Lecture (1)

The components of the human body

The main chemical composition of the human body consists mainly of six elements. The six elements are oxygen, carbon, hydrogen, nitrogen, calcium and phosphorous. The remainder consists of potassium, sulfur, sodium, chloride, magnesium, iron, and trace amounts of iodine, fluoride, copper and zinc. The large amount of oxygen and hydrogen in the body is present in the form of water.

The metal composition of the human body is illustrated in the following table:

Table (1) represents the metal composition of the human body;

Elements	Percentage	
Carbon	50	Major
Oxygen	20	
Hydrogen	10	
Nitrogen	8.5	
Calcium	4	
Phosphorus	2.5	
Potassium	1	Minor
Sulfur	0.8	
Sodium	0.4	
Chlorine	0.4	
Magnesium	0.1	
Iron	0.01	
Manganese	0.001	Trace
Iodine	0.00005	

The ionic constituents of tissues are represented by cations (each positively charged ion is called a cation) and include Na^+, K^+, Ca^{++}, Mg^{++}, Fe^{++}, Fe^{+++}, and trace amounts of Zn^{++}, Cu^{++}, and the anions (each ion carries a negative charge called anion) and include Cl^-,

HCO_3^{-1}, $H_2PO_4^-$, HPO_4^{--}, PO_4^{---}, SO_4^{--} and the anions of organic acids. It is important to know that Na^+ ions are the main cations in blood plasma and extracellular fluids, while K^+ is the main cation within cells (intracellular fluids).

Water Distribution in Human Body

Water constitutes 50-70% of the human body weight and this ratio is inversely proportional to the fat content of the body. Water is distributed throughout the body as a major component in intracellular fluids (50% of body weight) and in extracellular fluids (20% of body weight) and includes:

* Water in the blood: represents 75-80% of the blood.

• A fluid located between the interstitial tissue (lymph).

• Transcellular fluids (cerebrospinal fluid "CSF"), and digestive juice.

Water's Function & water's Equilibrium

Water is abundant in all tissues of the human body, so it is the necessary component for the structure of cells and represents the medium in which chemical reactions and transfer of substances take place, in addition, it is a good way to maintain body temperature and ionic balances in the body.

A person obtains water by; drinking water, from vegetables and fruits, and from the oxidation of food, and there must be a state of balance in the amount of water taken and lost, and this varies according to circumstances.

Water Balance for a Normal Human Adult

Water taken (ml/day)	Water Produced (ml/day)
1500 as fluid	300 – 400 from lungs
700 from food	300 – 400 from skin
200 from biological oxidation	200 from intestine
	1200 – 1500 from kidneys
Total = 2400	Total = 2400

It is noted that the amount of fluid taken is equal to the amount of fluid excreted, the amount of fluid taken up is controlled by thirst, and the amount of urine excreted is controlled by the antidiuretic hormone (Vasopressin).

If the amount of fluid taken is greater than the amount of fluid lost, edema (swelling in the body's cells) will develop, while if the fluid loss is more than the intake, as in case of diarrhea, vomiting and sweating, dehydration arises.

Lecture (2)

Methods of Expressing Concentrations

1. Percentage

It is divided into: Percent by Weight

Percent by Volume

The percentage by weight is defined as the number of grams of solute in 100 g of solution and the percentage by volume is the number of grams of solute in 100 milliliters of solution.

2. The mole or the Molar system

It is defined as the gram-molecular weights of the solute per liter of solution.

In biochemistry, the most commonly used terms are millimole (mm), micromole (µm) and milliequivalent (meq).

$$\text{Mole} = \frac{\text{gram}}{\text{gram/mole}}$$

$$\text{mmole} = \frac{\text{milligram}}{\text{milligram/millimole}}$$

$$\text{Molarity} = \frac{\text{number of moles}}{\text{number of liters}}$$

$$M = \frac{\text{weight} \times 1000}{V\ (\text{ml}) \times \text{molecular weight}}$$

Whereas:

M = Molarity or molar concentration

Weight = weight of solute in grams.

The molecular weight is denoted by the symbol (M.W.) and represents the molecular weight of the dissolved substance

V (ml) represents the volume of solvent in milliliters.

The final law is:

$$M = \frac{W \times 1000}{V(ml) \times M.W}$$

Normality: the number of equivalent weights of solute per liter of solvent.

$$N = \frac{\text{The equivalent}}{\text{liter}} = \frac{\text{milli-eq}}{\text{milliliter}}$$

$$N = \frac{W \times 1000}{V(ml) \times Eq.\ W}$$

Eq. W: represents the equivalent weight of the dissolved substance.

The acid's equivalent: It is the weight of the acid that liberates one atomic gram of hydrogen ion (one proton).

$$HCl \rightleftharpoons H^{+} + Cl^{-}$$

$$H_2So_4 \rightleftharpoons 2H^{+} + So_4^{-}$$

$$H_3Po_4 \underset{}{\overset{M.O}{\rightleftharpoons}} H^{+} + H_2Po_4^{-}$$

$$H_3Po_4 \underset{}{\overset{Ph.Ph}{\rightleftharpoons}} 2H^{+} + HPo_4^{-2}$$

$$H_3Po_4 \underset{}{\overset{CaCl_2}{\rightleftharpoons}} 3H^{+} + Po_4^{-3}$$

Calculate the equivalent weight of HCl given that the atomic weight of hydrogen = 1 and the atomic weight of chlorine = 35.5.

M.W for HCl = sum. of the atomic weights

= 1 + 35.5 = 36.5

$$\text{Acid Equivalent Weight} = \frac{\text{M.W}}{\text{number of hydrogen atoms}}$$

$$= \frac{36,5}{1} = 36.5$$

M.W for HCl is the same as Eq. W

The equivalent weight of the base: It is the weight of the base that liberates a gram - ion from the hydroxide (OH^{-}). More precisely, it is the weight of the base that gains or reacts with one proton.

$$KOH \longrightarrow K^{+} + OH^{-}$$

$$Al(OH)_3 \longrightarrow Al^{3+} + 3OH^{-}$$

$$Ba(OH)_2 \longrightarrow Ba^{2+} + 2OH^{-}$$

$$\text{Base Equivalent Weight} = \frac{\text{M.W}}{\text{number of hydroxide groups}}$$

Calculate the Eq. W of NaOH base if you know that the atomic weight of sodium is 23, the atomic weight of oxygen is 16, and hydrogen is 1.

M.W for NaOH base = 23 + 16 + 1 = 40

and Eq. W for NaOH base = 40

The M.W for NaOH base is the same as the equivalent weight.

Calculate the equivalent weight of aluminum hydroxide $Al(OH)_3$ given that the atomic weight of aluminum = 27, oxygen = 16 and hydrogen = 1.

M.W for $Al(OH)_3$ = sum. of atomic weights

= 27 + (16 + 1) x 3 = 78

$$Eq.\ W = \frac{78}{3}$$

Eq. W = 26

3. Molal Solution

It is the gram molecular weight of solute in 1000 grams of solvent.

$$\text{Molality} = \frac{\text{The number of moles of solute}}{\text{The number of kilograms of solvent}}$$

Examples of molar concentration (molarity) and normal concentration (normality).

Example: When 5 grams of sodium hydroxide NaOH is dissolved in 100 milliliters of distilled water (D.W), calculate the M and N of this solution if you know that the atomic weights of sodium, oxygen and hydrogen are as follows 23, 16, 1, respectively.

$$M = \frac{W \times 1000}{V\,(ml) \times M.W}$$

M.W NaOH = 23 + 16 + 1

= 40

$$M = \frac{5 \times 1000}{100 \times 40}$$

= 1.25 mole/L

$$N = \frac{W \times 1000}{V(ml) \times Eq.\ W}$$

$$\text{Base Equivalent Weight} = \frac{M.W}{\text{number of hydroxide groups}}$$

$$= \frac{40}{1}$$

= 40

$$N = \frac{5 \times 1000}{100 \times 40}$$

= 1.25 gram- equivalent / liter

Example: Dissolve 10 g of (Al $(OH)_3$ in 100 ml of distilled water (D.W) Calculate N & M if you know that the atomic weights of Al, O, H are 27, 16, 1, respectively.

$$M = \frac{W \times 1000}{V\,(ml) \times M.W}$$

M.W for base $Al(OH)_3 = 27 + (16 + 1)) \times 3$

$= 78$

$$\text{Eq. W for } Al(OH)_3 = \frac{78}{3} = 26$$

$$M = \frac{10 \times 1000}{100 \times 78}$$

$= 1.3$ mole/L

$$N = \frac{W \times 1000}{V\,(ml) \times Eq.\,W}$$

$$= \frac{10 \times 1000}{100 \times 26}$$

$= 3.8$ gram- equivalent/liter

Dilution Law

$M_1 V_1 = M_2 V_2$

$N_1 V_1 = N_2 V_2$

Example: Specific gravity of pure hydrochloric acid is 1.18, M.W 36.46, the percentage of HCl is 36%

$$\text{Molarity of liquids} = \frac{\text{Specific density x \% x 10}}{\text{M.W}}$$

$$\text{Normality of liquids} = \frac{\text{Specific density x \% x 10}}{\text{Eq. W}}$$

$$\text{M of HCl} = \frac{1,18 \times 36 \times 10}{36.46}$$

$= 11.8$ mole/L

Example: Prepare 1 M of hydrochloric acid in 100 ml distilled water from the information above.

$M_1 V_1 = M_2 V_2$

$11.8 \times V_1 = 1 \times 100$

$V_1 = 8.5$ ml

8.5 ml of HCl was withdraw and dilute to 100 ml with distilled water.

Example: Prepare 1 Normal in 100 ml of H_2SO_4 acid if you know that the molecular weight of H_2SO_4 acid is 98.7 and the specific gravity is 1.84 g and the percentage is 98%.

$$\text{W.M} = \frac{98.7}{2} = 49.35$$

$$N = \frac{\text{Specific density} \times \% \times 10}{\text{Eq. W}} = \frac{98 \times 1.84 \times 10}{49.35}$$

N = 36.8 gm-eq / L

$N_1 V_1 = N_2 V_2$

$36.8 \times V_1 = 1 \times 100$

V_1 = 2.7 milliliters

We withdraw 2.7 ml of H_2SO_4 acid and dilute it to 100 ml with distilled water.

Q 1: Prepare 0.8 normal of phosphoric acid H_3PO_4 in 500 ml distilled water, if you know that M.W = 98 and the specific density = 1.7 g and the percentage is 85%.

Q 2: Prepare 0.4 normal of barium hydroxide in 250 ml distilled water if you know that the atomic weights of oxygen, hydrogen, and barium are 16, 1, and 137, respectively.

Q 3: Prepare 5 normal of calcium hydroxide in 500 ml distilled water if you know that the atomic weights of oxygen, hydrogen and calcium are 16, 1, 40, respectively.

Lecture (3)

pH concentration

pH values: Sorensen (the Danish scientist) used a special system to express acidity and alkalinity, is the value of the acidic function and is defined as the negative logarithm of concentration.

$pH = -\log[H^+]$

Example: If the hydrogen ion concentration in an acidic medium is 10^{-2}, calculate the pH?

$pH = -\log[H^+]$

$PH = -\log 10^{-2}$

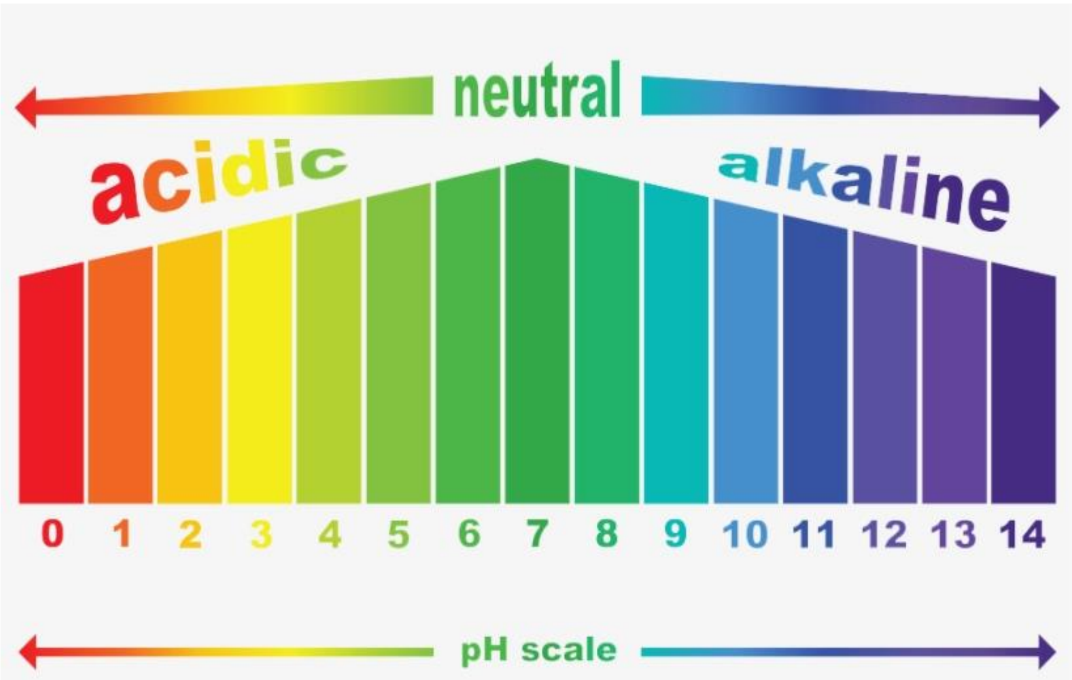
$PH = 2$

The pH value ranges from zero to 14.

acidic solution basic solution

0______________________7_____________________14

neutral solution



$$pH = -\log [H^+]$$

$$pOH = -\log [OH^-]$$

$$pH + pOH = 14$$

The normal pH of blood serum is PH = 7.4, it is slightly tended to the alkaline, or the pH of blood serum lies between (7.3 - 7.5). If pH is less than 7.3, the person will suffer from acidotic coma (acidosis), while if it is more than 7, the person will die, but if it increases more than 7.5 and reaches 7.8, then tetanus will occur, and this condition is called alkalosis.

The kidneys and lungs are the main organs responsible for the balance of acidity in the body, and therefore any damage to one of these organs may lead to a change in this balance.

Acidosis and alkalosis are not diseases, but rather a result of various types of disorders. The presence of acidosis or alkalosis is important evidence for doctors that there is a problem in patients.

Acidosis results in the following cases:

1. In the case of Diabetes Mellitus disease (D.M.) and severe hunger, 100 gm or more of beta-hydroxybutyric acid and acetoacetic acid per day can be produced by the body in these pathological conditions.
2. In chronic nephritis.
3. By taking acidic substances (as medications, especially aspirin).
4. In cases of lungs disease.
5. Emotional reactions such as anger, envy, crying, sadness and anxiety, all of which increase the acidity of the blood.

And when the acidity of the blood increases, even by a very small percentage, a disturbance occurs in the body and it becomes a suitable medium for bacteria, fungi and germs that love to live in an acidic environment, so the body does everything it can to equalize this acidity with the help of the kidneys that expel hydrogen ions through the urine, and orders the lungs to pump a large amount of oxygen to expel acidic carbon dioxide (CO_2). There are foods that increase the acidity of the blood, such as meat, refined sugar, processed foods, and alcohol.

Alkalosis arises from the following conditions:

1. Loss of stomach acid (HCl) in cases of severe prolonged vomiting

2. Loss of large quantities of carbon dioxide (CO_2) by increasing the breathing rate that occurs in the case of a lack of oxygen, in the case of high-altitudes and in the case of heart disease.

Most fruits, vegetables, some nuts, seeds, legumes, and whole grains are alkaline-promoting foods.

The body uses various mechanisms to regulate the acid-base balance in the blood. These mechanisms include:

1- Lungs

2- Kidneys

3- Buffering solutions.

Buffer solutions

Buffer solutions are defined as those solutions consisting of a weak acid and its salt or consisting of a weak base and its salt. The action of buffer solutions is the resistance to change in pH when an acid or base is added to it.

Example of buffer solutions:

Acidic buffer solution

Weak acid: **CH_3COOH** Salt of the weak acid: **CH_3COONa**

Alkaline buffer solution

Weak base**:** **NH_4OH** Salt of the weak base: **NH_4Cl**

Buffers of blood plasma

(HCO_3^-/H_2CO_3 , $HPO_4^{-2}/H_2PO_4^-$, protein/Proteinate$^-$, hemoglobin)

The first system of buffers present in the blood is the system of **bicarbonate - carbonic acid,** which present in large quantities in the blood (representing approximately 73% of the total regulating capacity of the blood), and it is of great importance in maintaining the blood pH within the normal range as the acidity of the blood plasma is 7.4.

Hemoglobin: (represents about 25% of the total regulating capacity of the blood) The red substance in the blood acts as a regulator in the circulatory system.

As for the other buffers present in the blood, which are **phosphate buffers** (representing > 1% of the total regulating capacity of the blood, which is important for the exchange of materials between cells), and **protein buffers** (representing about 1% of the total regulating capacity of the blood), their importance is very low compared to the buffers of bicarbonate.

Buffers of red blood cells

The pH of red blood cells is about 7.25 and Buffer solution is HCO_3^- / H_2CO_3 one of the most important factors is to maintain the pH of blood cells within the normal range compared to phosphate and protein.

Analytical Methods Used in Clinical Chemistry Laboratories

Analytical methods are divided into two types: Qualitative analysis methods and quantitative analysis methods.

Qualitative analysis methods: These are the methods that look at how to separate elements or substances from mixtures and identify them by separation, as well as identify the acid and basic potential present in one compound or a mixture consisting of several compounds. This can be done as follows:

(a) Using the senses: The senses can be a way to identify some known compounds. For example, through taste, we can identify two substances, one of which is sugar and the other is salt (sodium chloride), and it is also possible through color and crystalline shape to distinguish between two substances such as coal and sulfur.

(b) Use of chemicals: It is possible to use chemicals when the senses are unable to perform the necessary, for example, it is difficult to distinguish between silver nitrate and sodium nitrate, as they are similar in color and other natural characteristics, so it must be distinguished between them by other means. For example, such as the melting point and boiling point, or perform a chemical reaction with hydrochloric acid, where the first substance (silver nitrate) gives a white precipitate of silver chloride, and no precipitate is formed with the second substance (sodium nitrate).

Other chemical processes such as dissolution, precipitation and filtration can also be used to identify the presence of a substance or element.

Quantitative analysis methods: These are the methods concerned with the quantitative estimation of the elements or compounds present in a sample by quantitatively estimating these elements or compounds. For example, a phosphorous compound such as potassium phosphate can be estimated as a percentage of phosphorous.

Quantitative analysis methods are divided into several sections:

(1) Volumetric analysis:

In this method, all or a known part of the sample solution can be titrated with the standard solution until we get the end point at which the amount of the standard solution is exactly equivalent to the substance to be analyzed. The endpoint of reaction can be set:

a- By using colored chemical indicators.

b- By measuring the physicochemical properties of the solution. For example, by measuring the potential difference.

(2) Gravimetric analysis: in which the quantity of the element or compound can be estimated by a gravimetric process, after precipitation of the material, then separation and weighing, as this requires:

a. Use of inorganic precipitators.

b. Use of organic precipitators.

c. Electrodeposition.

(3) Absorption of photo-energy

It includes measuring the amount of photo-energy at a specific wavelength absorbed by the material to be analyzed, and the following can be used for this purpose:

a. Colorimetric methods

b. Ultraviolet spectroscopic methods

c. Infrared spectroscopic methods

d. X-Ray methods

(4) Emission of photo-energy

It includes excitation of matter to high levels of energy by means of photo or electrical energy, then returning it to a lower energy level, so it emits some of the absorbed energy, and it is a measure of the amount of matter, by the following methods:

a. Emission spectrography: where the material is excited using electric sparks.

b. Flame photometry: where the material is excited using flame, and after the material returns to a low-energy state, the amount of light emitted is measured.

(5) Analysis of gases

a. Volumetric method: in which the change in the volume of a substance is measured after gas sublimation or absorption.

b. The manometric method: the gas pressure or the change in this pressure is measured in this way.

(6) Electro-chemical methods

a. Polarography: The value of the electric current is measured as it is proportional to the concentration of the substance that is reduced or oxidized in an electrochemical reaction at the electrode.

b. Analysis by measuring the amount of electricity: the amount of electricity needed to complete the electrochemical reaction is measured.

c. Analysis by measuring the potential difference: In this type of analysis, the electric potential changing during the reaction is measured when the electrode is put in the solution, and the end of the reaction can be known, and thus the concentration of the reactants can be calculated.

d. Analysis by measuring the electrical conductivity: It is possible to know the end of the reaction by measuring the electrical conductivity during the reaction, and thus the unknown concentration of the reactant can be estimated.

(7) Chromatographic analysis (chromatography): is a word made up of two syllables, chromo, meaning color, and graphic, meaning writing. It was named by this name for historical reasons, as it was used initially to separate colored materials.

This type of analysis is used for separation a mixture into its components regarding their tendency to adsorption, partition, or exchange through an adsorbent surface. Chromatographic analysis methods are divided into:

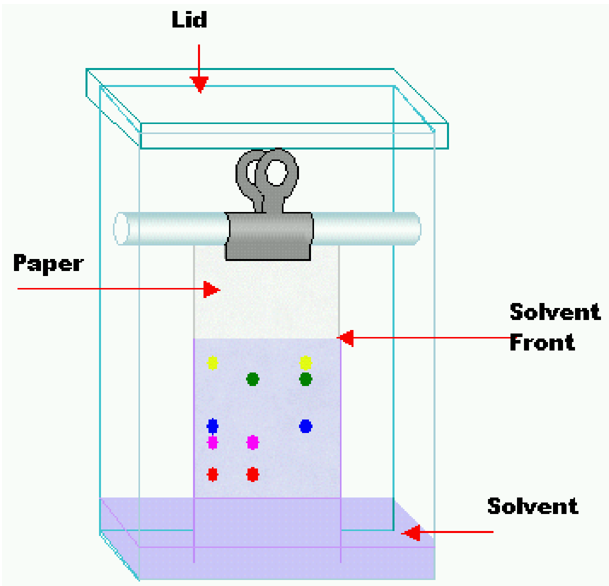
a. Adsorption chromatography

b. Ion exchange chromatography

c. Partition chromatography

d. Thin layer chromatography

e. Gas chromatography



Depending on the resource, the methods of analysis can now be classified into chemical methods and instrumental methods. Chemical methods involve chemical processes and use simple apparatus and glasses. A necessary part is the measurement of volume and mass. While the mechanical methods include the use of complex apparatus that depend on electricity and heat, where the energy that is related to the concentration of the sample must be measured.

Some advantages of chemical methods

a- The method shall be simple.

b- The method is accurate.

c- The devices used are simple.

Some advantages of mechanical methods

a- The appointment shall be quick.

b- A small sample can be used.

c- Complex samples can be analyzed.

d - Obtaining high sensitivity.

e- Obtaining reliable measurements.

Lecture (4)

Colorimetric analysis

Spectrum:

The human eye has the ability to see the radiant energy (light) in the visible region, confined between 400 and 750 nanometers(nm), but modern colorimetric analyzers can sense shorter wavelengths (known as ultraviolet) and longer wavelengths (known as infrared).

The sunlight, or the light emitted from the ordinary light bulb, is in fact a mixture of several radiant energies known as the spectrum with different wavelengths that the human eye distinguishes in the form of white light, and it is, in fact, only a group of spectra. The following table shows the relationship between wavelengths and the nature of their noticeable color for the spectrum regions (ultraviolet, visible and infrared).

Table (2) showing features of the visible, ultraviolet, and infrared spectrum;

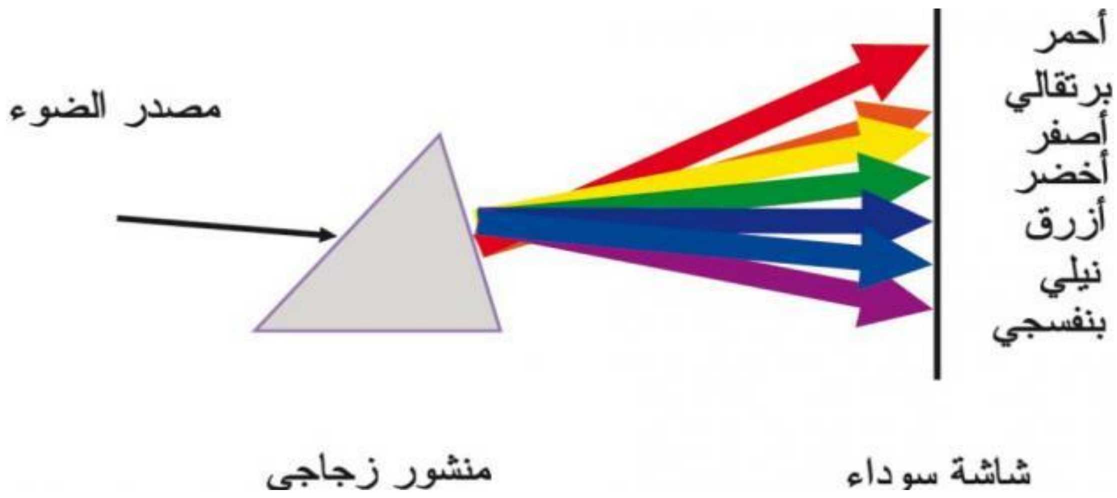
Noticeable color	Area name	Term	Wavelength in nanometer (nm)
Not watching	very short ultraviolet	Ultrashort UV	180 -220
Not watching	short ultraviolet	Short UV	220 - 320
Not watching	long ultraviolet	Long UV	320 - 400
purple	visible	Visible	400 - 440
blue	visible	Visible	440 - 500
green	visible	Visible	500 - 580
yellow	visible	Visible	580 - 600
orange	visible	Visible	600 - 620
red	visible	Visible	620 - 750
Not watching	infrared	IR	750 - 2000

On this basis, a solution appears green, for example, because it has permeability at wavelengths between 500-580 nm, but it absorbs light at other wavelengths.

On the same basis, the green substance reflects light in the 500-580 nm region and absorbs it in other regions of the spectrum.

Based on the foregoing, the **apparent color** of anybody depends on the ability to absorb one or more of the colors of the white light falling on it and the reflection or penetration of the remaining part in a way that leads to the appearance of the specific color for that body.

White light can be analyzed into its components of different color spectra by projecting a beam of light from a light source such as a tungsten lamp onto a glass prism, which separates it into different beams of light, each of which is known as the monochromatic beam.



BEER – LAMBERT'S LAW

The light wavelengths have different energies, from which the materials can absorb a certain part of it and reflect the other part, and this phenomenon applies to colored solutions only, as non-colored solutions do not have this ability to absorb, as it allows the incoming light to pass through almost 100%, and on this basis, the intensity of light the incident on the colored solution decreases significantly as a result of its absorption of part of the light beams that make it up, and the amount of absorbed light depends on two important factors:

a- The concentration of the solute in the solution.

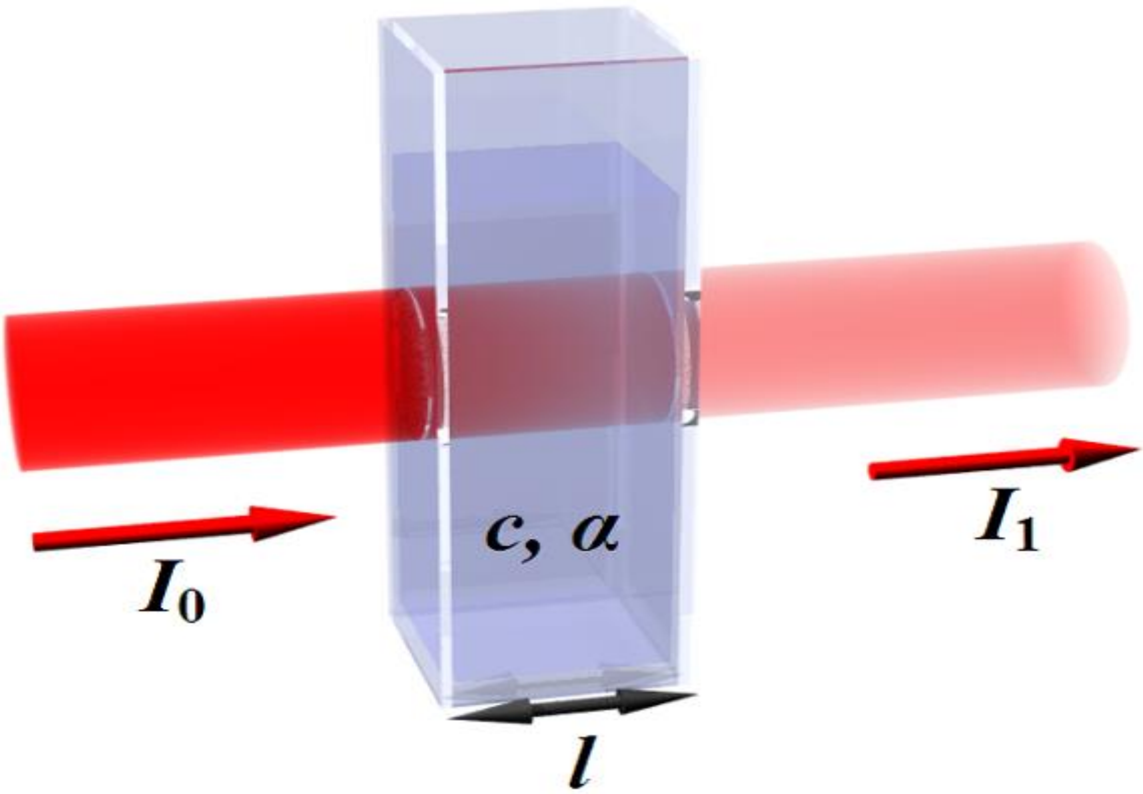
b- The thickness or depth of the solution through which the light penetrates during its path through the solution.

On this basis, the amount of absorbed light is directly proportional to the concentration of the colored solution, and this fact is the basic idea in Beer-Lambert's law.

If we consider (A) the unit in measuring the amount of absorbed light, and (C) the concentration of the solution, and (B) the thickness of the solution, the Beer-Lambert’s law can regulate the relationship between these factors with the following equation:

$A \propto B\ C$

$A = aBC$ or $a = Abc$



Where A = absorption capacity or absorbance.

a = Molar Absorptivity constant

B = Thickness of Solution

C = concentration of the solution

Based on this equation, (A) is a measure of the amount of light absorbed by the solution.

There are certain limits to the use of the Beer-Lambert's law that must be adhered to, as the law cannot be applied without following them, and the most important of these limits are:

1- Solutions must be colored in order for absorption and permeation to occur.

2- The solutions must have low concentrations, and on the contrary, the absorption is very high and cannot be measured within the range of the device (since the best devices do not measure an absorbance > 2).

3- The analyzer must have a good ability to generate a monochromatic beam of light of a high degree of purity to be projected onto the colored solution.

4- The colored solution must be clear, transparent and free from any turbidity or sediment.

Lecture - 5

Biochemistry

Biochemistry: It is one of the branches of natural sciences. Biochemistry is described as the science of chemistry of life, due to the connection of biochemistry to life. It is the intersection point between chemistry and biology. Biochemistry is defined as the chemistry of living things in plants and animals, as it is specialized in studying the chemical composition of the cell parts of various living organisms, whether simple such as bacteria, fungi, and algae, or complex such as humans, animals, and plants.

Clinical Chemistry

Clinical chemistry: It is one of the branches of pathology (also known as clinical biochemistry), and it is the science that deals with various body fluids in order to diagnose diseases. Therefore, it is necessary to know the method of collecting and preservating the different samples. When blood is collected, anticoagulants, or preservatives, are added to it in order to preserve the components of the blood. As for the urine, it is collected and preserved by adding preservatives, or it is frozen.

Urine (pH 6.5 - 8)

It is a solution that includes inorganic salts, organic substances, and water, which constitutes 96% of the urine composition, while the remainder of the solid materials constitute only 4%.

The urine is formed in the renal glomeruli, as there are millions of glomeruli in the kidney that filter the urine. The urine is temporarily stored in the bladder and then excreted by the urethra.

The organic part present in the urine consists of urea (on average about 35 g/day), uric acid and creatinine. The inorganic part is mostly salts (chloride salts, sulfate salts and ammonia) at an average of about 25 g / day.

The amount of urine excreted daily is about 1200 - 1500 ml, but this amount changes according to the Physiologically and Pathologically status. The amount of urine is affected by: **1.** the amount of fluid taken **2.** the type of food **3.** the air temperature **4.** the exercise.

Thus, protein-rich food increases the amount excreted from urine because it has a diuretic effect, as it increases the amount of urea formed. But if the air temperature increases, the amount of urine will decrease due to increased sweating. The same effect occurs when exercising.

The amount of daily urine excertion when food and fluid intake is normal is 1200-1500 ml/day.

An increase in the amount of urine is referred to as Polyuria (or profuse urine) and it occurs in the case of diabetes mellitus (D.M diabetes mellitus and Diabetes insipidus D.I). Decreased urine output is called oliguria and occurs in the case of fever, diarrhea, and vomiting. Complete absence of urine is known as anuria and occurs in kidney failure and lead poisoning.

Calculi

They are compact formations of chemical compounds that are often deposited in the following ducts and tissues:

Urinary Tract, Bladder, Prostate.

Biliary Tract & Pancreatic Duct.

Salivary gland.

Urinary Calculi

Urinary stones receive the most medical care and attention due to their common occurrence and the diversity of their chemical composition. The urine contains a lot of organic and inorganic salts that sometimes precipitate forming urinary tract stones, which consist of a well-defined nucleus consisting of bacteria, some blood clots, filiform fibers, or retinal cell clusters. Infection in the urinary system quickly increases with the presence of hard-to-dissolve salts, in which calcium oxalate is considered one of the most offensive in this regard. These stones can pass safely through the urinary tract in moderate cases, and surgery is required to remove the stone in severe cases.

The main factors that contribute to the formation of stones can be summarized as follows:

- Abnormal disturbances in internal metabolism caused by deposits of some substances such as cystine, uric acid, and cholesterol.
- Idiopathic hyperparathyroidism, resulting in increased calcium, (Hypercalcemia), which leads to an increased likelihood of stones forming, Hypercalculuria.
- Obstruction of the urinary tract leads to a decrease in the volume of urine excreted, which in turn leads to an increase in the possibility of deposition of salts in the urinary tract, especially in the ureters and bladder.
- Infections of the urinary system: It is often the starting point for the deposition of salts around the nucleus of bacteria. The deposition can take its place in the kidney itself, in the ureter, or in the bladder, and this stone often causes severe pain.
- Dehydration (the process of removing water in the human body) and this process can occur in the case of excessive dietary intake or excessive intake of some medical drugs. This in turn leads to an increase in salt deposits.
- Urinary stagnation: This stagnation may be a result of obstruction of the urinary tract, as the urine remains for a long time without movement that helps sedimentation occur.
- Changes in the hydrogen concentration of the urine have a significant impact on the deposition of salts. It is known that the basic medium helps to precipitate calcium oxalate, while the acidic medium helps to precipitate calcium phosphate and uric acid. These changes in pH occur as a result of bacterial infections that often lead to salt deposition at different pH concentrations.

Types of stones in the urinary system

Urinary stones are of several types:

1. Calcium salts stones:

It consists of the following compounds:

• Calcium oxalate with or without magnesium ammonium phosphate.

• Calcium phosphate.

• Calcium carbonate.

These calcium salts stones are among the most common stones in their occurrence, as they represent 70-90% of cases of urinary stones. Among the factors that contribute to its occurrence is the increase in the level of calcium as a result of goiter disease, and the deposition of calcium salt depends on the value of the hydrogen concentration of the urine. Calcium oxalate is deposited in the basic medium, while calcium phosphate is deposited in the acidic medium. In addition, the increased intake of oxalates present in the food leads to an increase in the possibility of precipitation of insoluble calcium oxalate, even if the process of excreting oxalates is proceeding in a normal state. Such cases can be treated by eating foods that contain a low level of calcium and oxalates, and treating thyroid disease, in addition to consuming large amounts of fluids to reduce the level of calcium in the urine. Calcium stones are large, hard, and very painful.

2. Uric acid stone:

It is formed from uric acid deposits as a result of disturbances in metabolism. It represents about 10% of cases of urinary stones, and the acidic medium of the urine contributes to the deposition of this type of stone, which is usually small and fragile and has a yellow-brown color. It can be treated by controlling the amount of uric acid and preserving the basic medium of the urine with a large amount of fluid intake.

3. Cystine stone:

Infection with this type of stones is rare in normal people, as the concentration of cystine in the urine is within its solubility, but due to birth reasons (or genetics), the concentration of cystine increases and exceeds its solubility, which leads to its precipitation.

Cystine stones are similar to uric acid stones, as they are small, fragile, and yellowish in color. The basic medium helps to dissolve them, unlike the acidic medium.

Prostate stone:

It consists of organic compounds and inorganic compounds (such as carbonates, calcium, magnesium and phosphates).

Bile duct stone (Gallstones):

They mainly consist of cholesterol and gallbladder pigments. Calcium phosphate and calcium carbonate may be mixed with them. They may contain traces of iron, copper, magnesium and other organic compounds.

The increase in the level of cholesterol contributes to a large extent in the formation of this type of stones, and the changes in the hydrogen concentration of the bile and the stagnation of the bile fluid in addition to infections in the bile duct are all considered essential factors in the formation of these stones, which are usually deposited in the course of the bile duct or in the gallbladder sac It is the same, and is usually waxy in texture, brittle and pale yellow in color.

Salivary gland stone:

It composes from calcium, magnesium, phosphate and carbonate salts and some organic substances.

Lecture (6)

Blood

It is a movable tissue in a closed system known as the circulatory system. If any rupture of blood vessels occurs here, there is a special mechanism designed to prevent blood leakage as a result of this rupture, with the initiative of coagulation immediately, as the factors causing coagulation are present in the blood itself and in the surrounding tissues. In blood vessels, and in order for the clotting process to be clearly understood, it is necessary to know these coagulation factors, which are protein substances in composition, except for calcium salts. In the blood there is fibrinogen and prothrombin in addition to calcium salts and antithrombin heparin (which is a protein substance that prevents clotting). Swimming in the blood plasma and vascular tissue cells contain the protein thromboplastin that helps the coagulation process, so if any wound or rupture occurs in the blood vessel, the blood flows out mixed with the surrounding tissue, which leads to the liberation of thromboplastin from the platelets and the ruptured tissue, which reacts immediately with prothrombin in the presence of ions calcium resulting a thrombin, which is the main substance in the coagulation process, as it works to convert fibrinogen blood to fibrin that is an insoluble, threadlike mass of protein forming clots. The coagulation mechanism can be summarized by the following interactions:

1. Stimulation of prothrombin

$$\text{Prothrombin} \xrightarrow[\text{Ca}^{++}]{\text{Thromboplastin}} \text{Thrombin}$$

2. Conversion of fibrinogen into fibrin

$$\text{fibrinogen} \xrightarrow{\text{Thrombin}} \text{fibrin (forms clot)}$$

It is clear from these equations that the presence of calcium ions is essential in the coagulation process. Therefore, preventing this coagulation in blood samples requires the addition of another substance that precipitates calcium ions and isolates them from performing their work, so the coagulation process stops immediately. Among these substances that precipitate calcium are: sodium oxalate, potassium oxalate, or sodium fluoride, which can be added in small amounts to obtain blood samples in a liquid, non-coagulated state. Such substances are known as anticoagulants.

In clinical chemistry, attention is directed to the basic chemical components of blood, which include water, protein (albumin, globulin, and fibrinogen), amino acids, fats, inorganic salts, and many waste products of metabolism, hormones, vitamins, and enzymes. The following table can be reviewed to clarify the chemical composition of blood, given that blood consists basically from the liquid part known as plasma (which is a transparent liquid substance that is somewhat yellowish in color, and its volume in the blood is about 55% of the total volume of human blood), in which the aforementioned chemical components and part are dissolved the second is the homogeneous spread of cells in the plasma, which includes red blood cells, white blood cells, and platelets. For a normal person who weighs 70 kg, his body contains about 6 liters of blood (6000 ml).

Anticoagulant factors

Anticoagulants, commonly known as blood thinners, are chemicals that prevent or reduce the occurrence of blood clotting, thereby prolonging the clotting time. Blood anticoagulants are used in the case of using samples of plasma or total blood, as required by the experiment. Therefore, an anticoagulant must be added to the blood tube as soon as it is drawn directly. The wall of the blood tube is usually covered with anticoagulant. It should be noted that the choice of anticoagulant must be based on consideration. This anticoagulant will not affect the chemical analysis and this point is very important.

Anticoagulants are used in the laboratory in some blood investigation, blood bags, medical and surgical instruments, including:

1- **Heparin**: It is an anticoagulant substance that is distinguished from other anticoagulants in that it does not interfere with clinical analysis tests. This substance is already present in most body tissues, but its natural presence in the blood is less than the percentage necessary to prevent its clotting when it flows as a result of a wound in the blood vessel. Heparin is generated from hepatic cells. It is present in the highest concentrations in the liver. It is also present in pulmonary cells. It was possible to separate and isolate it in the form of crystalline salt from liver and lung extract. Heparin is classified into the category of polysaccharides can be obtained commercially at the present time, in the form of a salt of sodium, potassium or ammonium salts.

The action of heparin is attributed to its: (A) Antithrombin, as it prevents the conversion of prothrombin to thrombin and thus prevents the formation of fibrin precipitate from fibrinogen, which is done with the help of thrombin, while this activity of heparin occurs in the presence of albumin as an assistant agent, (B) Anti-thromboplastin, which is the substance that aids the formation of thrombin. This phenomenon is due to the fact that heparin inhibits the dissolution of blood platelets containing thromboplastin.

Heparin is added at a rate of 20 units / ml of blood since it does not dissolve immediately, so its solution is often used and dried on the walls of the tube to be in direct contact with blood and its effect is the best possible, and its high prices and temporary effect are still among the most important obstacles to its use in analysis laboratories When compared with other most commonly used anticoagulants.

2-Oxalates: These include sodium, potassium, ammonium, or lithium oxalates. This anticoagulant act to precipitate calcium ions contained in the blood, whose presence is essential in the coagulation process.

Potassium oxalate is one of the most widely used anticoagulant in laboratories, as it can be added at a rate of 2 mg / 1 ml of blood.

A potassium oxalate solution can be prepared by dissolving 30 g of it in 100 ml of distilled water, then drawing 0.10 ml with a pipette from this solution and placing it in a test tube, which is then placed in an oven to dry at a temperature not exceeding 150°C in order to avoid the decomposition of oxalates and their conversion to carbonates at high temperatures. Thus, it loses its effectiveness as a good anticoagulant, and it is worth mentioning here that 0.1 ml of this prepared solution of potassium oxalate is sufficient to prevent 15 ml of blood from clotting.

3- Sodium fluoride (NaF): Sodium fluoride is considered an anti-glycemic agent in addition to its weak effectiveness as an anticoagulant. It can be used mixed with potassium oxalate when needed as a preservative to keep sugar from dissolving at a concentration equivalent to 2 mg / ml of blood. But if there is a need to use it alone as an anticoagulant only, then its concentration should be higher than that, equivalent to 6 to 10 mg/ ml of blood. There is no doubt that sodium fluoride should not be used in collecting blood samples for enzymatic pathological analyzes because it inhibits these enzymes and makes them lose their effective nature.

4-Ethylene Diamine Tetra Acetic Acid (EDTA):

EDTA is a chelating agent and is preferred for hematological exams in particular, as it works to preserve cellular components from damage. It is usually used in the form of disodium or dipotassium salt with a concentration of approximately 1 to 2 mg / 1 ml of blood. The effectiveness of this salt as an anticoagulant is attributed to its ability to bind with blood calcium and completely isolate it from playing its role in the coagulation process.

5-Citrate:

Like sodium citrate, it is in liquid form and is used in blood bags. It binds to calcium, but in a weaker way than EDTA.

Blood Functions:

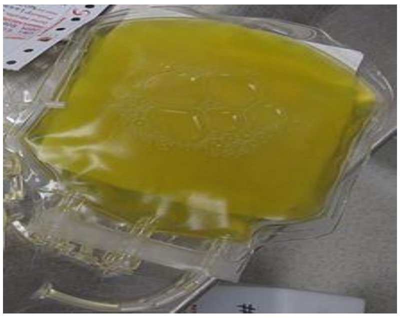
- Blood helps to transport materials: such as oxygen, fluids, food, hormones and vitamins to all organs of the body, and then returns it loaded with carbon dioxide and food waste after it is transformed into energy in the body.
- Water balance in the body: The blood maintains the water balance in the body, by transferring excess water from the gastrointestinal tract or excreting it through the skin in the form of sweat or through the kidneys in the form of urine.
- Regulating body temperature: through the secretion of sweat to moisturize the skin, or by increasing the burning of sugar in the blood in order to generate energy and raise the body temperature.
- Defending the body by producing antibodies that fight germs.
- Stopping bleeding through the production of elements that help in wound healing.

Serum and Plasma

Serum is a transparent liquid that tends to yellow due to the presence of bilirubin in the blood. It is the liquid substance resulting from the separation of the solid components of the blood from the liquid without adding any chemical anticoagulants to the blood sample drawn from the patient.

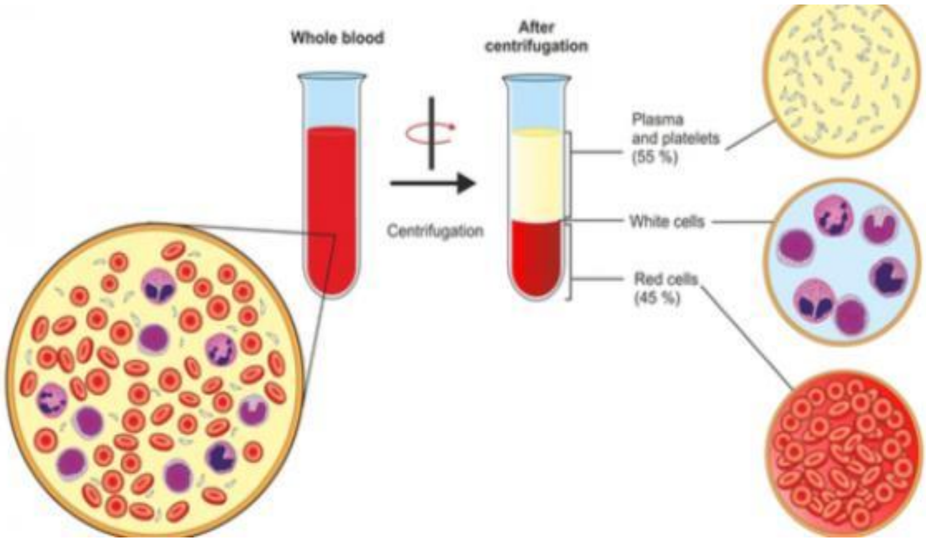
It is preferable to use blood serum in laboratory investigations instead of plasma, because the anticoagulant substances that are added to the blood to obtain the plasma may affect the results of the investigations because they interact with some enzymes in the blood plasma.

Plasma is one of the components of the blood. It is a transparent liquid substance that tends to yellow. Its volume in the blood is about 55% of the total volume of human blood, meaning that it constitutes almost half the volume of blood. Blood plasma has an important role in the transport of water, salts, and nutrients such as sugars, vitamins, hormones, and others.



The Difference Between Serum and Plasma

Plasma contains fibrinogen protein, while serum does not contain this protein, meaning that blood serum is a plasma without clotting factors. To obtain blood serum, the blood sample is transferred from the syringe to an empty test tube and left for 10 to 15 minutes at a temperature not exceeding About 37 °C (or room temperature), taking care not to shake the tube vigorously so as not to break and dissolve the red blood cells and lead to hemolysis. After about a quarter of an hour has passed, we will find that the solid part of the sample has become deposited on the wall of the tube and at the bottom, and the liquid part has become at the top, the tube is placed in a centrifuge and the sample is rotated for 5 to 10 minutes. After removing the sample from the centrifuge, you will find a yellow liquid at the top and the blood components are precipitated and coagulated at the bottom in red color (blood cells with fibrinogen protein), this liquid Yellow is serum, while to obtain plasma, blood is taken and an anticoagulant is placed on it, then a centrifugation process is performed on it, so the plasma is separated with fibrinogen protein to the top and blood cells to the bottom.



Collecting Blood Samples:

• From the veins: It is used in almost all examinations.

• From the arteries: it is usually used in gas tests, and an oximeter is also used in blood gas tests.

• By acupuncture: It is used to know the blood group.

How is Hemolysis prevented:

The color of blood serum is usually light yellow (pale) in the event that hemolysis occurs, the serum is colored reddish-pink according to the degree of breakage, then the contents of the red blood cells will transfer to the blood serum and thus give false results in the tests. There are methods used to prevent dissolving, namely:

• The syringe and needle must be clean and dry.

• The blood must be drawn slowly and steadily into the syringe.

• The needle must be removed from the syringe before transferring the blood into the tube.

The Chemical Composition of Blood:

1. Water 75-80%

2. Proteins - about 20% [Hemoglobin, fibrinogen, albumin, globulin].

3. Carbohydrates, about 0.1% [glucose].

4. Fat about 1-2% [Fats, Cholesterol, Phospholipids].

5. Inorganic salts, about 2%:

Sodium	Chlorides
Potassium	Sulfate
Calcium	Phosphate
Magnesium	Bicarbonate
Iron	

6. Wastes, about 0.5% [Carbon dioxide, urea, uric acid, creatinine, ammonia].

7. Enzymes [Catalase, Amylase, Maltase, Protease, Lipase].

8. Antibodies.

Lecture (7)

Electrolytes

Electrolytes are minerals that carry an electric charge when they are dissolved in the blood. Blood electrolytes, sodium, potassium, chloride and bicarbonate – help regulate the function of nerves and muscles (the transmission of nerve signals from the heart and muscles) and maintain acid-base balance and water balance.

Electrolytes are distributed in the form of solutions in all body fluids, as they are present in blood, lymph, internal cellular fluids, digestive juice and urine.

Ions (electrolyte): are atoms or particles charged with a positive or negative charge and is divided into:

* **Cation** "A positive ion" is an atom or group of atoms that has lost one or more electrons.
* **Anion** "A negative ion" is an atom or group of atoms that has gained one or more electrons.

Cations	Anions
It is the ion that carries a positive charge such as Na^+ and K^+ (they predominate) Ca^{+2}, Mg^{+2}	It is the ion that carries a negative charge such as Cl^-, HCO_3^-, $H_2PO_4^-$, HPO_4^{-2}, Proteinate⁻ and organic acid ions (present in small quantities).
The chief cation in plasma and extracellular fluids is Na^+ and in intracellular fluids is K^+.	The chief anion in plasma and extracellular fluids is Cl^-, HCO_3^-, while in internal fluids it is phosphate, protein^{-1}, sulfate SO_4^{-2}, bicarbonate HCO_3^- and very small amounts of chloride Cl^-.

Chloride (Cl^-):

Existence:

Chloride is found in the extracellular fluid and the main negative ion in this fluid is about 103 mmol/L out of the total concentration of negative electrolytes which is about 155 mmol/L.

Classification

Chloride is considered one of the negative ions, anions Cl^-, as it represents a large part of the group of electrolytes present in the blood plasma.

Chloride absorption

The chloride entering with food into the stomach is almost completely absorbed by the small intestine, where it moves to the blood through the circulatory system, and finally reaches the kidneys, where it is filtered and removed from the blood, but it is absorbed again by the proximal tubules, as is the case with useful filtered substances in the human body.

Chloride functions

- Chloride is an important factor in maintaining the proper distribution of water within the human body.
- Helps maintain Osmotic Pressure in the cells of the body.
- Helps maintain the natural balance between positive and negative electrolytes in the extracellular fluid, thus maintaining the vitality of the body's cells.
- Chloride helps balance the alkalinity and acidity of the body.
- The chloride ion also has important physiological roles, for example in the central nervous system.

Normal values for chloride in the serum (S. Chloride)

95-105 meq/L x 1 (T.U)

95-105 mmol/L x 1 (S.I.U)

Clinical Significance of Chloride:

Hyperchloremia is results from:

1. **Nephritis**, where the filtration does not occur naturally, which leads to an increase in its percentage in the blood plasma, but it is noticeable in chronic cases of this disease that the level of chloride decreases from its normal percentage, as a result of its loss through the urine and its non-absorption again after filtration due to damage to the cells microtubules.

2. **Prostatic Obstruction**: This condition occurs when the prostate gland becomes inflamed and swollen, leading to obstruction of the urinary tract and prevent passage of chloride to the outside.

Hypochloremia: it results from:

1. **Intestinal Obstruction**: As this obstruction in the small intestine prevents the absorption process from occurring normally, and thus the chloride does not pass into the blood, thus reducing its normal level.

2. **Diarrhea**: It includes most cases of pathological diarrhea in which the body loses large amounts of fluid containing essential substances, including chloride ions.

3. **Vomiting, sweating, fasting, and fever.**

4. **Addison's Disease**: It is a disease arising from a disorder of the adrenal gland adjacent to the kidney, which secretes the hormone adrenaline affecting the heart muscle. This disease is characterized by extreme weakness, wasting, and hypotension as a result of an imbalance between positive and negative ions.

Table showing the composition of electrolytes in blood serum

Negative ion (Anion)	**Concentration (meq/L)**	**Positive ion (Cation)**	**Concentration (meq/L)**
Cl^-	103	Na^+	143
HCO^{-3}	29	K^+	4.5
$Protein^-$	17	Ca^{++}	5
HPO_4^{--}	2	Mg^{++}	2.5
SO_4^{--}	1		
Organic acid	3		
Total	155	Total	155

Sodium (Na^+):

Sodium is the main positive ion in the extracellular fluid, as it performs several functions:

- Maintains the normal distribution of water in the tissue cells, thus regulating the fluid balance in the body.
- maintains the level of osmotic pressure in the cells of the body.
- Helps maintain blood pressure.
- It also supports the functioning of nerves and muscles.

The daily diet contains approximately 8 to 10 g of sodium chloride (130 to 260 mmol) which is absorbed from the gastrointestinal tract.

The body obtains sodium through food and drink and loses it mainly through sweat and urine. Healthy kidneys maintain a constant level of sodium in the body by adjusting the amount excreted from the urine, so sodium is considered a substance that has a certain renal threshold between 110 and 130 mmol /L, as it is filtered by the glomeruli and then reabsorbed by 80 to 85% by the proximal and distal renal tubules, so that reabsorption reaches approximately 99%, which is controlled by the aldosterone hormone.

The exchange of sodium ions with hydrogen ions H^+ is one of the most important processes that lead to acidifying the urine and making it acidic.

Normal values for sodium in the serum (S. Sodium):

136-155 mmol/L x 1 (S.I.U)

136-155 meq/L x 1 (T.U)

Clinical significance of sodium:

Hyponatremia sodium decreases in the following pathological conditions:

1. **Polyuria**, as is the case in Diabetes Insipidus.
2. **Diabetic Acidosis**, which is the condition present in diabetic urine, in which negative ions and positive ions are excreted together.
3. **Diarrhea**, where sodium is excreted in large quantities through the stool.
4. **Diseases of the renal tubules** that lead to a reabsorption of sodium after filtering it or not exchanging it with H^+ ions.

Hypernatremia sodium increases in the following pathological conditions:

1. **Hyperadrenalism** The disease is known as Cushing Syndrome, where sodium absorption is increased by the renal tubules as a result of excessive secretion by the adrenal glands of hormones that control reabsorption.
2. **Severe Dehydration**, where the body loses large amounts of water, resulting in an increase in sodium concentration.
3. **After treatment with sodium salts.**

Potassium (K^+):

Potassium is considered one of the main positive ions in the intracellular fluid, with an estimated concentration of about 150 mmol /L, and a concentration in red blood cells of about 105 mmol/L, and this is approximately 25 times higher than its level in blood serum, which is approximately 3.5 to 5.3 mmol /L. It does not leak due to the phenomenon of exudation in cell membranes, the presence of potassium is essential for the normal functioning of cells, nerves and muscles.

The body maintains the correct level of potassium by coordinating the amount of potassium consumed with the amount lost. Potassium is taken up through food and drink and is lost mainly through the urine. Some potassium is also lost through sweat and the gastrointestinal tract. The human body needs about 80 to 200 mmol per day of potassium. Absorption occurs in the intestinal tract. Healthy kidneys can adjust potassium excretion to suit changes in consumption. Thus, there is no renal threshold for potassium.

Normal values for potassium in the serum (S. Potassium)

3.5-5.3 mmol/L x 1 (S.I.U)

3.5-5.3 meq/L x 1 (T.U)

Clinical Significance of Potassium:

Hypokalemia is reduced in the following pathological conditions:

1. Prolonged Diarrhea.

2. Prolonged Vomiting.

3. Excessive secretion of the hormone aldosterone, a hormone originating from the adrenal glands that works to reduce the amount of potassium absorbed again after renal filtration (this is the opposite of what happens to sodium, where the amount absorbed increases again by secreting this hormone) and this phenomenon leads to a decrease in the level of potassium in the blood serum.

Hyperkalemia increases in the following pathological conditions:

1. Oliguria or anuria, **or obstruction of the urinary tract.**

2. Kidney failure.

Lecture - 8

Calcium

Calcium: It is one of the body's electrolytes, which are minerals that carry an electric charge when dissolved in body fluids such as blood, but most of the calcium in the body does not carry an electric charge.

The presence of calcium in the human body

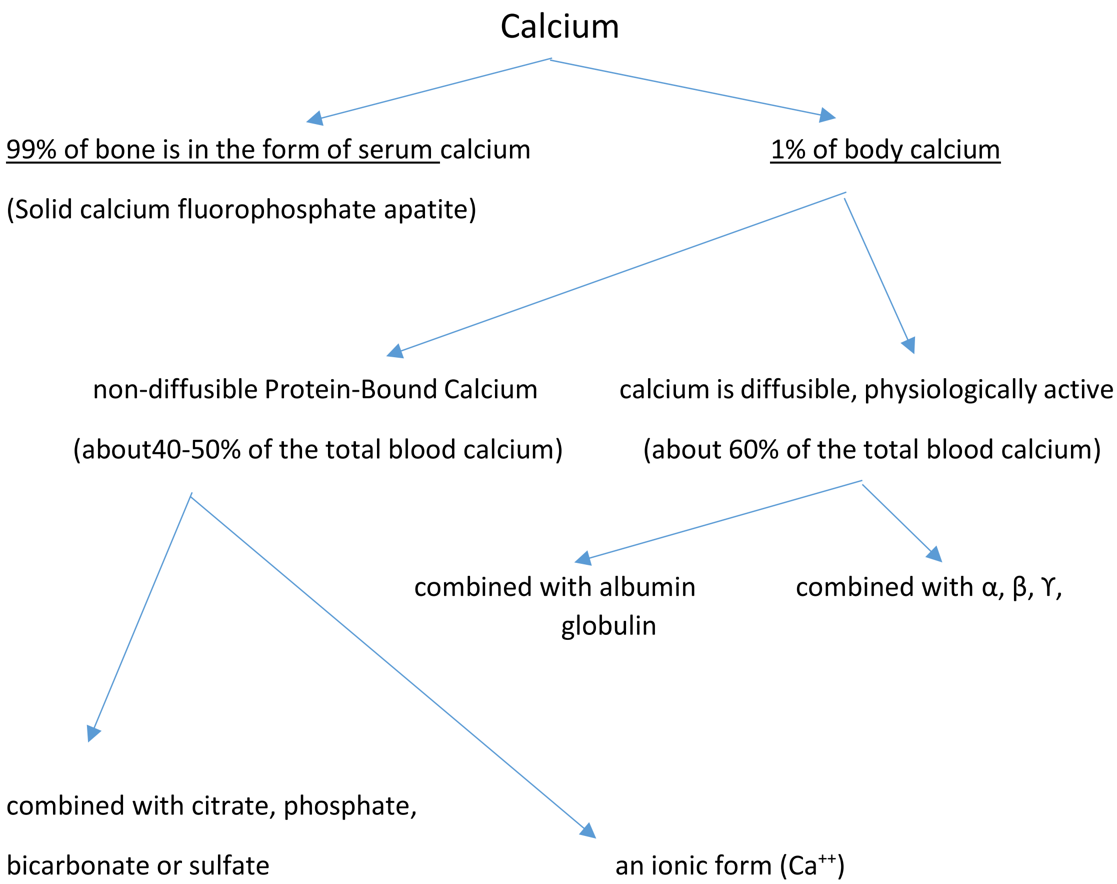
More than 99% of the total calcium and more than 80% of the total phosphorus in the human body is found in bone structure in the form of solid calcium fluorophosphate apatite. As for the remaining part of calcium and phosphorus, it represents the part that is transmitted in the blood through the circulatory system and is known as serum calcium, and it is present in two forms:

a. Non-Diffusible Protein-Bound Calcium: this part is about 40-50% of the total blood calcium.

b. Calcium is Diffusible, physiologically active, and exists either in an ionic form (Ca^{++}) or combined with citrate, phosphate, bicarbonate or sulfate, and this part represents about 60% of the total blood calcium.

It should be mentioned here that the estimation of total calcium in blood serum means total diffusible and non- diffusible calcium.

Serum calcium is estimated at about 5 milliequivalents / liter of blood serum out of about 155 milliequivalents / liter of serum, the total concentrations of positive ions in blood serum.



Absorption and Metabolism of Calcium

Both calcium and phosphorus maintain the balance of their levels in the blood, as the presence of any imbalance in the level of one of them leads to the emergence of imbalance in the other, and therefore they are closely related to each other, and therefore the process of absorption and metabolism can be explained to both in this field because this is justified. The low level of calcium is often accompanied by a high level of phosphorus, but this should not be taken as a general rule that applies in all cases, as there are many exceptions, including what happens during bone formation in the early stages of childhood, when the level of both calcium and phosphorus increases alike. Likewise, in the case of healing bone fractures, where their levels also rise, there are pathological cases in which the level of each of them decreases, as occurs in rickets disease, which is characterized by a low level of calcium and a low level of phosphorus to its lowest level of approximately 2 mg / 100ml. There is another similar pathological condition, which is the case of tetanus.

Tetany, which research indicates a low level of calcium and phosphorous together.

Calcium deficiency: Sometimes the lack of calcium comes from insufficient intake of this mineral in the daily diet, or because the body does not absorb enough of it through the digestive processes in the intestine, for reasons related to the extent of the digestive system's safety from diseases, the efficiency of the digestion and absorption processes in it, or the presence of food or drug elements that impede the absorption of calcium, or to increase the excretion of calcium with the urine for several reasons. When this happens, calcium is drawn from the bones into the blood to maintain a constant level of calcium in the blood. Also, every day, the body loses calcium through hair, skin, and nails, and through sweat, urine, and feces. So, each day, this lost calcium must be replaced by what the person eats.

The level of calcium in the blood is mainly regulated by two hormones: parathyroid hormone and calcitonin (from parathyroid cells).

Parathyroid hormone is produced by the four parathyroid glands, which are located around the thyroid gland in the neck. When the level of calcium in the blood decreases, the parathyroid glands produce more parathyroid hormone. Whereas, when the level of calcium in the blood increases, the production of parathyroid hormone by the parathyroid glands decreases. Parathyroid hormone does the following:

*Activating the release of calcium from the bones into the blood

*Cause the kidneys to excrete less calcium in the urine

*Activating the absorption of the digestive tract for a greater amount of calcium

Calcitonin is produced by the cells of the parathyroid gland, and it lowers the level of calcium in the blood by slowing bone breakdown, but to a limited extent.

Functions of Calcium

Calcium performs various important functions that can be summarized as follows:

1. It is considered the main element in the **calcification of bones** due to its contribution to its structure and formation.
2. It reduces the irritation of neuromuscular cells in the nervous system, as it is considered a **neuromuscular sedative agent**. In the event of a decrease in blood calcium from its normal rate, this leads to a state of involuntary contractions in the muscles of the body, which is known as muscle tetany.
3. It contributes effectively to the process of **blood clotting**, as calcium stimulates the secretion of thromboplastin from platelets, and it also works to convert prothrombin to thrombin, which is essential in coagulation.
4. **It activates some enzymes**, as its effectiveness increases with its presence in performing its vital tasks, such as the lipase enzyme, which is secreted by the pancreas to digest fats.
5. Works to **transport inorganic ions across cell membranes**.
6. **The work of the heart muscle**: Calcium keeps the heart muscle beating, while without calcium, the heart muscle in addition to other muscles in the rest of the body, will not be able to contract and relax. Calcium is also important in the constriction and expansion of blood vessels.

The absorption of both calcium and phosphorus occurs in the upper part of the small intestine, but the absorption of calcium is most intense in the duodenum, while the absorption of phosphorus is most intense in the lower part of the duodenum (jejunum), and the absorption of both calcium and phosphorus increases in the acidic medium, and decreases in the alkaline medium.

Levels Factors Affecting Ca^{++}

- pH concentration: where the absorption increases in the acidic pH and decreases in the basic pH, because calcium salts are more soluble in the acidic medium than they are in the alkaline medium.
- Vitamin D: The presence of this vitamin is essential in the process of calcium absorption, as the presence of vitamin groups helps the absorption process, and on the contrary, the absorption process is greatly reduced.

- Parathyroid hormone: There is a direct relationship and necessary effect for this hormone secreted by the parathyroid gland.
- Protein level in the blood: Since 50% of blood plasma calcium is almost united with protein, a deficiency in blood protein often leads to a decrease in the total calcium level, and there is no doubt that this deficiency directly affects that part of the calcium known as non-diffusible calcium.
- The level of phosphorous in the blood: There is apparently an inverse relationship between the level of calcium and the level of phosphorus, and of course there are several exceptions.

Normal values for total serum calcium

S. Calcium total 8.5-10.5 mg/dl x 0.25 (T.U)

2.1-2.6 mmol/L x 4 (S.I.U)

Clinical Significance of Calcium

The main clinical importance in measuring the level of calcium and its deviation from its normal level of 8.5-10.5 mg / dl of blood serum is in the diagnosis of two main diseases:

1. Rickets disease: where the level of calcium in the blood decreases, which leads to a defect in bone formation.
2. Tetany: This disease also arises due to a lack of calcium from its normal level, which leads to spasms in the muscles of the nervous system.

The following is a table that shows some of the pathological conditions that accompany the increase and decrease of calcium:

Hypocalcemia; Cases in which calcium increases	Hypocalcemia; Cases of calcium deficiency
Hyperparathyroidism	Tetany
Carcinoma	Rickets
Hypervitaminosis D	Pregnancy
Multiple Myeloma	Nephritis
	Osteomalacia

Phosphorus

It is the second most abundant element in the body after calcium, and the body needs it mainly to filter out toxins and repair tissues, and the body gets its need for it through food.

The presence of phosphorus in the human body

More than 80% of the total phosphorus is present in bone structure in the form of Ca-Fluorophosphate Apatite, while the remaining 20% represents the part that is transmitted through the blood circulation and is of two types:

1. Free Inorganic Phosphate PO_4^{-3}.

It is found mainly in the blood serum and is estimated at about 2.4 to 4.5 mg / dl of blood serum.

2. Organophosphate:

It is of several types, as there are organic Phosphate esters ($R - O - PO_3$), nucleic acids, nucleotides, and phospholipids.

These organic phosphates are found mainly in red blood cells, (erythrocytes) and are estimated at about 0.1-1.7 mg / dl of blood serum, while they are about 20-30 mg / 1 liter of whole blood.

Free phosphorous in the form of inorganic phosphate is estimated at about 2 meq/L of serum, out of a total anion of 155 meq/L of serum.

Functions of phosphorous:

1. It plays the role of a mediator in the process of carbohydrate metabolism and thus maintains the regulation of energy generation processes in the body.
2. Maintaining a regular heartbeat.
3. Helping the kidneys to purify the body of waste and toxins.
4. It plays the primary role in the formation of red blood cells, as it is one of the components of nucleic acids, phospholipids, phosphate esters, and nuclear salts.

5. Mineralization of bones.

6. Reduces the feeling of physical and sexual weakness: the natural levels of phosphorus in the body prevent fatigue, and it is also possible to reduce the symptoms of sexual weakness and improve sperm movement by eating phosphorus.

Absorption of Phosphorus

Absorption occurs in the upper part of the small intestine known as the jejunum. Absorption is affected by many factors, including:

1. pH: the absorption increases in the acidic medium and decreases greatly in the alkaline medium.

2. The presence of vitamin D: The presence of vitamin D helps a lot in the absorption process, as it increases with an increase in it and decreases with a decrease in it.

7. Calcium Levels: Both phosphorus and calcium maintain a balance of their concentrations, so that an increase in one of them leads to a decrease in the other in most cases.

Normal Values:

S. Inorganic phosphate:

2.5 – 4.5 mg/dl serum x 0.323 (T.U)

0.8 -1.4 mmol/L serum x 3.1 (S.I.U)

Clinical Significance of Phosphorus

The level of phosphorus is higher than its normal level, **hyperphosphatemia**, in the following diseases:

1. Hypoparathyroidism: Deficiency in the secretion of the parathyroid gland, accompanied by an increase in phosphorus.

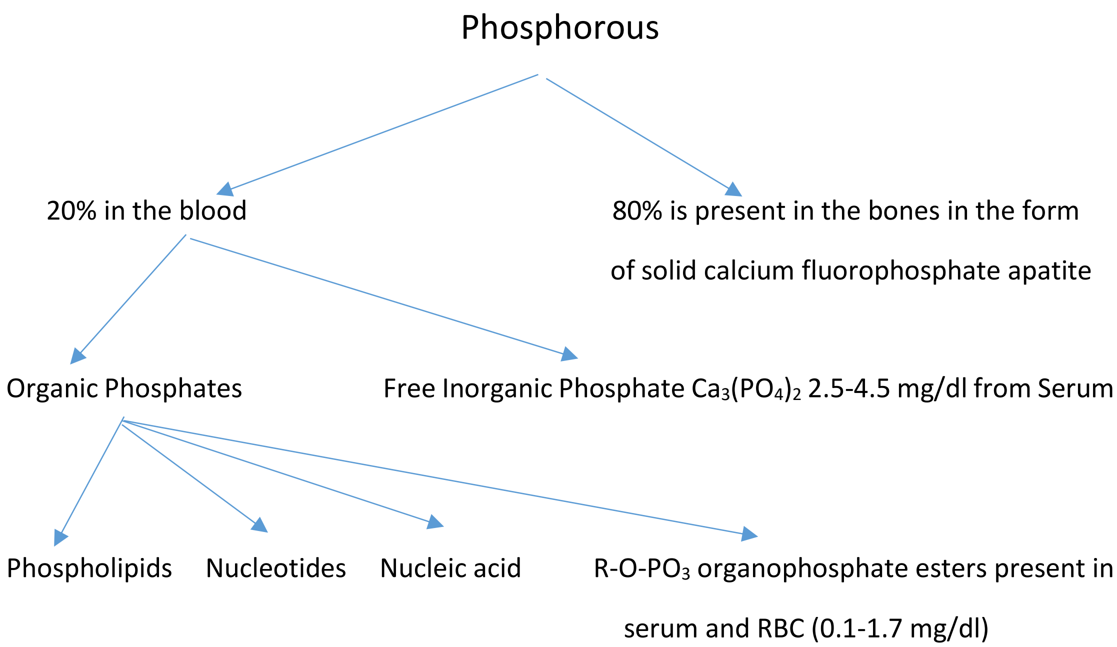
2. Renal disease: This includes acute nephritis. It should be noted here that calcium levels decrease according to the inverse relationship between calcium and phosphorus.

3. Hypervitaminosis D.

The level of phosphorus decreases from its normal level, **hypophosphatemia**, in the following diseases:

1. Hyper-parathyroidism, which is accompanied by a decrease in the level of phosphorus and an increase in the level of calcium.
2. Rickets the lack of phosphorous in this disease is attributed to a deficiency in vitamin D, which leads to a disturbance in the absorption of both phosphorus and calcium, and results in a decrease in their levels together.
3. Fanconi Syndrome is a disease characterized by a significant defect in the reabsorption of phosphorus after renal filtration, in addition to other metabolic substances.

A simple chart showing the distribution of phosphorous in the body:



Lecture No. (9)

Iron and Total Iron Binding Capacity

Presence of Iron:

Iron is one of the most important elements in the human body and is equivalent to approximately 4 to 5 gm of the weight of an adult who weighs 70 kg. About 75% of this relatively small weight of iron is found in the composition of hemoglobin and myoglobin (known as chromoprotein) and Haemenzyme (0.2% iron) such as cytochrome, cytochrome oxidase, peroxidase and catalase. Iron in these compounds plays a vital role in carrying oxygen, which makes it an essential element of Physiological aspect. As for the remaining 25% of iron, it is present in the form of stored iron known as ferritin. It consists of apoferritin and iron (clusters of phosphate and iron hydroxide) $Fe(OH)_3$-Fe-PO_4. Iron is stored in the liver and spleen. Ferritin is the main protein for storing iron. Iron in the body, which is in the form of a hollow ball whereas, the molecular dimensions of this ball allow the storage of the iron element in the form of clusters of iron hydroxide phosphate. The presence of sufficient amounts of stored iron is important for human health, as the lack of sufficient amounts of ferritin leads to depletion of iron stores in the body quickly.

Functions of Iron:

1. The iron in hemoglobin in the blood is in the state of ferrous (Fe^{+2}), which has the ability to bind to an oxygen molecule, turning into oxyhemoglobin. Oxyhemoglobin is transmitted through the blood from the lungs to various tissues of the body with low pressure of oxygen, which works to facilitate transport oxygen to these tissues under less basic conditions than they used to be. On this basis, hemoglobin iron acts as a carrier of oxygen from the lungs to various tissues.
2. It plays an important role in the production of red cells, as it constitutes about 75% of the iron in hemoglobin.
3. Iron is present in muscle tissues and helps in transporting the oxygen needed for their contraction. When iron is deficient, the muscles lose their flexibility, and muscle weakness is one of the most important symptoms of anemia.

4. Iron plays an important role in nourishing the hair roots with oxygen, and iron deficiency can lead to hair loss.

5. Iron also carries a benefit that lies in the treatment of insomnia, as it works to improve sleep by regulating the biological clock of the body. When there is a shortage of red blood cells, blood pressure decreases, and therefore the body may remain awake all night.

6. Iron has a great ability to change its chemical equivalence. Ferrous (Fe^{+2}) turns into ferric (Fe^{+3}) by losing one electron, just as ferric (Fe^{+3}) easily gains another electron and turns into ferrous (Fe^{+2}) again. This readiness to accept or lose electrons makes iron adapted to work in the system of electron transmission between the cells of the tissues of the body, especially the iron that is included in the composition of complex iron proteins such as cytochrome oxidase, catalase, and peroxidase, which contribute to tissue respiration.

Absorption and Storage of Iron

Iron absorption occurs in the duodenum and jejunum of the small intestine, although there are small amounts of it absorbed in the stomach, and the absorbed iron must be in the state of Ferrous (Fe^{+2}), and for this, ferric food must be converted to ferrous in the acidic medium of the stomach, as the pH concentration helps a lot in the reduction process. After the absorption of iron, it is oxidized immediately to ferric (Fe^{+3}) in the basal medium of the intestine and unites with a protein called apoferritin, forming ferritin, which is temporarily stored in the mucous cells of the small intestine. And according to the body’s need, the stored iron is released into the blood in another protein form known as (Transferrin), which is actually beta-globulin linked to two ferric ions by an ionic bond, forming a complex iron-protein called transferrin due to its transfer with the blood in the circulatory system to various storage places in body tissues such as liver and bone marrow, forming a dynamic balance between iron stores in the body.

If the body's tissues are overwhelmed with iron, the absorption process stops and most of the iron ingested through food (without absorption) is thrown out through the feces.

On the other hand, if there is a deficiency in the supply of ferritin in the mucous cells of the small intestine, as in the case of anemia, then absorption increases to compensate for the body's need.

• The body of an adult person needs about 12 mg of iron per day.

• The normal human body loses about 1 mg per day from skin and feces.

• An adult woman loses about 80 mg in each menstrual cycle.

• Pregnant women lose about 400 mg to the fetus.

Types of blood iron test

These tests include:

* Serum iron test

* Transferrin test

* Total Iron Binding Capacity (TIBC)

* Transferrin saturation

* Serum ferritin

Results of a blood iron test for a healthy person:

Iron in the blood is measured in micrograms of iron per deciliter of blood (µg/dl). The following are the normal levels for an iron test in the blood:

Examination	The normal range
Serum iron	70-180 µg/dl
Transferrin saturation	25-35%
The total iron binding capacity (TIBC)	250-400 µg/dl
Ferritin in men ranges	24 to 336 µg/L
Ferritin in women	11- 307 µg/L
Transferrin	170 to 370 µg/dl

Clinical Significance of Iron

The clinical importance of iron in the blood serum is directed to pathological conditions related to anemia, which result from many sources. There is anemia accompanied by an increase in the level of iron known as hemolytic anemia, and there is anemia accompanied by a decrease in the level of iron known as iron-deficiency anemia.

Normal values for serum iron (S. Iron)

70-180 µg/dl x 0.179 (T.U.)

13- 32 µmol/L x 5.59 (S.I.U.)

The pathological conditions directly related to an increase or decrease in iron can be summarized as follows:

Diseases in which iron is increased:

1. Hemolytic anemia: in which red blood cells break down, releasing their contents of hemoglobin iron, which leads to an increase in the proportion of iron in the blood serum, such as thalassemia.
2. Necrotic Hepatitis: The increase in iron in this disease is due to damage to the liver tissue and its inability to store transferrin. Therefore, it is released into the blood, causing an increase in the level of iron.
3. Hemochromatosis: In this disease, the ability to absorb iron increases as a result of an advanced disorder in which iron accumulates in tissues.
4. The pathological condition caused by low iron utilization as in lead poisoning.

Diseases in which iron is low:

1. Iron deficiency anemia: The low level of iron is due to a lack of intake of food containing iron or to a decrease in its ability to be properly absorbed as a result of chronic infections in the gastrointestinal tract.
2. Chronic Blood Loss: Where continuous blood loss leads to iron deficiency.

3. Kidney Nephrosis: Low iron is attributed to the loss of protein substances that filter and leak abnormally as a result of kidney damage.

4. Malignancies: The deficiency is attributed to an abnormal increase in tissue cells.

5. Pregnancy: where the fetus shares the protein substances stored in the body with its mother.

Total Iron Binding Capacity (TIBC)

Determination of TIBC:

It is known that iron in the blood serum is bound to the protein beta-globulin called Fe^{+3}-Transferrin, but only a third of this transferrin is in the state of union with iron almost in the normal state. On this basis, the amount of additional iron (estimated in micrograms / dl of blood serum) that has the inherent ability to unite with transferrin is the unsaturated iron-binding capacity and is abbreviated as (U.I.B.C). As for the total iron-binding capacity (TIBC), it represents the total iron in blood serum plus iron that can bind.

TIBC = Serum Iron + UIBC

Based on this definition, the TIBC determination method requires two stages:

- Determination of iron in a serum sample.
- Determination of bondable iron.

By combining the two results, it is possible to obtain the value of TIBC, which is of clinical importance in knowing the human body's ability to accept iron intake through food or through treatment for anemia diseases. The TIBC value is high in iron deficiency anemia and low in liver diseases such as cirrhosis, nephrosis, and malignancies.

Normal values for total capacitance (S.TIBC)

250-400 µg/dl x 0.179 (T.U)

70 – 45 µmol/L x 5.59 (S.I.U.)

Lecture No. (10)

Carbohydrates

Carbohydrates represent the main source of energy in the body, and carbohydrates are defined as polyhydroxy aldehydes or ketones, or those substances that are produced when hydrolyzed polyhydroxy aldehydes or ketones.

The general formula for carbohydrates $(CH_2O)_n$ is one water molecule per carbon atom, meaning that it consists mainly of C, H, and O, and the ratio of H to O is the same as its ratio in water.

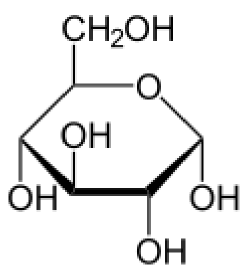
Classification of carbohydrates

Monosaccharides	Oligosaccharides	Polysaccharides
(one sugar unit)	(2-10 sugar units)	(more than 10 sugar units)
Glucose, glyceraldehyde, ribose, fructose	maltose, lactose, sucrose, raffinose	glycogen, starch, gums, insulin, saliva, cellulose

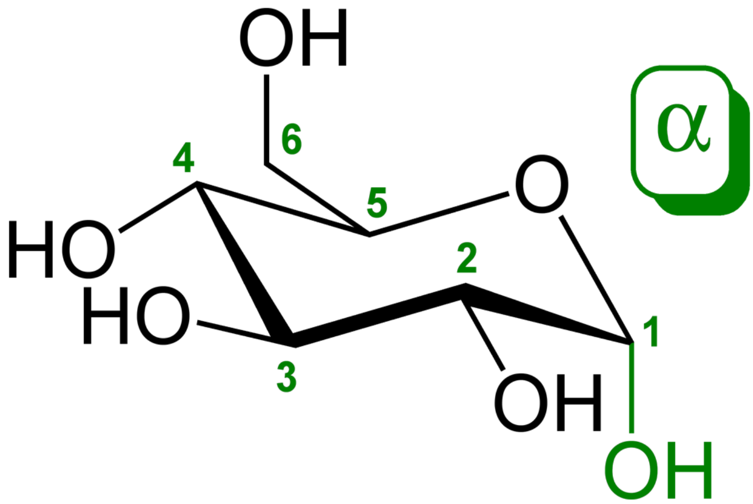
1. Monosaccharide:

It is the simplest type of sugar that cannot be broken down by hydrolysis (it includes only aldehyde or ketone). The simplest type of monosaccharide is glucose (hexose), which consists of six carbon atoms and is characterized by its sweet taste.

Haworth's formula for glucose



Chair conformation:



Monosaccharides →
- Trioses, such as glyceraldehyde
- Tetroses, such as erythroiys
- Pentoses, such as ribose
- Hexoses, such as glucose
- Heptoses
- Octoses

2. Oligosaccharides:

They are those sugars that, upon hydrolysis, produce (2-10) simple sugar units, and the link between these sugar units is by means of a Glycosidic bound, and these sugars are characterized by being low in sweetness.

Oligosaccharides →
- Disaccharides (2-sugar unit) such as maltose, lactose and sucrose
- Trisaccharides (3-sugar unit) as raffinose.

Disaccharides: It is a linear link between monosaccharides, and this link is very special by means of a Glycosidic bound, such as:

Maltose: glucose + glucose

Sucrose: glucose + fructose

Lactose: glucose + lactose

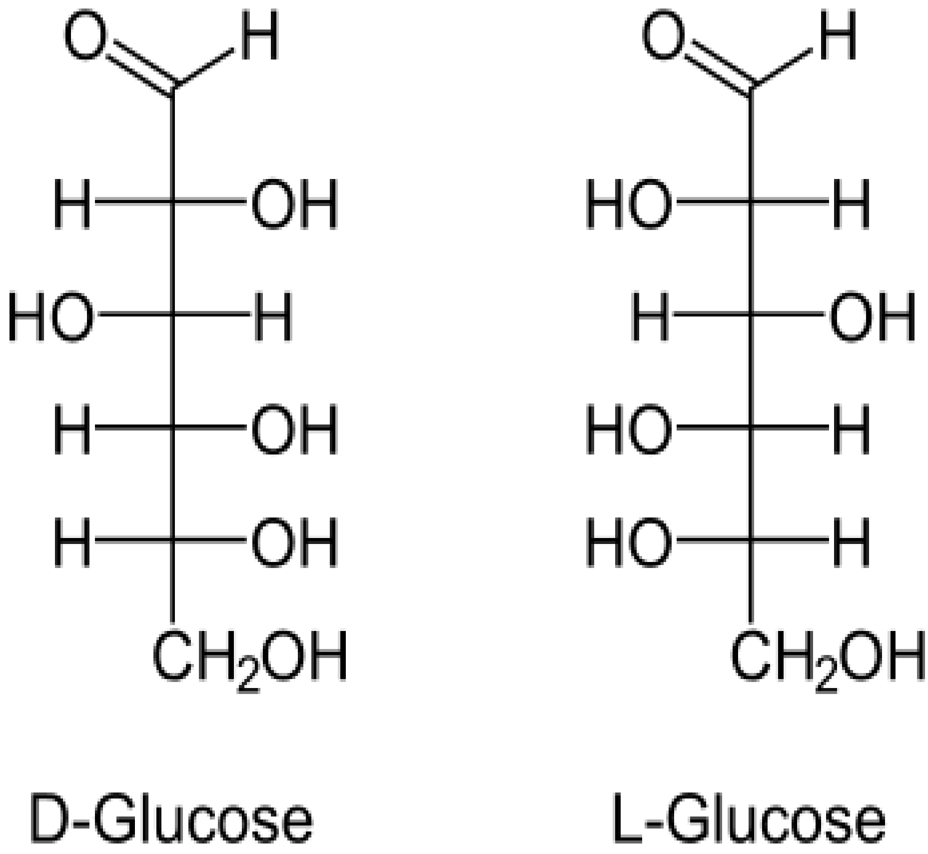
3. Polysaccharides: These are sugars that, upon hydrolysis, produce many monosaccharides (more than 10 sugar units), such as: starch in plants, glycogen in animals, and insulin. In all cases, the link between the sugar units is by means of a glycosidic bound.

Food sources of carbohydrates: rice, flour, corn, potatoes.

Sucrose (sugar cane and beets), lactose (milk and dairy products), glucose (fruits, honey, corn syrup), fructose (fruits and honey)

Glucose

Glucose is one of the carbohydrate compounds that constitute the main food and energy source for the people of the whole world. Glucose has a critical molecular formula that is $C_6(H_2O)_6$, as it contains one water molecule for every carbon atom. On this basis, it was classified as a carbohydrate. Glucose belongs to the class of monosaccharides that contain six carbon atoms known as hexose, which are derivatives of aldehydes. It is called aldose. It is clear from the study of glucose in stereochemistry that this compound forms stereoisomers in the form of two stereoisomers that are similar in chemical composition and different in stereoscopic formation (Fisher's project).



Fisher's Project

The specialization in the designation (D) and (L) refers to the location of the hydroxyl group on the carbon atom adjacent to the CH_2OH group located at the bottom of the molecule (glucose D in relation to the hydroxyl groups written on the right, and glucose L in relation to the hydroxyl groups written on the left).

Metabolism of Glucose

Absorption of monosaccharides occurs in the mucous membranes of the small intestine, where the disaccharides are transformed into monosaccharides in that region. The absorption is almost complete and occurs under the control of another enzymatic process. After absorption, the glucose is transferred through the vein to the liver, where it is transformed into animal starch (glycogen). Glycogen is stored there according to the body’s need, or metabolized into carbon dioxide and water to provide the body with the necessary thermal energy, or transformed into keto acids, amino acids, and proteins, or transformed into fat and stored in the form of adipose tissue. The process of absorption and metabolism can be summarized in the following schematic form:

Monosaccharides glucose (hexose) →

- It is converted into glycogen stored in the liver
- Converts to CO_2 and H_2O to provide the body with energy
- Converts into ketone acids, amino acids and proteins
- Converts into fat and is stored in the form of adipose tissue

Glycogenesis: It is the process of converting the sugar glucose into animal starch (glycogen).

Gluconeogenesis: It is the process of forming the sugar glucose from non-carbohydrate sources such as amino acids and fatty acids.

Glycogenolysis: It is the process of breaking down glycogen and converting it into glucose and other intermediates.

Glycolysis: It is the process of converting glucose sugar by blood cells into lactate and pyruvate.

Regulation of Blood Glucose Concentration:

It is possible to maintain the level of glucose in the blood in the state of fasting (without food and drink for a period of not less than eight hours, as the levels of glucose decrease in the blood), which will lead the pancreas to stop secreting insulin whereas, alpha cells secrete the hormone glucagon, which is the hormone responsible for breaking down glycogen to glucose again (by the person withdrawing a quantity of glycogen stored in the liver and also withdrawing a small amount of glycogen stored in the kidneys, where glycogen turns into glucose-6-phosphate, which in turn into glucose by the action of the enzyme for that and which is present in each of the tissues of the liver and kidney, known as glucose-6-phosphatase)

Glucose-6-Phosphatase

Glycogen → Glucose-6-Phosphate → Glucose

Glycogenolysis →

← Glycogenesis

When the level of glucose in the blood rises as a result of absorption in the intestine, the process of glycogenolysis stops and is replaced by the process of glycogenesis, and the excess glucose is transferred to the liver, where it is transformed and stored in the form of glycogen in the liver and muscles.

Diabetic patients are tested in the morning, where the patient must be fasting (without breakfast). This test is called Fasting Blood Sugar, and it is symbolized by F.B.S. It is in the range of 65-110 mg / dl of blood serum.

S. Glucose (fasting)

65-110 mg/dl x 0.0555 (T.U)

3.6-6.1 mmol/L x 18 (S.I.U)

Lecture (11)

Hormones affecting glucose concentration

There are a group of hormones that affect the concentration of glucose in the blood, which can be summarized as follows:

(1) Insulin: It is secreted by the beta cells (β-cells) in the pancreas, from the islets of Langerhans, and it is a protein hormone that helps the process of glycogenesis and lipogenesis, and as a result of its work, a decrease in the level of glucose in the blood. And if there is a clear deficiency in insulin secretion (as happens in the case of diabetes mellitus), then the level of glucose when fasting rises from its normal level and results in a disease known as hyperglycemia, where the body is unable to metabolize carbohydrates properly. Insulin and the amount of glucose in the blood have an inverse relationship.

(2) Growth Hormone, adrenocortico-trophic stimulating hormone. And both hormones are secreted by the anterior pituitary gland, and they have an anti-insulin effect that works to raise the level of blood glucose. The relationship between the amount of these two hormones and the amount of blood glucose is a direct relationship.

(3) Hydrocortisone: Which is secreted by the adrenal cortex, where it helps in the process of forming neutral glucose (gluconeogenesis). The relationship between this hormone and the level of glucose is a direct relationship.

(4) Adrenal hormone (Epinephrine): Which is secreted by the adrenal marrow, and it helps the process of dissolution of glycogen into glucose, leading to an increase in the level of glucose in the blood. The relationship between them is a direct relationship.

(5) Glucagon: It is secreted by alpha cells in the pancreas, and its action is anti-insulin, as it helps the process of dissolution of glycogen into glucose, which leads to an increase in the level of blood glucose. The relationship between this hormone and blood glucose is a direct relationship.

(6) Thyroxine (T4): Which is secreted by the thyroid gland, which helps in the dissolution of glycogen, thus raising the level of glucose in the blood, and this hormone increases the rate of absorption of glucose in the small intestine, which also leads to an increase in the level of glucose in the blood. The relationship between them is direct.

Glucose tolerance test (GTT).

In patients with mild cases of diabetes, the fasting blood glucose level is within the normal range, but when they eat a meal rich in carbohydrates, they are unable to produce a sufficient amount of insulin to help the carbohydrate metabolism process quickly, and therefore the blood glucose level rises to the abnormal level. In other words, this patient suffers from low glucose tolerance, and on this basis, a new test was created which called (glucose tolerance) to help diagnose moderate and mild cases of diabetes, noting that the normal value of glucose tolerance is 180 mg / dl.

Here are the short steps for this test:

- The patient is given a dose of 50 gm or 100 gm of glucose by mouth. Absorption occurs quickly, leading to an increase in the concentration of glucose in the blood within half an hour to an hour. This alerts the pancreas to secrete other quantities of insulin, which in turn leads to a gradual decrease in glucose in the blood after an hour approximately.

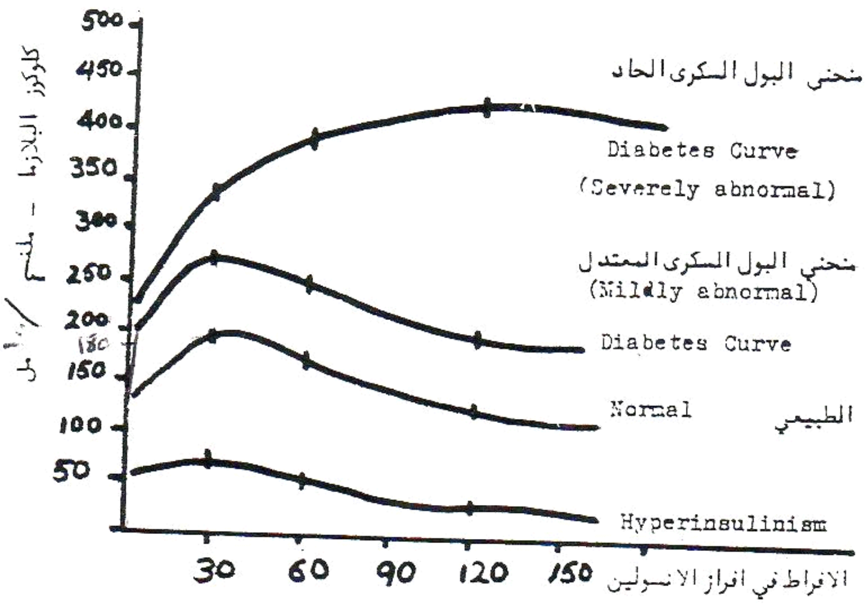


Diagram of a glucose tolerance test

- Since the amounts of insulin now are more than the body needs, the blood glucose level tends to drop below the fasting average after 1.5 to 2 hours, and then return to its normal level within approximately three hours.

The normal value for glucose tolerance in healthy individuals is approximately 180 mg/dl in serum.

Hyperglycemia: It is a condition where the blood glucose level is higher than its normal level, more than 120 mg / dl, and it occurs in the case of D.M and severe suffering.

Hypoglycemia: It is a condition of low blood glucose level below its normal level, less than 65 mg / dl, and it occurs in the condition of fasting (12-24 hours) and increased insulin intake.

Glycosuria: is a condition characterized with high blood glucose level above 180 mg/dl with excretion of glucose with the urine.

Clinical Significance of Glucose:

The most important diseases that are mainly related to an increase in the level of glucose sugar in the blood plasma is diabetes mellitus, which is characterized by a decrease in effective insulin levels in the blood, as this deficiency leads to the inability of glucose to enter the muscle cells to form glycogen and liver cells, and this in turn leads to disruption of the processes of metabolism of proteins and fats, which leads to an increase in the generation of ketone bodies (ketosis) and to the occurrence of diabetic coma. In addition to this, there is a relationship between heredity and formation of this disease.

Sources of glucose in the body:

- Liver glycogen
- Muscles glycogen
- Kidneys

Processes that add glucose to the blood:

- Absorption by the intestine.
- Glucose from liver glycogen (glycogenolysis).
- Glucose formed in the liver from amino acids and other substances (gluconeogenesis).

Processes that remove glucose from the blood:

- Oxidation process in tissues to produce energy.
- Deposition in the form of glycogen in the liver and muscles.
- Converting to fat and storing in the form of adipose tissue.
- Manufacture of lactose, glycol fats and nucleic acids.
- Glycolysis: the breakdown of glucose by blood cells into lactate and pyruvate.
- Excretion of glucose with urine, if the level of glucose in the blood exceeds 180 mg / 100 ml, this is called the Kidney threshold.

Diabetic patients are tested in the morning, where the patient must be fasting (without breakfast). This test is called Fasting Blood Sugar, and it is symbolized by F.B.S. It is in the range of 65-110 mg / dl of blood serum.

S. Glucose (fasting)

65-110 mg/dl x 0.0555 (T.U)

3.6-6.1 mmol/L x 18 (S.I.U)

Diabetes mellitus

In general, D.M. is defined as insulin insufficiency.

Classification:

1. Insulin Dependent Diabetes Mellitus (I.D.D.M): Hypoinsulinism is also called, juvenile diabetes and it is also called type 1 diabetes, which is a chronic condition in which the pancreas produces a small amount of insulin, or does not secrete it at all (defined as a lack or absence of

insulin circulating in the blood circulation, as the pancreas fails to respond to glucose load). Insulin is a hormone required to allow glucose to enter cells for energy production. Therefore, insulin treatment is necessary, and this type of diabetes usually occurs during childhood and adolescence. Several factors, including heredity and some viruses, may contribute to type 1 diabetes. Type 1 diabetics patients suffer from sharp and frequent high and low blood sugar.

2. Non-Insulin Dependent Diabetes Mellitus (N.I.D.D.M): It is also called diabetes mellitus (D.M.), or type 2 diabetes. In case of type 2 diabetes, two interrelated problems appear: the first problem is the inability of the pancreas to secrete an adequate amount of insulin (insufficiency of insulin), which is the hormone responsible for regulating the movement of sugar into the cells. The other problem is that the cells do not respond to the hormone insulin properly. The second type of diabetes can be controlled by following a diet, exercising, decrease weight, and eating healthy food. If a healthy diet and exercise did not control blood sugar, then it needs from a person to take diabetes medications or insulin therapy.

Clinical picture of diabetic patients

- Polyuria
- Polydipsia
- Polyphagia.

Lecture No. (12)

Lipids

Lipids are defined as those substances that are characterized by their inability to dissolve in water, but rather dissolve in non-polar fatty solvents such as ether, chloroform, boiling alcohol and benzene. Chemically, lipids are defined as esters of fatty acids with alcohol (and these fatty acids it may be saturated or unsaturated). Fat is present in all animals.

Estrification = fatty acid + glycerol.

$$R\text{-}OH + R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}OH \longrightarrow R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}OR + H2O$$

Lipids consist of C, H, O, like carbohydrates, in addition to P, N sometimes. The ratio of H to O is very high, so it gives more energy than carbohydrates.

Lipids classification

Lipids

- Simple lipids: They are esters of fatty acids with alcohol
  - Fats, oils
  - waxes
- complex lipids: which are esters of fatty acids with alcohol which other groups Such as phosphates, nitrogen, sugars and proteins
  - Lipoproteins
  - Sulfolipids
  - Glycolipids
  - Phospholipids
- conjugated lipids: an example which are steroids vitamins D, K, F and cholesterol

Types of blood plasma lipids:

1. Fatty acids (F.A): such as stearic acid, oleic acid, and palmitic acid.

2. Triglycerides = glycerol + 3 fatty acids

3. Phospholipids:

F.A — phosphate group — nitrogenous base (increases water solubility)
|
F.A

4. Cholesterol

5. Lipoprotein → LDL
→ HDL

Digestion and absorption of fats:

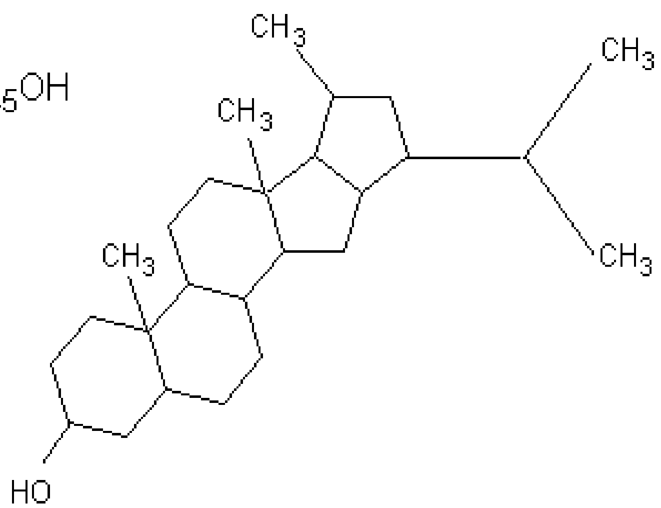
The main fat present in food is a long chain fatty acid (F.A) and glycerol. Absorption and digestion of fatty substances occur in the small intestine. The fat leaves the stomach in the form of large droplets, after which the bile salts emulsify the large droplets into more and smaller drops. The enzyme lipase secreted by the pancreas digests the triglycerol into smaller droplets and forms monoglycerol.

Free fatty acids and a little glycerol pass from the retinal membranes to the epithelial cells, and then pass into the lymphatic channel and into the blood.

Cholesterol

The chemical formula

$C_{27}H_{45}OH$



Classification of cholesterol:

Cholesterol belongs to the class of derived lipids and consists of a steroid unit which consists of a distinct steroid nucleus in the form of A, B, C and D rings. Cholesterol composes of (Chole: bile, Sterol: solid alcohol). On this basis, cholesterol means (solid bile alcohol) or bile fatty alcohol.

Presence of cholesterol:

Cholesterol is found in most tissues in humans, and the largest amount of it is found in the brain (about 14% of the white matter) and in the nervous tissue (about 10% of the spinal cord), and it is about 1-5% of the composition of the bile.

As for its presence in the blood, it is with the rest of the fats 1-2% of the components of the blood, and its presence in the blood is in two forms:

(1) Free Cholesterol: It is equivalent to a third of the total cholesterol originally present in the blood (1/3 of the total cholesterol).

(2) Cholesterol Esters: They are equivalent to two-thirds of the total cholesterol in the blood (2/3 of the total cholesterol).

It should be noted that cholesterol is found in a large number of foodstuffs, such as egg yolk, meat, animal fats, and dairy products such as milk, butter, and cheese.

Biosynthesis of Cholesterol

The human body does not depend on nutrients to obtain its need for cholesterol, but rather it manufactures it internally from simple organic substances that contain the acetyl unit (CH_3CO), such as amino acids, fatty acids and carbohydrates, as all these substances contribute to the manufacture of cholesterol internally and in many places in the human body (liver, skin, intestines, and tissues of the male gonad "testis" and female gonad "ovary"). Cholesterol is the original source in the formation of bile acids (which play the important role in the digestion of fats) and steroid hormones (progesterone and estrogen).

The liver of a normal adult makes about one gram of cholesterol per day, while the rest of the tissues make about half a gram of it. On this basis, the liver is the largest internal source of cholesterol. The amount of cholesterol ingested through food and absorbed through the intestines is estimated at about (0.8) grams per day in normal cases related to appropriate food and proper digestion and absorption processes.

Cholesterol metabolism, absorption and final fate in the body:
Cholesterol absorption occurs in the alimentary tract and is transmitted through the blood circulation to the liver, where part of it is transformed into bile salts by converting it into bile acids, which are of great importance in the process of emulsification and digestion of fats in the small intestine. 90% of the salts of the gallbladder in the small intestine are reabsorbed again and transferred to the liver again in turn known as the enterohepatic circulation. While the extra amount of cholesterol excretes by feces, and this process calls partial elimination of cholesterol.

Cholesterol synthesis, its metabolism and ultimate fate:

cholesterol manufactured internally from amino and fatty acids and carbohydrate

cholesterol coming from ingested food substances such as egg yolk

the gut is a pool of cholesterol

absorption occurs in the gastrointestinal tract

through the blood circulation

liver

converts cholesterol to

bile acids, then to bile salts

is reabsorbed by about 90%.

the internal hepatic circulation

Small intestine (Fats get emulsified)

Large intestine

Excess cholesterol is removed from the body's need

through defecation as a part of the process of partial excretion

أ.م.د. ثائرة ادريس يونس

Factors affecting blood cholesterol levels:

- Genetic defect in lipoprotein metabolism as a result of internal diseases in the internal secretion system of the endocrine glands. Liver diseases and kidney diseases also contribute to the occurrence of this defect in the concentration of cholesterol.
- Imbalance in the secretions of some hormones, especially the following:

* Thyroid hormone, thyroxine, as it has an opposite effect on the concentration of cholesterol. Patients who suffer from hypothyroidism are often accompanied by a significant increase in cholesterol concentration (Hypercholesterolemia).
* The female sex hormone (estrogen) lowers blood cholesterol levels.

Normal Values for cholesterol

Serum total cholesterol(S. Cholesterol)

150-250 mg/dl serum x 0.0259 (T.U)

3.87-6.47 mmol/L serum x 38.7 (S.I.U)

Clinical Significance of Cholesterol:

Its clinical importance is directed towards atherosclerosis, as it rises above its normal level, similar to heart diseases in general.

The following is a review of the most important pathological conditions in which cholesterol increases, **Hypercholesterolemia**

1. Atherosclerosis: In it, cholesterol is deposited in the blood vessels, which leads to damage, and the arteries are affected in particular, so blood does not flow through them.
2. Heart disease: Cholesterol increases due to its deposition, which leads to double disturbances in blood circulation.
3. Diabetes mellitus: Cholesterol increases as a result of the high percentage of proteins and fats in which metabolic processes are disturbed, and as a result of this metabolic dysregulation, it turns into cholesterol.

4.Nephrotic syndrome: The increase is attributed to the increase in lipoproteins, which contain cholesterol in high proportions.

5. Gallstones and bile duct obstruction: The increase is attributed to the decrease in bile emptying into the small intestine as a result of this obstruction.

As for the most important pathological conditions in which decreases in the blood (**hypocholesterolemia)**, they are:

(1) Severe Hepatitis: The liver is unable to manufacture cholesterol due to damage to its tissue.

(2) Excessive secretion by the thyroid gland of the hormone thyroxine, which has an adverse effect on the concentration of cholesterol, as its increase leads to a decrease in the concentration of cholesterol in the blood.

Ketone bodies

The term ketone bodies refer to ketone acid, acetoacetic acid, acetone, and beta-hydroxy butyric acid (acetone is derived from a non-enzymatic process of decarboxylation of acetic acid).

Which is made by the liver from fatty acids during periods when food intake is low (such as fasting, low-carbohydrate diets, starvation, intense and prolonged exercise, and people with untreated or insufficiently processed type 1 diabetes) is the process of making sugar from non-carbohydrate sources to provide energy for the body). These ketone bodies are rapidly picked up by extrahepatic tissues (ketone bodies cannot be used by the liver for energy) due to low blood sugar and converted to acetyl-CoA and then entered into the citric acid cycle and oxidized in the mitochondria in the cells of the body in order to turn into energy needed by the body and its organs to carry out their functions, (ketone bodies can be used by the cells of the body to produce the energy they need).

The main source of manufacturing ketone bodies is the liver, followed by the spleen, the brain, and finally the kidney. The liver produces ten to forty times more ketone bodies than the rest of the organs.

The blood contains a few percent milligrams of ketone bodies, and the daily excretion of ketone bodies does not exceed 0.1 gm. This means that what is used of ketone bodies in the peripheral tissues (external) equals or balances what is produced by the liver sometimes in certain cases, such as starvation, food rich in fatty substances, and severe diabetes. The production of fatty acids increases, and thus the ability of the liver to the production of ketone bodies does not become equal to the process of consuming ketone bodies in peripheral tissues. Under these conditions, an increase in ketone bodies is produced in the blood, which is called Ketonemia, also ketone bodies excrete with the urine resulting in ketonuria. All these conditions call ketosis.

Ketone bodies have a distinctive odor, which can be detected by the breath odor of individuals with ketoacidosis, which is similar to the odor of nail polish remover that usually contains acetone or ethyl acetate. In the case of patients with diabetes, the patient excretes about 120 grams of ketone bodies in the urine per day, which are mainly acetic acid, beta-hydroxy butyric acid, and acetone, which constitutes a very small part.

__Lecture No. (13)__

Proteins

The name protein is derived from the Greek word proto, meaning "first". Certainly, proteins come in the first place among the basic components of living matter (protoplasm), and living things would not survive without them.

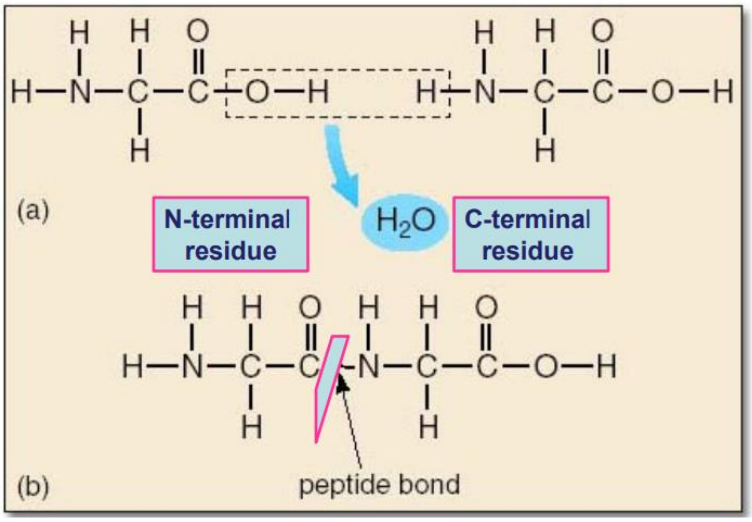
Proteins: They are organic compounds that contain C, H, O, N and in addition to sulfur, phosphorus, and iodine, as well as other elemental components present in some proteins.

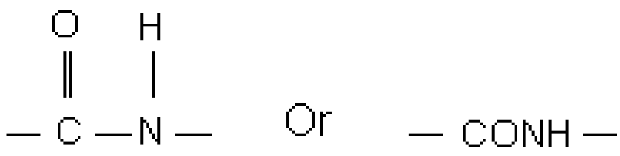
Proteins are the vital material necessary for building and regenerating all animal and plant cells (repairing damaged ones). It is the only source that provides the body with the nitrogen necessary for the formation and repairment of body tissues.

Chemical nature of proteins:

The structural units in the chemical structure of protein are the Alpha-Amino Acids. They are polymers of these amino acids. These amino acids are connected to each other by peptide bonds, which are long chains containing 50 to several thousand amino acid molecules, as the molecular weight of proteins ranges from 6000 to 40,000,000 Daltons, so proteins are considered huge biomolecules.

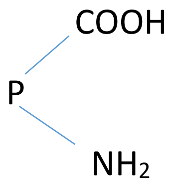
The following is an illustration of this link in the amino acid molecules





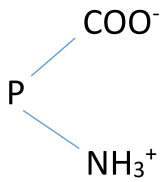
Peptide Linkage

The dipeptide molecule represents a simple unit for protein synthesis. It is clear from this simple unit that the protein molecule has two sides, an acid side(-COOH)and a base side (-NH_2). On this basis, a simplified design of the protein molecule can be developed as follows:



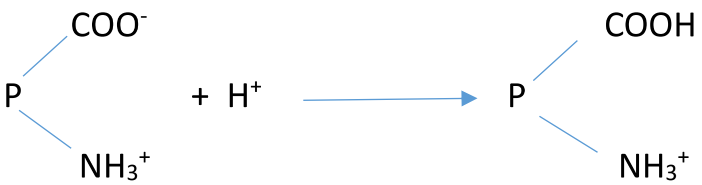
Design of a protein molecule

If this design is taken into account, the protein will behave like ionizable molecules. If the protein is placed in an equal potential field, it will behave as follows:



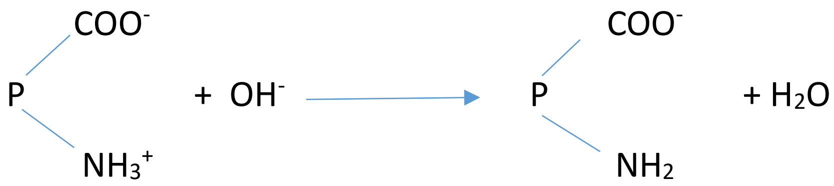
Zwitter ion

This state is called the case of the ion zwitter because it is an amphoteric ion with a positive electric charge at one end and a negative one at the other. This means that the protein molecule will behave as a positive ion if it is placed in an acidic medium.



cation

It behaves as an anion if placed in an alkaline medium:



anion

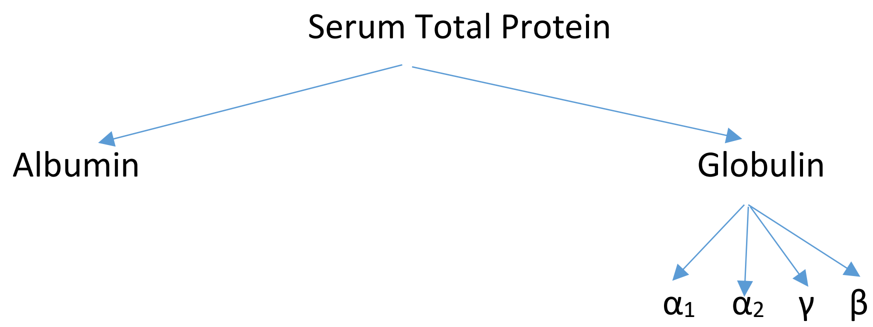
Origin & Presence of Proteins

Living matter, especially plants, produces proteins in nature, and animals have a limited ability to form them, as they consume them as food and convert them into types of proteins.

Proteins are found in the cells of living organisms. They constitute the bulk of the solid matter in the muscles of the body, tendons, ligaments, and cartilages, in addition to the equivalent of 20% of the blood composition, and about half of the solid matter included in the structure of the brain, nervous tissue, bones, hair, and nails.

Classification of proteins:

Serum proteins can be classified as follows:



Proteins are divided into two main classes based on their structure

1. Simple proteins: These are proteins that, upon hydrolysis, produce only amino acids or derivatives of those acids, such as albumins and globulins.

2. Conjugated proteins: These are proteins consisting of a simple protein associated with a nonprotein substance. This non-protein group is called the addition group or the prosthetic group. When the prosthetic group is an organic group such as: nucleoproteins (present in the nuclei and cytoplasm of living cells) and associated with nucleic acids such as RNA and DNA, lipoproteins (present in blood serum), glycoproteins (the presence of sugar as a bond group with protein) there are these Proteins in skin, bone, connective tissue, and blood.

And when the prosthetic group is an inorganic group such as metalloproteins, it includes some minerals such as iron, copper and magnesium, such as heme proteins (hemoglobin, ferritin), and phosphorylated proteins (Phosphoprotein) these proteins contain 10% of phosphorus and are found in egg yolks and milk.

Normal values for proteins

S.Total Protein:	6 – 8 g/dl x 1	(T.U)
	60-80 g/L x 0.1	(S.I.U)
S.Albumin :	3.6-5.2 g/dl x 10	(T.U)
	36- 52 g/L x 0.1	(S.I.U)
S.Globulin:	2.4-3.7 g/dl x 10	(T.U)
	24-37 g/L x 0.1	(S.I.U)

Clinical significance of proteins

Hyperproteinemia occurs in the following cases:

1. Dehydration: where the total protein level reaches 10 or 15% of its normal level and dehydration can occur in the event of a lack of water intake or in the case of water loss resulting from severe vomiting, severe diarrhea or as a result of the condition advanced diabetic acidosis, and Addison's disease.

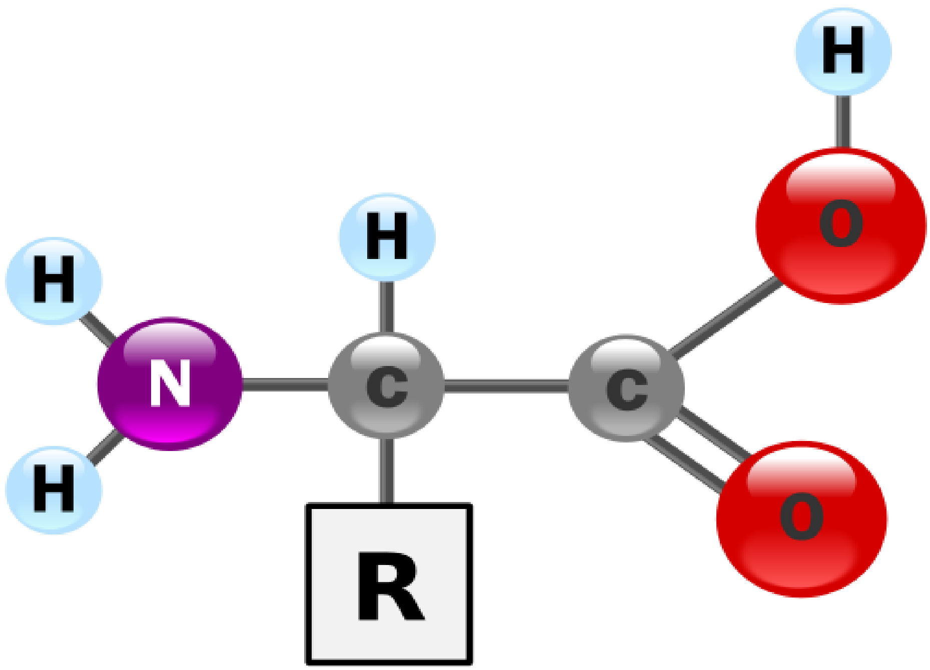
2. Cancer diseases, such as multiple myeloma, up to 10 g / 100 ml of blood serum.

Hyoproteinemia occurs in the following cases:

1. Nephrotic Syndrome, which leads to the loss and leakage of albumin in large quantities through the damaged tissue of the kidney, and therefore the protein level is lower than its normal level.

2. Burns and cases of severe bleeding, as protein decreases in the case of intestinal diseases in which absorption is disrupted as a result of inflammation of the intestine.

Amino Acids (A.A)



They are considered the basic building blocks of proteins, and amino acids are chemically composed of an acid group that is a carboxyl group (-COOH) and a basic amine group (-NH_2), amino acids form a distinct part of the human body, the number of amino acids is 22 amino acids that make up the proteins in the human body. All amino acids are classified into two different groups of amino acids.

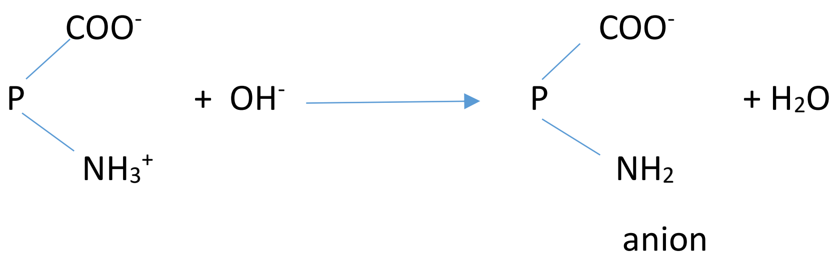
Essential amino acids (E.A.A), numbering 8 amino acids, which are those amino acids that are not made in the human body but are taken through food. Therefore, food is the main source of essential amino acids such as lysine, tryptophan, isoleucine, phenylamine, methionine, Leucine, valine and threonine. These amino acids are found in milk, red meat, poultry, fish, nuts, lentils, peanuts and beans.

Non-Essential Amino Acids (N.E.A.A) are 14 amino acids, and they are those amino acids that are made in the human body and are called non-essential because the human body is able to adequately manufacture them and does not need to obtain them from food sources such as: Alanine, Serine, Cysteine Cystine, Tyrosine, Arginine, Aspartic Acid, Glutamine and Glycine.

Electrophoresis

Electrophoresis is used in clinical chemistry for the purpose of separating the protein fractions that make up the total protein in blood serum. Electric migration (electrophoresis) is defined as the migration of suspended particles in solutions towards opposite poles of charge.

The basic idea in the separation process is based on considering proteins as large molecules that carry negative electric charges if they are placed in an alkaline solution:



On this basis, the protein parts of different components and types will behave as negative ions if an electric current is passed through them. Therefore, they are attracted and migrated towards the positive electrode, the anode, and their kinetic speed depends on (1) the density of the electric charge on the surface of the protein mainly and on several other factors, including (2) the intensity of the passing electric current, (3) the pH of the buffer solution, in addition to (4) the molecular weight of the separated protein part, and (5) the supporting medium. There are several types of support media used in this process:

- Starch-gel
- Polyacrylamide gel
- Agar-gel
- Cellulose acetate paper

Cellulosic migration is used more than others in clinical chemistry laboratories at the present time due to its ease of availability and obtaining it in the form of rectangular sheets with regular pores suitable for the movement of large protein molecules such as enzymes, lipoproteins and hemoglobin.

The difference in the negative density on the protein parts of the blood serum works according to the difference in their attraction and speed of movement towards the positive electrode. Based on this method, the blood serum proteins can be separated into the following parts:

1. Albumin
2. Globulin Fraction

   (α_1)

   (α_2)

   β

   γ

It appears from this sequence that the albumin are the fastest moving protein parts towards the positive pole, followed by α_1, α_2, β, and finally γ, which hardly move due to its low negative density.

Normal values for separated protein fractions in serum:

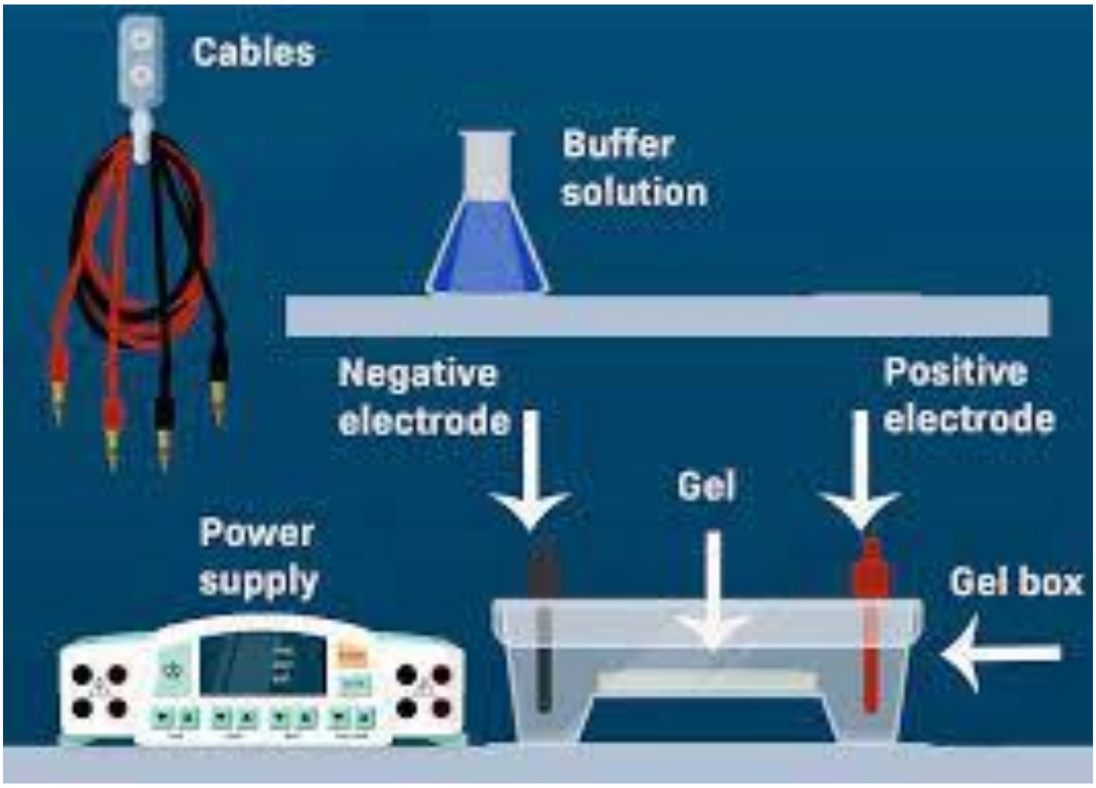
Albumin: 3.5-5 g/dl of blood serum

Globulin: Alpha-1 = 0.17-0.33 g/dl of blood serum

Alpha_2 = 0.42-0.9 g/dl of blood serum

βeta = 0.52-1.05g/dl of blood serum

gama = 0.71-1.65g/dl of blood serum.



Electrophoresis Device

Lecture No. (14)

Enzymes

Enzymes: They are protein compounds in nature and are present in small quantities in the body and increase the speed of chemical reactions without changing the equilibrium point in the reaction or reducing or changing the chemical composition of the reaction components. One molecule of the catalase enzyme can break down five million molecules of hydrogen peroxide in just one second.

Each enzyme has its own active site, at which the enzyme shows the highest levels of effectiveness, and each enzyme has a special substance on which it works called the substrate. Most enzymes have a pure protein composition, but most of them need aids in order to show all their effectiveness and these aids are called cofactors (or activator or coenzyme) and are of two types:

- Inorganic cofactor such as chloride or Mg^{+2}, Mn^{+2}, Cu^{+2}, Co^{+2}, Zn^{+2} and these enzymes are called metalloenzyme.
- Organic cofactors such as nicotinamide adenine dinucleotide (NAD) is the coenzyme of the LDH enzyme.

Enzyme Classification

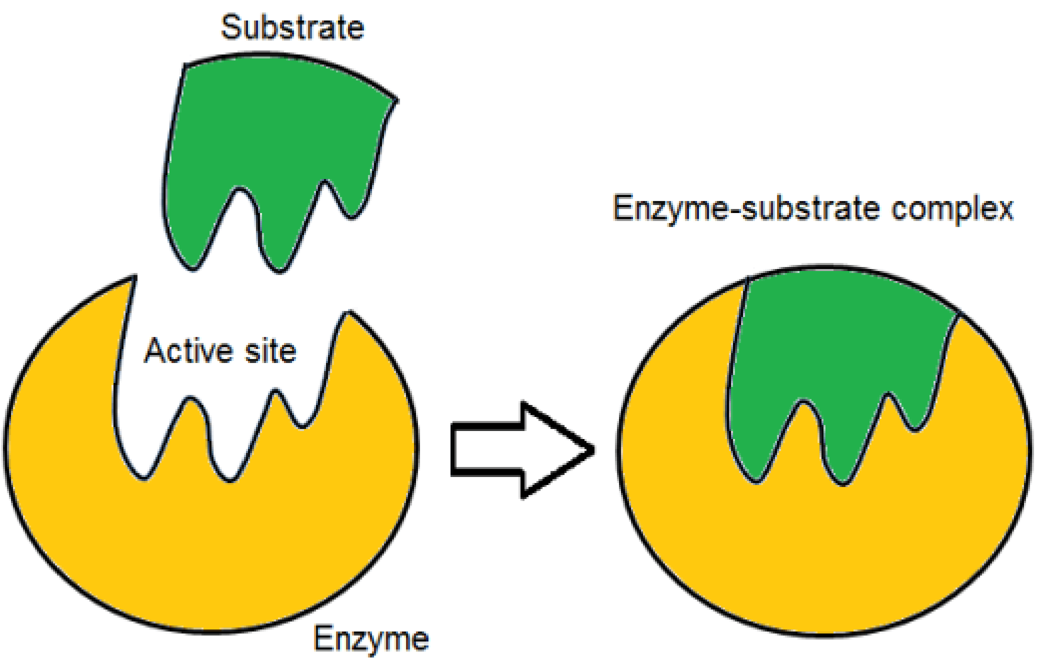
- Oxidoreductase enzymes such as the enzyme LDH, (dehydrogenase)
- Transferase enzymes such as GOT, GPT
- Hydrolyzed enzymes such as amylase, ALP, and ACP
- Lyases such as pyruvate carboxylase
- Engineering or isomeric enzymes Isomerases (some affect the cis and some affect the trans).
- Ligases: the formation of a new bond by linking two molecules together.

Factors affecting enzyme activity

1. The bond between the enzyme and the substrate, in which the enzyme shows most of its activity:

$$E + S \rightarrow ES \rightarrow E + P$$

Enzyme Substrate Free enzyme Product



Lock & Key Model

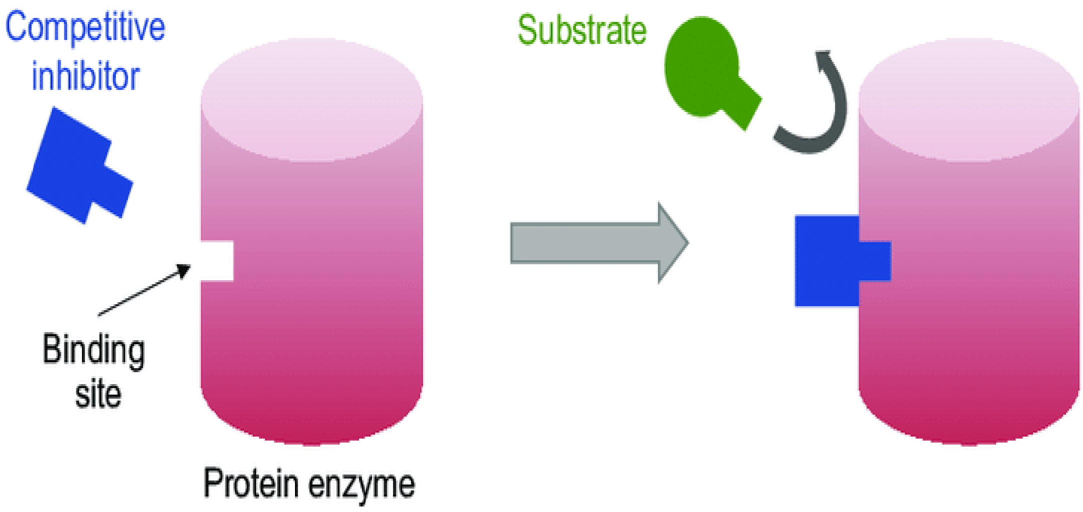
2. Concentration of enzyme: the amount of enzyme does not affect the equilibrium state of the reaction, but it affects the time required to complete the reaction.

3. Temperature: Every reaction needs an optimum temperature at which the enzyme shows 100% activity. Any slight deviation in temperature (1-2 degrees) can lead to an error in the result at a rate of 10-20%. If the temperature is increased much more usually, it can lead to a process of enzyme damage called denaturation.

4. pH Function Each enzyme works at a specific pH function in order to show the highest activity. For example, pepsin enzyme works in acidic conditions, but is inactive in basic conditions.

5. Coenzyme or activators: Each enzyme works very well when special substances are present, which may be organic or inorganic. An example of NAD is the coenzyme of LDH.

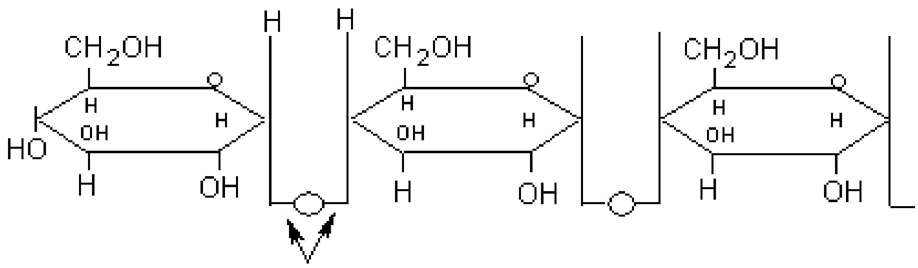
6. Inhibitors: Some substances that reduce the effectiveness of the enzyme or make it ineffective are called inhibitors. These inhibitors may be competitive or non-competitive.



Amylase

Amylase Classification:

The amylase enzyme belongs to the group of hydrolytic enzymes (hydrolases) that help to break down carbohydrate compounds such as starch and glycogen into simpler sugars such as glucose and maltose. This enzyme was called amylase in relation to the amylose it works on, and amylose is a starch that contains two types of chains of glucose molecules called glucosan (the glucosan molecule consists of D-glucose units linked together by carbon atoms 1 and 4 located next to the other glucose molecule, as in the case of amylose or These units may be linked in a way that includes carbon atoms 1 and 4, in addition to another side link that includes carbon atoms 1 and 6, as in the case of amylopectin. The structure of amylose can be explained as follows:



1.4 Linkage

The structural formula for amylase shows linked glucose molecules

by (1, 4) which is a glucosan bond

Amylase Synthesis:

The amylase enzyme consists of three vital organs:

• The pancreas: It is considered the main source of amylase, as it is found in high concentration and is secreted by the acinar cells of the pancreas and poured into the intestinal tract at the duodenum, where it performs its work as an aid in the digestion of starchy materials and their conversion into simple sugars.

• Salivary Glands: These glands secrete effective amounts of this enzyme, which begins with its initiative in analyzing carbohydrates while they are still in the mouth and esophagus.

• Liver: The liver also secretes small amounts of amylase which helps break down carbohydrates and make them easier to digest.

General Properties of Amylase:

*Amylase, like other enzymes, shows maximum activity at 37°C, although it continues to be effective up to 50 °C.

* The effectiveness of amylase is most intense at pH between 6.9-7.0, and its effectiveness decreases completely in alkaline and acidic medium.

* Amylase is considered a metallo-enzyme because it is affected by the presence of positive metal ions, and in particular it is affected by the presence of Ca^{+2} ions, which help to integrate its functional

effectiveness. Also, amylase shows remarkable activity in the presence of a group of negative inorganic ions such as HPO_4^{-3}, ClO_3^-, NO_3^-, Br^-,Cl^-.

* Amylase is characterized by its small molecules, its molecular weight ranges from 40,000 to 50,000 Daltons, and for this reason it passes through the glomeruli and is easily filtered. This is the reason attributed to the presence of amylase in the urine in the natural state.

* All anticoagulants - with the exception of heparin - inhibit the activity and effectiveness of this enzyme, as citrates, oxalates and EDTA inhibit its effectiveness by about 15-20%. On this basis, the methods of amylase analysis must be based on the use of blood serum or plasma obtained from heparin, and it must not use other types of plasma.

Clinical Significance of Amylase

The clinical importance of determining the level of amylase in blood serum is concentrated mainly in the relationship of this enzyme to pancreatic diseases and its importance in evaluating pancreatic function. The level of amylase rises above its normal level when acute pancreatitis occurs. This rise is temporary and is at its highest level during a period ranging from 8 to 72 hours, and the concentration of amylase reaches a peak height within 24 to 30 hours from the onset of feeling sick, and the rise continues for several days, then the level decreases and returns to normal within a period not exceeding three days, this is due to the ability of the enzyme to leak through the kidneys into the urethra (urine). For this reason, blood samples used to measure amylase activity should be collected from the patient as soon as possible in order to have reliable diagnostic value and take into consideration.

In chronic pancreatitis, amylase levels are lower than in the case of acute inflammation, but higher than normal in general. The amylase enzyme also rises in the case of pancreatic obstruction and pancreatic cancer. There is another clinical significance of amylase in diagnosing mumps. The mumps tumor blocks salivary gland secretions of amylase, which then passes into the blood, causing a noticeable increase.

As for the low level of amylase, it has been observed in many liver diseases, such as abscess of the liver, acute hepatocellular damage, liver cirrhosis, liver cancer, and bile duct cancer.

Unit of Measurement of Amylase

Amylase, like other enzymes, is measured in units of effectiveness instead of the weight units that are usually used in measurements of other blood components. On this basis, amylase is measured in a unit known as the Amylase Unit, defined as the unit that equals the amount of amylase that breaks down 10 mg of starch within 30 minutes. If the period is a quarter of an hour, the definition becomes that the amylase unit is equal to the amount of amylase that decomposes 5 mg of starch within 15 minutes under reaction conditions of 37°C and pH = 7.0.

Normal Values for Serum Amylase: 30-110 U/L

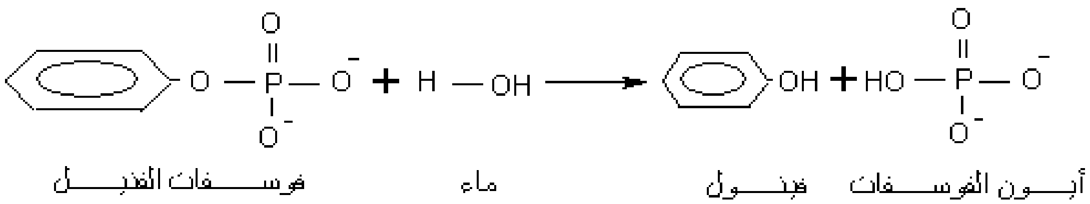
Normal values for amylase in the urine (measured in units per hour):

2.6-21.2 U/H

ALKALINE PHOSPHATASE (ALP)

Classification:

Alkaline phosphatase belongs to the class of hydrolases enzymes that help in the cleavage of compounds containing the phosphate ester or acyl bond. Upon cleavage of this bond, another simultaneous cleavage occurs in the hydroxyl bond (-OH) of the water molecule, resulting in the formation of a phenolic compound similar to alcohol. (The pH function at which the alkaline phosphatase enzyme works is 9.6).



Biosynthesis of ALP

Alkaline phosphatase is found in several tissues of the body, especially in cell membranes. It is also found in high concentrations in the epithelial membrane of the intestine, liver, osteoblasts, and tubules. As for the alkaline phosphatase found in the blood serum of adults, it originates mainly from the liver and the bile duct, in addition to the small amounts originating from the bones that make their way into the blood.

The presence of this enzyme in the urine is attributed to its secretion by the renal tissue cells (small renal tubules) and not to its filtering by the renal glomeruli, as it does not pass.

Functions of Alkaline Phosphatase (ALP)

* Facilitates the process of transporting metabolites across cell membranes, particularly lipids.

* Facilitates the process of hardening of the bones.

Properties of Alkaline Phosphatase

• The optimal activity of the basic phosphatase at the pH concentration is 9.6-10.

• alkaline phosphates show maximum effectiveness at a temperature of 37°C.

• The activity of this enzyme is activated by the presence of some bivalent metal ions such as Mg^{+2}, Mn^{+2}, and Co^{+2}. The particular magnesium ion, Mg^{+2}, is characterized by the optimal activity of this enzyme, and for this reason it is preferable to add it to the analysis methods used in the assays of this enzyme.

• Negative non-metallic ions such as PO_4^{-3}, borate, oxalates and cyanide are considered inhibitors of the activity of this enzyme and should not be used in the preparation of blood plasma. It is preferable to use serum for this purpose.

Clinical Significance of Alkaline Phosphatase

The importance of alkaline phosphatase estimation is concentrated in diagnosing two types of pathological conditions:

1. Bone Disease: Most bone diseases are characterized by a significant increase in the level of this enzyme in the blood serum. Among the most important of these diseases are:

a. Piaget's disease: It is an inflammation of the osteitis deformans, in which the osteoblastic cells swell in their attempt to rebuild the necrotic bone. As a result of this necrosis, the alkaline phosphate enzyme leaks into the blood serum, causing an increase of about 10 to 25 times more than the upper limit of its normal level in the blood serum.

b. Rickets disease: ALP increases to about 2-4 times more than the normal limit for the enzyme, and it has been observed that this increase quickly disappears when treated with vitamin D.

c. Bone Cancer: As this enzyme rises to its highest levels, indicating the significant abnormal increase in the bone tissue cells, which leak what they contain of this enzyme into the blood serum.

2. Hepatobiliary Diseases: The increase in this enzyme in such pathological conditions is attributed to the fact that the liver tissue is considered one of the main sources of alkaline phosphatase, and any defect that affects it leads to abnormal leakage of this enzyme into the blood. Among the most important of these diseases are:

a. Obstructive jaundice: Where there is a significant increase in the effectiveness of this enzyme in such a pathological condition.

b. Biliary Obstruction: This blockage can be due to external causes, such as the presence of a stone in the passage of the gallstone duct, a carcinoma, or fibrosis of the bile duct. Thus, this enzyme originating from the cells of the bile duct leaks into the blood, reaching 10 or 12 times more than its normal level. Recent studies have indicated that when this blockage occurs, the liver alerts to the formation of other amounts of ALP, which leads to its entry into the bloodstream, and its level in the blood serum rises. As for the internal causes of the obstruction of the bile duct it may be a result of acute or chronic hepatitis, or cirrhosis of the liver, the increased enzyme level is less than as external causes, as the level is estimated to be about 2.5 times more than the normal level.

There are normal cases and not pathological of high levels of this enzyme, such as:

1. Pregnancy: The increase is estimated at about 2 to 3 times more than the normal level, and the increase is due to the secretion of this enzyme by the placenta.
2. Growth of Children: The ALP level in children is estimated to be about 1.5 to 2.5 times more than the level in adults, and this increase is due to the growth of bone tissue cells.

Normal Value for Alkaline Phosphatase in Blood Serum:

Alkaline phosphatase activity = 20-140 U/L

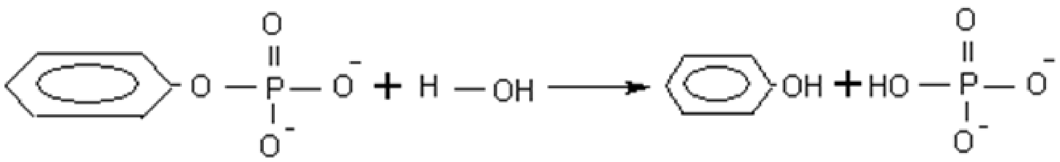
Alkaline Phosphatase Unit:

It is the unit that liberates 1 mg of phenol within 15 minutes under the reaction conditions of a temperature of 37°C and a pH = 9.6.

ACID PHOSPHATASE (ACP)

Classification:

The acid phosphatase belongs to the hydrolytic enzymes (hydrolases). It is thus, like the alkaline phosphatase, that works on the cleavage of the compounds containing the Acyl or Phosphate- ester bond. During this cleavage, another cleavage occurs in the hydroxyl bond of the water molecule, which leads to the formation of phenol Alcohol-like compound) (The pH at which the acid phosphatase enzyme works is 4.9).



Biosynthesis of ACP

Acid phosphatase is formed by many tissues in the human body. High concentrations of its activities are found in the liver, spleen, red blood cells, platelets, bone marrow, prostate gland and milk. It is also present in high concentrations in semen and urine.

The prostate gland is considered one of the richest sources of this enzyme, as it contributes about a third to half of the amount of enzyme present in the blood serum of healthy males.

The presence of the other part of this enzyme in the serum of males and females is attributed to the liver and as a result of the dissolution and destruction of red blood cells and platelets.

Properties of ACP

- The optimum pH for the activity of this enzyme differs in relation to its source. For example, the prostate enzyme has a clear pH ranging between 4.8 and 5.1, in which its effectiveness is most intense. In general, the optimum pH for this enzyme can be determined as acidic, around 5, and it loses its nature at a pH higher than 7.0.
- The best temperature for its maximum effectiveness is 37°C, and it loses its nature above 50°C.
- The acid phosphatase works on the same substrates as the alkaline phosphatase enzyme, as it analyzes a number of phosphate esters and turns them into phenols.
- Acid phosphatase is active with the same alkaline phosphatase stimulants such as Mg^{+2}, Co^{+2}, and Mn^{+2}. Negative ions such as oxalates, cyanide, borates, and phosphates all inhibit its effectiveness. Therefore, blood serum should be used instead of plasma to avoid the use of these inhibitors.
- Due to the importance of acid phosphatase in diagnosing prostate cancer, it is important to distinguish between the increase in prostatic enzyme and the increase in enzyme activity that is not related to other sources. There are a number of chemicals that work to inhibit one type without the other, as the prostatic enzyme is affected quickly and loses its effectiveness in the presence of the compound L- tartrate. On this basis, the test can be done using tartrate to stop the work of prostate acid phosphatase, and the test can be done without tartrate, and thus it is possible to measure the effectiveness of the prostatic enzyme is calculated by calculating the difference between the two test results,

and this method is one of the most used methods to distinguish between the prostatic enzyme and other types.

Clinical Significance of Acid Phosphatase;

1. Prostate cancer.
2. Female Breast cancer.
3. Bone diseases (as Biaget disease and Bone Cancer).
4. Hperparathyrodisim.

Normal Value for Acid Phosphatase: 2.5-11.7 U/L

Acid Phosphatase Unit:

It is the unit that releases 1 mg of phenol within one hour under reaction conditions of 37^{o}C and pH = 4.9.

TRANSAMINASES (GOT and GPT)

Glutamate Oxalacetate Transaminase: GOT

Glutamate Pyruvate Transaminase: GPT

Aminotransferases (Transaminases): is an enzyme whose function is to transfer the amine group from amino acids to alpha-ketone acids. It is found in all tissues and blood serum.

GOT and GPT Classification:

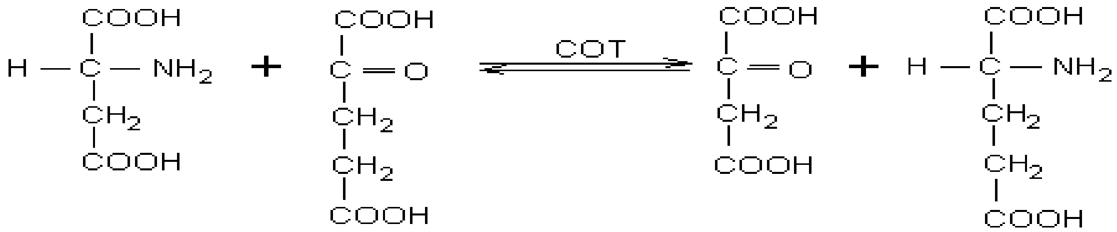
GOT and GPT enzymes belong to the class of enzymes called transaminases, which are newly called transferases. This group of enzymes is called transaminases because they help transfer the amino group (NH_2^-) from the amino acid to the alpha-keto site of the keto acids, and thus the amino acids are converted into alpha-ketone acids. This transformation is considered one of the main functions of these enzymes within the processes of protein metabolism in the human body within.

GOT: Now called Aspartate Transaminase (AST)

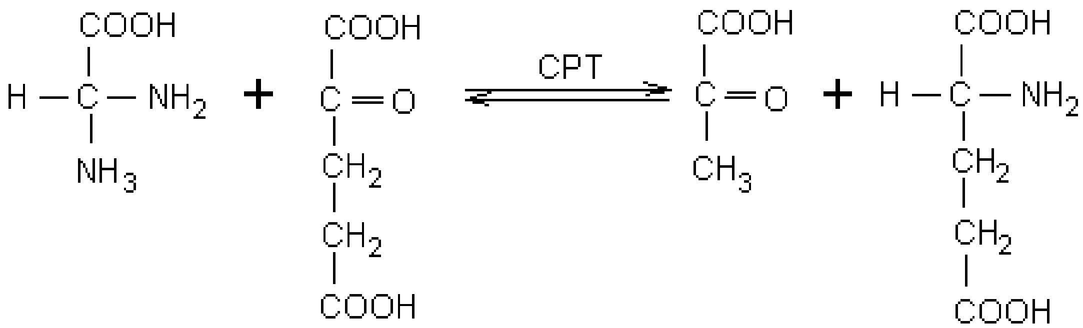
GPT: Now called Alanine Transaminase (ALT)

But the abbreviations GOT and GPT are still in general use.

It is worth mentioning that the reactions supported by each of the two enzymes are reversible reactions, but the balance of GOT and GPT reactions is biased towards the formation of aspartate and alanine, respectively. Here are the interactions that GOT and GPT help make:



aspartic acid (amino acid) | ketoglutaric acid (alpha keto acid) | oxaloacetic acid | glutamic acid



alanine acid (amino acid) | ketoglutaric acid (alpha keto acid) | pyruvic acid | glutamic acid

Sources of Transaminases:

Both GOT and GPT are found naturally in a number of body tissues. They are found in blood plasma, bile, and cerebrospinal fluid. The main sources of each are as follows:

- GOT: The most important source of GOT in blood serum is the heart, (cardiac muscle). The heart muscle is rich in the largest concentrations of this enzyme. The liver, skeletal muscles, and kidneys contain effective amounts of this enzyme.
- GPT: The liver is one of the most important sources of this enzyme, although it is present effectively in each of the skeletal muscles, heart and kidneys.

GOT Properties:

- Substrate that GOT works on is aspartic acid and alpha-keto-glutaric acid.
- GOT shows its optimal effectiveness at a temperature of 37^{o}C and at a pH of 7.4.
- Most anticoagulants negatively affect the activity of this enzyme, such as oxalates, acetate and borates. Therefore, it is preferable to use blood serum instead of plasma to assess the effectiveness of this enzyme.

GPT Properties:

- Substrate that GPT works on is alanine acid and alpha-keto-glutaric acid.
- The optimal activity of this GPT enzyme is achieved in the same conditions that achieved the optimal effectiveness of GOT. The temperature is 37^{o}C and PH = 7.4 are the appropriate conditions for the activity of this enzyme.
- The effect of anticoagulants on the effectiveness of GPT is the same as their effect on GOT. Therefore, blood serum remains preferable to plasma in estimating the effectiveness of GPT.

Clinical Significance of GOT

The clinical importance of GOT estimation comes in the clinical diagnosis of heart diseases in the first degree, as it is considered of great specificity in such cases. The clinical importance of increasing this enzyme can be summarized in the clinical diagnosis of three groups of human diseases.

1.Heart disease: as Myocardial Infarction.

2. Liver Diseases: as in viral hepatitis, liver cancer, liver cirrhosis, obstructive jaundice, and biliary obstruction.

3. Muscular Diseases: as in muscular atrophy.

Normal Value for GOT:

GOT = 5-46 U/L

The unit of measure for the effectiveness of GOT and GPT:

Each of the two enzymes is measured in an enzymatic unit known as the International Unit and is defined as follows:

The International Unit: is the activity of the enzyme that produces 1 micromol of pyruvic acid for the GPT enzyme and produces 1 micromol of oxaloacetic acid for the GOT enzyme under reaction conditions of 37^{o}C and pH = 7.4 within one minute per liter.

Clinical Significance (GPT): It increases in these diseases:

* Infectious Hepatitis: Where damage occurs in the liver cells, which leads to leakage of GPT into the blood, resulting in a significant increase in the effectiveness of this enzyme.

* Liver cirrhosis and bile duct cirrhosis.

* Obstructive jaundice.

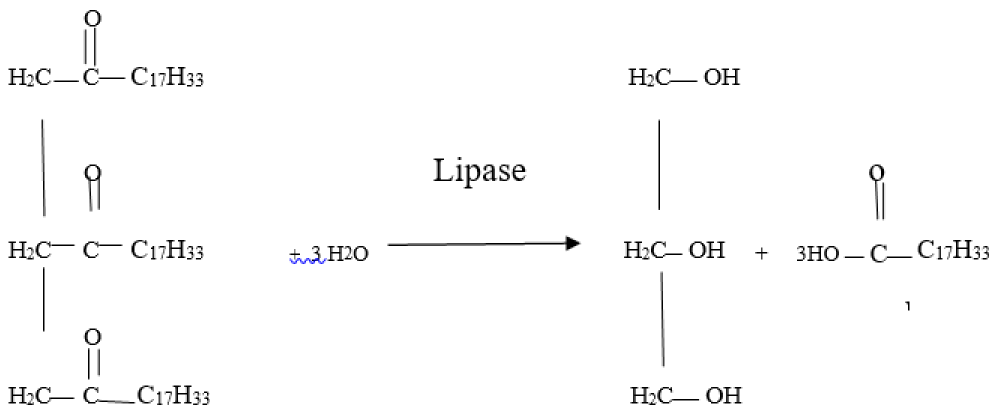
* Liver Cancer.

Normal Value for GPT:

GPT = 5-49 U/L

Lipase

This enzyme belongs to the class of hydrolytic enzymes that work on analyzing glycerol esters of long-chain fatty acids, thus converting them into simpler substances as part of the basic lipid metabolism that occurs in the small intestine, which results in It mainly contains oleic acid, and thus fats are considered the basic materials on which the lipase enzyme works.



triolein glycerol oleic acid

Lipase Source:

Lipase is formed by pancreatic acinar cells and preserved in it in the form of fermented granules (Zymogen granules) that are released in the pancreatic duct to empty into the duodenum with pancreatic fluid containing alkaline HCO_3^- ions. The end of the pancreas duct is shared with the end of the bile duct, but there is a secondary pancreatic duct, its contents are poured separately into the duodenum.

Studies in the past indicated that the lipase enzyme is activated in the presence of bile salts, albumin, and Ca^{+2} ions, as the bile salts emulsify fats well, which makes them spread in the form of a fatty emulsion in an aqueous medium that helps the lipase to attack it easily. From its work on preserving the nature of the enzyme itself, it prevents the process of Denaturation of the enzyme.

Properties of the Lipase Enzyme:

- Optimal activity of the lipase enzyme is at pH = 8.2 and the temperature is 37^oC.
- Lipase activity is activated by the presence of bile salts, albumin and calcium ions Ca^{++}.
- The effectiveness of the lipase is inhibited by the presence of hemoglobin, and for this reason, the blood serum must be free of any impurities from hemolysis.

Clinical Significance of Lipase:

Measurements of lipase activity in blood serum have the same clinical significance as measurements of amylase enzyme activity, which is directly related to acute pancreatitis, in which the activity of each of these two enzymes rises. The effectiveness of the lipase remains high in general for 10 to 14 days after the onset of inflammation, then it begins to decrease and return to normal. On this basis, if the blood serum was not withdrawn from the patient within three days of the onset of disease symptoms, resorting to measuring lipase activity is necessary and of clinical importance that cannot be dispensed with in diagnosing the disease.

The increase in lipase activity in acute pancreatitis can be explained by the following two mechanisms:

- The direct absorption of lipase from damaged pancreatic tissue cells into the bloodstream.
- The occurrence of lipase absorption from the small pancreatic ducts as a result of obstruction of the main pancreatic duct affected by inflammation.

Pathological conditions in which lipase is increased in the blood serum:

(1) Acute pancreatitis

(2) Carcinoma of the Pancreas

(3) Pancreatic duct obstruction

Normal Value for Serum Lipase: 0-160 U/L.

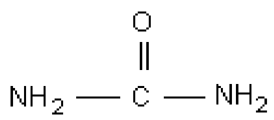
Lecture No. (15)

Non-Protein Nitrogenous Compounds (NPN)

They include; Urea, Uric acid, Creatine, and Creatinine.

Urea

Formula:



Biosynthesis of Urea:

Urea $(NH_2)_2CO$ is formed inside the human body in liver cells from ammonia gas generated as a result of deamination of amino acids

NH_2CH_2COOH $\xrightarrow{\text{Deamination}}$ NH_3 $\longrightarrow$ $(NH_2)_2CO$

amino acid ammonia urea

The formation of urea is the main means to get rid of the amounts of nitrogen in excess of the body's need, which is excreted outside through the urine.

Classification of Urea:

Urea belongs to the category of non-protein nitrogenous compounds, which include, in addition to urea, creatine, creatinine, uric acid, ammonia, and amino acids. It has been customary nowadays to express urea as urea nitrogen so that it is possible to distinguish between the amount of nitrogen present in urea and the amount of nitrogen present in non-protein nitrogen compounds. Urea nitrogen is called Blood Urea nitrogen (BUN).

The molecular weight of urea = 60 and the molecule contains two nitrogen atoms with an atomic weight of 28

$\therefore$ Amount of urea nitrogen (BUN) = 60/28 = 2.14

The amount of urea nitrogen that can be converted to urea is multiplied by 2.14. In short, BUN equals half of urea.

Clinical Significance of Urea

The determination of urea in blood serum is currently considered one of the most common screening tests for the purpose of evaluating kidney function. This test is always required along with the creatinine estimation test, as each of the two tests helps the other in diagnosing kidney disease.

The level of urea in the blood (Hyperuremia), which is called excessive uremia, is elevated above its normal level in a number of kidney diseases, such as: acute or chronic nephritis, polycystic kidney infection, nephrosclerosis, tubular necrosis, and glomerulonephritis, as well as an elevated level of urea in infections of the urinary tract (UTIs), such as: obstruction of the urinary tract the urinary tract is blocked by the presence of calculi or an enlarged prostate gland (in men) or as a result of tumors that may affect the ureter or bladder.

Glomerular Filtration of Urea

Renal filtration is one of the most important functions of the kidney, as waste products from metabolism come through the blood to the glomeruli, where they are filtered and flow through the small renal tubules and out without being reabsorbed, but what happens to urea is that it is partially reabsorbed through the cells of the renal tubules, which leads to not relying entirely on the urea test in evaluating the renal filtration function and resorting to examining creatinine, which is completely filtered without being reabsorbed by the renal tubules. As for useful substances such as glucose, they are filtered and completely reabsorbed by the renal tubules, to be returned to the circulatory system for use.

The substances that are reabsorbed are: glucose, amino acids, phosphates, electrolytes such as: hydrogen ion (H^+), H_2O,Cl^-, Na^+, Mg^{+2}, Ca^{+2}, HCO_3^-.

The substances that are not reabsorbed are:

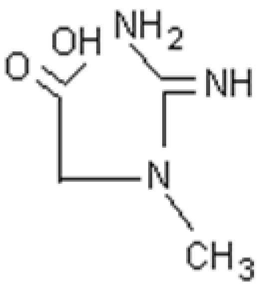
Urea (partial absorption), creatinine and non-protein nitrogenous compounds.

Normal Values for Serum Urea

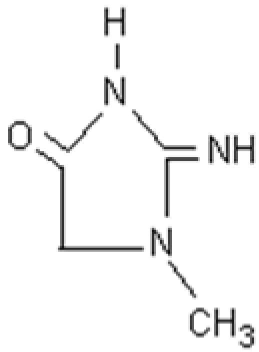
S.Urea	20-45 mg/dl x 0.166	(T.U)
	3.3-7.5 mmol/L x 6	(S.I.U)

Creatine and Creatinine

Formula:



CREATINE



CREATININE

Classification:

Both creatine and creatine belong to non-protein nitrogenous compounds that remain in the blood at relatively low concentrations in healthy people.

Sources and Biosynthesis

Creatine is formed internally in the liver and pancreas from three amino acids: Arginine, Glycine, and Methionine. After creatine formation, it travels to the blood vessels, where it is distributed to many cells in the human body, especially muscle cells, and there it turns into creatine phosphate. This process is called creatine phosphorylation.

Creatine and creatine phosphate are about 400 mg per 100 gm of fresh muscle, and both compounds automatically convert to creatinine at a rate of 2% per day. On this basis, creatinine is considered a waste product derived from creatine, which is excreted by the kidneys to the outside, it is the least changeable nitrogen compound in the blood, so its value is almost constant for a person.

Diagram showing the biosynthesis of creatine and creatinine

arginine glycine methionine

(in the liver and pancreas) Creatine

through blood

Creatine phosphate → 2% pre day → Creatinine

(in muscles) It acts as a storage of high energy

(considered a waste product from creatine) which is excreted out through the kidneys

Clinical Significance of Creatinine

After its formation, creatinine is transported to the kidneys through the blood, where it is filtered there by the renal glomeruli and excreted out through the urine without being reabsorbed by the small renal tubules to any significant extent, which gives high results for creatinine clearance rates, compared to filtering urea (which gets partial reabsorption).

When creatinine levels in the blood plasma rise above their normal limits, the small renal tubules contribute with the kidney to excrete creatinine. For this reason, creatinine levels in renal diseases do not rise in general unless there is significant damage to the kidney that prevents it from filtering and excreting wastes. Any level of creatinine higher than 2 to 4 mg per 100 ml of blood serum suggests moderate to severe renal damage. This decrease in creatinine sensitivity can be compensated for by the creatinine clearance test (C.C.T), which is considered one of the most sensitive tests to measure the percentage of renal filtration, Glomerular Filtration Rate (GFR). It is concluded from the foregoing that creatinine is of clinical importance, especially for kidney diseases of all kinds, such as nephritis, obstruction of the urinary tract by stones, malignant or non-malignant tumors, or infections of the prostate and bladder.

Normal Values for Creatinine

S. Creatinine 0.7-1.4 mg/dl x 88.4 (T.U)

62-124 µmol/L x 0.0113 (S.I.U)

Clinical Significance of Creatine

The amount of creatine in the blood serum represents a small part of the non-protein nitrogenous compounds, and recent studies indicate that the high or low levels of its natural levels in the blood are not related to all kidney diseases, and therefore there is no clinical significance in this matter.

The main clinical importance of creatine is concentrated in muscular diseases, where its levels rise above normal limits when severe muscle damage occurs, and among these muscular diseases is muscular dystrophy, in which the level of creatine in the blood rises in addition to other quantities that are excreted from the body. Through the urine, as studies show that 1400 mg of creatine is excreted within 24 hours, noting that the normal person excretes about 200 mg of creatine within 24 hours.

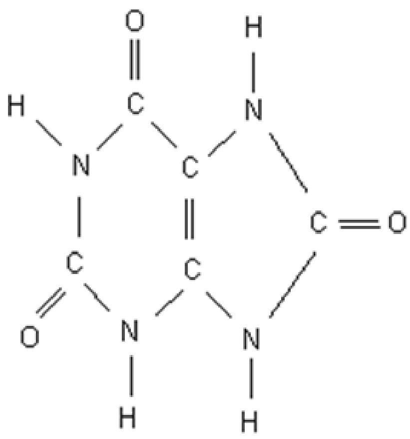
Normal Values for Creatine

S. Creatine 0.5-0.9 mg/dl x 88.4 (T.U)

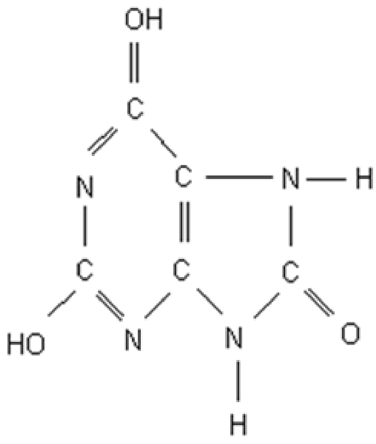
44.2 - 89.3 µmol/L x 0.0113 (S.I.U)

Uric Acid

Formula



Keto - form



Enol - form

Classification:

Uric acid belongs to the non-protein nitrogenous components of blood.

Biosynthesis of Uric Acid;

Uric acid is one of the end products of purine metabolism in the human body. It is one of the waste materials that is characterized by the difficulty of its solubility, and most of it must be excreted through the urine.

The formation of uric acid takes its place in the liver through two main ways:

Endogenous Pathway:

Uric acid from the process of purine metabolism, which is present in the synthesis of nucleic acids that make up nucleaoprotein molecules.

Exogenous Pathway:

Uric acid from purines taken through food (especially meat rich in these substances).

It is possible to follow the following diagram that shows the steps of uric acid formation. From this diagram, it is clear that the formation of uric acid depends on the effectiveness of a liver enzyme (Xanthine oxidase). This fact is used medically in the treatment of patients with gout resulting from an increase in uric acid from its normal level and depositing in the joints.

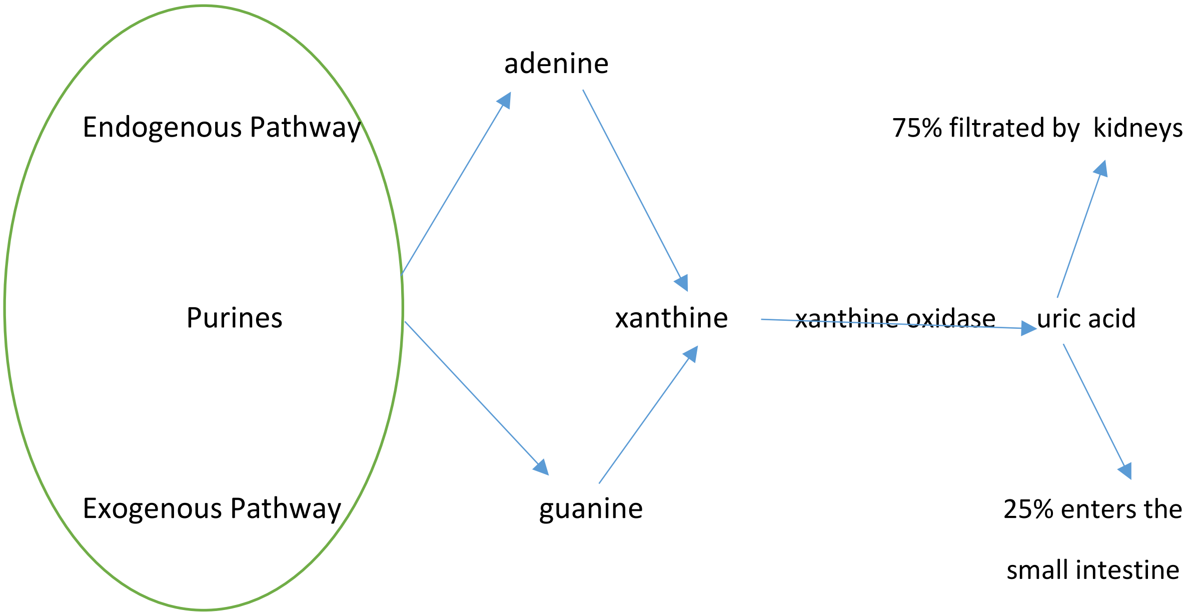


Diagram showing the formation of uric acid

Origin and Fate of Uric Acid

The purines that make up uric acid have an internal and external origin, and these are transformed into adenine and guanine, which are transformed in the liver, with the presence of the enzyme xanthine oxidase, into uric acid, which is transported by the blood to the kidneys, where approximately 75% of the total uric is filtered, while the other part, approximately 25%, is transferred to the small intestine, where it occurs uricolysis is caused by the microorganisms that live there. As for the filtered part of the kidney, it is absorbed again by the small renal tubules, at an estimated rate of 90% of the total renal filtrate. The presence of uric acid in the urine is attributed to its excretion by the efferent cells of the renal tubules.

Clinical Significance of Uric Acid

The main clinical importance of determining uric acid in blood serum is the diagnosis of gout, which is a disease in which the level of uric acid rises to 6.5 to 10 mg/dl of blood serum, noting that the normal level is between 3-7 mg / dl of blood serum.

The causes of high uric acid level, hyperuricemia, are attributed to the following:

- Increased purine formations, which are the main substances in the formation of uric acid.
- Increased intake of meat containing purines.
- Decreased renal filtration of uric acid and urates as a result of kidney failure. All these reasons lead to an increase in the formation of uric acid and then its deposition in the joints, especially the joints of the foot and the knee, which constitute the painful pathological symptoms of gout, also known as gout disease.
- Uric acid also rises in carcinoma diseases.

The Normal Values of Uric Acid:

S. Uric acid	3-7 mg/dl x 60 (T.U)
	180-420 µmol/L x 0.0166 (S.I.U)

Liver Function Tests

Liver tests can be classified as follows:

1. Tests and examinations that indicate the extent of damage to the hepato-cells.

   It includes examinations of aminotransferase enzymes known as transaminase, which include both GOT and GPT, which are released into the blood when there is damage or rupture in the liver cells.

   On this basis, both enzymes. (GOT, GPT) levels are significantly higher than normal in the case of liver diseases, such as:

- Viral Hepatitis of all kinds.
- Liver cirrhosis or liver fibrosis

2. Tests and examinations indicating dysfunction of the liver. These examinations include the following:

* Tests of Conjugatin Capacity of the Liver

The most important of these tests is total bilirubin, direct and indirect bilirubin.

It is known that bilirubin in general increases and rises above its normal level in the case of jaundice, which may result from infection with acute or viral hepatitis, or as a result of obstruction of the bile duct by a gallstone, or the presence of a carcinoma that leads to leakage of the substance bile into the bloodstream, causing the skin sclera (the white area of the eye) to be dark yellow, which alerts the patient to the need to treat this emergency with a doctor.

3. Examination of the excretion ability of the liver, while the most important examination in this field is the examination known as the BSP-Test (Bromsuion Thalein Excretion Test). Intravenously, at a rate of 5 mg per kilogram of the patient's weight (if the patient weighs 70 kg, he is injected with 350 mg of BSP). It has been observed that 5% of the amount of the dose given remains in the blood stream of the normal person after 45 minutes have passed, while the liver stores the other quantities in the bile sac. This process depends not only on the integrity of the liver cells in unloading their cargo of this dye in the bile sac, but also depends on the blood flow inside and outside the liver and on the integrity of the bile duct.

4. Tests that indicate the ability of the liver to manufacture protein substances, such as:

* Total Protein.
* Albumin.
* Globulin (except gamma-globulin).

5. Tests and examinations of bile stasis:

These tests indicate the failure of the bile pigments to reach the duodenum as a result of internal or external hepatic factors. The most important of these tests is the determination of enzymatic levels of alkaline phosphatase and nucleotides, whose levels rise significantly in cases of bile stasis.

*Alkaline phosphatase.

* S- Nucleotides

Bilirubin

Presence:

Bilirubin is found in very small quantities in the blood serum, causing the light-yellow color that characterizes the serum. In addition, bilirubin is considered one of the components of the bile stored in the gall-bladder, as it is the main pigment among the pigments of the yellow matter.

Formation and Metabolism of Bilirubin:

Bilirubin originally consists of damaged red blood cells, which are known to live for approximately 126 days only, and then fragmented at a rate of one million per day, releasing about 6 gr of hemoglobin. In this way, the body gets rid of the aging cells, as the cells of the reticulo-endothelial system, especially those found in the liver, spleen, and bone marrow, it devours the red blood cells and converts the released hemoglobin into bilirubin according to the following steps: hemoglobin turns into heme and globin, and iron separates from the heme forming biliverdin, which turns into bilirubin, which leaves the reticulo-endothelial system to pass into the blood, and albumin is combined with a weak bond (Albumin – Bilirubin), and thus it travels in the blood within the circulatory system and is known as unconjugated - Bilirubin. Then it reaches the liver, where it is combined with glucuronic acid, forming bilirubin-diglucuronide, which is known as conjugated bilirubin, which is emptied and stored in the bile sac. On this basis, any obstruction in the bile duct causes the cessation of emptying of this dye, which leads to its return to the bloodstream and an abnormal increase in its percentage, forming what is known as obstructive jaundice.

The conjugated bilirubin stored in the bile sac moves within the bile secretion to the small intestine to contribute to the process of digestion of fats. It is transformed into urobilinogen, part of which is reabsorbed to the liver and kidneys, where it is excreted through the urine. As for the other part, it moves to the large intestine and is transformed into urobilin. and is excreted through the feces.

Normal Value of Total Bilirubin in Serum

S. Total Bilirubin 0.3-1 mg/dl x 17.1 (T.U)

5-17 µmol/L x 0.06 (S.I.U)

S. Direct Bilirubin (Conjugated Bilirubin)

0-0.3 mg/dL x 17.1 (T.U)

0-5 µmol/L x 0.06 (S.I.U)

S. Indirect Bilirubin (Unconjugated Bilirubin)

0.3-0.7 mg/dL x 17.1 (T.U)

5-12 µmol/L x 0.06 (S.I.U)

Clinical Significance of Bilirubin

The occurrence of any disorders or obstruction in the metabolism of bilirubin leads to the occurrence of jaundice, which is characterized by an increase in bilirubin in the blood and the appearance of an orange-brown pigment on the skin, Sclera (the white eye layer) and the mucous membranes. The abnormal metabolism of bilirubin is one of the most important causes of jaundice.

The following is a review of the most important types of jaundice

- Hemolytic jaundice: The increase in bilirubin is due to the breakdown of red blood cells and the occurrence of acute or chronic hemolytic anemia. In both cases, hemoglobin is released from the blood outside the red blood cells, causing an increase in the formation of bilirubin. In this case, only unconjugated bilirubin rises. The cause of jaundice may be caused by a neonatal jaundice.

- Hepatic jaundice: The increase in bilirubin is due to the failure of the liver in its ability to conjugate bilirubin with glucuronic acid and store it in the form of conjugated bilirubin in the bile sac. Viral hepatitis is also one of the most important causes of hepatic jaundice. Liver cirrhosis also leads to an increase in bilirubin, in such a case both conjugated and unconjugated bilirubin rise.

- Obstructive jaundice: the increase here is due to obstruction of the common bile duct or the ducts branching from it due to stones, spasms, or narrowing. In all these cases, the liver is unable to excrete unload its load of conjugated bilirubin in the bile sac, which leads to its return to the blood and an increase in its level beyond the normal limit and the occurrence of obstructive jaundice. In such a case, only conjugated bilirubin rises.