found in about 1% of hospitalized patients. In most cases the cause is related to drugs, including salicylates, allopurinol, x-ray contrast agents, and glyceryl guaiacholate. Forced diuresis, used mainly in the treatment of suicide-attempt patients and renal colic, may result in hypouricemia. Total parenteral nutrition can cause profound hypouricemia in some patients.

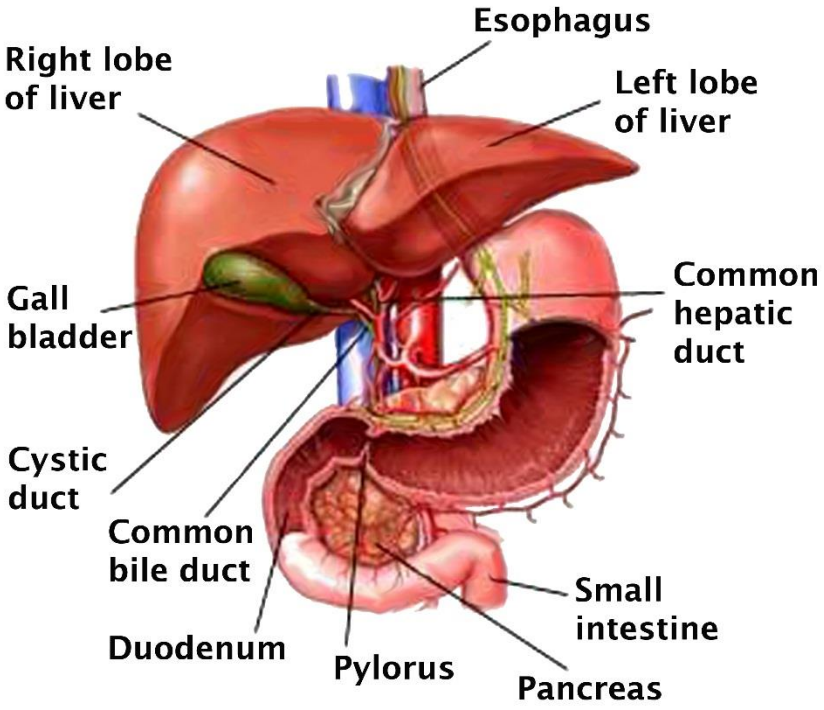
Several malignant diseases have been associated with hypouricemia, including Hodgkin's disease, sarcoma, glioblastoma, and a variety of carcinomas. In multiple myeloma, light chains most likely cause tubular epithelial damage and Fanconi syndrome. Other malignancies have also been associated with tubular dysfunction and increased renal clearance of urate. The inappropriate secretion of antidiuretic hormone that accompanies some malignancies may lower serum uric acid. Decreased xanthine oxidase activity, acquired after the development of a malignancy, appears to be an uncommon mechanism.

Hypouricemia produces no symptoms or known morbidity. Its fortuitous discovery on automated chemistry screening requires no therapy but should alert the physician to search for an underlying cause.

Liver (Hepatic) functions tests

Deflation :-The liver is the largest glandular organ of the body it weight about (1.36kg) .It is reddish brown in color and is divided in to lobes of unequal size and shape .Blood is carried to the liver via two large vessel called the hepatic artery and the portal vein.





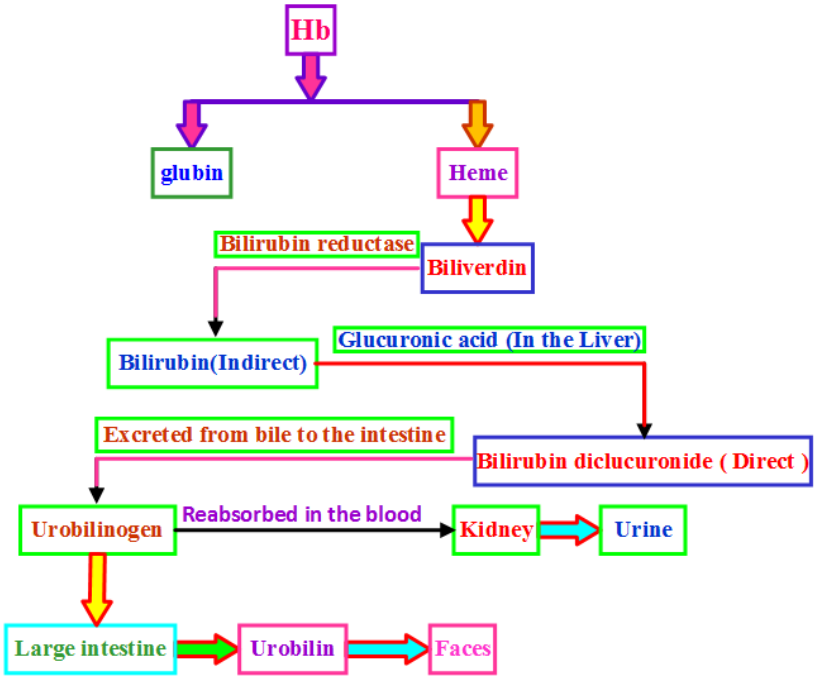
The liver has many functions some of the functions are to produce substances that break fats ,convert glucose to glycogen , produce urea filter harmful substances from the blood (such as alcohol), make certain amino acids ,storage of vitamins and minerals (vitamins A,D,K and B12) and maintain a proper level or glucose m the blood. The liver is also

responsible for producing cholesterol ,it produce about 80% of the cholesterol in body.

- Several diseases states can affect the liver and to identification this diseases must be performance some examination or name liver function test/this examination can be divided in three group:
  1. Liver damage function ;include (enzyme transaminase GOT and GPT)
  2. Liver dyes function ; include (liver conjugation capacity measure bilirubin (direct and indirect)
  3. function depended on liver ability to industrialization for example Total protein and Albumin .

1. Determination pf serum bilirubin : -

- **Definition**:- Bilirubin is a waste product derived from the breakdown of hemoglobin in the reticuloendothelial system (spleen, bone marrow and Kupffer's cells in the liver) .
- **Synthesis and production**: The bilirubin molecule formed in the spleen is non-polar and only a slightly soluble in water at body pH, therefore, it's called free (untonjugated or indirect bilirubin). To accomplish the translation of this molecule from the spleen to the liver, it must be soluble, therefore, free bilirubin is solubilized by formation complex with albumin. This complex dissociates in liver, and bilirubin is conjugated with glucuronic acid by glucuronly transferase enzyme (by formation in ester linkage between glucuronic acid and the propionic acid side chain of bilirubin). The resulting polar, waste soluble bilirubin glucuronide is as known as conjugated or direct reacting bilirubin .
- **Excretion:-** Most of conjugated of direct reacting bilirubin is activity excreted from the liver into bile duct to the intestine where it is reduced by bacteria to urobilinogen and urobilin. Bilirubin is excreted with feces while urobilinogen is reabsorbed from the liver to the blood stream and excreted via the kidney.



Clinical significant: -

1. Normal case:-
   The normal range of Total Serum Bilirubin (TSB) is 0.0 to 1 mg/dL , s.Direct bilirubin is 0.0 to 0.2 and s.Indirect bilirubin is 0.2 to 0.8 mg/dL
2. Abnormal case : -
   Hyperbilirubinemia:- It can be seen in two cases : -
   A. Subclinical Jaundice:- In this case the con. of TSB is 1.1 to 2.0 mg/dL.
   B. Jaundice:- It can be seen in three cases when the con. of TSB more than 2.0 mg/dl.
      a) Pre-hepatic jaundice :- In Direct bilirubin > Direct bilirubin, example haemolytic jaundice
      b) Hepatic jaundice :- Direct bilirubin > In Direct bilirubin, example: hepatic disease.
      c) Post-hepatic jaundice:- Increased of Direct bilirubin, example: obstructive jaundice.

Determination of serum transaminase enzyme activities : -

✯ Transamination is a term given to the process in which the amino group is transferred from an a-amino acid to a-keto acid. As a result a different α-amino acid and α-keto acid are formed. All naturally occurring a-amino acids can take apart in such reactions. This process is catalyzed by enzymes referred to transaminase or amino transferase, which plays a key role in intermediary metabolism as it provides a means for the synthesis and degradation of amino acids in living cells. Two clinically important examples are GOT and GPT.

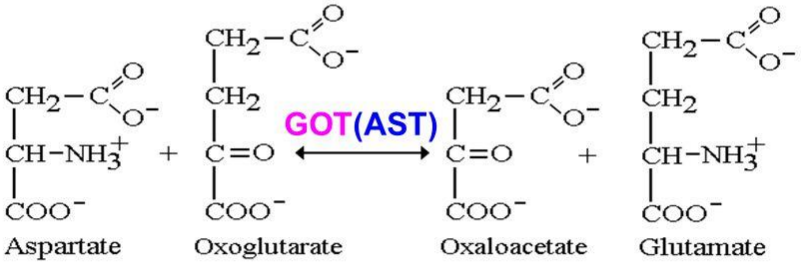
Glutamate oxaloacetate transaminase(GOT)enzyme:

It's called also aspartate amino transferase (AST), catalyzed the following reaction:

2. GOT

- **(serum glutamate oxaloacetate transaminase)**

/ Aspartate aminotransferase (AST)



- **The enzyme properties** : -
  a) It acts on the substrate; L-aspartic acid + α- Keto glutaric acid
  b) AST activity is widely distributed in human tissues: kidney, liver, skeletal muscle and the heart being the richest sources .
  c) The optimum conditions of maximum enzyme activity are: pH= 7.4 and temp.=37°C.
  d) The enzyme activity is inhibited by anticoagulants, therefore, serum preferred to use rather than plasma.
  e) The enzyme stability : 3 days in 25°C, 1 week in 5°C and 1 month in -25°C.
- **The enzymes GOT and (GPT) unit-:**

The enzyme activity is measured by international unit , which may be defined as : The activity of enzyme that produced 1µmol of oxaloacetic acid or (pyruvate) from aspartic acid or (alanine) respectively at 1 min per lit. of serum under certain conditions of tem. 37°C and pH=7.4

- **Clinical significant:**
  1. Normal case:- the normal range of s. GOT is 15-37 IU/L
  2. Abnormal cases:-The enzyme clinical usefulness is largely restricted to the diagnosis of heart and Fiver diseases. The most information is gained when the enzyme measured simultaneously with other enzymes, particularly GPT, CPK, LDH and ALP. However, high level of GOT is observed in :
     a) Heart diseases:-S.GOT was increased after myocardial infarction MI.

GOT begin to rise 5-8 hrs. after a MI occurs, and the peak activity occurs at (24-36 hrs.), then return to normal level usually follows in (4-5) days unless other attack occurs. The GOT activity is proportional with the cardiac muscle damage.

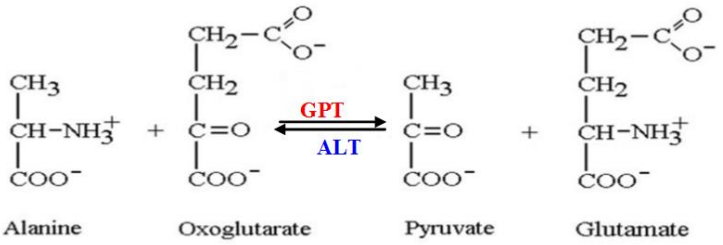
b) Liver diseases:- Large amount of GOT may be released into the blood. Very high levels are observed in acute liver diseases, while lesser elevation are seen in chronic liver disease. The most common entities are listed below: -
    1) Infection hepatitis
    2) Toxic hepatitis.
    3) Bile duct obstruction
    4) Liver cirrhosis and cancer .

c) Muscular disease :-S.GOT was increased in muscular dystrophy .

Glutamate pyruvate transaminase (GPT) enzyme:

It is also called alanine amino transferase (ALT), catalyzed the following reaction:

Alanine transaminase (ALT)



- **ALT or sGPT (serum glutamate pyruvate transaminase)**

GPT (ALT) catalyses the transfer of amino-groups from alanine to 2-oxoglutarate and thus the formation of glutamate and pyruvate.

The enzyme properties :

GPT properties are similar to these of GPT except

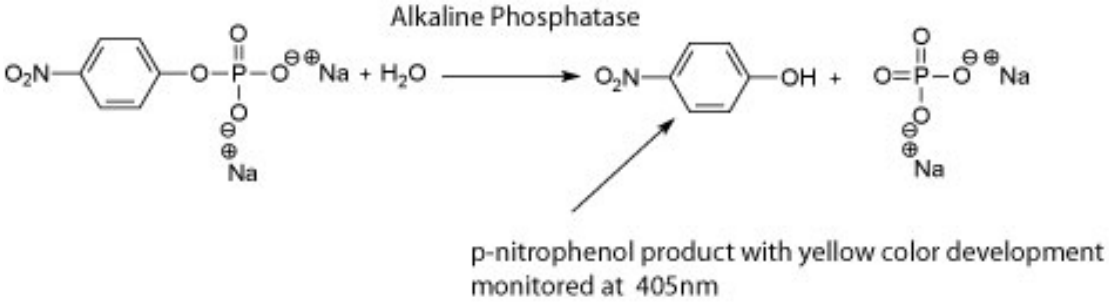
1) GPT found in a highest's con. ln the liver in spite of its active occurrence in skeletal muscles heart and kidney.
2) The substrate of GPT is L-alanine + α-keto glutaric acid

Clinical significant : -

1) Normal case:- The normal range of s.GP f is 20- 35 IU/L.
2) Abnormal case:- The GPT activity in tissues is generally less than GOT. Significant elevation of s.GPT occur in sever acute hepatitis where the enzyme is released into the circulation. However GPT level is increased in the following diseases : -
    a) Infection hepatitis
    b) Liver cirrhosis and biliary cirrhosis. The GPT is usually elevated to a lesser extent than the GOT. Some physicians, use the ratio GOT ; GPT
    c) Obstructive jaundice
    Both GPT and GOT are moderately increased. The level of GOT in this case is about the same magnitude as that seen after a myocardial infract coronary of heart or heart attack, so an associated rise in GPT may help to differentiate these two conditions.
    d) Liver cancer.

Determination of serum alkaline phosphatase

a) Definition:- The group of enzyme in the blood, which catalyze the breakdown of phosphate esters bond, are known collectively as phosphatase
b) The clinically important phosphatase is divided into two groups depending on the pH at which they are most active. The group of phosphatase most active;pH:10-)is called alkaline phosphatase (ALP) while the most active at pH:5 is called acid phosphatase (ACP).



ALP properties

a) Optimal activity of it is exhibited at a pH of approximately 10.0 and temperature 37° C.
b) ALP requires Mg^{+2} ,Mn^{+2} and Co^{+2} for activation.
c) ALP activity is inhibited by Ca^{+2}, PO_4^{-3} , $C_2O_4^{-2}$,EDTA, CN^- and F^- , therefore they should be avoided during preparation of plasma .
d) The assays of ALP activity uses p-nitrophenyl phosphate or phenyl phosphate or α-naphthyl phosphate as a substrate.

e) ALP is found in the blood serum and plasma. bone, kidney, liver, mammary gland, intestine. Lungs ,spleen, leucocytes, adrenal cortex.

✯ However, it is found chiefly in the bone and liver.

✯ ALP helps the transference of metabolites through cells, tissues and bone calcification.

❖ **King Armstrong unit of ALP activity : -**

One unit being the mg of phenol liberated by 100 Ml of serum in 15 min under specified conditions (pH=10 & temperature = 37°C

❖ **Clinical significant : -**

1. Normal case:-the normal range of s.ALP is (adults 3-l3KUA/dL, children 6-25 KUA/dL).
2. Abnormal cases : - Increased s.ALP : -
   1) Bone diseases
   2) Paget's diseases: increased 10-15 time than normal value.
   3) Rickets: increased 2-4 time than normal value.
   4) Bone cancer d-Osteomalasia
   5) Hepatobiliary diseases
   6) Obstructive jaundice b-Biliary obstructive
   7) Pregnancy: increased bone formation
   8) Growing children

✯ **Decreased s.ALP : -**

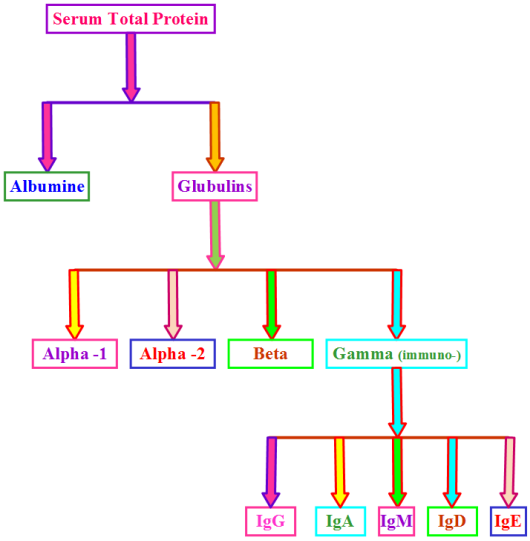
a) Hypothyroidisn
b) Chronic nephritis
c) Vit.C deficiency

✯ **Deamination of serum total proteins:**

➢ **Definition:-** Proteins are polymers of α-amino acids occurring in both soluble and insoluble state in the body . Only tests for the soluble proteins presently are performed on a routine basis in clinical chemistry laboratory because of the emphasis on fluid rather than solid-tissue samples. The three common fluids that submitted for these analysis are serum, urine and cerebrospinal fluid (CSF).

➢ Serum (as contrasted with plasma) is deficient in those coagulation proteins, which are, consumed during the process of blood coagulation.

➢ Therefore s.protein will be approximately 0.25 gm/dL lower than for plasma protein because of the absence of fibrinogen . Serum protein can be analyzed in total , in groups as illustrated in the figure:-



Synthesis:-

✯ Many proteins including albumin, fibrinogen and most globulins are formed in the liver.

✯ **Separation of proteins** :

There are many technical methods used for separation s.protein types are summarized below:

1) Salt fractionation

Based on the solubility of protein groups in certain salts .Albumin is soluble in sodium sulphate and ammonium sulphate, while globulin is precipitate at it.

2) Electrophoresis :

Simple and important method to quantitative serum proteins. It is include the separation of proteins in an applied electric field depending on the separation of proteins in an applied electric field depending on the charge density and charge type on the protein surface. The leads to various speed of protein migration in the electric field.

3) Ultra-centrifugation :

This method depending on the differences in molecular weight and molecular shape of the protein type therefore, when they centrifuged in a high speed, they will separate from each other.

4) Chromatography : The separation is depending on the differences in volume shape change and electric change of protein type of and their flow rates through the gel chromatography.

5) Gel filtration : -

Different type of protein will separate depending on their molecular mass. Large molecules will filter first ,by gel while small one discharged later from the gel porous by certain ionic strength.

6) Immunochemical analysis :

This technique is depending on the radial diffusion spied of proteins in a small porous on the gel. F

✯ **Clinical significant:**

1. Normal case : The normal range of s.total protein is 6.2-8 g/dl.
2. Abnormal cases:
   A. **Hypoproteinemia** : It is involve a decrease serum total protein levels less than 6.2 g/dl.
      1) Over-hydration:- the concentration of all fraction's protein is proportionately decreased due to relative water excess.
      2) Kidney diseases as in the nephritic syndrome large masses of albumin may be lost m the urine as a result of kidney damage.
      3) Sever burns, extensive bleeding, fever and necrosis where increased breakdown of protein.
      4) Sever malabsorption
      5) Sever protein deficiency (protein starvation)
      6) Increased requirement, as in growth, pregnancy and hyperthyroidism.
      7) Drugs: estrogen therapy has been reported to decrease the total soluble proteins.
   B. **Hyperproteinemia:-** It is involve an increase of serum total protein levels more than 8g/dL
      1) Dehydration:-The total protein is increased and the rise being reflected proportionately in all protein fractions, dehydration may result from, a decrease in water intake, as occurs in frank water depletion or from excessive water loss, as occurs in: vomiting, sever diarrhea and diabetic acidosis.
      2) Multiple myeloma:-In this state, the total protein may increase to over 10 g/dl. due to over production of proteins.
      3) Cirrhosis of the liver
      4) Certain chronic diseases: In this case, the immunoglobulin is mostly increased.
      5) Aretefacutal stasis during venepuncture, stasis induced by keeping the tourniquet on far too long during venepuncture causes fluid to escape into the extra vascular compartment, leading to hemoconcentration and falsely raised protein conc.
      6) Drugs like, clofibrate, digitalis, epinephrine, steroids, progestin, insulin and thyroxin.
      7) Exercise:-An increase of (6-12%) occurs with vigorous exercise of short duration.
      8) Vertical vs horizontal position:-Total s.protein is reported to be lower by (0.4-0.8 g/dl) with the subject supine than when in the erect position.

✯ This phenomenon is usually a scribed to hemoconcentration when in the erect position

Determination of Serum Albumin

- Definition:- Albumin is the most prevalent protein (about 60% by weight) ,has a low molecular weight (66.000 D), the biologic half time is 20 day.,
- Albumin functions:
  1) **Regulatory function**:- Regulate the osmotic pressure of plasm and distribution of water between blood plasma and the tissues.
  2) Transport function:- Albumin is a non-specific transport mechanism for many physiologic substances as drugs, antibiotics, various ions (Ca^{+2} ,Mg^{+2}, P^{-5}), amino acids, fatty acids, bilirubin, uric acid and hormones.
  3) Catalytic function:- The wide range of enzyme present in plasma are proteins.
  4) Structural function:- Alb. Also precursor for tissue proteins such collagen (fibrous protein found in connective tissues) and α-keratin.
  5) Defense function :-The immunoglobulins are antibodies, which provides a defense against infection such as thrombin and fibrinogen.

Clinical significant -:

1) **Normal case:-** The normal range of serum alb. is (3.8-5.4 g/dl), serum glob. is (2.5-3.5 g/dl) and the ratio alb./glob. (1-1.5)
2) **Abnormal cases**:- The following table shows the relationship of s.protein concentrations to diseases.

Total protein − Albumin = Globulin

Disorder	Total protein	Albumin	Globulin
Dehydration	High	High	High
Multiple myeloma	High	Normal	High
Hepatic damage, certain chronic infection, cirrhosis	Normal	Low	High
Renal diseases, in adequate diet, intestinal malabsorption, nephritic syndrome	Low	Low	Normal
Massive burns, extensive bleeding, dilution	Low	Low	Low

Serum Sodium
principles, normal values, clinical significance and functions.

Sodium (Na^+) is the main electrolyte in the extracellular compartment (ECC) and its level represents the relative content of sodium in relation to water. Sodium loss in excess of water loss or water gain will result in hyponatraemia,

Sodium intake by food ,drinks and added salt with food .A normal neonate requires about 2-4 mmol/kg of sodium daily the premature infant may need up to 6 mmol/kg day, because of the high losses.

- ➢ Sodium is most often found outside the cell, in the plasma of the blood stream (non-cell part).
- ➢ Sodium regulates the total amount of water in the body. Many processes in the body, especially in the brain, nervous system, and muscles.
- ➢ A Normal blood sodium level is 135 - 145 milli Equivalents/liter (mEq/L).

Conditions of Sodium Imbalance:

1) *Hypernatremia*:

Increased concentration of sodium, this term may be defined as a plasma (Na^+) above 140 mmol/l occurs whenever there is excess sodium in relation to water. There are numerous causes of hypernatremia; these may include kidney disease, too little water intake, and loss of water due to diarrhea and/or vomiting, injection of sodium chloride and in severe fever.

Symptoms of high sodium levels (hypernatremia) include:

- Thirst
- Urinating (peeing) very little
- Vomiting
- Diarrhea
- Confusion
- Muscle twitching
- Seizures

Without treatment, extremely high levels of sodium may lead to a coma and become life-threatening.

2) *Hyponatremia:*

decreased concentration of sodium, this term may be defined as a plasma (Na^+) below 130mmol/l occurs whenever there is a relative increase in the amount of body water relative to sodium. This happens with some diseases of the liver and kidney, in patients with congestive heart failure, in burn victims, severe burns excessive sweating, overdose of diuretics drugs and diabetes mellitus, excessive depletion of sodium and water causes oedema.

Symptoms of low sodium levels (hyponatremia) include:

- Weakness
- Fatigue
- Confusion
- Muscle twitching
- Seizures

Without treatment, extremely low levels of sodium may also lead to a coma and become life-

Clinical features

Despite the arbitrary division, hyponatremia is considered acute if it develops within 48 hours or chronic if it takes longer.

- The former leads to cerebral oedema, causing nausea and malaise when Na+ is 125–130 mmol/L.
- Headache, dullness, convulsions, coma and death may occur when serum Na+ is below 110–115 mmol/L.
- Although chronic hyponatremia is considered asymptomatic above this level, there may be subtle symptoms at higher Na+ concentrations (0.120 mmol/L) (e.g. lethargy and dizziness) and a greater risk of falling, possibly due to unsteadiness.
- Sodium is an essential nutrient involved in the maintenance of normal cellular homeostasis and in the regulation of fluid and electrolyte balance and blood pressure (BP)
- The human body requires a small amount of sodium to conduct nerve impulses, contract and relax muscles, and maintain the proper balance of water and minerals. It is estimated that we need about 500 mg of sodium daily for these vital functions

function of sodium in the blood

Sodium plays a major role in the body. It helps in

1- Maintaining normal blood pressure
2- Supports the functioning of your nerves and muscles,
3- Regulates the fluid balance in your body.

The normal level of sodium in the blood ranges from 135 to 145 milliequivalents per liter (mEq/L)

What sample for Sodium (Na^+) is needed?

1. This test is done on the patient's serum.

   A random sample can be taken.

2. Heparinized plasma and whole blood without sodium heparin may be used.
3. Twenty-four hours of urine samples may be collected without the addition of preservatives.

   Can store the serum or urine at 2° C to 4 °C.

4. Other samples can be:
   a- Feces.
   b- Sweat.
   c- Gastrointestinal fluids.

Serum Potassium

Definition

Potassium, a metallic inorganic ion with atomic weight of 39, is the most abundant cation in the body. The vast majority of potassium is in the intracellular compartment with a small amount in the extracellular space. Normal serum potassium is 3.5 to 5.5 mEq/L; however, plasma potassium is 0.5 mEq/L lower. While total body potassium is lower in females and in older patients, serum potassium concentration is independent of sex and age.

The potassium intake by food from added salt with food the potassium output by skin, urine, normal stool . The potassium is the intracellular cation and the normal values in the ICF (intra cellar fluid) is about (25-30) times than in ECF (extra cellar fluid) normal values is (3.2-4.6 mmol/l).

1-Hyperkalemia:

increased concentration of potassium levels can define as plasma (K+) above 5.0mmol/l and this increased are most often associated with kidney failure, in which potassium levels build up and cannot be excreted in the urine. When collection blood samples must not be refrigerated until serum has been separated refrigeration promotes the loss of potassium from the erythrocytes producing hemolysis pathological causes of hyperkalemia occurs in poorly controlled diabetes mellitus insulin lack promote the loss of k+ from cells and leukemia.

2-Hypokalemia:

may defined as plasma (K+) below 3.0mmol/l. Decrease concentration of Potassium levels can affect the nervous system and heartbeat, hypokalemia occurs in many diseases such as gastrointestinal secretion (vomiting, diarrhea) in urine (thiazide diuretics or acute renal failure) and cardiac arrhythmias.

Serum potassium functions

Potassium is a type of electrolyte which plays a crucial role in various bodily functions such as proper nerve and muscle function, regularity of heart rate, maintain normal blood pressure

Functions

1- Maintaining normal blood pressure.

2- Transmitting nerve signals between organs.

3- Controlling muscle contractions.

4- Ensuring optimal water balance within the system.

5- Balancing pH in the body between acidity and alkalinity.

6- Upholding accurate heart rate i.e. pulse.

7- Regulating proper digestion processes

Clinical significance of serum potassium

In states of health, serum potassium (K^+) is tightly regulated, typically between 3.5 and 5.0 mEq/L (1). Homeostatic maintenance of serum K^+ is important for many physiologic processes, such as

- cardiac conduction and
- inotropy, smooth muscle tone,
- neuronal signaling

Potassium is important for heart function. This test may be ordered if a person has signs of high blood pressure or heart problems. Small changes in potassium levels can have a big effect on nerve and muscle activity, especially the heart.

A potassium test may be used to monitor or diagnose conditions associated with abnormal potassium levels. These conditions include kidney disease, high blood pressure, and heart disease.

Serum Calcium

Reference Range

Calcium concentration, both total and free, is characterized by a high physiological variation, depending on age, sex, physiological state (eg, pregnancy), and even season (owing to the seasonal variation of vitamin D, which is directly involved in the regulation of calcium concentration). Therefore, separate reference intervals have been established according to the age and sex of the individual being tested.

Total calcium reference ranges are as follows ·

- < 10 days: 7.6-10.4 mg/dL; 1.9-2.6 mmol/L
- Umbilical: 9-11.5 mg/dL; 2.25-2.88 mmol/L
- 10 days-2 years: 9-10.6 mg/dL; 2.3-2.65 mmol/L
- Child: 8.8-10.8 mg/dL; 2.2-2.7 mmol/L
- Adult: 9-10.5 mg/dL; 2.25-2.62 mmol/L (Values tend to be reduced in elderly persons.)

Possible critical values for total calcium are < 6 mg/dL or >13 mg/dL

Calcium provides to the skeleton and calcium ions play a role in metabolic processes.

 Occurrence of calcium in the body:

1- Calcium is an electrolyte cation

2- More than 99% of the calcium in the body is present in the bones as calcium fluorophosphates apatite.

3- The remainder 1% of the calcium found as:

A. Protein –bound calcium especially albumin (40-50%) from the amount of Ca+2

B. Free calcium fraction (complexes and ionized) the complex calcium bound with bicarbonate or bound with sulfate (60% amount of Ca+2). The calcium bound with protein and free calcium (total calcium in serum must be determined

Absorption and metabolism of calcium

The Ca+2 and balance values ,the low calcium values the higher phosphorous level but this relation not always ,there is two cases Ca+2and both increase or decrease.

1- In the formation of bones calcium and higher values

2- In the rickets disease calcium and phosphorus decrease level in the body and decrease in tetanus disease . The calcium and phosphorous absorbed in the upper small intestine duodenum maximal absorption of calcium and phosphorous maximal absorption in the jejunum .The absorption of calcium and phosphorous increases in acidic medium and decreased in alkaline medium .

Factors effecting calcium level

1- The PH of the medium (acidic increase , alkaline decrease) .

2- Presence of vitamin D essential for calcium absorption increased level of vitamin D promote calcium absorption calcium binding protein .

3- Parathyroid hormone ; increase parathyroid hormone effected to increase the absorption of calcium and phosphorous in the body .

4- The level of protein in blood ; the calcium in plasma bound with albumin therefor decrease the protein level often show decrease the calcium level .

5- The higher calcium level low phosphorous level but this not always.

6- The normal value for calcium (9-11)mg/100ml, (2.1-2.6)mmol/l.

Function of calcium

The calcium in the body have many function

1- The main component in the formation of bon .

2- Inter the operation of blood clotting the calcium need for the formation of thrombin

3- Transfer of inorganic ion .

4- Promote some enzymes in the body.

Clinical significance of calcium

A. Increase of Calcium (too much calcium in the blood) symptoms include kidney stones, abdominal pain, and depression. Also, too much calcium can be associated with heart disturbances.

B. Decrease of Calcium is usually associated with eating disorders or lack of parathyroid hormone. Symptoms include weakness, muscle spasms, and heart rhythm disturbance.

C. Rickets: this disease cause when calcium level decrease which cause error in the formation of bones the reason of this decrease (decrease vitamin D parathyroid hormone or protein .

D. Tetanus: This disease occur also when calcium level decrease .

Definition of Total Calcium Test

Total Calcium Test measures the amount of calcium bound to certain proteins in the blood, which is a routine metabolic test.

Calcium is one of the most important minerals in the body as the individual needs calcium for healthy bones and teeth, and calcium is also necessary for the function of nerves, muscles and the heart. It is worth noting that about 99% of calcium in the body is stored in the bones, while the remaining 1% is found in the blood. High or low blood calcium levels above the normal level indicate thyroid diseases, bone diseases, kidney diseases, and others.

It is worth noting that there are two types of calcium tests: ionized calcium test, which measures the level of calcium not bound to proteins, and total calcium test. The test is performed by taking a blood sample.

How to Prepare for the Test

Your health care provider may tell you to temporarily stop taking certain medicines that can affect the test. These medicines may include:

- Calcium salts (may be found in nutritional supplements or antacids)
- Lithium
- Thiazide diuretics (water pills)
- Levothyroxine
- Vitamin D

Symptoms of high blood calcium include:

- Vomiting and nausea.
- Frequent need to urinate.
- Increased thirst.
- Loss of appetite.
- Constipation.
- Abdominal pain.

Symptoms of low blood calcium include:

- Tingling sensation in the lips, tongue, fingers and feet.
- Irregular heartbeat.
- Muscle pain.
- Muscle cramps.

Serum Chloride, S. CL^-

Definition

Chloride is an inorganic anionic halogen in the human body that is essential for metabolism (the process of converting food into energy). It also helps maintain the body's acid-base balance. The amount of chloride in the serum is carefully controlled by the kidneys.

Its atomic weight is 35.5. It is distributed exclusively within the extracellular fluid (ECF) compartment, which consists of the blood/plasma (or serum) compartment and the interstitial fluid compartment. Chloride is the major sodium-bound anion in the ECF (see Figure 197.1). Normal serum chloride concentrations range from 96 to 106 mEq/L.

Clinical Significance

The serum chloride value, like the serum sodium value, is a *concentration* measurement (e.g., the amount of chloride/liter of plasma water). Therefore, the serum chloride concentration can be elevated above the normal range—hyperchloremia—either by the addition of excess chloride to the ECF compartment or by the loss of water from this compartment, and vice versa. The serum chloride concentration can be reduced below the normal range—hypochloremia—by the loss of chloride from the ECF or the addition of water to this compartment. This means that one cannot evaluate total body chloride stores from the serum chloride concentration. Clinical parameters must be used in conjunction with serum chloride values to assess the significance of hypochloremia or hyperchloremia.

Chloride has a major physiological significance, which includes regulation of osmotic pressure, electrolyte balance and acid-base homeostasis. Chloride is present in all body fluids, and is the most abundant extracellular anion which accounts for around one third of extracellular fluid's tonicity.

Chloride is an essential electrolyte, playing a key role in maintaining cell homeostasis and transmitting action potentials in neurons. It can flow through chloride channels (including the $GABA_A$ receptor) and is transported by KCC2 and NKCC2 transporters.

Chloride is usually (though not always) at a higher extracellular concentration, causing it to have a negative reversal potential (around −61 mV at 37 °C in a mammalian cell). Characteristic concentrations of chloride in model organisms are: in both *E. coli* and budding yeast are 10–200 mM (dependent on medium), in mammalian cells 5–100 mM and in blood plasma 100 mM.

Chloride is also needed for the production of hydrochloric acid in the stomach.

The concentration of chloride in the blood is called serum chloride, and this concentration is regulated by the kidneys. A chloride ion is a structural component of some proteins; for example, it is present in the amylase enzyme. For these roles, chloride is one of the essential dietary mineral (listed by its element name *chlorine*). Serum chloride levels are mainly regulated by the kidneys through a variety of transporters that are present along the nephron Most of the chloride, which is filtered by the glomerulus, is reabsorbed by both proximal and distal tubules (majorly by proximal tubule) by both active and passive transport.

Conditions of Chloride Imbalance

1) ***Hyperchloremia:***

Increased concentration of chloride Elevations in chloride may be seen in diarrhea, certain kidney diseases, urinary obstruction, prostatic obstruction, cardiac condition and sometimes in over activity of the parathyroid glands.

What does a high chloride level mean?

If your results reveal that you have higher-than-normal levels of chloride in your blood, it may indicate that you have:

- Dehydration.
- Kidney disease.
- Cushing's syndrome.
- Metabolic acidosis.
- Respiratory alkalosis.

It's important to remember that a high chloride result doesn't necessarily mean that you have a medical condition. Certain situations and medications can also increase your chloride levels.

2) ***Hypochloremia:***

Decreased concentration of chloride is normally lost in the urine, sweat, and stomach secretions. Excessive loss can occur from heavy sweating, vomiting, adrenal gland, polycythemia and kidney disease.

What does a low chloride level mean?

If your results reveal that you have lower-than-normal levels of chloride in your blood, it may indicate that you have:

- Heart failure.
- Lung diseases, like emphysema.
- Addison's disease.
- Metabolic alkalosis.

It's important to remember that a low chloride result doesn't necessarily mean that you have a medical condition. Certain situations and medications can also increase your chloride levels.

What is a chloride blood test?

A chloride blood test (serum chloride) measures the level of chloride in your blood.

Electrolytes are minerals that carry an electrical charge when dissolved in a liquid. Electrolytes in your blood — chloride, sodium, potassium and bicarbonate — help control nerve and muscle function, maintain the acid-base balance (pH balance) in your blood and maintain water balance.

The amount of chloride in your blood is often measured along with other electrolytes to diagnose or monitor certain medical conditions, including:

- Kidney disease.
- Heart failure.
- Liver disease.
- High blood pressure.

Why do I need a chloride blood test?

Your healthcare provider may order a chloride blood test as part of a routine blood panel. They can also order a chloride blood test if you have symptoms of an acid or fluid imbalance, including:

- Experiencing multiple instances of vomiting.
- Having diarrhea.
- Feeling very tired (fatigue).
- Feeling weak.
- Experiencing dehydration.
- Having difficulty breathing.

What does a chloride blood test tell you?

The results of a chloride blood test, alongside the results of other electrolyte tests, can help diagnose a condition related to an imbalance of acids or fluids in your body.

Enzymes

- ***Enzymes*** are proteins that catalyze increase the rates of chemical reactions in enzymatic reactions.
- ***Enzymes*** are synthesized by all living organism, all enzymes are proteins and denaturation by such factors as heat, concentrated urea solution, organic solvents and such as action.
- ***Some enzymes*** have different from called isoenzymes; when two different proteins from different tissues, coded by different gens act on the same substrate these are termed isoenzymes these isoenzymes may be separated by their different physical or chemical properties,
- ***Enzymes*** which are used in the cells which make them are called intracellular enzymes, other cells produce enzymes and secrete them to other parts of the body these enzymes are described as extracellular.

❖ *Types of Enzymes*

There are three main categories of enzymes:

A. Metabolic enzymes:

which are produced within the body

are responsible for running the body at the level of the blood, tissues and organs. They are required for the growth of cells and repair and maintenance of all the body's organs and tissues.

Metabolic enzymes take protein, fat, and carbohydrates and transform them into the proper balance of working cells and tissues. They also remove worn-out material from the cells, keeping them clean and healthy.

B. Digestive enzymes:

which the body produces etabolic enzymes Digestive enzymes Aid in the digestion of food and the absorption and delivery of nutrients throughout the body. The most commonly known digestive enzymes are secreted from the pancreas into the stomach and small.

C. Food enzymes:

are derived solely from raw fruits, vegetables, and supple mental sources. Like digestive enzymes; they enable the body to digest the food by breaking down the various nutrients — proteins, fats, carbohydrates, and vitamins and minerals - into smallest compounds that the body can absorb. They are absolutely essential in maintaining optimal health.

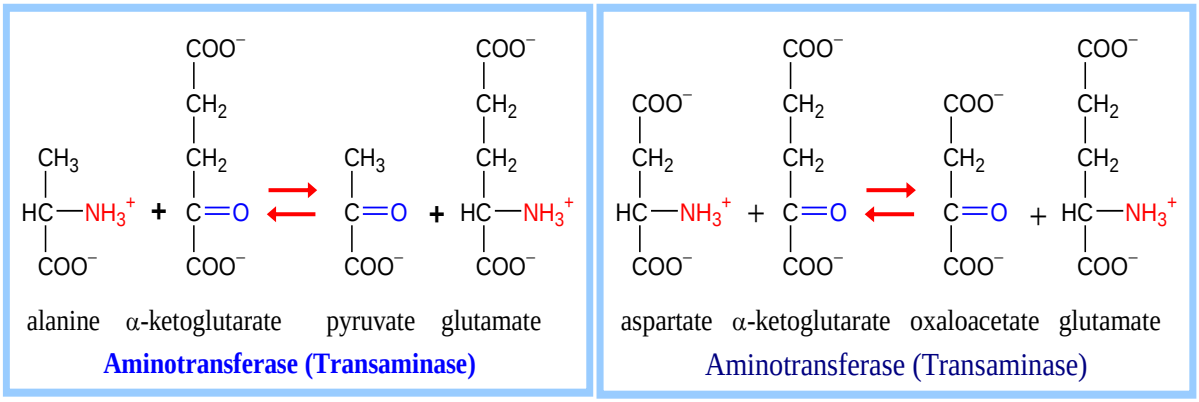
→ ***All enzymes are classified to six classes, characterized by the type of reaction that catalyze such as:***

- ✓ Oxidoreductases.
- ✓ Transferases.
- ✓ Hydrolases.
- ✓ Lyases.
- ✓ Isomerases.
- ✓ Ligases.

1. Oxidation and reduction.

Enzymes that carry out these reactions are called oxidoreductases. Oxidoreductases: general name for enzymes that catalyze reactions in which one molecule is oxidized while the other is reduced. Enzymes of this type are often called oxidases, reductases, and dehydrogenases.

2. ***Transferases:*** Remove groups (not including H) from substrates and transfer them to acceptor molecules (not including water). These enzymes, called transferases, move functional groups from one molecule to another. For example, alanine aminotransferase shuffles the alpha-amino group between alanine and aspartate:



3. ***Hydrolysis:*** These enzymes, termed hydrolases, break single bonds by adding the elements of water.

4. ***Lyases:*** Formation or removal of a double bond with group transfer:
   add or remove of groups to form double bonds (not by hydrolysis). The functional groups transferred by these lyase enzymes include amino groups, water, and ammonia. for example, in the removal of amino groups from amino acids.

5. ***Isomerization*** of functional groups:
   Isomerases: catalyze the rearrangement of bonds within a single molecule.

6. ***Ligases: Single*** bond formation by eliminating the elements of water: ligate two substrates at the expense of ATP hydrolysis.

   → Hydrolases break bonds "by adding the elements of water; ligases carry out the converse reaction, removing the elements of water from two functional groups to form a single bond.

- ***Enzyme nomenclature: -***

→ The nomenclature of enzymes by using the name of the substrate or group on which the enzymes acts, and then adding the suffix - ase

→ Thus the enzyme hydrolyzing urea was called urease, with the exception of some enzymes, such as pepsin, trypsin, thrombin and lysozyme which does not contain this suffix - ase.

Clinical significance of enzyme

assays Enzymes are the preferred markers in various disease states such as myocardial infarction, jaundice, pancreatitis, cancer, neurodegenerative disorders, etc. They provide insight into the disease process by diagnosis, prognosis, and assessment of response therapy. Enzyme assays are performed to serve two different purposes: (i) to identify a special enzyme, to prove its presence or absence in a distinct specimen, like an organism or a tissue (ii) to determine the amount of the enzyme in the sample.

Enzyme inhibition

Enzyme inhibitor is defined as a substance which binds with the enzyme and brings about a decrease in catalytic activity of that enzyme.
The inhibitor may be organic or inorganic in nature.
There are three broad categories of enzyme inhibition.
1. Reversible inhibition.
2. Irreversible inhibition.
3. Allosteric inhibition.

What is the clinical significance of plasma enzymes?

Abnormal levels of plasma enzymes are highly suggestive of damaged cells and provide clues to parts of the body that may be involved in disease processes. Enzyme levels are measured in the clinical laboratory to identify the site of damage and to quantify the amount of damage

Enzymes as catalysts :

→ A catalyst is a chemical that increases the rate of a chemical reaction without itself being changed by the reaction. The fact that they aren't changed by participating in a reaction distinguishes catalysts from substrates, which are the reactants on which catalysts work. Enzymes catalyze biochemical reactions.

→ An enzyme catalyzed reaction as follows:

Substrate (S) ; Enzyme (E) ; Product(P)

→ The substrate undergoes chemical change to from product the of the reaction in the absence of the enzyme very little or no product will be form , but in the presence of the catalyzing enzyme E , the reaction will be produced and the product will formed at the rate which will depend on the concentration of the enzyme and other factors such as:

1) substrate concentration
2) temperature
3) PH

→ The reaction is reversible and produced in other forward or reverse direction depended on the value of the equilibrium constant Keg = P/S most enzymes catalyzed reactions involve two substrates and usually two products are formed.

Enzyme activities in plasma:

The activity observed is governed by the following factors.

1. The rate of release of the enzyme form cells.
2. The volume of distribution of the enzyme in ECF.
3. The rate of removal of the enzyme from plasma by catabolism.
4. The presence in the plasma factors which may affect the method of assay like inhibitors or activators of enzyme activity.