وزارة التعليم العالي والبحث العلمي
الجامعة التقنية الجنوبية
المعهد التقني العمارة
قسم / التمريض

الحقيبة التدريسية لمادة Clinical chemistry

Lesson year - First Courese 2

تدريسي المادة

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الفصل الدراسي / First Courese 2

Clinical chemistry جدول مفردات مادة

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General Aims

This course aims to give basic knowledge in clinical chemistrt through theoretical and practical studies.

Target group:

Nursing departments / First Courese 2

Educational techniques used:

1- Blackboard and pens
2- interactive whiteboard
3- Data Show
4- Laptop

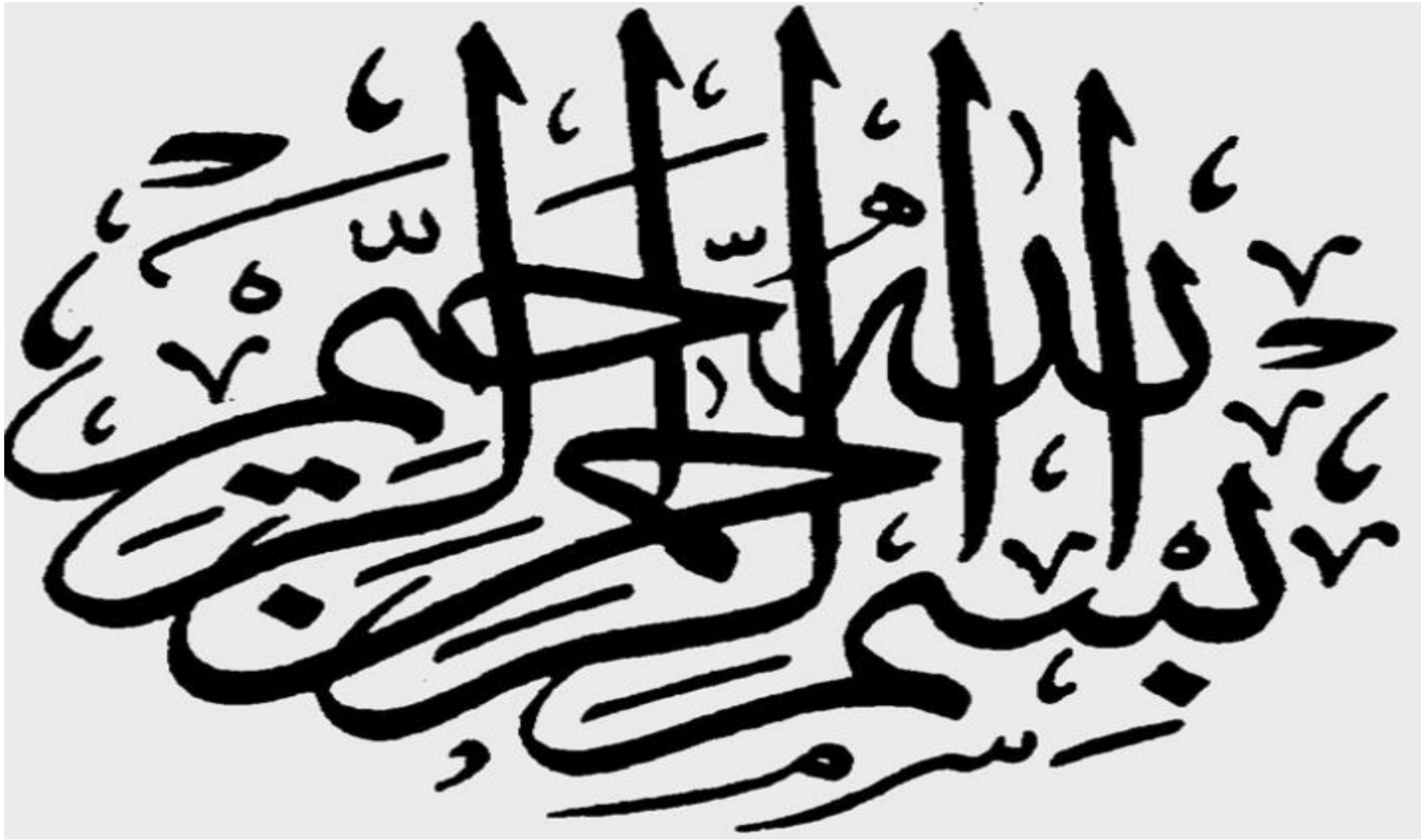
Lecture time: The time of the lecture for one class is four hours , distributed two houre in theoretical and two practicl hours.

Activities used:

1- Interactive classroom activities
2- Home Work

Evaluation methods:

1- Answer the questions posed as a class activity at the end of the lecture.
2- Conducting exams at the end of each semester.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Introduction to Clinical Chemistry

*The analysis of individual constituents, proteins, enzymes, nutrients, waste products, metabolites, hormones, etc. in blood or body fluids that provides information regarding the function or integrity of a tissue or organ.

* The clinical chemistry laboratory measures change in biochemical compounds as an indicator of health status or disease processes.

*Clinical Laboratory plays an integrated role in the diagnosis, prognosis, treatment, and long-term management of disease

Objectives

Understanding of:

o The principal methods to characterise patient samples

o The major disorders and pathological states encountered by clinical biochemists

o The major organ systems involved in disease

o Clinical diagnosis and prognosis

o Aspects of therapies used

o To display knowledge of human body chemistry levels under healthy and abnormal conditions

Why are Clinical biochemistry tests ordered?

- Diagnosis
- Monitor progression of disease
- Monitor effectiveness of treatment
- To identify complications of treatment
- To check the accuracy of an unexpected data
- To prevent malpractice
- To conduct research: response to new drugs

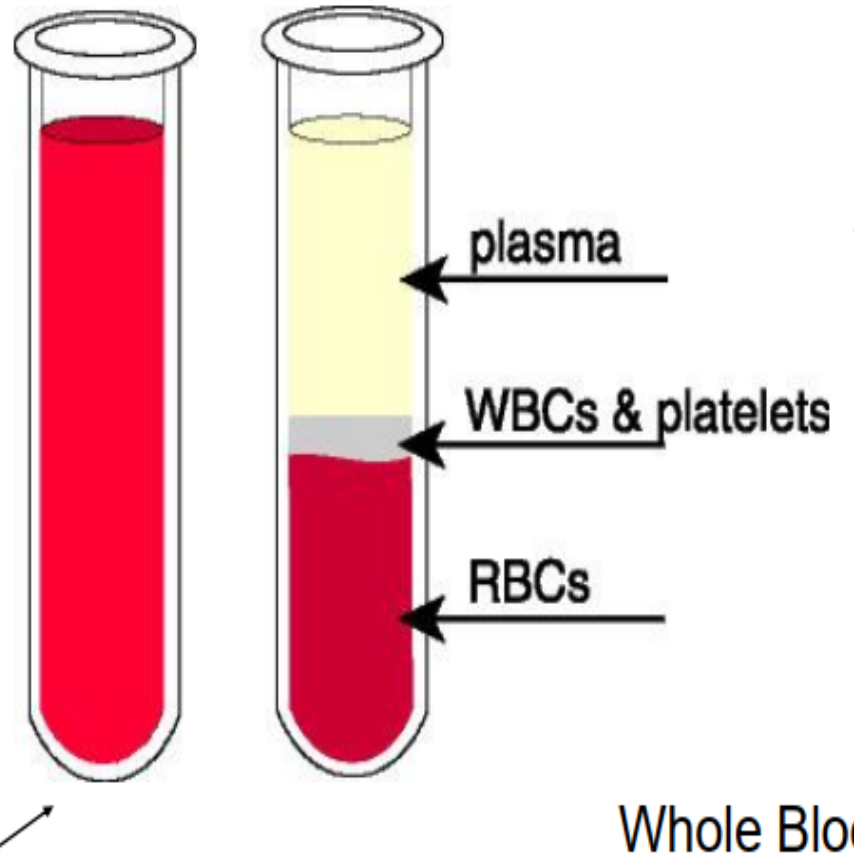
What kind of Biological Specimens?

Blood

- Urine
- Cerebrospinal Fluid
- Gastric Juice
- Gall stone
- Kidney Stone
- Stools/Feces
- Sputum & Saliva
- Synovial Fluid (joint fluid)
- Tissue Specimen

The Clinical Biochemistry Process

- Clinical history and physical examination
- Blood sample taken
- Tests requested
- Barcode label attached to blood tube
- Transported to lab



Whole Blood

Plasma is fluid component of blood. Comprises ~55% of total volume of whole blood. Contains proteins, sugars, vitamins, minerals, lipids, lipoproteins and clotting factors.

95% of plasma is water

Whole Blood after centrifugation

Note: clotting has been prevented

Factors affecting of parameters

- Age.
- Sex.
- Ethnicity.
- Physiological conditions (at rest, after exercise, standing, lying).
- Sampling methods (with or without using tourniquet).
- Storage and age of sample.
- Container used, for blood sample, anticoagulant.
- Method of analysis.

CLINICAL LABORATORY SUPPLIES

-In today's clinical chemistry laboratory, many different types of equipment are in use.

-The following is a brief discussion of the composition and general use of common equipment found in a clinical chemistry laboratory, including thermometers, pipettes, flasks, beakers, and dessicators.

*Thermometers/Temperature

The predominant practice for temperature measurement uses the Celsius (°C) scale; however, Fahrenheit (°F) and Kelvin (°K) scales are also used.The SI designation for temperature is the Kelvin scale.

Common Temperature Conversions

Celsius (Centigrade) to Fahrenheit	**°C (9/5) + 32** (multiply Celsius temperature by 9; divide the answer by 5, then add 32)
Fahrenheit to Celsius (Centigrade)	**(°F – 32)5/9** (subtract 32 and divide the answer by 9; then multiply that answer by 5)

Kelivin (°K)= 273.15 +(°C)

Some laboratory procedures, such as enzyme determinations, require precise temperature control.

Glassware and Plasticware

1 Laboratory glassware.

Pipettes

Pipettes are glass or plastic equipment used to transfer liquids; they may be reusable or disposable. Although pipettes may transfer any volume, they are usually used for volumes of 20 mL or less; larger volumes are usually transferred or dispensed using automated pipetting devices.

Micro Pipettes

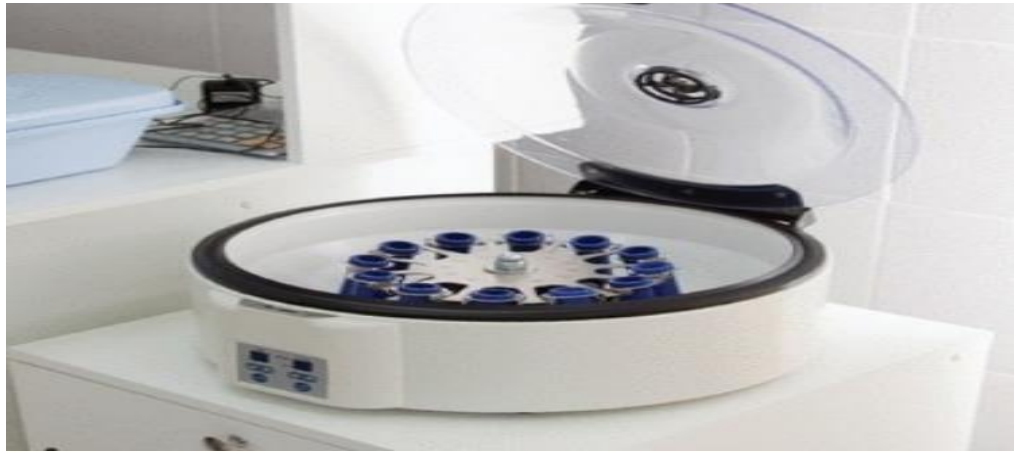
Disposable transfer pipettes.

Syringes

disposable tips

Centrifugation

Centrifugation is a process in which centrifugal force is used to separate solid matter from a liquid suspension. It is used to prepare samples, blood and body fluids, in clinical chemistry for analysis and also to concentrate urine sediment in urinalysis for microscopic viewing.



CENTRIFUGATION

Analytic balance.

Types of Samples

- venipuncture, is the act of obtaining a blood sample from a vein using a needle attached to a collection device or a stoppered evacuated tube.

- These tubes come in different volume sizes: from pediatric sizes (≈150 µL) to larger 5 mL tubes. The most frequent site for venipuncture is the medial antecubital vein of the arm.
- A tourniquet made of pliable nonlatex rubber flat band or tubing is wrapped around the arm, causing cessation of blood flow and dilation of the veins, making for easier detection.
- The gauge of the needle is inversely related to the size of the needle; the larger the number, the smaller the needle bore and length.

-In addition to venipuncture, blood samples can be collected using a skin puncture technique that customarily involves the outer area of the bottom of the foot (a heel stick) for infants .

-A sharp lancet device is used to pierce the skin and an appropriate capillary or microtainer tubes are used for sample collection.

- Analytic testing of blood involves the use of whole blood, serum, or plasma.

Whole blood, as the name implies, uses both the liquid portion of the blood

called plasma and the cellular components (red blood cells, white blood cells, and platelets).

- This requires blood collection into a vacuum tube containing an anticoagulant.

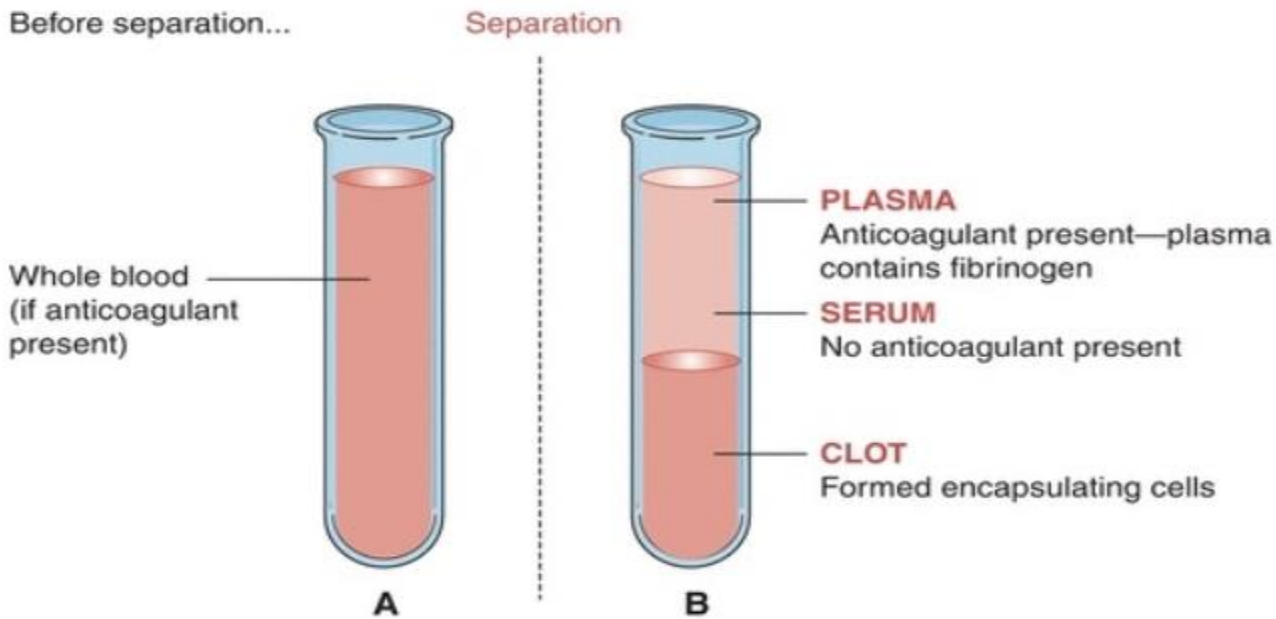
- Complete mixing of the blood immediately following venipuncture is necessary to ensure the anticoagulant can adequately inhibit the blood's clotting factors.
- As whole blood sits or is centrifuged, the cells fall toward the bottom, leaving a clear yellow supernatant on top called plasma.
- If a tube does not contain an anticoagulant, the blood's clotting factors are active in

forming a clot incorporating the cells.

- The clot is encapsulated by the large protein fibrinogen.
- The remaining liquid is called serum rather than plasma .
- Most testing in the clinical chemistry laboratory is performed on either plasma or serum.
- The major difference between plasma and serum is that serum does not contain fibrinogen (there is less protein in serum than plasma)
- And some potassium is released from platelets (serum potassium is slightly higher in

serum than in plasma).

- It is important that serum samples be allowed to completely clot (≈20 minutes) before being centrifuged. Plasma samples also require centrifugation but do not need to allow for clotting time .



Blood sample. (A) Whole blood. (B) Whole blood after separation

-Arterial blood samples measure blood gases (partial pressures of oxygen and carbon dioxide) and pH. Syringes containing heparin anticoagulant are used instead of evacuated tubes because of the pressure in an arterial blood vessel.

-Proper patient identification is the first step in sample collection.

The importance of using the proper collection tube, avoiding long time tourniquet application, drawing tubes in the proper order, and proper labeling of tubes cannot be stressed strongly enough.

-Having patients open and close their fist during phlebotomy is of no value and may cause an increase in potassium and, therefore, should be avoided.

-In addition, the proper antiseptic must be used. Isopropyl alcohol wipes, for example, are used for cleaning and disinfecting the collection site

then soap and water as the disinfectant).

- Urine is the next most common fluid for determination. Most quantitative

analyses of urine require a timed sample (usually 24 hours); a complete sample (all urine must be collected in the specified time) can be difficult because many timed samples are collected by the patient in an outpatient situation.

-Creatinine analysis is often used to assess the completeness of a 24-hour urine sample because creatinine output is relatively free from interference and is stable.

-The average adult excretes 1 to 2 g of creatinine per 24 hours.

-Urine volume differs widely among individuals.

Common Clinical Laboratory Hazards and Waste Disposal

- It is very important to protect laboratory worker from hazards.

-The laboratory hazards fall into three main categories: chemical hazards, biological hazards, and physical hazards.

-The major chemical hazards in laboratories are the cleaning agents, anesthetic gases, disinfectants, drugs, and solvents.

-The persons working in laboratory are exposed to chemical hazards during their usage or due to improper storage.

- Biological hazards involve exposures to infectious samples, animal diseases transmissible to humans, and biological agents used during experimental procedures that include viral vectors, etc. .
- The laboratory personnel encounter the physical hazards due to accidental spill of corrosive reagent, broken glassware, etc. (Fig. 1.1).

The major precautions that can be followed while working in laboratory are:

1. Proper labelling of chemicals.
2. The worker should avoid mouth pipetting and should take care not to blow out pipettes containing potentially infectious material like serum.
3. The gloves, mask, protective eyewear, and gowns must be used while drawing blood from a patient.
4. Proper installation of fire extinguishers, grounding of electrical wires, etc.
5. The reuse of the syringes should be avoided, and needles should be disposed off in the containers without touching.

6. Completely incinerate infectious tissues.

7. The discarded tube or infected material should not be kept unattended or unlabelled.

8. All sharp objects and infectious samples should be disposed off properly.

9. Immediately use laboratory first aid in case of accidental exposure to any hazard

10. The laboratory workers must be trained for proper handling and disposal of biohazardous materials including the patient specimens. (Note the hazard warning symbol on reagents.)

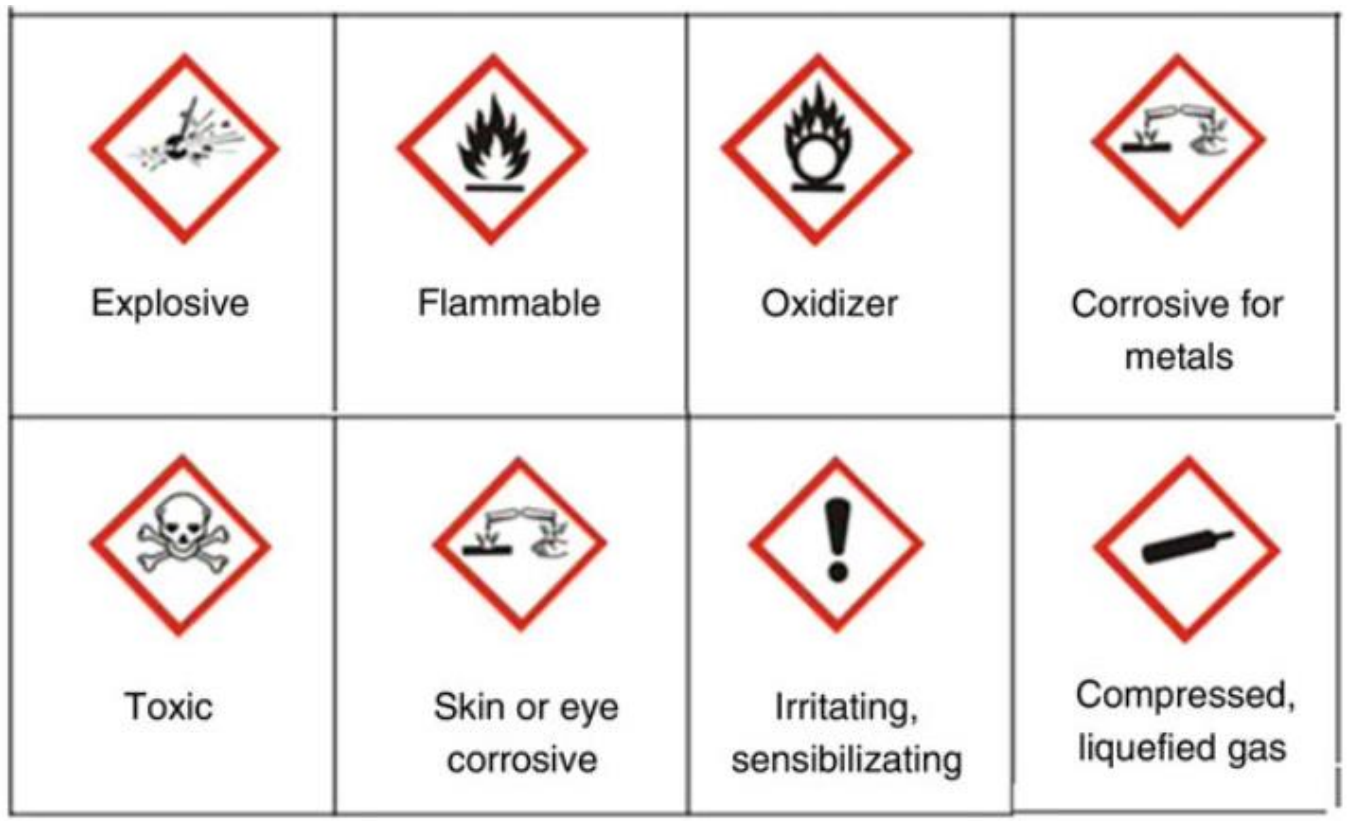


Fig. 1.1 Hazard warning symbols

Laboratory first aids

S. no	Accident/injury	First aid
1.	Alkali splash on the skin	Wash with tap water for 15 min followed by 5% acetic acid solution
2.	Acid splash on the skin	Wash with tap water for 15 min followed by 5% sodium carbonate solution
3.	Phenol burn	Wash with plenty of tap water. Then use polyethylene glycol with water
4.	Splashes in the eyes	Wash with plenty of tap water and sterile saline. Then seek professional doctor's help
5.	Injury due to broken glass	Wash wound immediately with disinfectant
6.	Burn	Wash with plenty of tap water and cover with sterile dressing

Laboratory wastes may be hazardous in nature. It should be disposed off in appropriate plastic bin bags:

1. Black waste bin bag – Contaminated medicine, general waste, leftover food and peels of fruits, outdated medicine, any noninfectious material, etc. should be discarded in these waste bins.

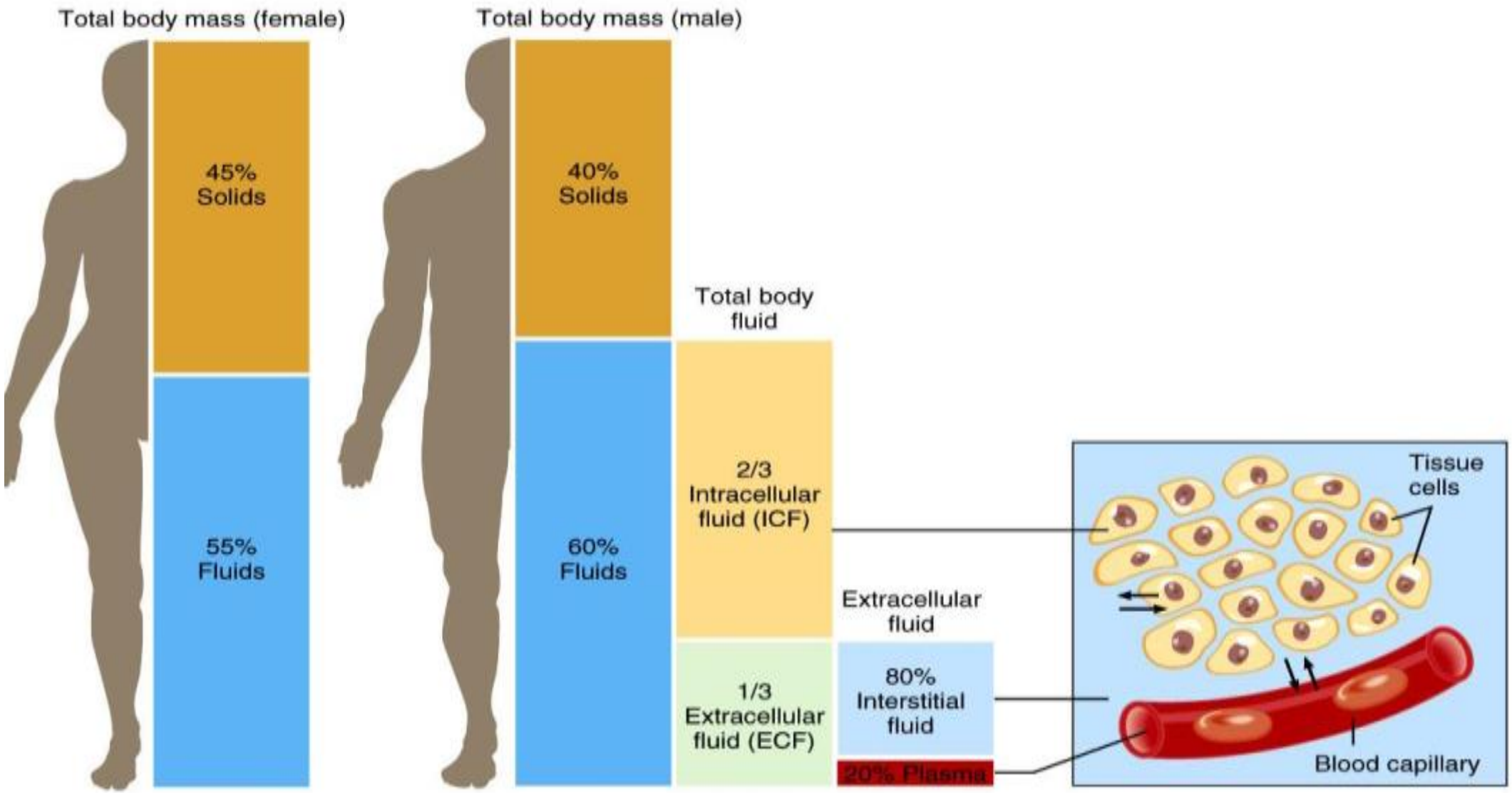
2. Red waste bin bag – Plastic waste such as catheters, urinary catheter, suction catheter, injection syringes, tubing, IV bottles, used or discarded blood containers, microbiology culture, etc. 3. Blue waste bin bag – All broken glass bottles and articles, surgical blades, glass syringes, needles, and any sharp material.

4. Yellow waste bin bag – Empty vials, ampoules, gloves, infectious waste, human anatomical wastes, organs, body parts, dressing, bandages, gauze, items contaminated with blood/body fluids, microbiological and biotechnical wastes, etc.

Body Fluid

- Body fluids are liquids originating from inside the bodies of living humans.
- They include fluids that are excreted or secreted from the body.
- Human blood, body fluids
-Total amount of fluids in the human body is approximately 70% of body weight
- Body fluid has been divided into two compartments –
1- Intracellular fluid (ICF)
- Inside the cells, 55% of total body water
2- Extracellular fluid
- Outside the cells, 45% of total body water

Composition of body fluids



(a) Distribution of body solids and fluids in an average lean, adult female and male

(b) Exchange of water among body fluid compartments

Composition of body fluids

- Organic substances

Glucose ,Amino acids ,Fatty acids ,Hormones ,Enzymes

- Inorganic substances(Na,K,Ca,Mg,Cl,PO4,SO4)

*** Extracellular fluid**

1- Interstitial fluid

Present between the cells, Approximately 80% of ECF2

2- Plasma

Present in blood ,Approximately 20% of ECF

3- Also includes (Lymph , synovial fluid , cerebrospinal fluid)

Composition of body fluids/ Extracellular fluids

Extracellular fluids (Interstitial Fluid) :

Also known as intercellular fluid and tissue fluid is fluid between the cells of multi-cellular organisms which delivers materials to the cells, intercellular communication, and removal of metabolic waste.

- Interstitial fluid consists of a water solvent containing amino acids, sugars, fatty acids, coenzymes, hormones, neurotransmitters, salts, as well as waste products from the cells.

- This fluid presents as gel-like extracellular matrix.

The exchange of material across the capillaries occurs at high rate by diffusion in both directions.

- acting as a media for intercellular communication.

Intracellular Fluid

- The cytosol or intracellular fluid is the liquid found inside the cells .

- Physiological Function : The cytosol has no single function and instead it is the site of multiple cell processes including metabolic processes (such as glycolysis, gluconeogenesis) . It is also involved in signal transduction from the cell membrane to sites within the cell .

The body fluid composition of tissue varies by

- Tissue type: lean tissues have higher fluid content than fat tissues.
- Gender: males have more lean tissue and therefore more body fluid.
- Age: lean tissue is lost with age and body fluid is lost with it.

Functions of the Blood

1. The main function of the blood is to maintain intracellular homeostasis by:

a). Carries O2 and nutrients (glucose, amino acids, lipids, and vitamins) to the cells.

b). Carries CO2 and other wastes (nitrates, creatine, nucleic acid) away from the cell.

2. Providing intercellular communication in the body: carries hormones (secreted by endocrine glands) to the target organs.

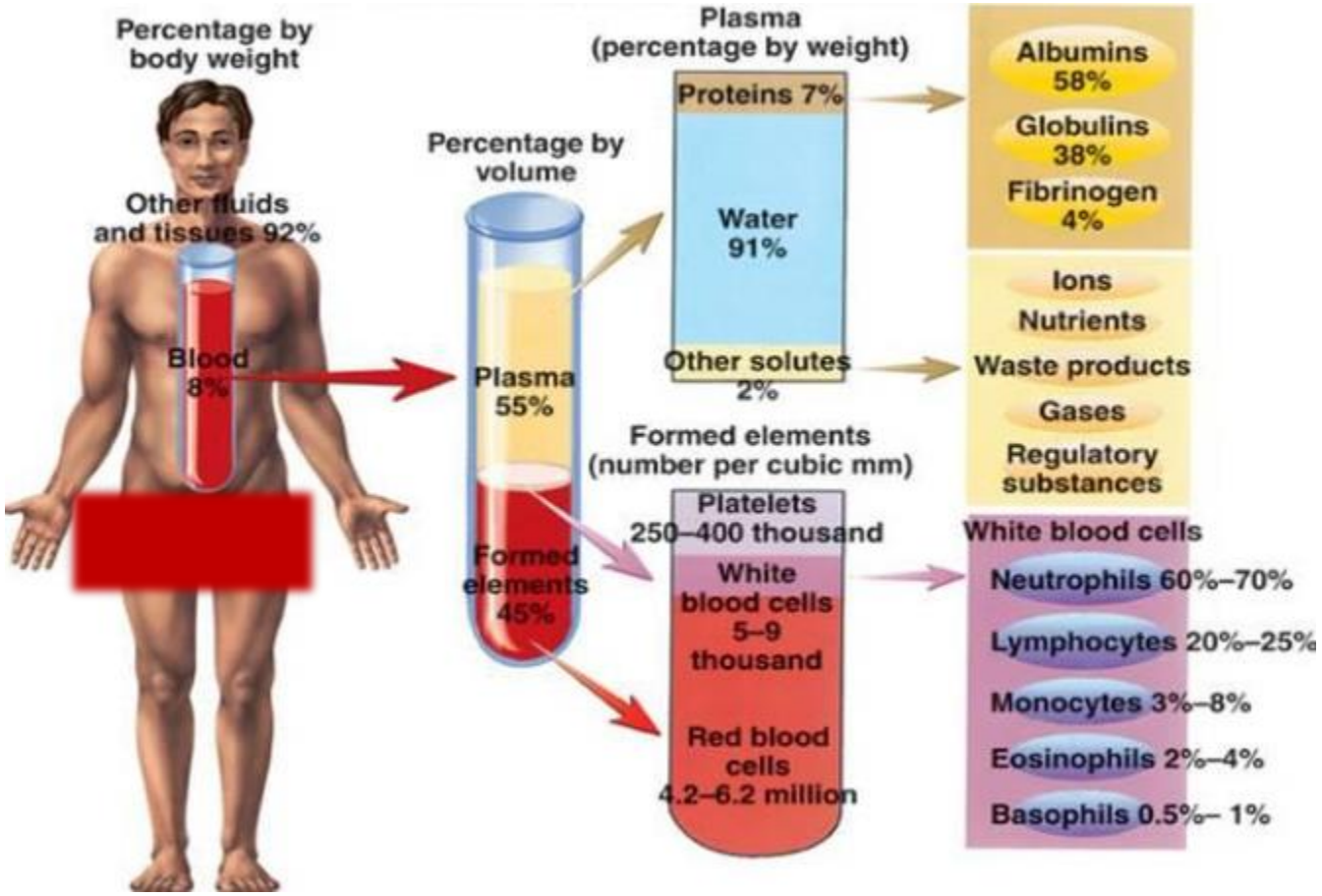
3. Protection and defense: it allows cells and immunological proteins to transport from place to place where need them.

4. Self repair mechanism: clotting cascade.

5. Blood is a fluid connective tissue. It circulate continually around the body, allowing constant communication between tissues distant from each other.

6. Blood makes up about 7% of body weight (about 5.6 liters in a 72 Kg man).

Blood Components



Formed Elements (Cellular Content of Blood)

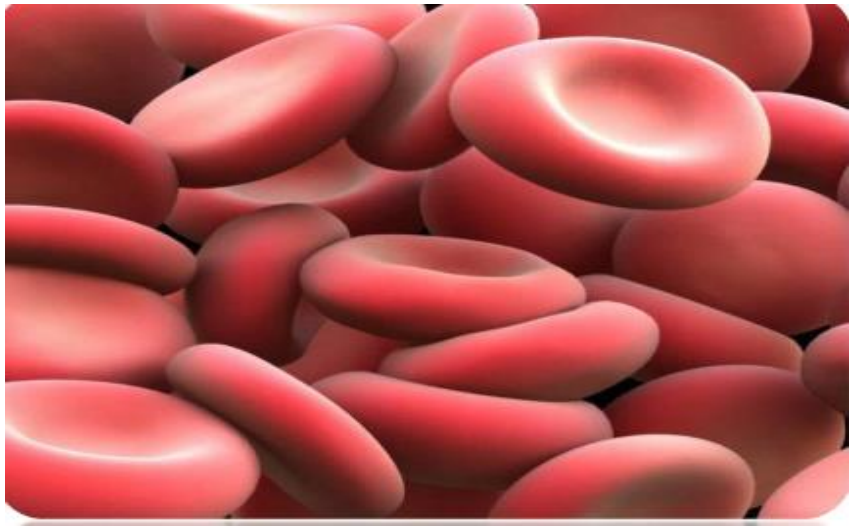
- There are three types of blood cell:

1. Erythrocytes (Red Blood Cells =RBC).
2. Platelets (thrombocytes)
3. Leukocytes (white blood cells = WBC) they include monocytes, lymphocytes, neutrophils, eosinophils, and basophils

Source of Blood Cells Mature blood cells have a relatively short life spine.

- Blood cells are synthesised mainly in the red bone marrow.
- Some lymphocytes, additionally are produced in lymphoid tissue.
- The organ or system responsible for synthesis blood cells are called hematopoietic system and the process of blood cell formation is called hematopoiesis.

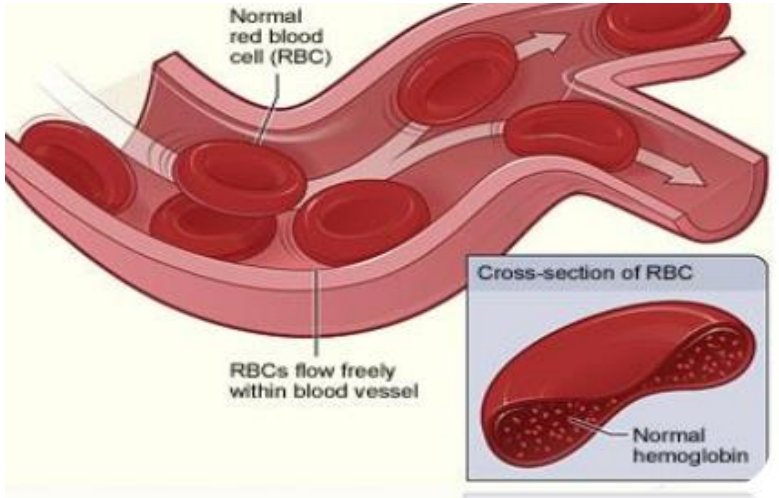
Normal red blood cell (RBC)



Biconcave shape of RBC

Life Span and Formation of Red Blood Cells

- Erythrocytes are produced in red bone marrow
- Their life span in circulation is about 120 days.



Hemolysis

Hemolysis is the release of hemoglobin from red blood cells, giving the plasma/serum a pink to red color. Hemolysis must be avoided during sample collection, transportation, and storage, as it causes changes in measurement.

Hemoglobin (Hb)

- Hb is the most important constituent of red blood cells. It is responsible for transport of O2 from lungs to tissues and CO2 from tissues to lungs.
- The normal value in a normal male adult is 13-18 g\100ml and in female is 11.5-16.5 g\100ml.
- Molecules of hemoglobin is large and complex. They are made up of heme and globin.
- Heme is made up of iron (in ferrous form) and porphyrin.
- Globin is a protein that has 4 polypeptides chains (2 alpha and 2 beta).
- Each RBC carries about 280 million Hb molecules, therefore each RBC has ability to carry over a billion O2 molecules.
- Hb with O2 is called oxyhemoglobin, and Hb without O2 called deoxyhemoglobin.

Hemoglobin degradation

Reactions and Steps Involved in Heme Degradation

1. Conversion of Heme to Biliverdin

- Heme oxygenase breaks down heme, releasing biliverdin, CO, and iron.

- Heme degradation begins with the enzyme heme oxygenase, which breaks down heme into biliverdin, carbon monoxide (CO), and iron.

- This reaction involves the cleavage of the heme ring and the release of biliverdin as a product.

Reaction: Heme + O2 → Biliverdin + Fe3+ + CO // Enzyme: Heme oxygenase

2. Reduction of Biliverdin to Bilirubin

- Biliverdin reductase converts biliverdin into bilirubin, which is a yellow pigment.

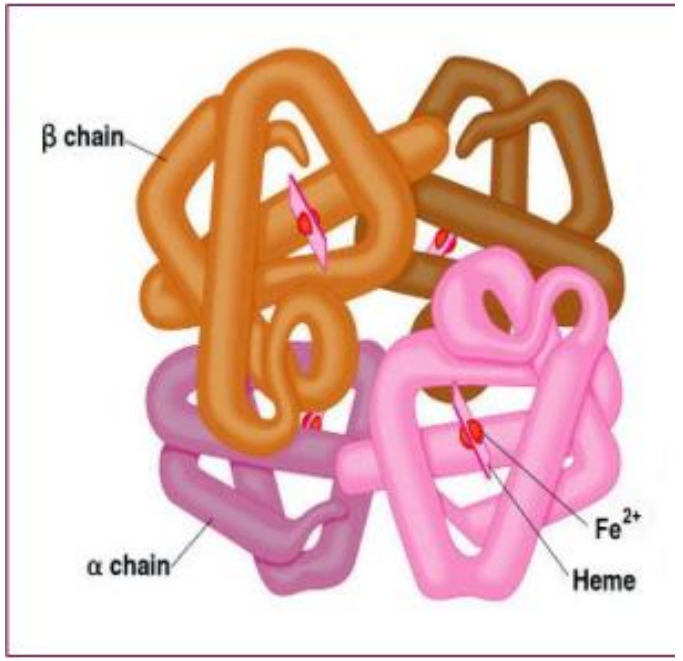
- Biliverdin reductase is responsible for the reduction of biliverdin to bilirubin.

- This enzymatic reaction involves the transfer of electrons from NADPH to biliverdin, resulting in the formation of bilirubin.

Reaction: Biliverdin + NADPH + H+ → Bilirubin + NADP+ + H2O // Enzyme: Biliverdin reductase

Coagulation (blood clotting)

• Coagulation of blood is very important for stoppage of bleeding from an injured blood
vessel. The process of coagulation is complex and involves many steps and many factors (most of which is proteins).
• These clotting factors activate each other in specific order resulting in the formation of prothrombin activator.
• Prothrombin activator is the first step in the final common pathway of blood coagulation.
• In the final common pathway, the prothrombin activator converts prothrombin (present in the plasma) to thrombin (an enzyme).
• Thrombin acts on the plasma protein fibrinogen and converts it into insoluble fibers of fibrin these fibers form a meshwork in which blood get entangled to form a sold clot.



Hb Structure

what does anticoagulation mean?

Anticoagulants

Whole blood or plasma sample investigations need use of anticoagulants while collecting sample. Some common anticoagulants are:

(a) Ethylenediaminetetraacetic acid: It removes calcium ions by and block coagulation.

(b) Heparin: Heparin inhibits conversion of prothrombin to thrombin.

(c) Sodium fluoride: This anticoagulant is considered when glucose estimations are carried out in blood samples. Sodium fluoride inhibits glycolysis by inhibiting activity of enolase enzyme and hence preserves blood glucose levels.

(d) Sodium or potassium oxalate: Sodium, potassium, and even lithium oxalates precipitate, calcium ions and inhibit blood coagulation.

Urine

- Urine is the excretory product of the body produced by the process of filtration, reabsorption, and tubular secretion.

- Urine can be collected and examined easily, and

presence of certain substances in the urine may indicate the metabolic state of the body.

- Urine sample is collected in clean vials.

- Arandom sample is usually taken for routine clinical examination; however, firstmorning urine is preferred for urinalysis and microscopic analysis, since it is

generally more conc.

Urine Formation

- Urine formation is a blood cleansing function.
- Normally, about 26% of cardiac output enters the kidneys to get rid of unwanted substances.
- Kidneys excrete the unwanted substances in urine.
- Normally, about 1 to 1.5 L of urine is formed every day.
- Urine is a liquid excreted by the kidneys, collected in the bladder, and excreted from the body through the urethra.

Urinary Excretion

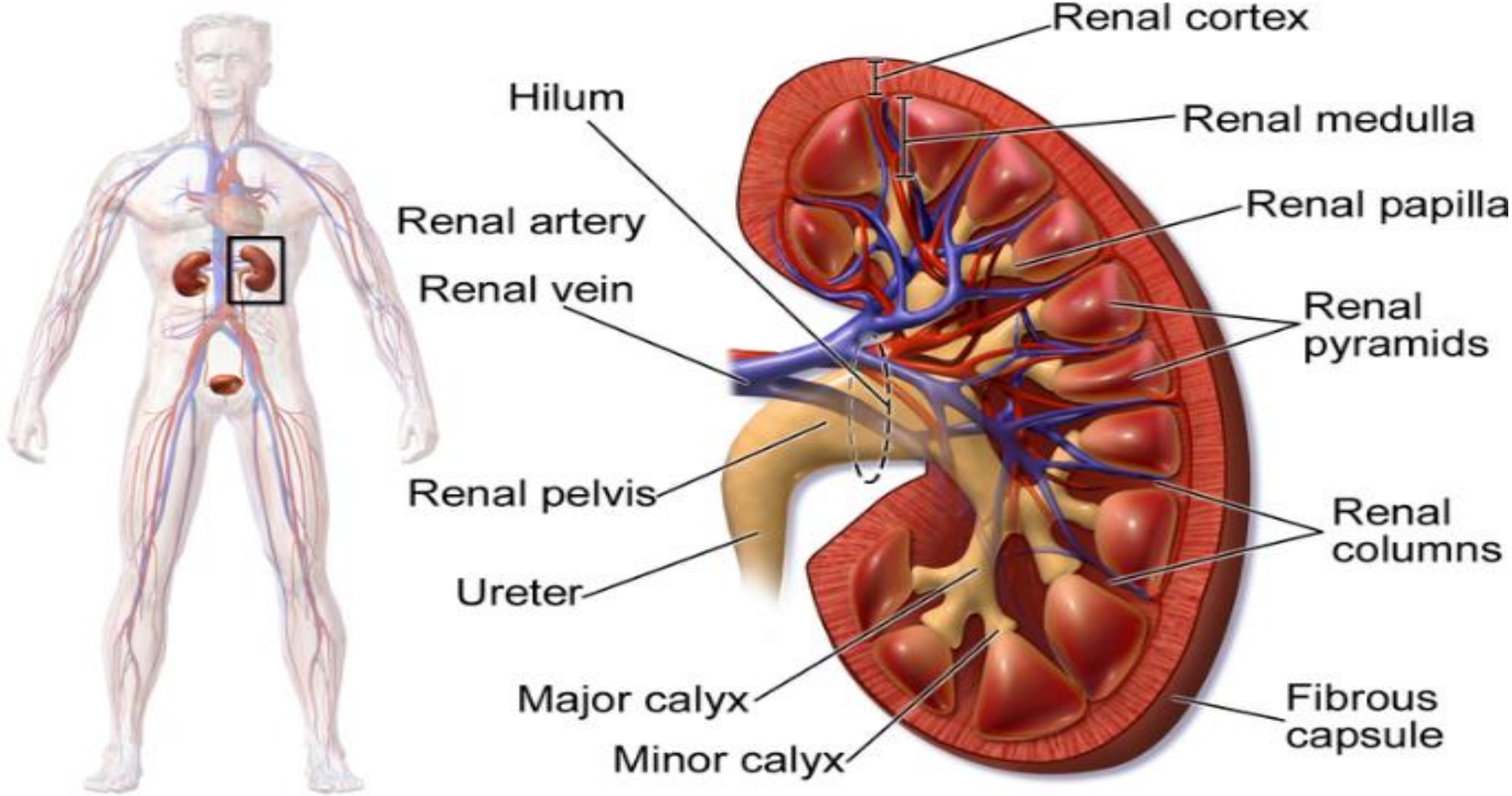
- The primary route in which the body eliminates substances is through the kidneys.
- The main function of the kidney is the excretion of body wastes and harmful chemicals into the urine.
- The functional unit of the kidney responsible for excretion is the nephron. Each kidney contains about one million nephrons.
- The nephron has three primary regions that function in the renal excretion process: the glomerulus, proximal tubule, and the distal tubule .

Three processes are involved in urinary excretion

- Filtration :-Filtration takes place in the glomerulus, which is the vascular beginning of the nephron. Approximately one-fourth of the blood flow from cardiac output circulates through the kidney, the greatest rate of blood flow for any organ.

- Secretion :- which occurs in the proximal tubule section of the nephron, is responsible for the transport of certain molecules out of the blood and into the urine.

- Reabsorption:- Reabsorption takes place mainly in the proximal convoluted tubule of the nephron. Nearly all of the water, glucose, potassium, and amino acids lost during glomerular filtration reenter the blood from the renal tubules.


Renal cortex
Hilum
Renal medulla
Renal artery
Renal papilla
Renal vein
Renal pyramids
Renal pelvis
Renal columns
Ureter
Major calyx
Fibrous capsule
Minor calyx

Physical Examination of Urine

Color and Odor

- Normal urine is colorless to straw colored due to presence of urochrome.
- Slight change in color occurs in fever, dehydration jaundice, or vitamin B-complex therapy which adds riboflavin (deep yellow color).
- Food beverages and drugs may impart a specific odor to urine.
- The smell of normal urine is aromatic. The smell of urine changes depending on the person taking medication or something else.

Appearance

- Normally freshly voided urine is clear and transparent, but it may become turbid if exposed for a long time due to the bacterial action on urea present in urine to convert it into ammonium carbonate.
- The presence of white cells, red cells, or epithelial cells makes urine cloudy.
- Fat globules give urine milky appearance.

Specific Gravity

- Specific gravity of urine is measured by urinometer. Specific gravity of normal urine is between 1.002 and 1.026 and depends upon state of hydration, diet, fluid intake, drugs, etc.

- Severe dehydration, diabetes mellitus, adrenal insufficiency,diabetes

insipidus, and chronic nephritis increase specific gravity .

Volume

- Normal healthy individual excretes about 800–2000 ml of urine/day. Daily urinary excretion depends upon intake of fluid volume, loss of fluid, solute load, climatic condition, fever, or intake of drugs.

- The term polyuria is used if urinary output is more than 3000 ml/day.

pH :- Normal range of urinary pH is 4.5–7.5.

- Various factors like heavy meals, heavy exercise, metabolic acidosis, or chronic respiratory acidosis influence urine pH greatly. Normally freshly voided urine is acidic.

Urine chemical analysis

Normal urine has various organic and inorganic constituents.

- The normal inorganic constituents are chloride, phosphates, sulphates, calcium, Ammonia ,etc.,

-while organic constituents are urea, uric acid, and creatinine.

- Urea is formed in the liver as a result of amino acid metabolism. It reacts with some acids, such as nitric acid, to form ammonium nitrate, and with oxalic acid to form urea oxalate.
- Creatinine is a compound formed from creatine by losing a water molecule from creatine.
- Amino acids are found in urine either as free amino acids, such as aspartic acid and histidine, or as bound amino acids, such as methionine and glutamic acid.
- oxalic acid.
- In pathological cases, the following organic compounds appear: glucose in diabetes, albumin in kidney diseases, bile salts and Bilirubin in liver diseases, and blood in kidney, bladder and urinary tract diseases.

Urin analyses

checks for:

- Acidity (pH). The pH level indicates the amount of acid in urine.
- Concentration. A measure of concentration shows how concentrated the particles are in your urine. A higher than normal concentration often is a result of not drinking enough fluids.

- Protein. Low levels of protein in urine are typical. Small increases in protein in urine usually aren't a cause for concern, but larger amounts might indicate a kidney problem.

Sugar. The amount of sugar (glucose) in urine is typically too low to be detected.

- Ketones. As with sugar, any amount of ketones detected in your urine could be a sign of diabetes and requires follow-up testing.

- Bilirubin. Bilirubin is a product of red blood cell breakdown. Usually, bilirubin is carried in the blood and passes into your liver, where it's removed and becomes part of bile. Bilirubin in your urine might indicate liver damage or disease.

Electrolytes of the body fluids

What are electrolytes?

Electrolytes are minerals that have an electric charge when they are dissolved in water or body fluids, including blood. The electric charge can be positive or negative. You have electrolytes in your blood, urine (pee), tissues, and other body fluids.

-Common human electrolytes are sodium,Iron , chloride, potassium, calcium.

- Electrolytes in body fluids are charged , It can be:

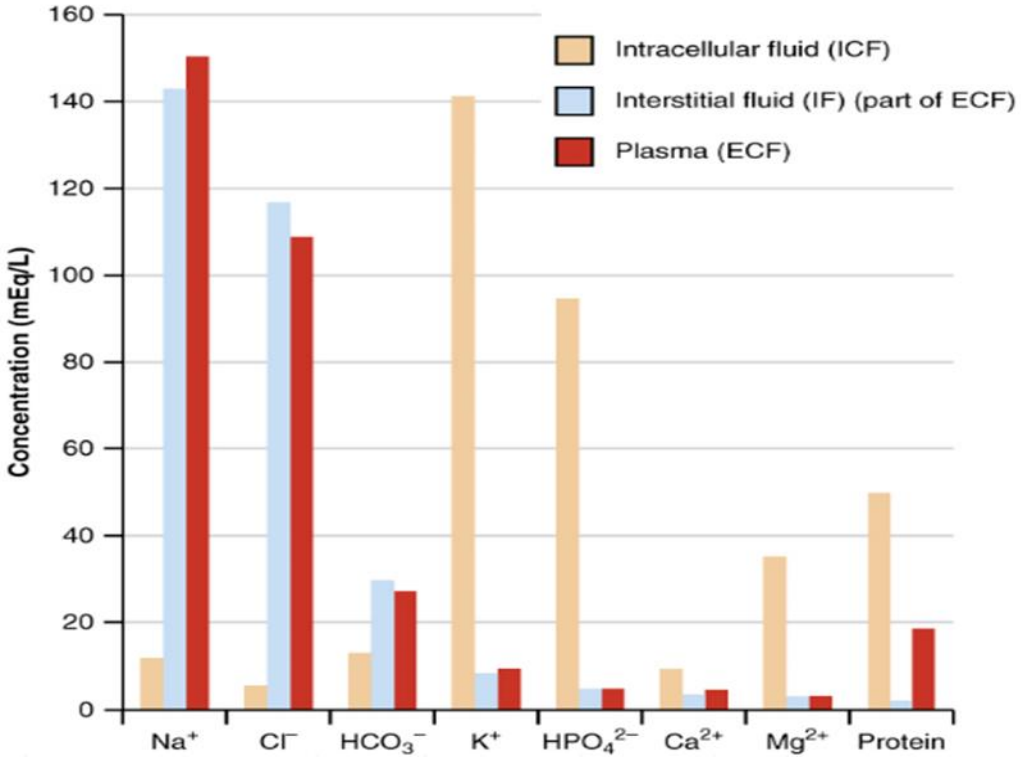
Cation - positively charged electrolyte, e.g .Na+, k+,Ca+2

Anion - negatively charged electrolyte, e.g, Cl- , HCO3- po4-3

The chief extracellular cation is Na+

The chief intracellular cations are k+

- Cl- is the anion outside cells whereas phosphates constitute the bulk of intracellular anions.



* Electrolytes are important because they help:

1-Balance the amount of water in your body

2-Balance your body's acid/base (pH) level

3-Move nutrients into your cells

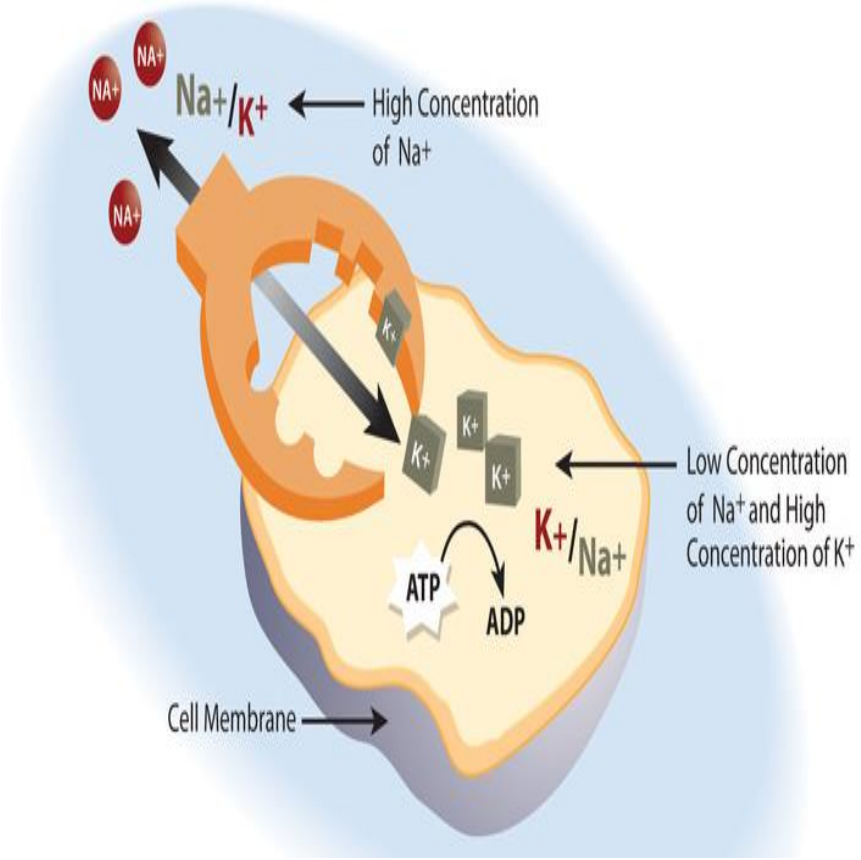
4-Move wastes out of your cells

5-Support your muscle and nerve function

6-Keep your heart rate .

7-Keep your blood pressure stable

8-Keep your bones and teeth healthy

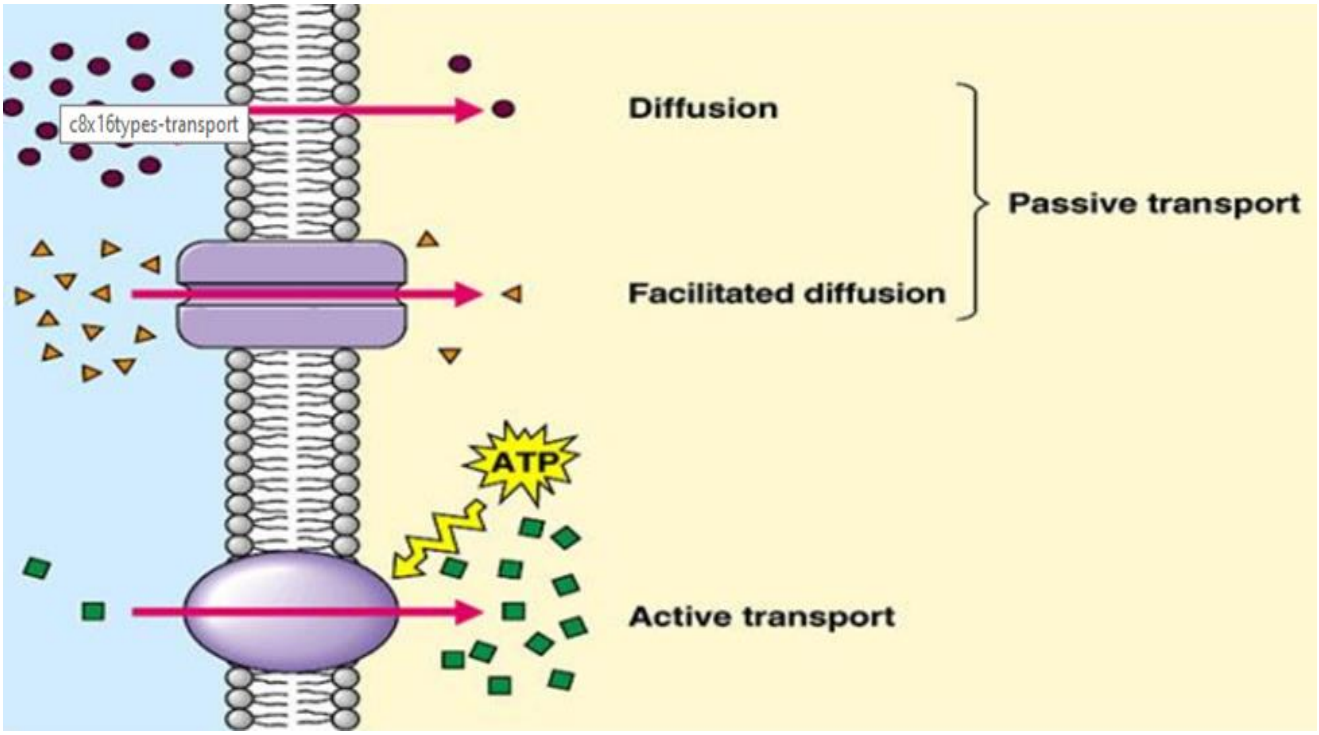


The Sodium-Potassium Pump

- The main electrolytes in body include: (Na,K, Fe, Ca, Cl,PO4 ,Mg,……)

*Note :You get these electrolytes from the foods you eat and the fluids you drink.

Movement of body fluids



Membrane transport processes:

1-**passive transport** it is the movement of substances across a membrane from higher to lower concentration (down a concentration gradient) ,it does not require metabolic energy.

Passive transport

A- simple diffusion :-It is the movement of substances from a region of high concentration to a region of low concentration. Generally, simple diffusion of water, gases, and other small uncharged molecules across plasma membranes can occur in the absence of transport proteins.

B- facilitated diffusion :-It is a transport of substances across a biological membrane from an area of higher concentration to an area of lower concentration by a carrier proteins.

2- Active transport:

It is the movement of substances across a membrane against gradient (from low concentration to high concentration). Active transport requires energy and involves specific carrier proteins.

Movement of fluids due to:

1) Hydrostatic pressure:- It is physiological processes that regulate fluids intake & output as well as movement of water substances dissolved in it between the body compartments

2) osmotic pressure:- The pressure exerted by the flow of water through a semi-permeable membrane separating two solutions with different conc… of solute

It is pressure which forces the water to move from where there is little dissolved solute to where there is lots dissolved solutes.

NOT1 -Osmosis: It is diffusion of a solvent (usually water molecules) through a semipermeable membrane from an area of low solute concentration to an area of high solute concentration.

NOT2-The amount of osmotic pressure exereted by a solute is proportional to the number of molecules or ions.

* A question? Cells are about 75 percent water and blood plasma is about 95 percent water. Why then, does the water not flow from blood plasma to cells?

- ## What is an electrolyte imbalance?

An electrolyte imbalance means that the level of one or more electrolytes in body is too low or too high. It can happen when the amount of water in body changes. The amount of water that you take in should equal the amount you lose. If something upsets this balance, may have too little water (dehydration) or too much water (overhydration).

-Some of the more common reasons why you might have an imbalance of the water in body include:

1-Some medicines
2- Severe vomiting and/or diarrhea
3- Heavy sweating
4- Heart, liver or kidney problems
5- Not drinking enough fluids, especially when doing intense exercise or when the weather is very hot
6- Drinking too much water.

*Note: The most common electrolyte imbalances are in sodium and potassium. Electrolyte imbalances are referred to with the prefixes "hypo" (low) and "hyper" (high), combined with the scientific name of the electrolyte.

*What are the different types of electrolyte imbalances?

The names of the different types of electrolyte imbalances are:

Electrolyte	Too low	Too high
Calcium	Hypocalcemia	Hypercalcemia
Chloride	Hypochloremia	Hyperchloremia
Magnesium	Hypomagnesemia	Hypermagnesemia
Phosphate	Hypophosphatemia	Hyperphosphatemia
Potassium	Hypokalemia	Hyperkalemia
Sodium	Hyponatremia	Hypernatremia

*Disorder of Electrolyte (Na, K, Fe, Ca, Cl)

-Electrolyte imbalance, or water-electrolyte imbalance, is an abnormality in the concentration of electrolytes in the body.

-Electrolytes play a vital role in maintaining homeostasis in the body.

The importance of electrolytes

They help to regulate heart and neurological function, fluid balance, oxygen delivery, acid–base balance and much more. As follows:

1- Sodium : Na+ is the most abundant cation in the ECF, and largely determines the osmolality of the plasma.

-Hypernatremia:- Early symptoms may include a strong feeling of thirst, weakness, nausea, and loss of appetite.

-Hyponatremia symptoms include a decreased ability to think, headaches, nausea, and poor balance

2- (K)Potassium is the major intracellular cation. Like Na+, K+ would eventually diffuse across the cell membrane until equilibrium is reached.

Note - The Na+/K+-ATPase ion pump moves three Na+ ions out of the cell in exchange for two K+ ions moving into the cell as ATP is converted to ADP.

-Hyperkalemia:- can cause an abnormal heart ,which can result in cardiac arrest, kidney failure and death.

- hypokalemia Symptoms may include feeling tired, leg cramps, weakness, and cardiac arrest.

3-calcium (Ca^{2+}) in our bodies, and much of it is found in our skeletal system. .Plasma calcium is an essential component of coagulation pathways.

-Calcium, which helps make and keep bones and teeth strong.

Note -Three hormones, PTH (Parathyroid hormone), vitamin D, and calcitonin, are known to regulate serum Ca^{2+} by altering their secretion rate in response to changes in ionized Ca^{2+}.

-PTH secretion in blood is stimulated by a decrease in ionized Ca^{2+}, and conversely, PTH secretion is stopped by an increase in ionized Ca^{2+}. The **importance of(PTH)parathyroid hormone in the kidneys**

1-In the kidneys, PTH conserves Ca^{2+} by increasing tubular reabsorption of Ca^{2+} ions.

2-PTH also stimulates renal production of active vitamin D.

* NOT- Body fluids are neutral in charge. Thus, cations, or positively charged ions, and anions, or negatively charged ions, are balanced in fluids.

*NOT-The most common cause for hypocalcemia is hypoparathyroidism. , vitamin D deficiency, kidney failure, pancreatitis.

4-Chloride (Cl-) is the extracellular anion. Chloride is a principal contributor to the osmotic pressure gradient between the ICF and ECF and plays an essential role in maintaining hydration.

- Hyperchloremia is causes of : Loss of body fluids from vomiting, diarrhea, sweating or high fevers.

-Low levels of chloride (hypochloremia) may be a sign of: Heart failure. Lung disease. Addison disease, a condition in which your body's adrenal glands don't produce enough of certain types of hormones.

5- Iron involved in the transfer of oxygen from the lungs to tissues. Iron in the body is found in hemoglobin and myoglobin. Hemoglobin is the protein in red blood cells responsible for carrying oxygen to the tissues from the lungs. Myoglobin is a protein found in muscles that is used for storage of oxygen.

- Iron deficiency anemia:- symptoms may include: Weakness, Pale skin, Chest pain, fast heartbeat or shortness of breath, Headache, Cold hands and feet.

- Haemochromatosis is an inherited condition where iron levels in the body slowly build up over many years, This build-up of iron, known as iron overload, can cause unpleasant symptoms. If it is not treated, this can damage parts of the body such as the liver, joints, pancreas and heart.

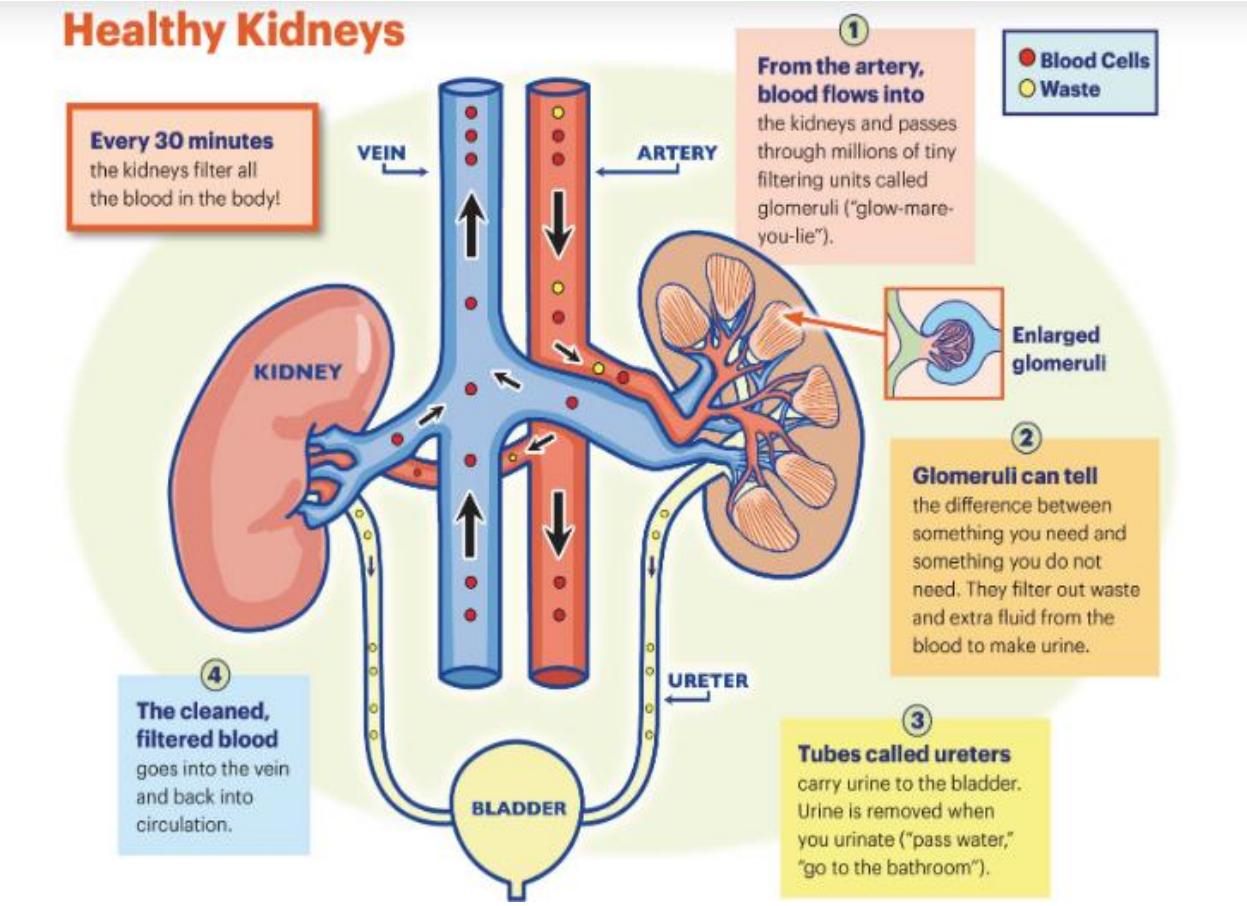
Normal electrolyte levels

Name	Chemical symbol	Plasma	CSF	Urine
Sodium	Na^+	136.00–146.00 (mM)	138.00–150.00 (mM)	40.00–220.00 (mM)
Potassium	K^+	3.50–5.00 (mM)	0.35–3.5 (mM)	25.00–125.00 (mM)
Chloride	Cl^-	98.00–107.00 (mM)	118.00–132.00 (mM)	110.00–250.00 (mM)
Bicarbonate	HCO_3^-	22.00–29.00 (mM)	—	—
Calcium	Ca^{++}	2.15–2.55 (mmol/day)	—	Up to 7.49 (mmol/day)
Phosphate	HPO_4^{2-}	0.81–1.45 (mmol/day)	—	12.90–42.00 (mmol/day)

What are the kidneys?

The kidneys are two bean-shaped organs that filter your blood. Your kidneys are part of your urinary system.

Your kidneys also help balance your body's fluids (mostly water) and electrolytes.



What is the function of the kidneys? & Why are the kidneys important?

1- kidneys remove wastes and extra fluid from body.

2- kidneys also remove acid that is produced by the cells of the body .

3- maintain a healthy balance of water, salts, and minerals—such as sodium, calcium, phosphorus, and potassium—in the blood.

4- kidneys also make hormones that help control blood pressure , keep your bones strong and healthy.

Note1:- Without this balance, nerves, muscles, and other tissues in the body may not work normally.

Note2: have two kidneys that filter blood, removing wastes and extra water to make urine.

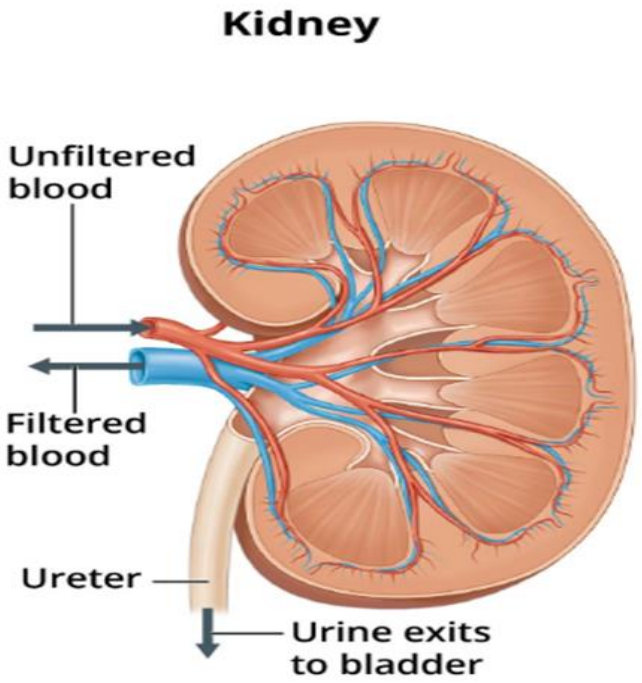
*Unfiltered blood flows into kidneys

through the renal artery and

filtered blood exits through renal vein.

The ureter carries urine from

the kidney to your bladder.



How much water should I drink to keep my kidneys healthy?

On average, males should drink about 13 cups (3 liters) of water each day. On average, females should drink about 9 cups (a little over 2 liters) of water each day.

- ## The kidney function test (KFT)

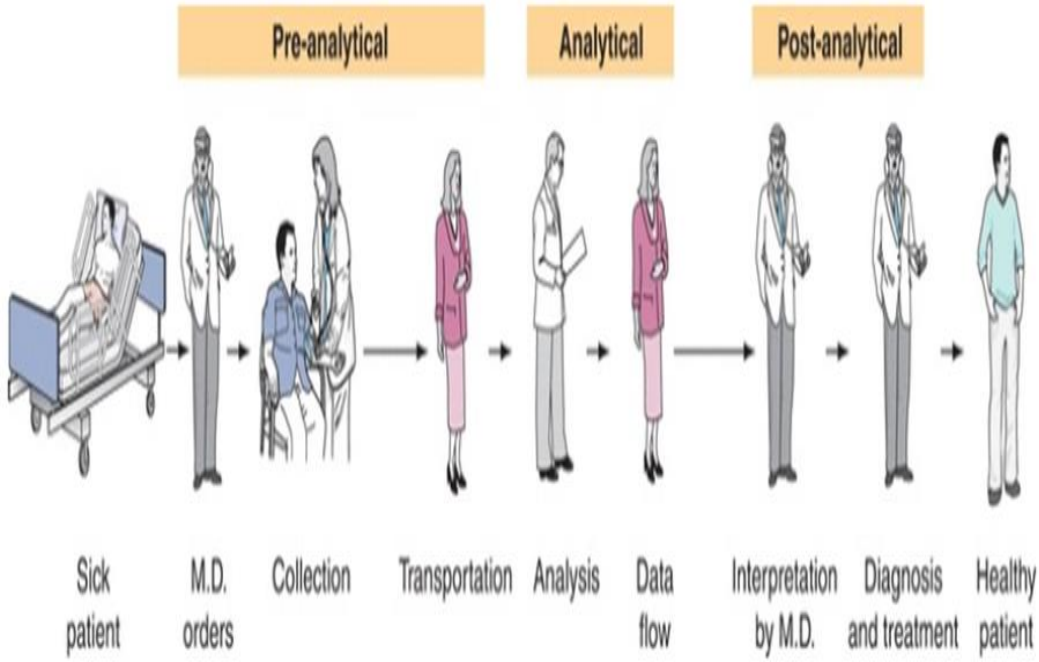
The kidney function test (KFT) is one such test that uses urine and blood samples.

1-Urea. 2- Creatinine. 3- Sodium. Potassium.

4-Some laboratories also measure chloride and bicarbonate routinely,

5-albumin :urine indicates kidney damage

-*These blood tests are called a 'renal profile', 'renal function test', or 'urea and electrolytes' ('U&E' for short).



- **Routine kidney function blood test**

Two simple tests can check how well your kidneys are functioning.

-The first is a blood test called estimated glomerular filtration rate (eGFR) .Estimated glomerular rate (eGFR) is a blood test measuring creatinine (a waste product from the digestion of dietary protein and the normal breakdown of muscle tissue) from which kidney function levels can be estimated.

-the second is a urine test known as the ~~urine albumin-creatinine ratio~~ (uACR). ~~Albumin to creatinine ratio~~ (ACR) measures the albumin (a kind of protein) in your pee. Having too much albumin may mean your kidney's filtering units have been damaged by disease.

Both tests are needed to have a clear picture of your kidney health.

plasma proteins

What are proteins?

Proteins are important building blocks of all cells and tissues. Proteins are necessary for body's growth, development, and health.

- Blood contains albumin and globulin.
- Albumin proteins keep fluid from leaking out of your blood vessels.
- Globulin proteins play an important role in your immune system.

- **CLASSIFICATION OF PROTEINS**

Three major types of classifying proteins:

A- Based on the functions .

(Enzymes or catalytic proteins, Transport proteins, Hormonal proteins, Storage proteins, Defense proteins, Receptor proteins for hormones, viruses, Immunoglobulins, Genetic proteins,…)

B. based on chemical nature and solubility.

It is based on the amino acid composition, structure, shape and solubility properties.

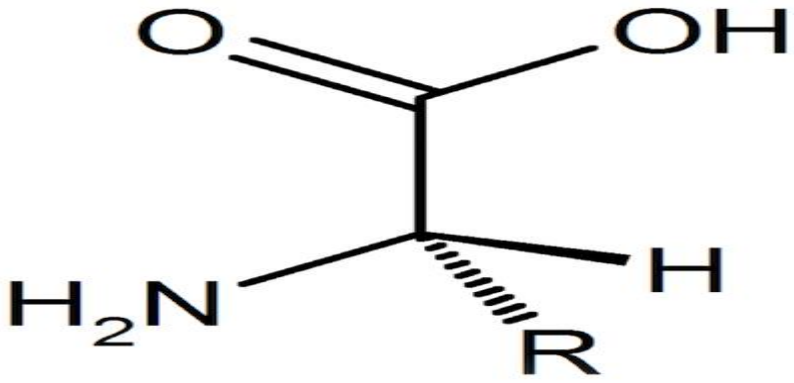
C. Nutritional classification of proteins : These proteins have all the essential amino acids.

NON ESSENTIAL	ESSENTIAL
Alanine	Histidine
Arginine	Isoleucine
Asparagine	Leucine
Aspartate	Lysine
Cystine	Methionine
Glutamic	Phenylalanine
Glycine	Threonine
Ornithine	Tryptophan
Proline	Valine
Serine	
Tyrosine	

Essential Amino Acids :-that you must obtain by eating various foods.

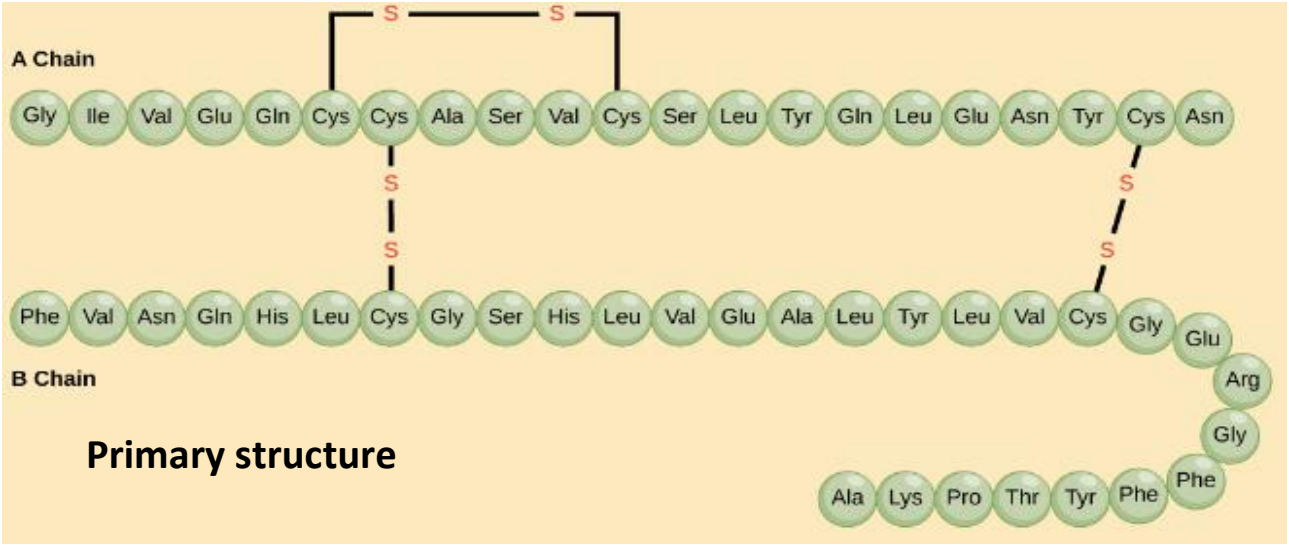
Non-Essential Amino Acids :- synthesized by the body

* All amino acids have a basic structure consisting of an amino group, a carboxylic group, a hydrogen atom, and an R group around a central carbon. It is the R group which distinguishes one amino acid from another. Sometimes referred to as a side chain, the R group is characterized by a number of different properties based on polarity, charge, size, and solubility



Orders of protein structure

simply the sequence of amino acids in a polypeptide chain.

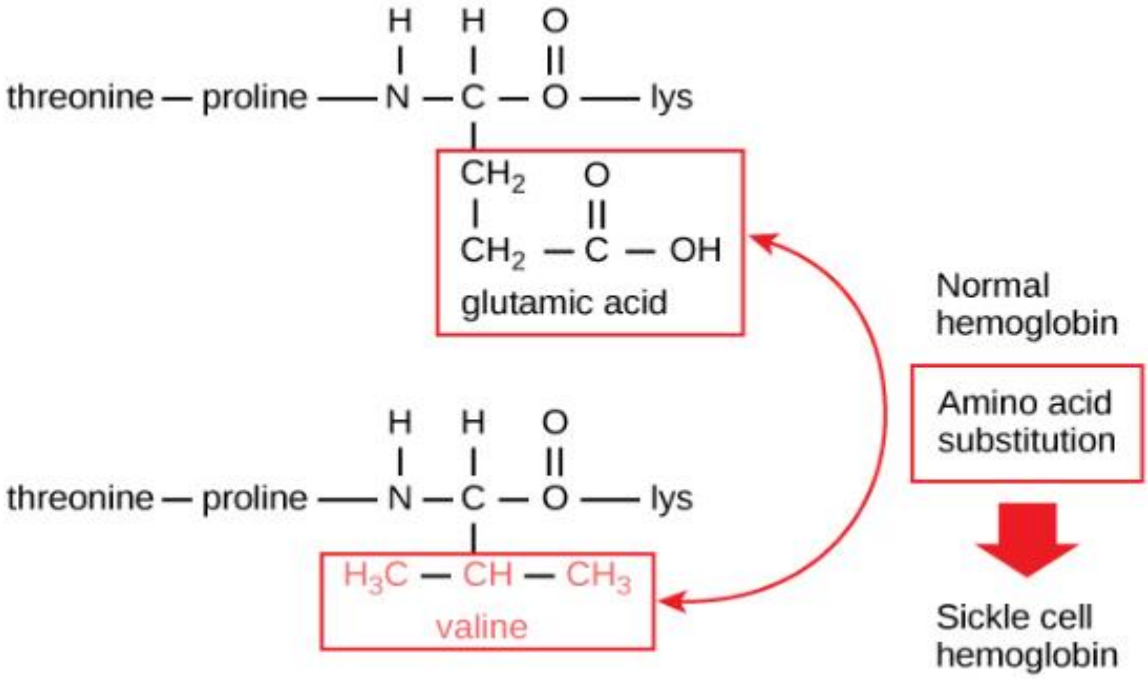


Primary structure

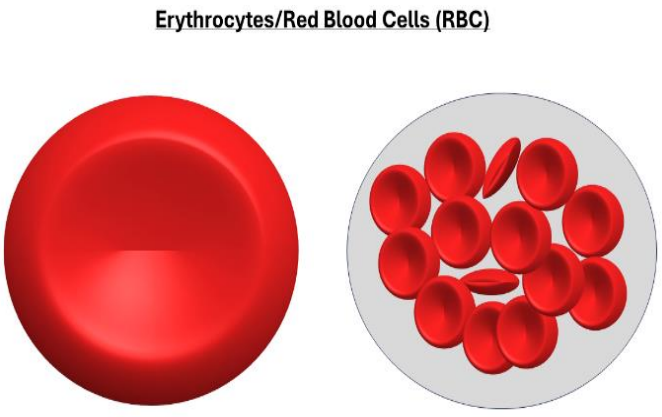
-The sequence of a protein is determined by the DNA of the gene that encodes the protein .

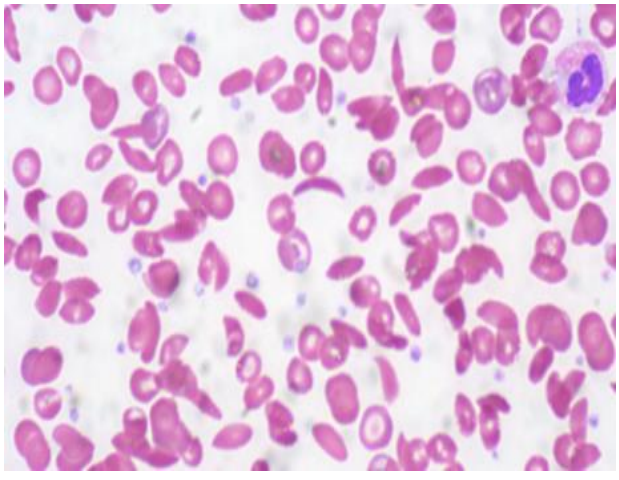
- A change in the gene's DNA sequence may lead to a change in the amino acid sequence of the protein.

-For instance, a single amino acid change is associated with **sickle cell anemia**, an inherited disease that affects red blood cells. In sickle cell anemia, one of the polypeptide chains that make up hemoglobin, the protein that carries oxygen in the blood, has a slight sequence change. The glutamic acid that is replaced by a valine.



These occur because the glutamic acid-to-valine amino acid change makes the hemoglobin molecules assemble into long fibers





What body fluids have protein?

NO	Body fluid	Number of proteins in dataset
1	Amniotic fluid	192
2	Bronchoalveolar lavage fluid	65
3	Cerebrospinal fluid	204
4	Milk	71
5	Nipple aspiration fluid	37
6	Plasma/Serum	418
7	Saliva	175
8	Seminal fluid	155
9	Synovial fluid	63
10	Tear	84
11	Urine	244
	Sum	1,708

Total Protein Test

The total protein test measures your albumin and globulin levels.

- High levels may mean you have inflammation or infection.

-Low levels may suggest kidney problems, malnutrition, and several other possible conditions.

Methods of measure protein

1-UV absorption

2-Biuret methods: detection of reduced copper.

3-Colorimetric dye based methods: direct detection of the color change

4-Fluorescent dye methods: direct detection of increase in fluorescence associated with the bound dye.

*Purpose of the total protein test

It's one of the tests that make up your comprehensive medical panel (CMP). It may be ordered if you have:

1- weight loss

2-Tiredness

3- edema: which is swelling caused by extra fluid in your tissues ,symptoms of kidney or liver disease

4- The total protein test measures the total amount (albumin ,globulin).

,This test is known as the "A/G ratio."

plasma proteins

plasma is the liquid medium of blood (55-60)% the main difference between plasma and serum is the presence or absence of fibrinogen.

* The term plasma proteins refers to the proteins of the blood plasma circulating between the blood and the interstitial fluid compartments.

-the plasma proteins can be separated into three groups—namely albumin, globulins and fibrinogen.

albumin

Albumin is exclusively synthesized by the liver.

Plasma albumin performs osmotic, transport and nutritive functions

1- Osmotic function : albumin plays a predominant role in maintaining blood volume and body fluid distribution. Decrease in plasma albumin level results

in a fall in osmotic pressure, leading to enhanced fluid retention in tissue spaces, causing edema.

2- Transport functions : Plasma albumin binds to several biochemically important compounds and transports them in the circulation. These include free fatty acids, bilirubin, steroid hormones, calcium and copper.

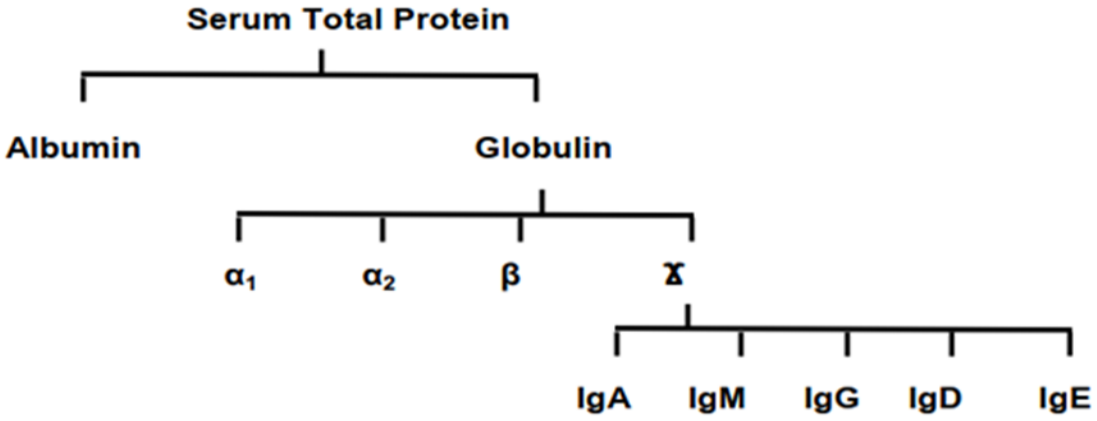
3-Nutritive functions : Albumin serves as a source of amino acids.

GLOBULINS

three types of globulin —alpha, beta, and gamma. Alpha and beta globulins are **transport proteins,** and perform other diverse functions. Gamma globulins have a vital role in **natural and acquired immunity** to infection.

IMMUNO GLOBULINS :- defense system

CLASSES OF IMMUNOGLOBULINS Humans have five classes of immuno-globulins—namely IgG, IgA, IgM, IgD and IgE.



Fibrinogen

Is an important soluble plasma clotting factor precursor, which is converted to a thread like protein called fibrin on contact with a sticky surface.

What Does Plasma Do?

Plasma is carry nutrients, hormones, and proteins to the different parts of the body.

1- It carries away the waste products of cell metabolism from various tissues to the organs responsible for detoxifying and/or excreting them.
2- -plasma is the vehicle for the transport of the blood cells through the blood vessels.
3- Clotting Factors and Inhibitors:The clotting factors in plasma cause a blood clot.
4- Plasma proteins keep the blood pH alkaline .
5- Plasma proteins can also supply amino acids if required by being broken down by macrophages.

What are abnormal proteins? Proteinopathy

proteinopathy (disease) , protein conformational disorder, or protein misfielding disease, is a class of diseases in which certain proteins become structurally abnormal, and thereby disrupt the function of cells, tissues and organs of the body.

- These include destabilizing changes in the primary amino acid sequence of the protein, post-translational modifications (such as hyper phosphorylation), changes in temperature or pH, an increase in production of a protein

-accumulate in organs or organ systems such as the heart, kidneys, nervous system or gastrointestinal tract.

* **What are the types of protein disorders?**

Protein misfolding is believed to be the primary cause of

1-Alzheimer's disease. is the most common cause of dementia.

2- Parkinson's disease. is a movement disorder of the nervous system that worsens over time.

3-Huntington's disease. The movement disorders related to Huntington's disease may cause movements that can't be controlled, called chorea. Chorea are involuntary movements the arms and legs, the face and the tongue.

4-Creutzfeldt-Jakob disease:- also known as CJD, is a rare brain disorder that leads to dementi.

Metabolism

Metabolism: “change" is the set of life-sustaining chemical reactions in organisms. **The three main functions** of metabolism are:

1-the conversion of the energy in food to energy available to run cellular processes;

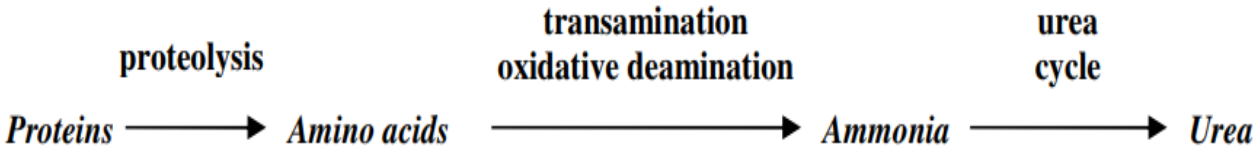
2-the conversion of food to building blocks of proteins, lipids, nucleic acids, and some carbohydrates.

3- the elimination of metabolic wastes.

Metabolic reactions may be categorized as

-catabolic—the breaking down of compounds (for example, of glucose to pyruvate by cellular respiration).

- anabolic—the building up (synthesis) of compounds (such as proteins, carbohydrates, lipids, and nucleic acids).



Amino acids

Amino acids are molecules that combine to form proteins. Amino acids and proteins are the building blocks of life. When proteins are digested or broken down, amino acids are the result. The human body then uses amino acids to make proteins to help the body:

1-Break down food

2-Grow

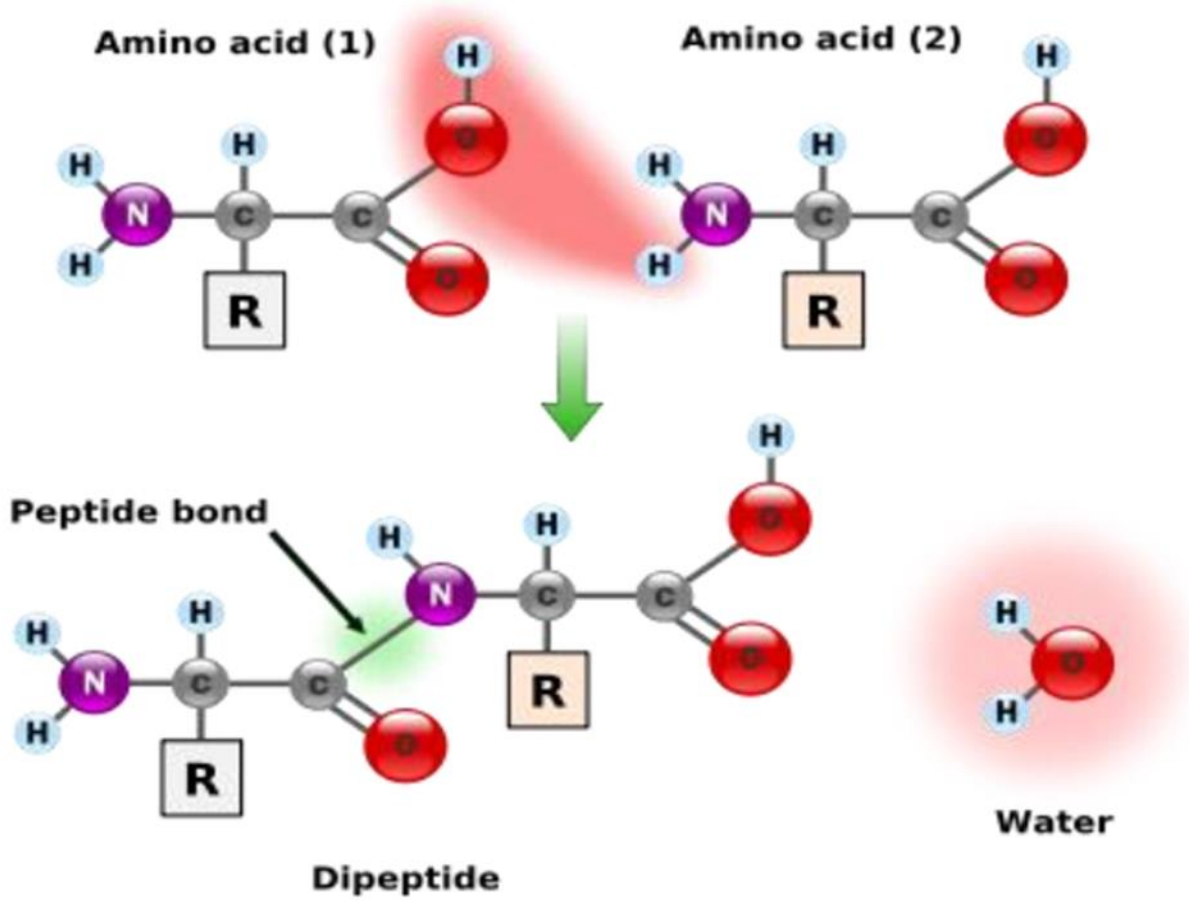
3-Repair body tissue

4-Perform many other body functions

Amino acid metabolism

Amino acids are a group of organic compounds containing two functional groups—amino and carboxyl. The amino group (—NH2)

is basic while the carboxyl group (—COOH) is acidic in nature.



amino acid catabolism

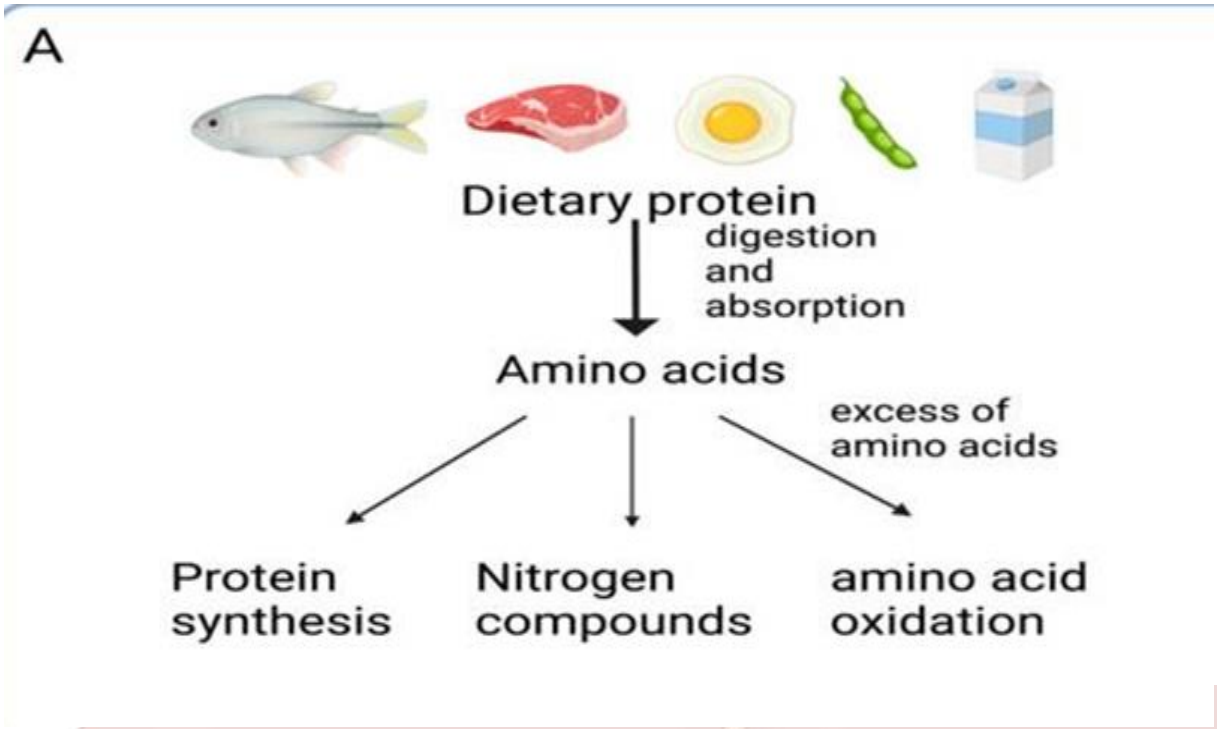
Upon fasting or when amino acids are ingested in excess of the amounts required, their catabolism serves as an energy source.

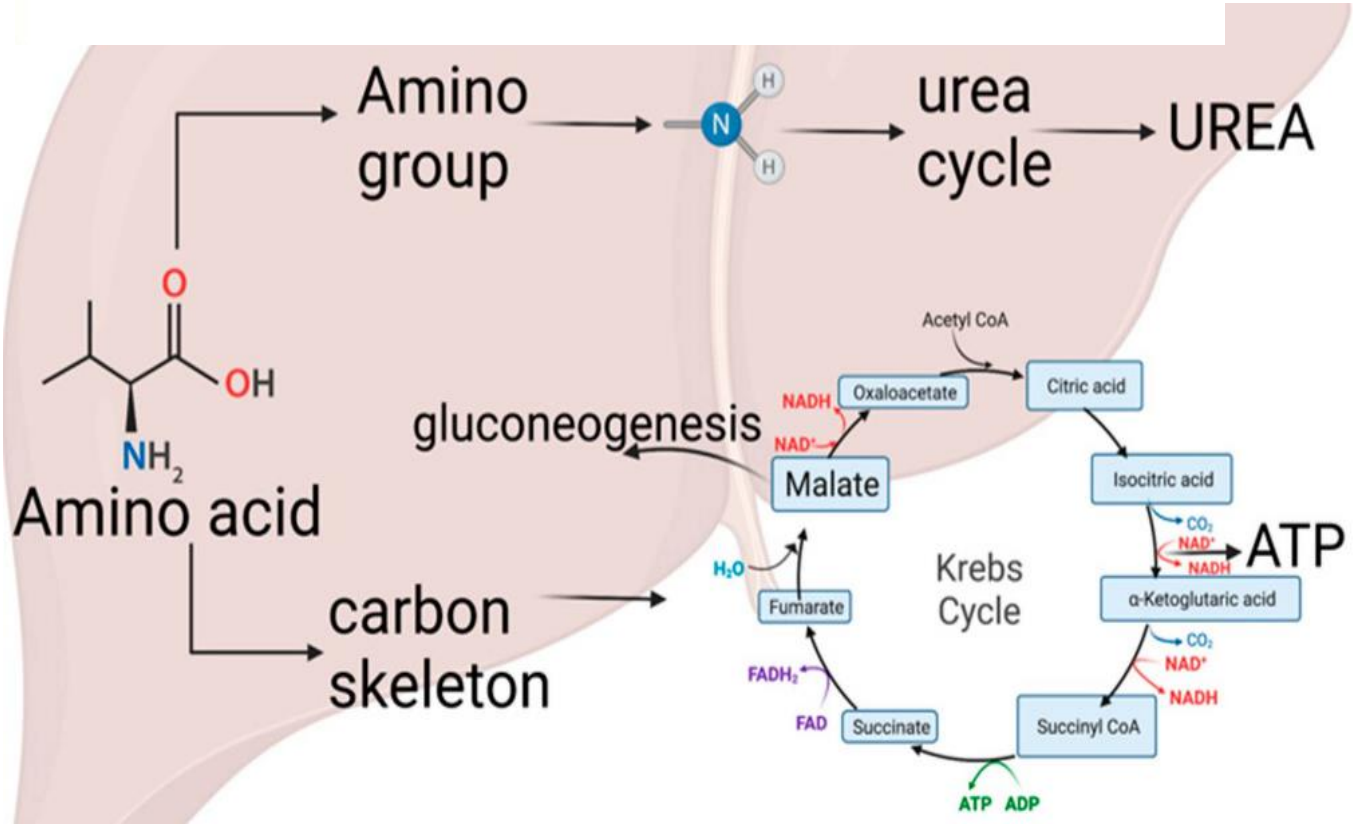
- When amino acids are used for energy production, they undergo the loss of their amino groups; their remaining carbon skeletons have two primary fates:

1- gluconeogenesis .

2-oxidation to synthesize ATP.

-For this reason, there must be a balance between the synthesis and continuous degradation of proteins in the body to ensure the maintenance of optimally functioning proteins.





* In the catabolism of most amino acids

- the first stage the removal of the α-amino group constitutes and occurs via two major enzymatic pathways: transamination and oxidative deamination.

- a second stage, the carbon skeletons of the amino acids are channeled into the tricarboxylic acid cycle to obtain energy in the form of ATP, and some serve as substrates for the gluconeogenic pathway.

Elimination of ammonia

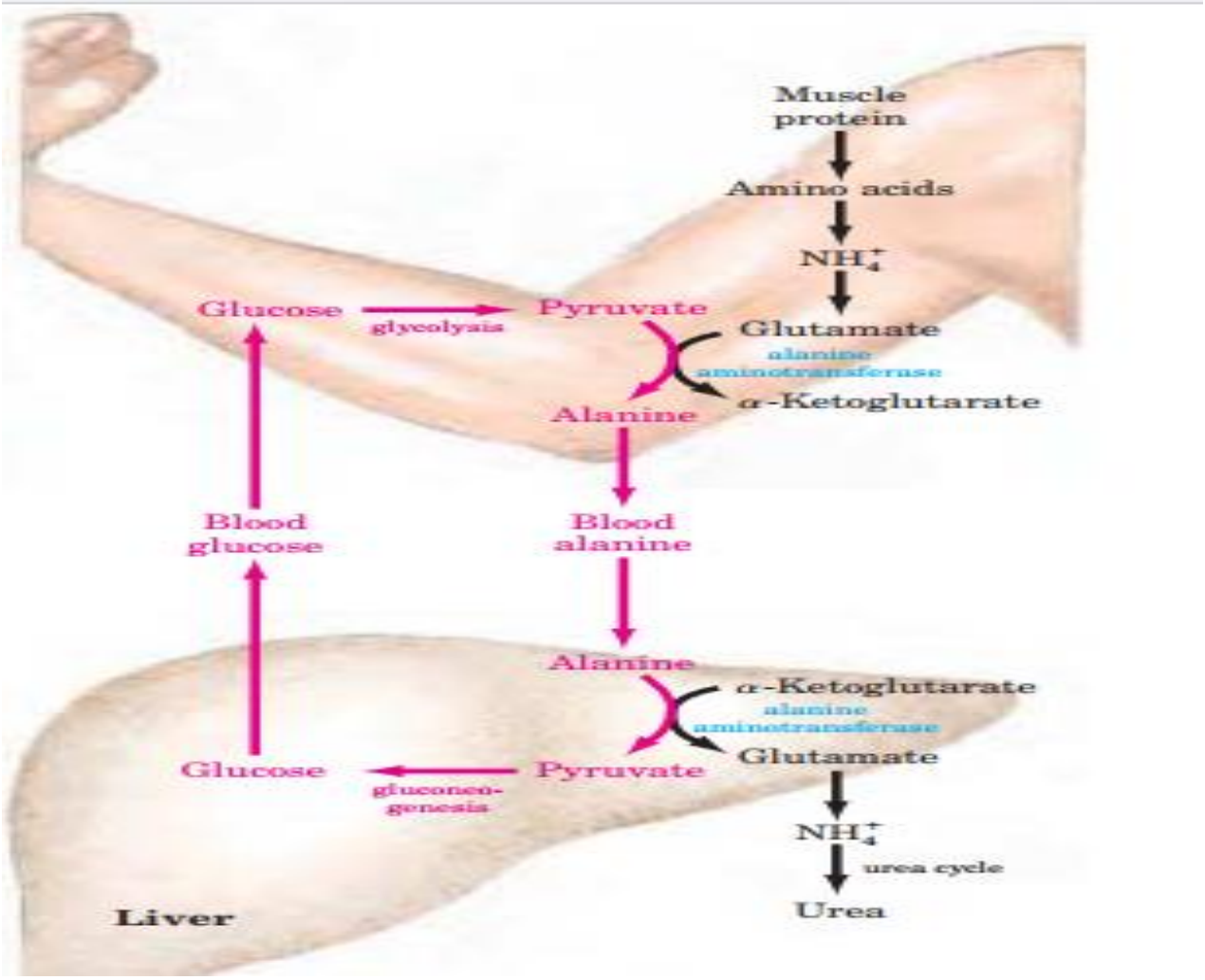
Ammonia can be produced by

1-the break-down of amino acids,

2- by the gut bacteria in humans.

- If the level of ammonia in the blood becomes too high, then it becomes toxic to the brain.

-The urea cycle removes ammonia from the blood and makes urea, which is eventually excreted as urine. This cycle is carried out by the cells of the liver.

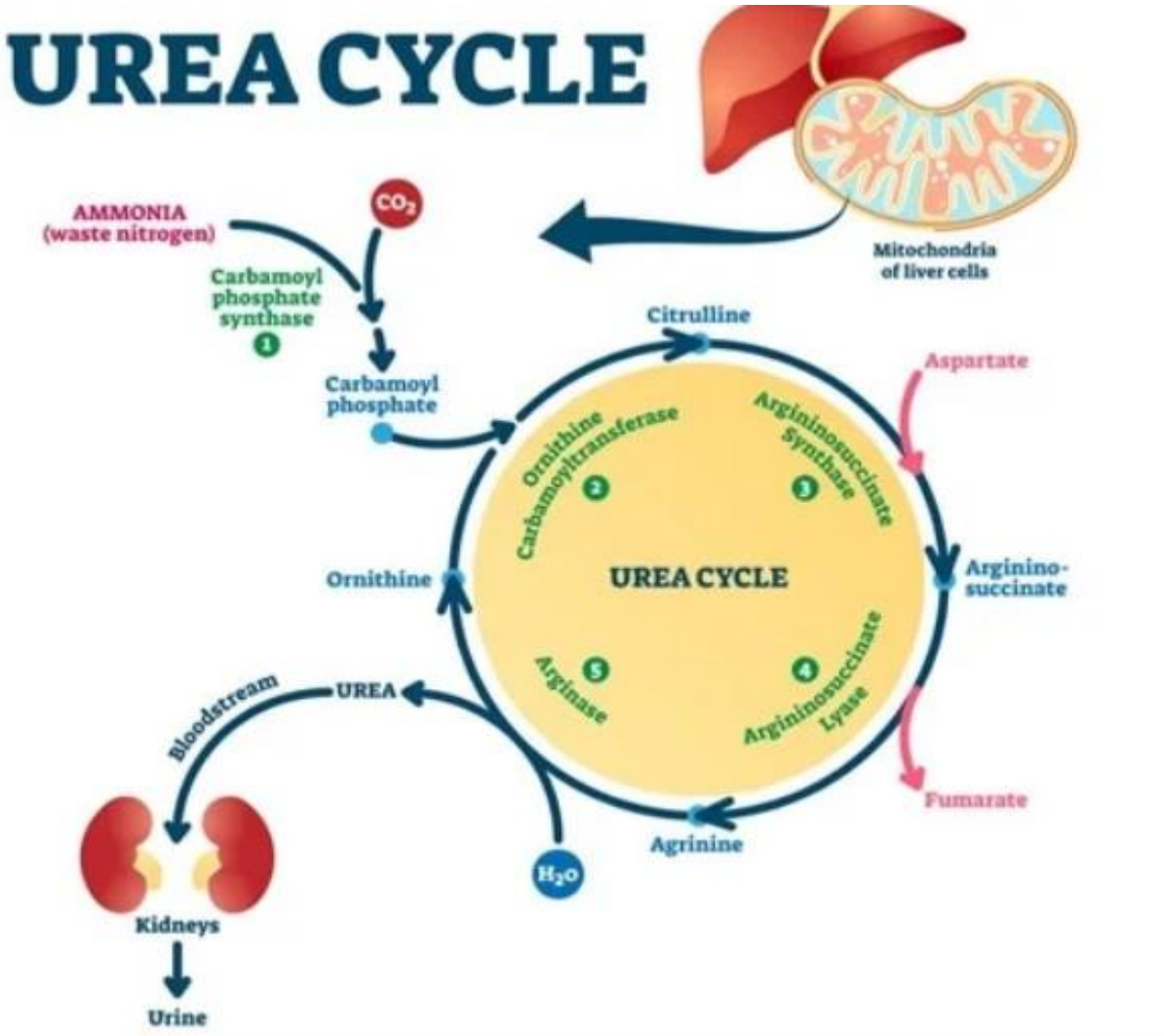


$$2CH_3CHNH_3^+COO^- + O_2 \rightarrow 2CH_3COCOO^- + 2NH_4^+$$

Alanine → Pyruvate

What is Urea Cycle?

The urea cycle, also known as the(ornithine cycle), is a vital metabolic pathway responsible for the conversion of ammonia into urea. It role in the body's mechanism to eliminate excess nitrogen.



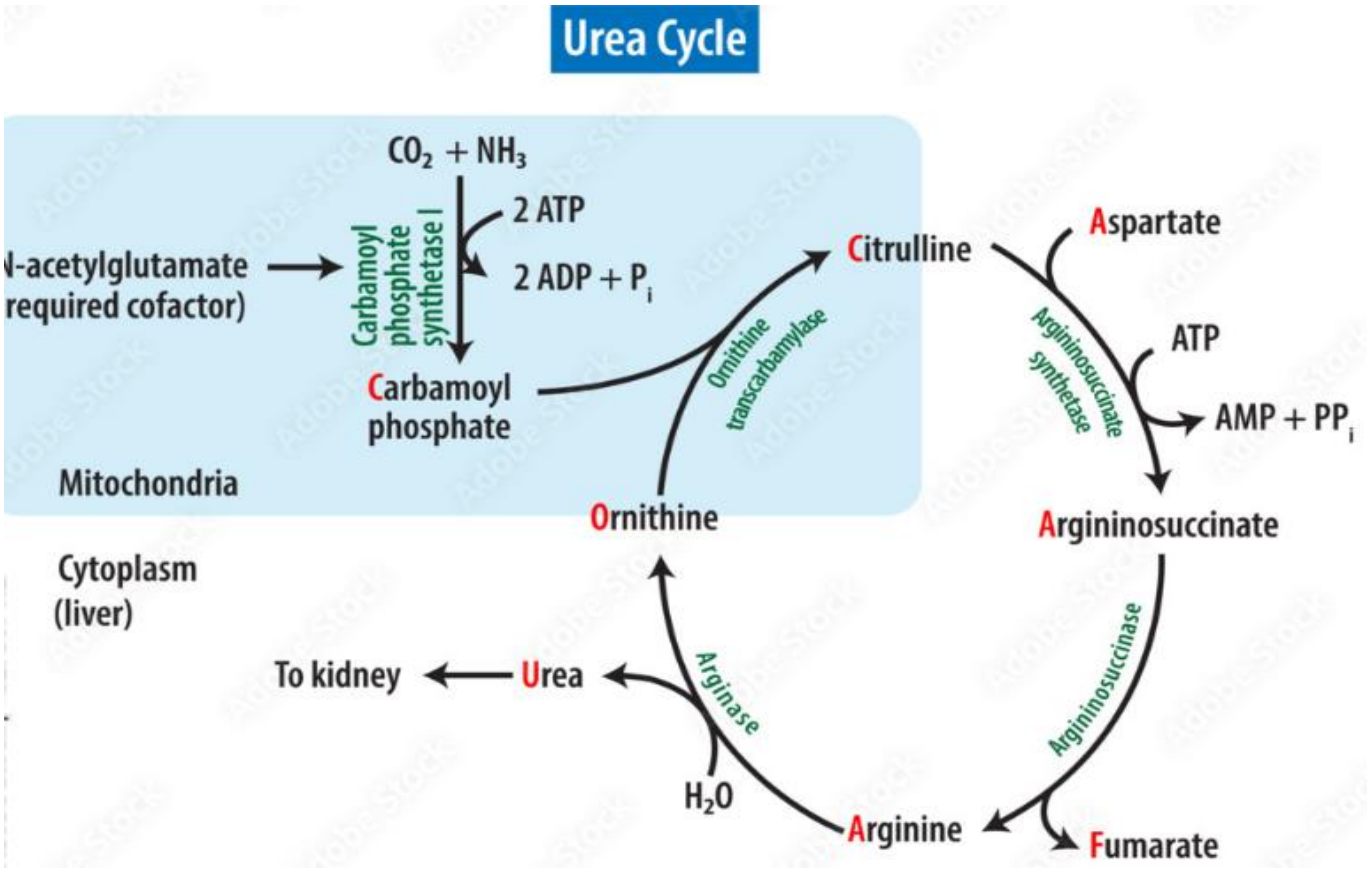
-Urea (H_2NCNH_2) is the major disposal form of amino groups derived from amino acids and accounts for about 90% of the nitrogen-containing components of urine.

-Thus, the overall equation of the urea cycle is:

$NH_3 + CO_2 + \text{aspartate} + 3\ ATP + 3\ H_2O \rightarrow \text{urea} + \text{fumarate} + 2\ ADP + 2\ Pi + AMP + PPi + H_2O$

Step by Step Reactions of the urea cycle

Step	Reactants	Products	Enzyme/Co-factors	Location
1	$NH3 + HCO_3^- + 2ATP$	carbamoyl phosphate + 2ADP + Pi	CPS1	mitochondria
2	carbamoyl phosphate + ornithine	citrulline + Pi	OTC (with zinc and biotin)	mitochondria
3	citrulline + aspartate + ATP	argininosuccinate + AMP + PPi	ASS	cytosol
4	Argininosuccinate	arginine + fumarate	ASL	cytosol
5	arginine + H2O	ornithine + urea	ARG1 (with manganese)	cytosol



Disorders of the Urea Cycle(UCD)

1-Genetic defects in the enzymes involved in this cycle can lead to a range of disorders.

2-These disorders are primarily characterized by an inability to effectively process ammonia, leading to its accumulation in the body. blood (hyperammonemia).

3-In a healthy person, the liver makes several enzymes to change nitrogen into urea, which is then removed from the body in urine. This process is called the urea cycle.

4- Untreated, the high amounts of ammonia can cause brain damage, coma and eventually death.

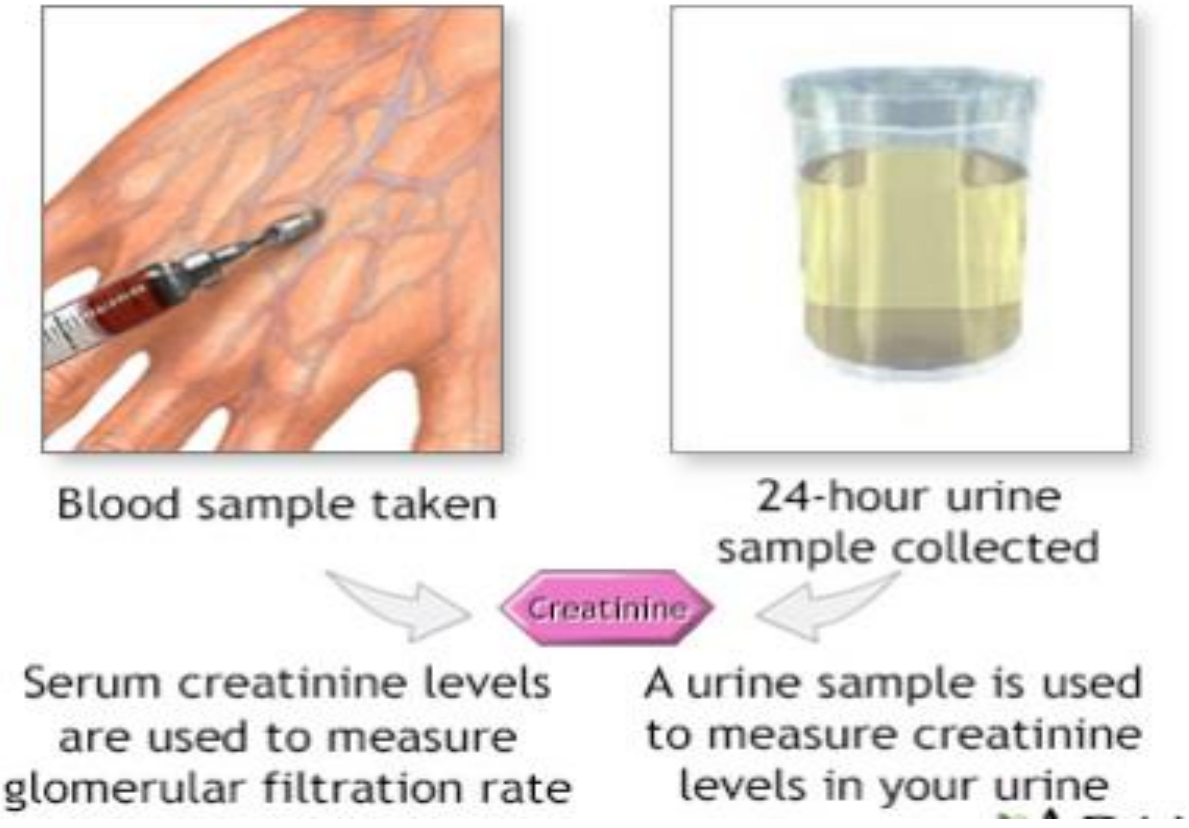
Non-protein compounds of nitrogen

Blood serum contains compounds of nitrogen other than proteins and peptides. **Urea**,**creatinine**, **uric acid**, **ammonia** are the most important of them and have implications in clinical biochemistry.

Creatinine

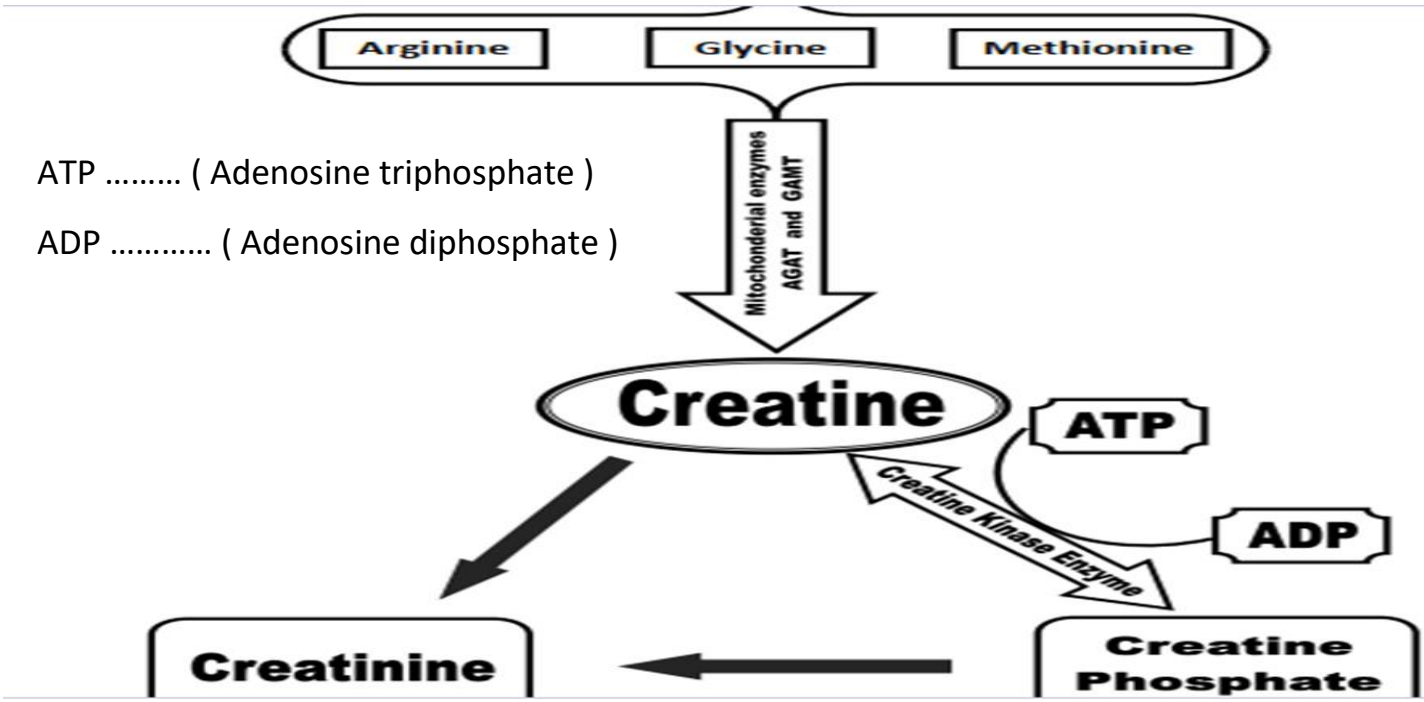
Creatinine is formed in muscles by irreversible non-enzymatic dehydration and cleavage of phosphate from creatine phosphate, which serves in muscle as a source of energy for muscle contraction .

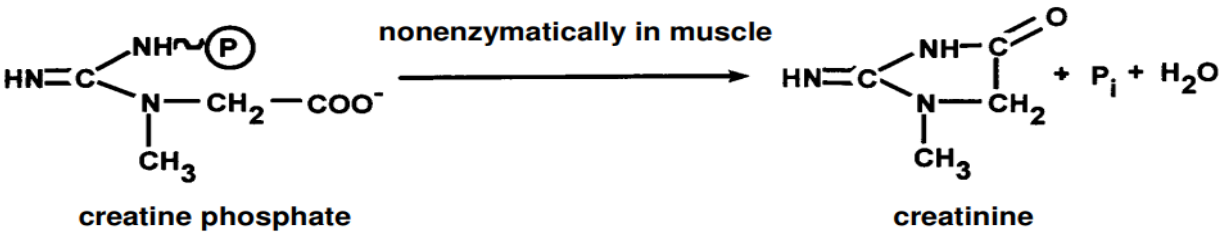
- The creatinine blood test measures the level of creatinine in the blood. This test is done to see how well your kidneys are working.
- Creatinine in the urine can be measured with a urine test.



ATP …… (Adenosine triphosphate)

ADP …… (Adenosine diphosphate)





Uric acid – blood

-Uric acid is a chemical created when the body breaks down substances called purines.

- Purines are normally produced in the body and are also found in some foods and drinks.

-Most uric acid dissolves in blood and travels to the kidneys. From there, it passes out in urine.

If your body produces too much uric acid or does not remove enough of it, you can get sick. A high level of uric acid in the blood is called hyperuricemia.

* What Uric Acid Level Indicates Hyperuricemia?

- A uric acid level of 6.8 mg/dl or higher means you have **hyperuricemia**.

- A normal serum urate level for females is 1.5 to 6.0 mg/dL.

- For males, it is 2.5 to 7.0 mg/dL.2

Enzymes

An enzyme is a protein that acts as a biological catalyst by accelerating chemical reactions.

-The study of enzymes is called enzymology.

Main characteristics of an enzyme:

1-It is a protein and destroyed by heating.

2-It acts only on one kind of substance called the substrate. and the enzyme converts the substrates into different molecules known as products.

3-It acts as a catalyst, so it can be used again and again.

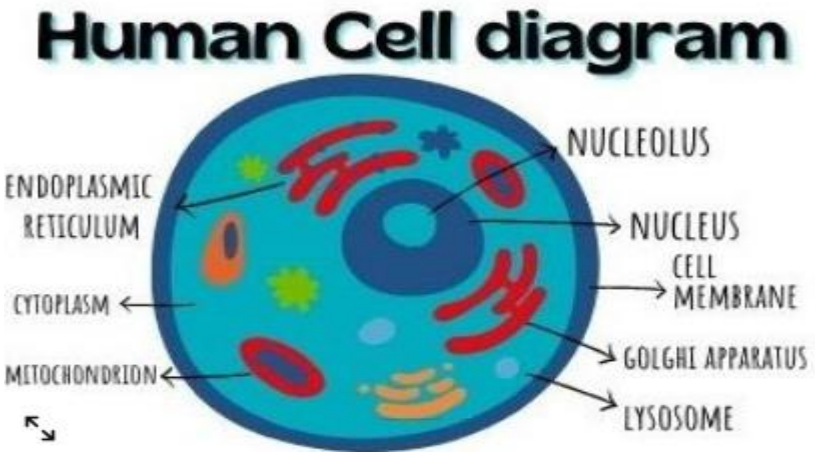
4-It only affects the rate of a chemical reaction.

- Almost all metabolic processes in the cell need enzyme catalysis in order to occur at rates fast enough to sustain life.
- Most commonly used enzyme names have the suffix “ase ”attached to the substrate of the reaction (for example, glucosidase and urease).
- Any substance that speeds up a biochemical reaction without being a reactant is called a catalyst. The catalysts for biochemical reactions in living systems are known as enzymes. They are thus known as biological catalysts or biocatalysts.

* Enzymes are sometimes considered under two broad categories :

(a) Intracellular enzymes –They are functional within cells where they are synthesized.

(b) Extracellular enzymes – These enzymes are active outside the cells.



Clinical Enzymology

clinical enzymology refers to measurement of enzyme activity for the diagnosis and treatment of diseases.

- In general, most enzymes are present in cells at much higher concentrations than in plasma.

- Measurement of their levels in plasma indicates whether their tissue of origin is damaged leading to the release of intracellular components into the blood.

•Factors Affecting Results Of Plasma Enzyme Assays

A-Analytical factors:_

1. substrate concentration 2. product concentration

3. enzyme concentration 4. reaction temperature

5. reaction pH 6. presence of activators or inhibitors

B- Non-disease factors

1. Age: Plasma AST activity is higher in the neonatal period than in adults. Plasma ALP activity is higher in children than in adults.

2. Sex : Plasma GGT activity is higher in men than in women. Plasma CK activity is also higher in males.

3. Race/ethnicity: Plasma CK activity is higher in black people than in whitepeople.

4. Physiological conditions: Plasma ALP activity rises during the last trimester of pregnancy.

5. Several enzymes, such as AST and CK, rise in plasma during and immediately after labour or strenuous exercise.

***Cofactors**

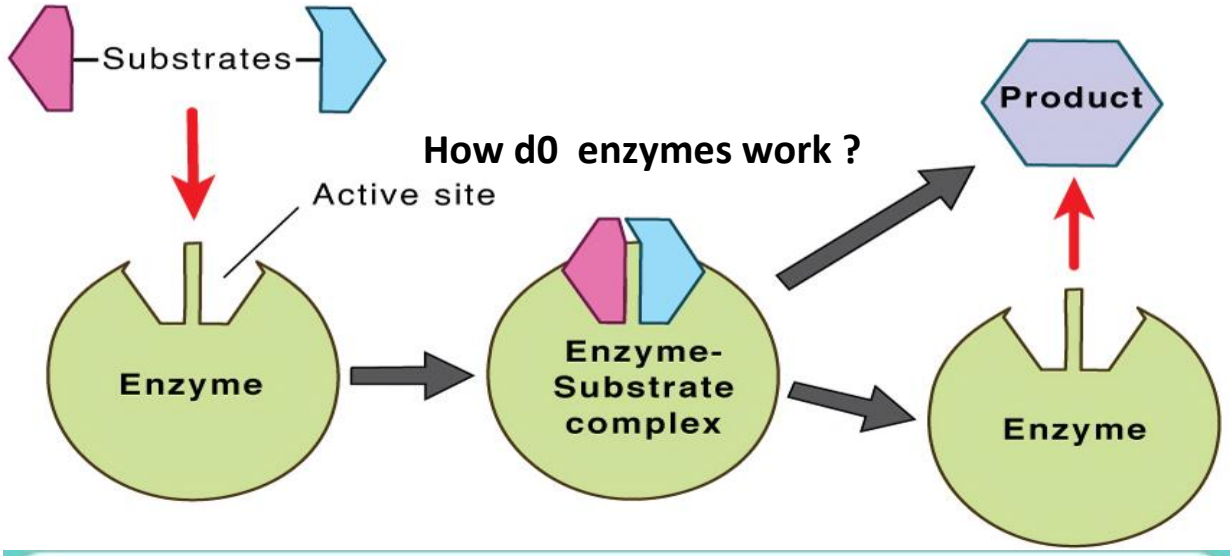
Some enzymes require a non-protein part for their functioning, known as cofactors. Cofactors are essential for the functioning of the enzyme. An enzyme devoid of a cofactor is an apoenzyme, while an enzyme with its cofactor is called a holoenzyme.

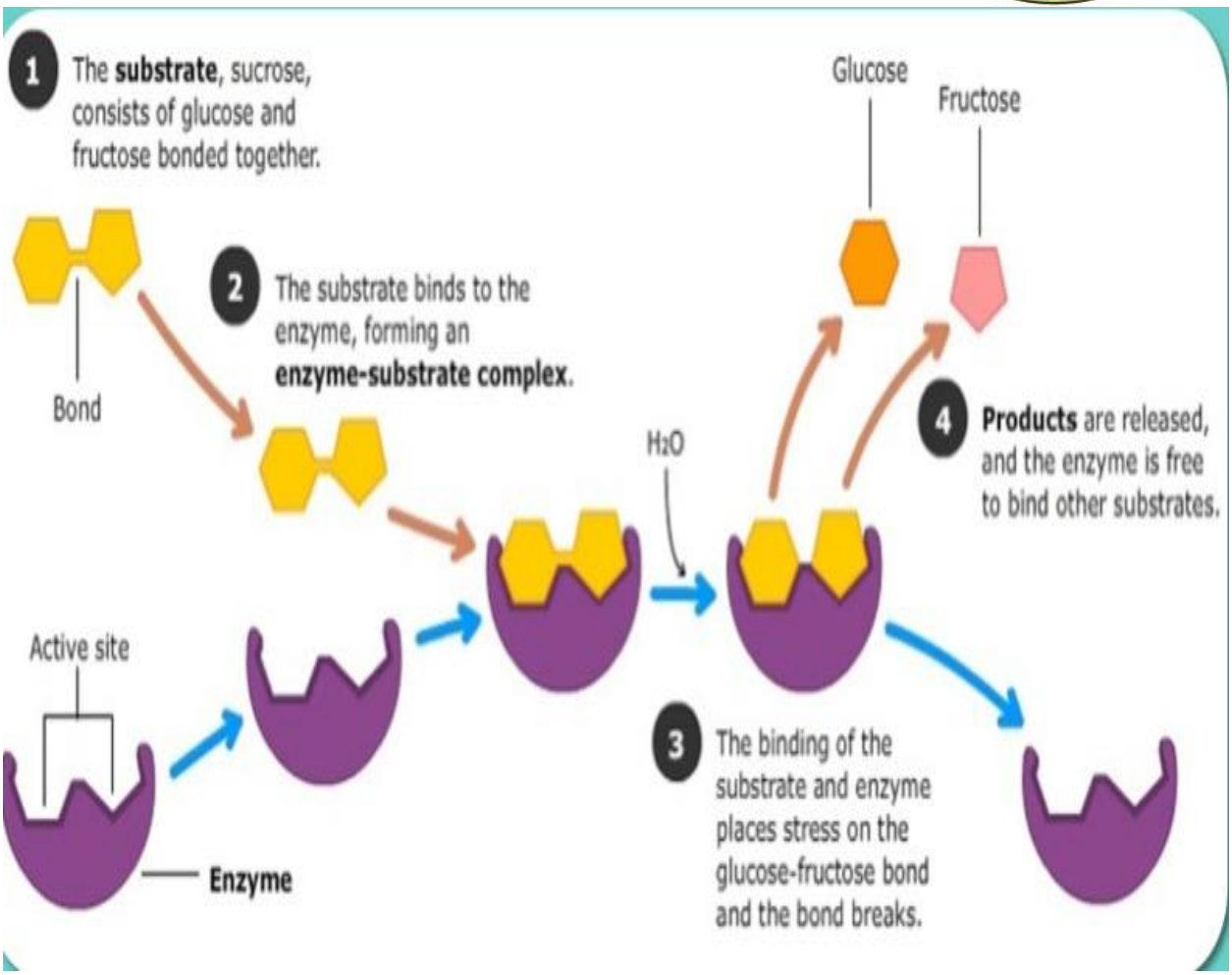
there are <u>three types</u> of cofactors:

1) Prosthetic Groups: They remain tightly bound to an enzyme all the time. Example FAD

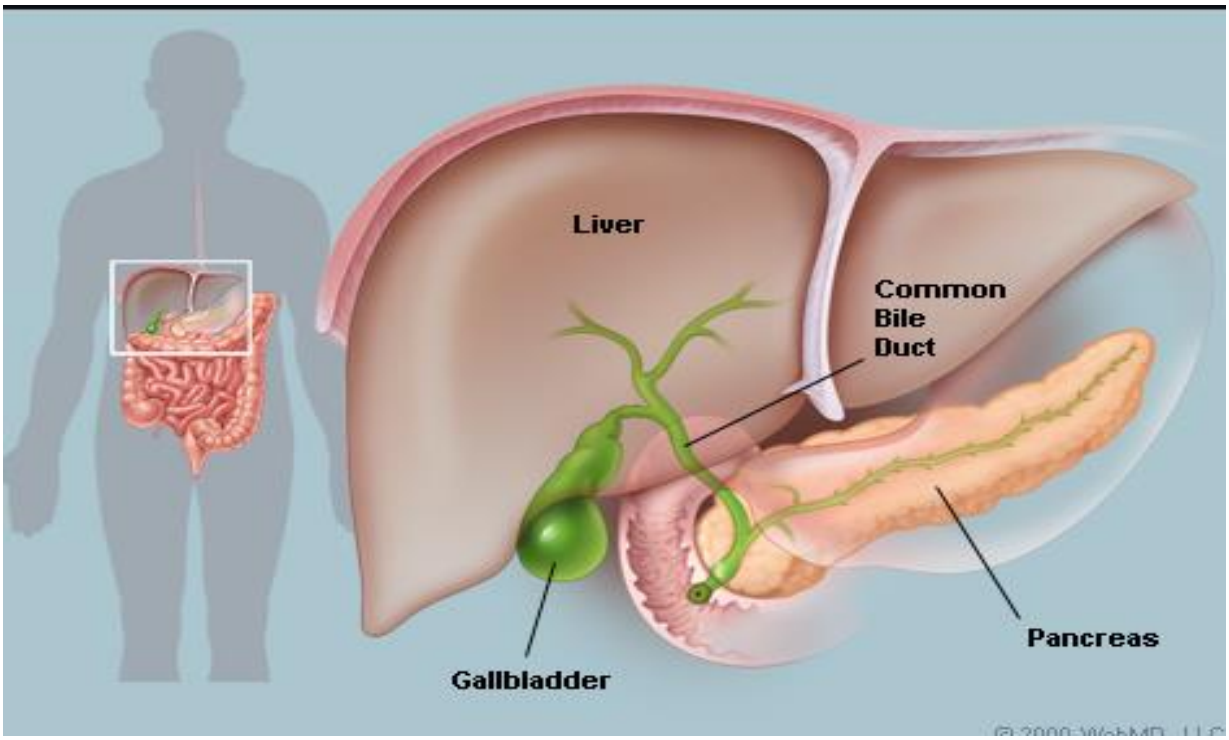
2) Coenzyme: They bind to an enzyme only during catalysis. Example NAD+

3) Metal Ions: Certain enzymes require a metal ion at their active site for catalysis. Example Zn2+





Liver



Liver structure / Overview of Liver

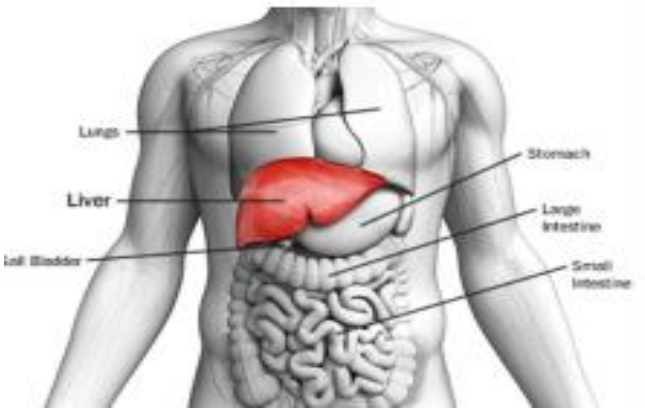
*Largest internal organ in human body.

* Located in the right upper quadrant of the abdominal cavity below the diaphragm.

* A reddish brown organ, divided into 4 lobes.

* Contains an extensive Reticuloendothelial system for the synthesis and breakdown of blood cells.

- Weighs 1.44 - 1.66 kg
- Connected to hepatic artery and portal vein
- Capable of regeneration
- Many functions
- Site of many diseases



Functions of the Liver

1- Metabolizes, or breaks down, nutrients from food to produce energy, when needed.

2-Removes potentially toxic by products of certain medications.

3- Produces most proteins needed by the body.

4- Produces bile, a compound needed to digest fat and to absorb vitamin A, D, E and K.

5- Synthesis of cholesterol, phospholipids and triglycerides.

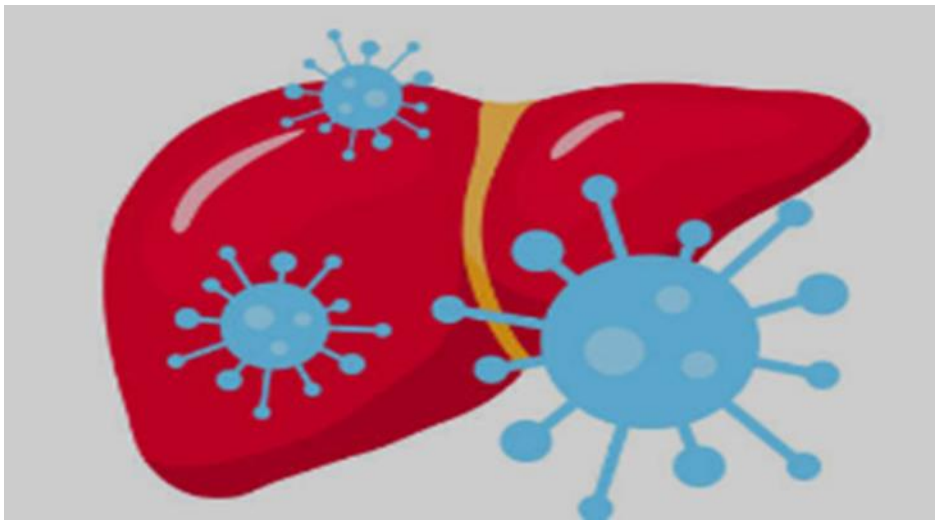
6-Produces most of the substances that regulate blood clotting.

7-Helps the body fight infection by removing bacteria from the blood.

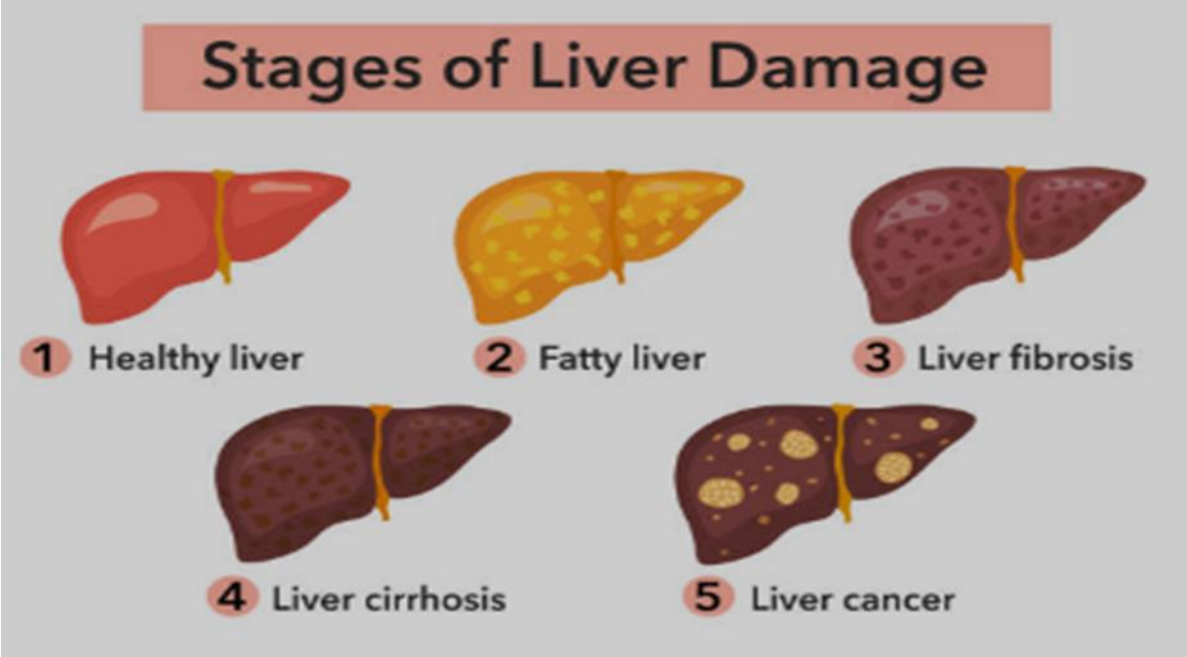
8-Prevents shortages of nutrients by storing vitamins, minerals and sugar.

The most common disease processes that affect the liver are:

-hepatitis, which may be acute or chronic, or a combination of both, in which there is damage to and destruction of liver cells. There are five viruses that cause the different forms of viral hepatitis: hepatitis A, B, C, D and E.



- cirrhosis, in which fibrosis leads to shrinkage of the liver, decreased numbers of hepatocytes and hence decreased hepatocellular function. The most common causes are hepatitis and other viruses, and alcohol abuse.



*** Patients with liver disease often present with characteristic symptoms and signs, particularly jaundice, the yellow-orange discolouration of the skin caused by a high plasma concentration of bilirubin.**

Clinical biochemistry laboratory blood tests

What is the benefit of laboratory blood tests in clinical biochemistry?

1- Provide information about the state of a patient's liver.

2- Can detect presence and follow progress of liver disease.

3- A request for LFTs will provide results for enzymes, bilirubin and proteins.

4-Can assist in differentiating biliary tract obstruction, acute, and chronic disease.

5-To support doctors in diagnosing and treating diseases.

Liver enzymes

Enzymes For Diagnosis Liver diseases

A- Markers of hepatocellular damage ALT , AST:-Enzymes which are normally present inside the hepatocytes released into the blood when there is a hepatocellular damage.

B. Markers of cholestasis:-

1- Alkaline phosphatase, ALP

2 -Gamma glutamyl transferase (GGT) :

- It is involved in amino acid transport across the membranes.

- Gamma-glutamyl-transferase is found mainly in biliary ducts of the liver, kidney and pancreas. Y-GGT increased in liver diseases especially in obstructive jaundice.

3- 5-nucleotidase: The enzyme hydrolyses nucleotides to nucleosides at an optimum pH of 7.5. increased in hepatitis and highly elevated in biliary obstruction. unaffected by bone disease.

Types of Liver Enzymes: -

1-Alanine aminotransferase (ALT): Also known as serum glutamate-pyruvate transaminase (SGPT), it breaks down amino acids and supports the production of energy.

2-Aspartate aminotransferase (AST): Also known as serum glutamic-oxaloacetic transaminase (SGOT), this enzyme plays a key role in metabolizing amino acids.

4-Alkaline phosphatase (ALP): It plays a role in developing hard tissue and maintaining bone health. The alkaline phosphatases are a group of

enzymes that hydrolyse organic phosphates at high pH. They are present in most tissues , the cells of the hepatobiliary tract, intestinal wall, renal tubules and placent.

5-Gamma-glutamyl transferase (GGT): This enzyme helps metabolize glutathione, an antioxidant that plays a role in immunity and cell repair.

6-Lactate dehydrogenase (LDH): Present in almost all your body tissues, LDH helps cells make energy.

ALP Levels:- ALP is present in the bones as well as the liver. Elevated levels are associated with:

1-Cirrhosis 2-Hepatitis 3-Blockage in bile ducts

Lower levels of ALP in the body may be caused by nutritional deficiencies.

Gamma glutamyl transferase (GT or GGT)

Gamma-glutamyltransferase (GGT) is a liver enzyme, which is located on the plasma membranes of most cells and organ tissues, but more commonly in hepatocytes, and as a marker of excessive alcohol.

- Produced by liver, kidney and pancreas.
- It is used to confirm hepatitis.
- Increases in cholestasis.
- Alcohol and drugs such as phenytoin (anti-epileptic) induce enzyme activity.
- Eight hours fasting is recommended because GGT drops after eating.

GGT Levels

GGT levels are often checked to assess alcohol abuse or liver damage. It may indicate one of the following underlying issues:

1- Hepatitis 2- Cirrhosis 3- Pancreatitis

4-Diabetes 5- Heart failure 6- Alcohol use disorder (AUD)

Lower levels of GGT are not a sign of a health issue.

Aminotransferases (AST & ALT)

▪ Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT), Present in cells and leak into the blood when cells are damage due to inflammation, virus infection and cell death.

▪ AST is synthesized by liver cells, cardiac muscle and skeletal muscles.

▪ AST is less sensitive biomarker than ALT for liver damage.

▪ Myocardial infarction (heart attack) and muscle damage lead to increase AST level in serum.

What is aspartate transferase (AST)?

Aspartate transferase (AST), also known as aspartate aminotransferase, is an enzyme that exists in your liver, heart, brain, pancreas, kidneys, muscles and many tissues in your body.

What is an AST blood test? : to help assess the health of your liver.

- Common names for an AST blood test include:

Aspartate transferase (AST). Aspartate aminotransferase (AST).

Serum glutamic-oxaloacetic transaminase. SGOT.

Aspartate transaminase.

What does it mean if my AST level is high?

A high AST level may indicate any of the following liver conditions:

1-Alcohol-induced liver injury. 2 -Hepatitis (liver inflammation).

3-Cirrhosis (scarring of the liver). 4 -Taking medications that are toxic to your liver.

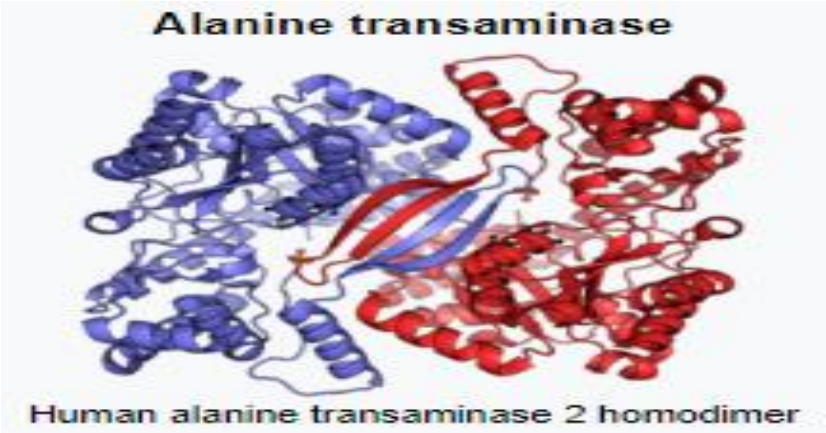
5-Liver tumor or liver cancer.

Alanine aminotransferase (ALT, SGPT)

-Alanine aminotransferase (ALT) is generally the most useful enzyme for identifying the presence of hepatocellular damage.

-Alanine aminotransferase (ALT) is the clinical chemistry gold standard for detection of liver injury or hepatotoxic effects.

-ALT is commonly measured clinically as part of liver function tests.



How is aspartate transferase (AST) different from alanine transferase (ALT)?

While both are known as liver enzymes, AST is found in more parts of your body than ALT. For this reason, higher-than-normal levels of ALT tend to be a more specific indicator of liver conditions than higher-than-normal AST levels.

Alkaline phosphatase (ALP)

▪ Liver is not sole source of ALP activity.

▪ Present also in bile duct, bone, small intestine, placenta and kidney.

▪ Normal physiological elevation during growing children and during pregnancy (3rd trimester of pregnancy).

▪ Increases in

1-Cholestasis (flow of bile from liver is reduced or blocked)

2- Inflammation 3-Cirrhosi 4-Alcoholic hepatitis

Bilirubin

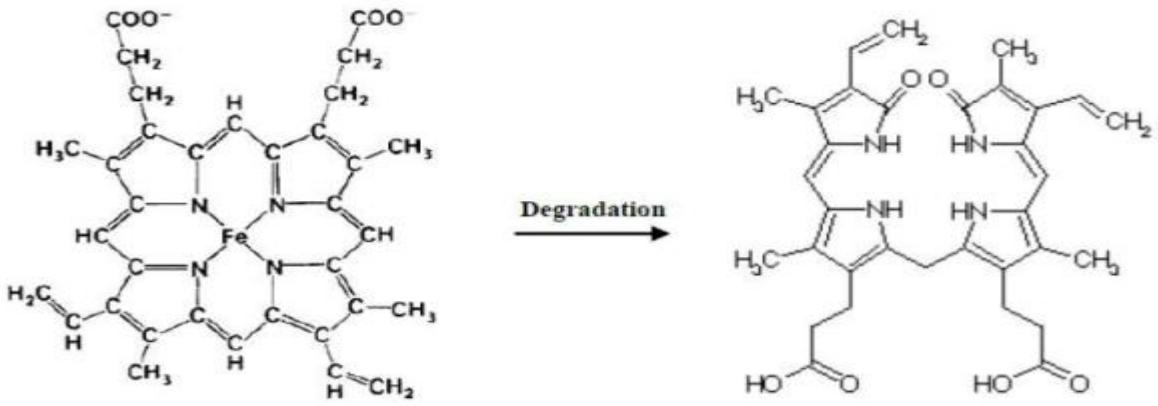
▪ Bile pigment

▪ Bilirubin produced from haem degradation, mainly found in haemoglobin

▪ Insoluble in water and is transported in the blood bound to albumin

▪ Taken up by liver cells and conjugated (more water soluble)

▪ Conjugated bilirubin excreted into bile to help in food digestion.



Heam
(Fe-protoporphyrin IX)

Bilirubin
(lipophilic)

Type of bilirubin in serum

1-Direct bilirubin is conjugated or water soluble bilirubin (rapidly reaction).

2-Indirect bilirubin is unconjugated or water insoluble bilirubin (slowly reaction).

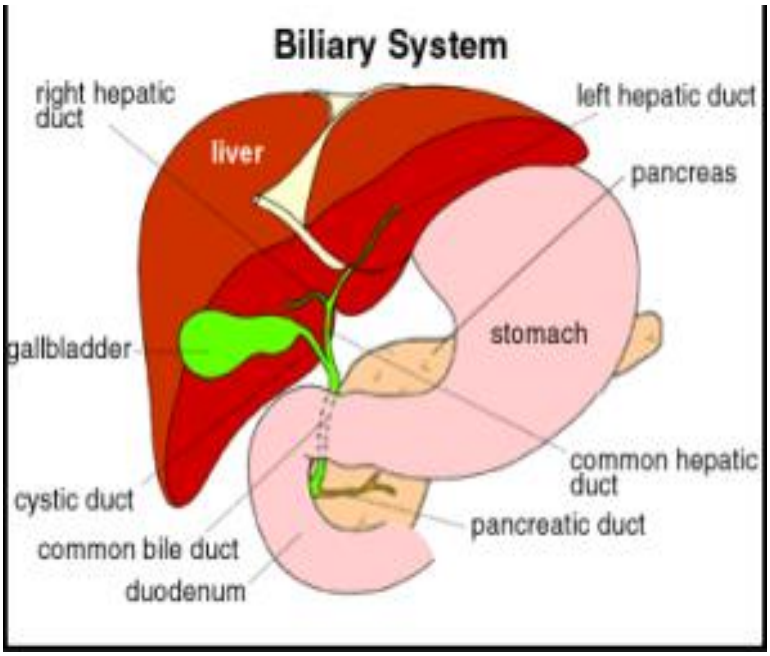
▪ Both conjugated and unconjugated bilirubin are measured given total bilirubin.

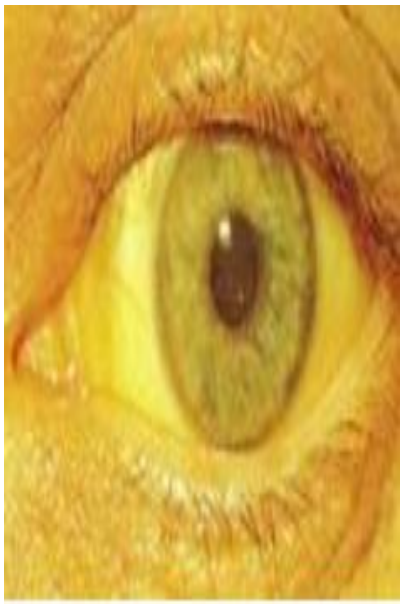
▪ Unconjugated bilirubin calculated by subtracting Direct from total so called indirect.

▪ Knowing the level of each type of bilirubin has diagnostic important. ..

Jaundice

- Jaundice due to increased levels of bilirubin in bloodstream
- Yellow colour of skin or sclera
- Detectable when bilirubin concentration is > 40 µmol/L





Three main reasons for Jaundice

1- Haemolysis

▪ Increased bilirubin production caused by haemolysis gives unconjugated hyperbilirubinemia

▪ Commonly happen in babies

▪ Bilirubin is neurotoxic (high levels in babies can result in brain damage)

▪ A rapidly rising bilirubin in a neonate should be carefully monitored

▪ Phototherapy used to breakdown bilirubin if > 200 µmol/L

2- Failed conjugation

A-Result of hepatocellular damage due to cancer , cirrhosis or hepatitis

B- Bilirubin that is conjugated is not efficiently secreted into bile but leaks to blood

C-Most common causes of acute jaundice, as a result of hepatocellular damage,

seen in adults are:

- Viral hepatitis - Paracetamol poisoning

3. Biliary obstruction (cholestasis)

A- Gallstones can partially or fully block the bile duct which prevents passage of bilirubin into intestine.

B-Direct bilirubin will back to liver and then to circulation elevating its level in blood and urine.

C- If blockage complete, bilirubin and ALP are raised.

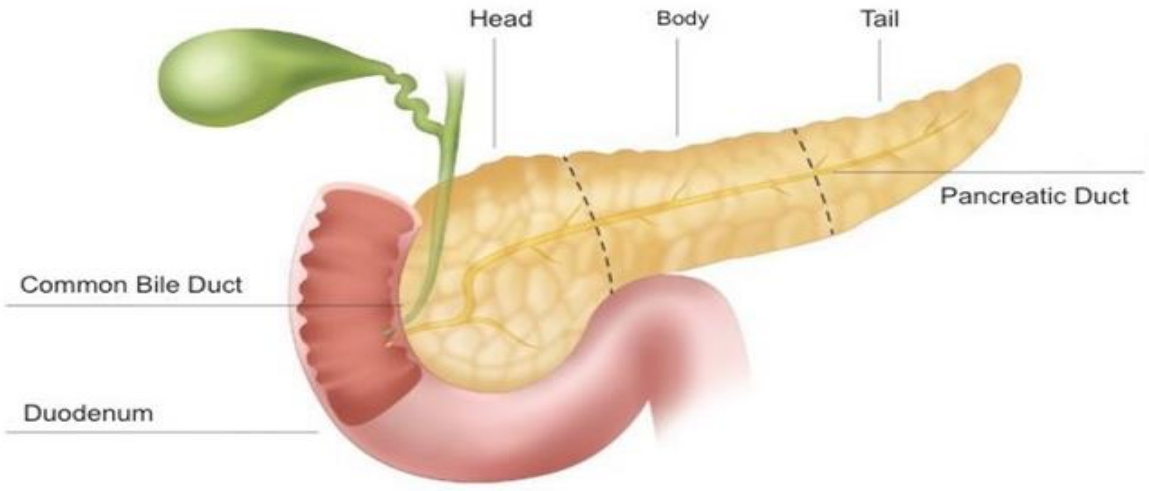
D- If blockage partial, bilirubin may well be within the reference range.

Diagnostic Enzymes In Different Diseases

What is the benefit of estimating enzymes in people?
Enzyme estimations are helpful in the diagnosis of:-

1) Liver diseases	2) Myocardial Infarction	3) Muscle diseases
4) Bone diseases	5) Cancers	6) GI Tract diseases

Enzymes For Diagnosis Pancreatic Diseases



1. Amylase

- catalyzes the hydrolysis .

- Plasma amylase is derived from the pancreas and salivary glands. Thus, pancreatic juice and saliva contain high concentration of amylase.

- Estimation of plasma amylase activity is mainly use to diagnosis of acute pancreatitis.

- **Causes of Raised Plasma Amylase Activity**

1- Acute pancreatitis. 2– Severe glomerular impairment.

3-Acute abdominal disorders. 4-Inflammation of the gall bladder.

5- Perforated peptic ulcer. 6- Intestinal obstruction.

7-Salivary gland disorders .

2. Lipase

- Lipase is a single chain glycoprotein .

- Lipase is derived from the pancreas but is more specific for pancreatic pathology than amylase.

- lipase has a longer half-life than amylase , therefore may be more useful in the diagnosis of acute pancreatitis and carcinoma of the pancreas.

- serum amylase is increased in mumps, pancreatic disease or due to

some other cause, whereas lipase is increased only in pancreatitis.

-Therefore, the determination of both amylase and lipase together

helps in the diagnosis of acute pancreatitis.

3. Trypsin

-Trypsin is a serine proteinase that hydrolyze the peptide bonds formed by the carboxyl groups of lysine arginine with other amino acids.

-Increased in pancreatic disease.

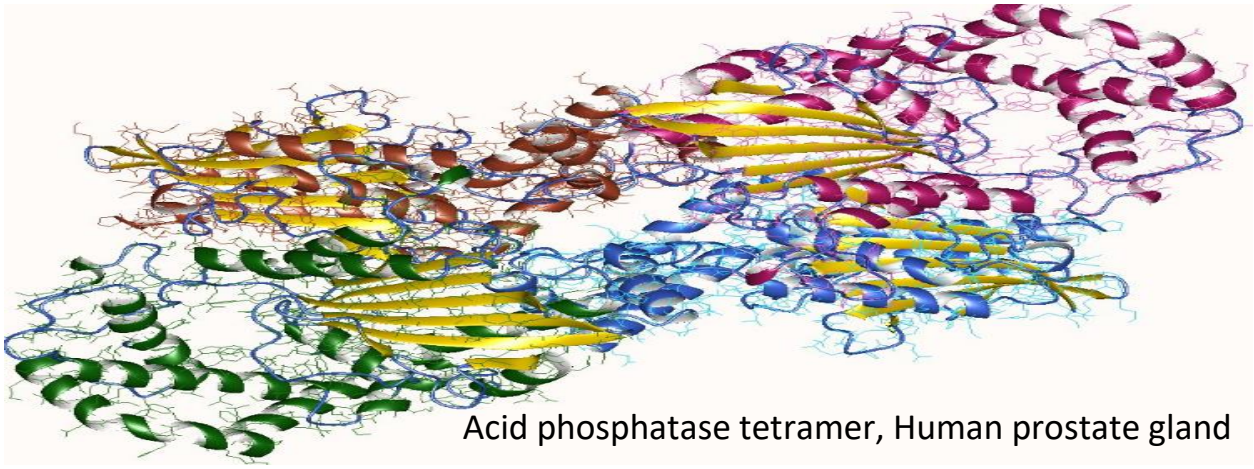
Enzymes For Diagnosis Of Prostate Diseases

- **Acid Phosphatase(ACP)** :Include all phosphatases that hydrolyze

phosphate esters with an optimum pH of less than 7.0.

- It is produced by Primarily in prostate gland. It is also found in erythrocytes, platelets,leukocytes, bone marrow, bone, liver, spleen, kidney, and intestine.

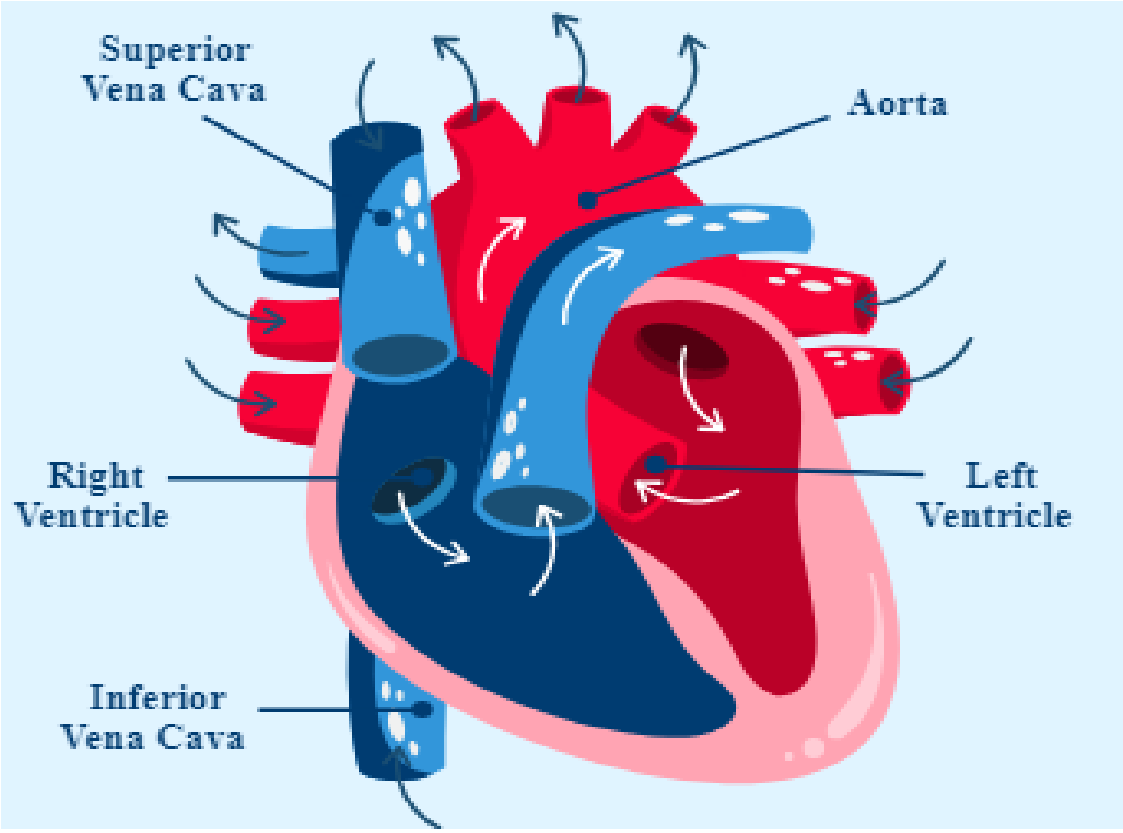
The ACP test is used primarily to diagnose and assess conditions such as cancer of the prostate (diagnose and monitor the effect of the treatment), certain bone diseases (Paget's disease), prostatitis (infection or inflammation of the gland), hyperparathyroidism, and benign hypertrophy of the prostate gland (BPH).



Acid phosphatase tetramer, Human prostate gland

Heart

heart is a vital organ. It is a muscle that pumps blood to all parts of your body. The blood pumped by your heart provides your body with the oxygen and nutrients it needs to function. Your heart is about the size of a clenched fist, and weighs between 300 and 450 g.



Major cardiac enzymes and proteins

Certain enzymes (CPK, LDH, and SGOT) are released from the heart muscle cells when it is injured ("heart attack").

Myoglobin	LDH (also called LD)
CPK (also called CK) Creatinine kinase	Troponin

*Myoglobin: - is an iron- and oxygen-binding protein found in the muscle tissue

and in almost all mammals. It is related to hemoglobin, which is the iron- and oxygen-binding protein in blood, specifically in the red blood cells. The only time myoglobin is found in the bloodstream is when it is released following muscle injury.

*LDH (also called LD); - An intracellular enzyme present in nearly all metabolizing cells in the body. The highest concentration of enzyme is located in the heart, skeletal muscle, liver, kidney, brain, and erythrocytes.

* **Cardiac troponin**:- This protein is by far the most commonly used biomarker.

the best biomarker for finding a heart attack.

Enzyme markers of cardiac disease

- Plasma Enzymes For Diagnosis Of Myocardial Infarction : Enzyme assays for the diagnosis of Acute Myocardial Infarction are:
  1. Creatine kinase (CK).
     -Creatine Phosphokinase (CK/ CPK)
     -Phosphocreatine serves as energy reserve during muscle contraction
     -Mainly useful in detecting damage to myocardial and skeletal muscle tissue
     -It is composed of two polypeptide chains designated M (muscle) and B (brain)
  2. Creatine kinase-MB (CK-MB) isoenzyme
  3. Lactate dehydrogenase (LD) :-Present in almost all tissues
  -LDH catalyzes the reversible conversion of pyruvate and lactate.
  -Most often measured in myocardial infraction.
  4. Aspartate aminotransferase (AST).

Carbohydrates

What Are Carbohydrates?

-Carbohydrates are the major components of plant tissue, making up to 60% to 90% of the dry matter (DM). Carbohydrates are the basic energy source in animal cells.

-Carbohydrates are the most abundant organic molecules in nature. They are primarily composed of the elements carbon, hydrogen and oxygen.

-They are the most abundant dietary source of energy (4 Cal/g) for all organisms.

-Carbohydrates are precursors for many organic compounds (fats, amino acids).

-Carbohydrates — fiber, starches and sugars — are essential food nutrients. Your body turns carbs into glucose (blood sugar) to give you the energy you need to function.

CLASSIFICATION OF CARBOHYDRATES

Carbohydrates are often referred to as saccharides (sugar).

carbohydrates can be classified as (1) monosaccharide, one unit of sugar; (2) disaccharide, two monosaccharides; (3) oligosaccharide, three to fifteen monosaccharides; and (4) polysaccharides, large polymers of simple sugars.

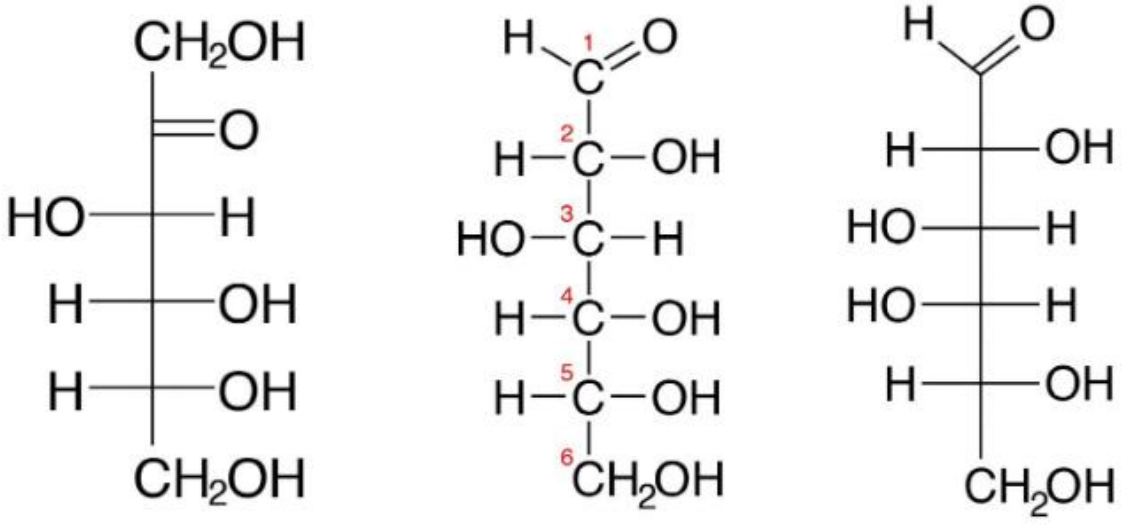
1. Monosaccharides , one unit of sugar.

-Monosaccharides can be subdivided based on the number of carbon (C) atoms. The following list shows the prefixes for numbers of carbons in a sugar.

A-Triose (3 C) B - Tetrose (4 C) C- Pentose (5 C; e.g., Xylose and Ribose)

D-Hexose (6 C; e.g., glucose, fructose, galactose, and mannose).

*Most monosaccharides in animal tissues are of 5 C and 6 C sugars.
The three hexoses that are nutritionally and metabolically important are glucose, fructose, and galactose .



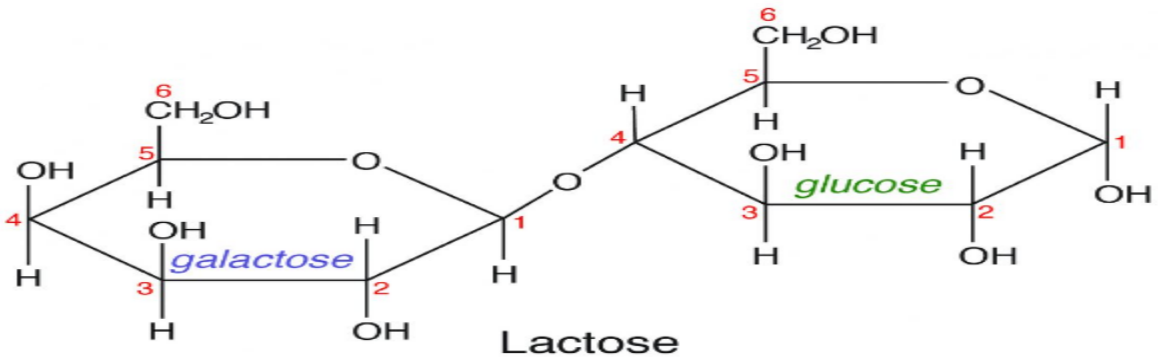
2. Disaccharides are made up of two monosaccharides bonded together by a glycosidic (covalent) bond. The following are some of the common disaccharides:

A-Sucrose-glucose + fructose (e.g., table sugar)

B-Lactose-glucose + galactose (milk sugar)

C-Maltose-α-D-Glucose + β-D-Glucose (malt sugar)

D-Cellobiose-β-D-Glucose + β-D-Glucose (cellulose)



3. Oligosaccharide are made by bonding together three or more (3 to 15) monosaccharides bonded together.

Raffinose (glucose + fructose + galactose; 3 sugars)

Stachyose (glucose + fructose + 2 galactose; 4 sugars)

D. Polysaccharides, as their name implies, are made by joining together large polymers of simple sugars. (starch , glycogen ,Cellulose ,)

What are the different types of carbohydrates?

Foods and drinks can have three types of carbohydrates:

1-Fiber. 2-Starches. 3-Sugars.

Fiber and starches are complex carbs, while sugars are simple carbs.

Fiber

Plant-based foods — like fruits, vegetables and whole-grain products — contain fiber. Animal products, including dairy products and meats, have no fiber.

Starches;- Starches are complex carbohydrates that also give your body vitamins and minerals (micronutrients).

Sugars

Sugars are a type of simple carbohydrate. Your body breaks down simple carbohydrates quickly. As a result, blood sugar levels rise — and then drop — quickly. After eating sugary foods, you may notice a burst of energy, followed by tiredness.

Limiting sugar is essential to keep your blood sugar levels in the healthy range. The American Heart Association recommends:

-No more than 25 g (6 teaspoons or 100 calories) per day of added sugar for most females.

-No more than 36 g (9 teaspoons or 150 calories) per day of added sugar for most males.

What do carbohydrates do?

Carbs are body's main source of fuel. They give the energy you need to function. Here's how the process works:

1-When you eat carbs, your digestive system begins to break them down.

2-Your bloodstream absorbs the carbs (now called glucose or blood sugar).

3-Your body releases insulin, which directs the glucose to your cells for energy.

4-If you have extra glucose, your body will store it in your muscles or liver. Once you max out glucose storage in those places, your body converts extra glucose to fat.

5-Carbohydrate digestion begins in the mouth, where salivary **amylase** starts the breakdown. After breaking down throughout the digestive system, monosaccharides are absorbed into the bloodstream. As carbohydrates are consumed, the blood sugar levels increase, stimulating the pancreas to secrete **insulin.**

Normal Blood Sugar Levels	
Time of Test	**Target Blood Sugar**
Fasting (before eating or drinking anything in the morning)	60-95 mg/dL (3.3 – 5.3 mmol/L)
1 hour after a meal	Less than 140 mg/dL (7.8 mmol/L)
2 hours after a meal	Less than 120 mg/dL (6.7 mmol/L)

High blood sugar (hyperglycaemia)

It is where the level of sugar in your blood is too high. It mainly affects people with diabetes .

- The amount of carbs you consume affects blood sugar. Taking in a lot of carbs can raise blood sugar levels. High blood sugar **(hyperglycemia)** .

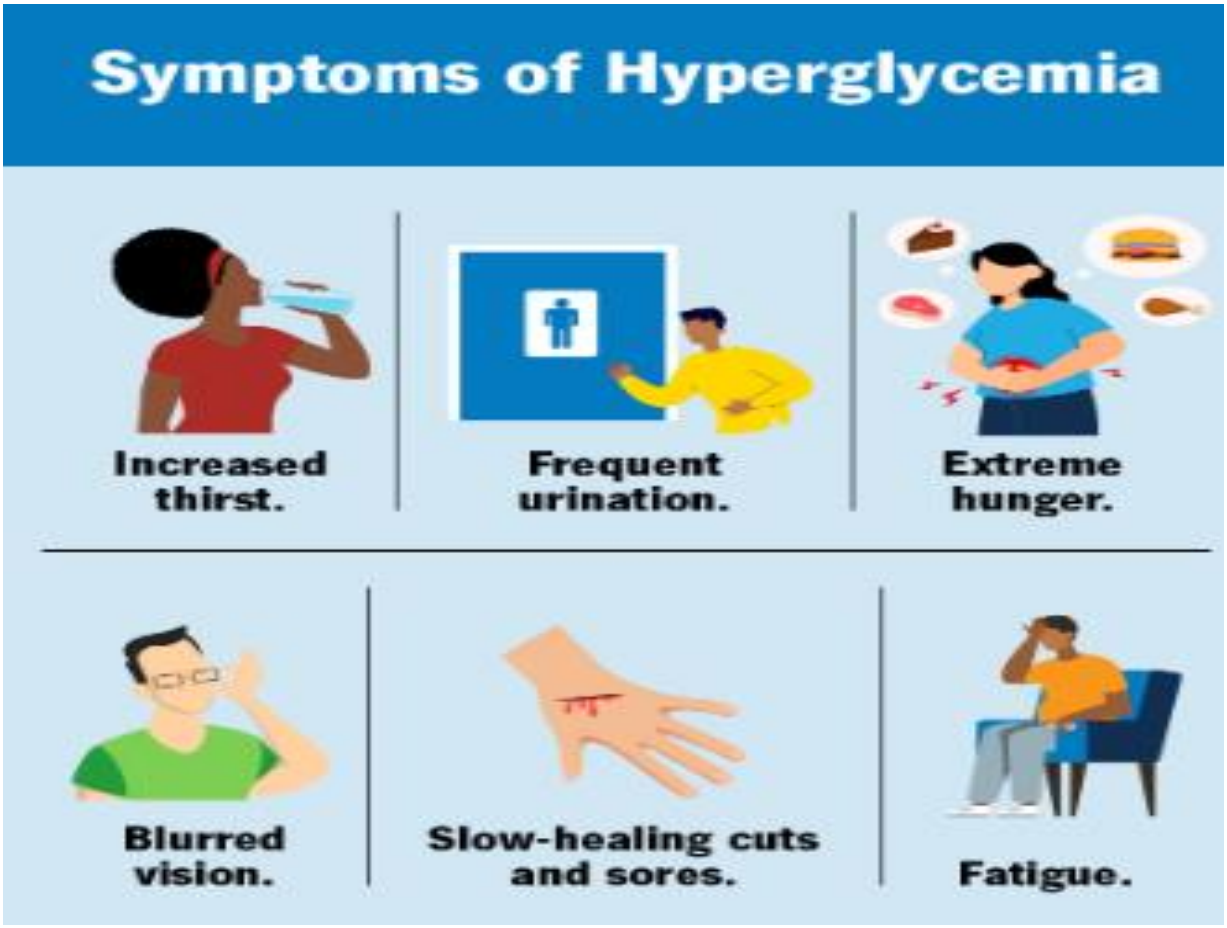
What is hyperglycemia (high blood sugar)?

-Hyperglycemia happens when there's too much sugar (glucose) in your blood. It's also called high blood sugar or high blood glucose. This happens when your body has too little insulin (a hormone) or if your body can't use insulin properly (insulin resistance).

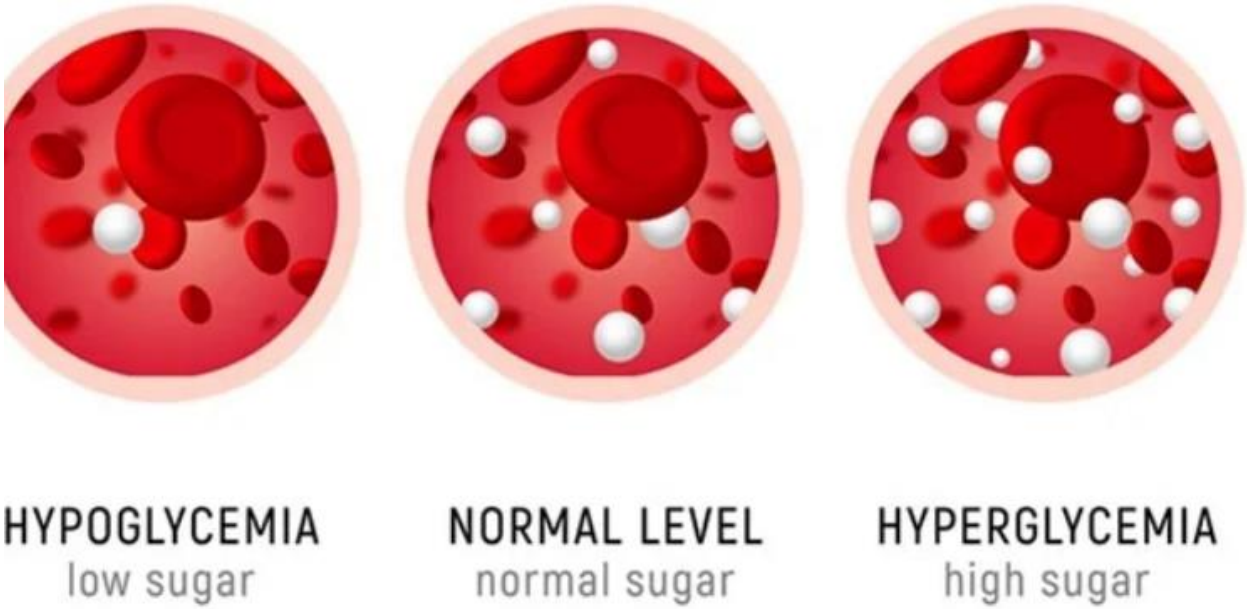
-Hyperglycemia usually means you have diabetes.

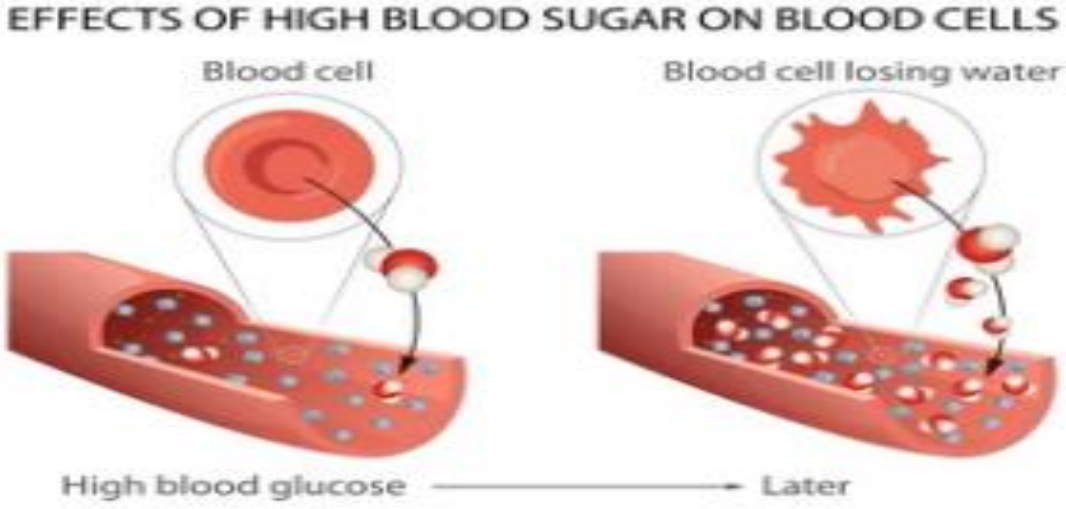
-If you have hyperglycemia that's untreated for long periods of time, it can damage your nerves, blood vessels, tissues and organs.

What are the signs and symptoms of hyperglycemia?



Effect of high blood sugar on blood cell





Hypoglycemia (Low Blood Sugar)

Hypoglycemia (low blood sugar) is common in people who have diabetes. But it can also sometimes affect people without diabetes. You need to treat hypoglycemia as soon as possible by consuming carbohydrates. If it's left untreated, severe low blood sugar can be life-threatening.

- Some people who don't consume enough carbs have low blood sugar **(hypoglycemia).**

What is hypoglycemia (low blood sugar)?

Hypoglycemia happens when the level of sugar (glucose) in your blood drops below the range that's healthy for you. It's also called low blood sugar or low blood glucose. Hypoglycemia is common in people with diabetes, especially Type 1 diabetes.

-For most people with diabetes, hypoglycemia is when your blood sugar level is below 70 milligrams per deciliter (mg/dL) or 3.9 millimoles per liter (mmol/L).

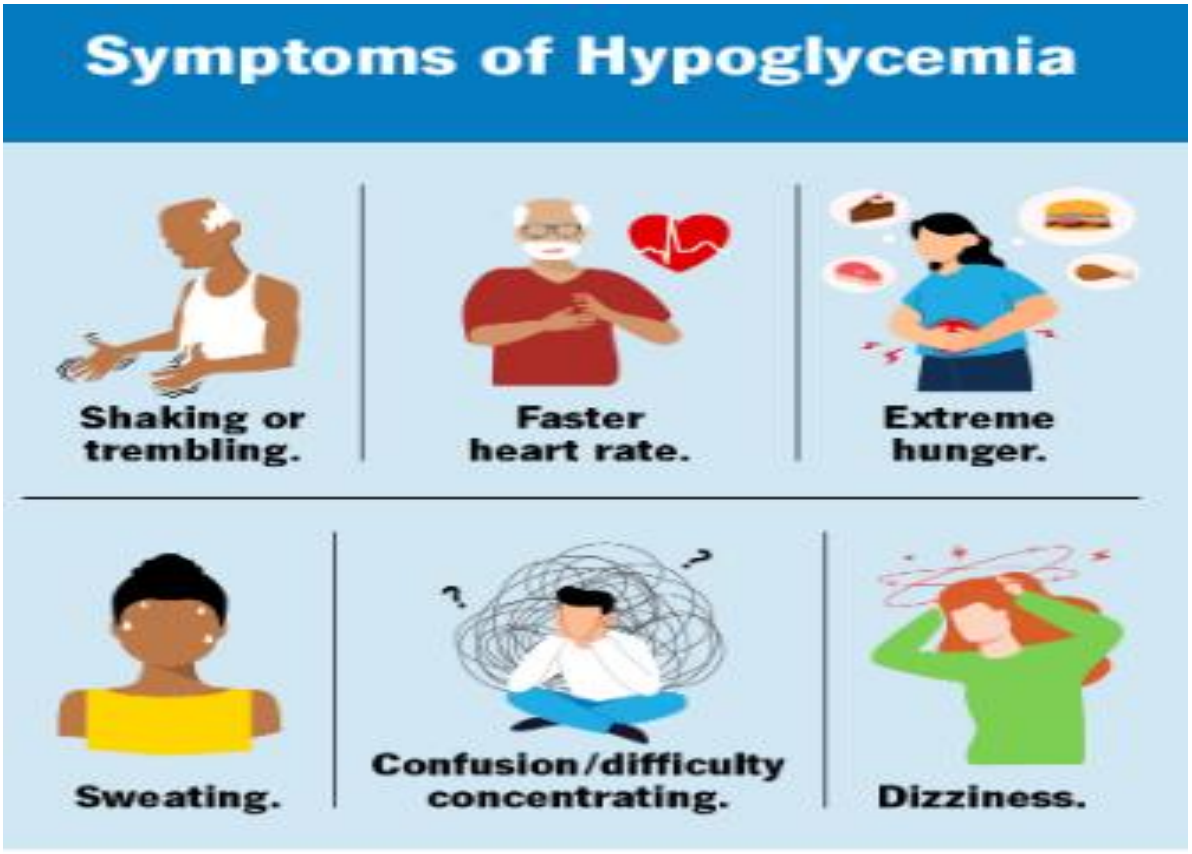
-For most people without diabetes, hypoglycemia is when your blood sugar level is below 55 mg/dL or 3.1 mmol/L.

What are the signs and symptoms of hypoglycemia (low blood sugar)?

Symptoms of hypoglycemia can start quickly, and they can vary from person to person. they provide good warnings ,The signs include:

1-Shaking or trembling. 2 Faster heart rate 3-Sweating

4- Extreme hunger (polyphagia). 5-Dizziness . 6-Confusion or trouble concentrating.



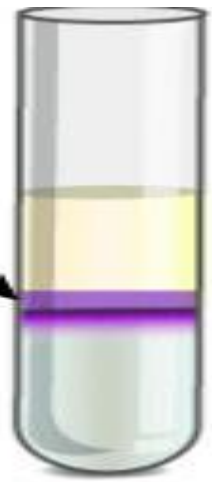
Tests for Carbohydrate

- **Molisch test**

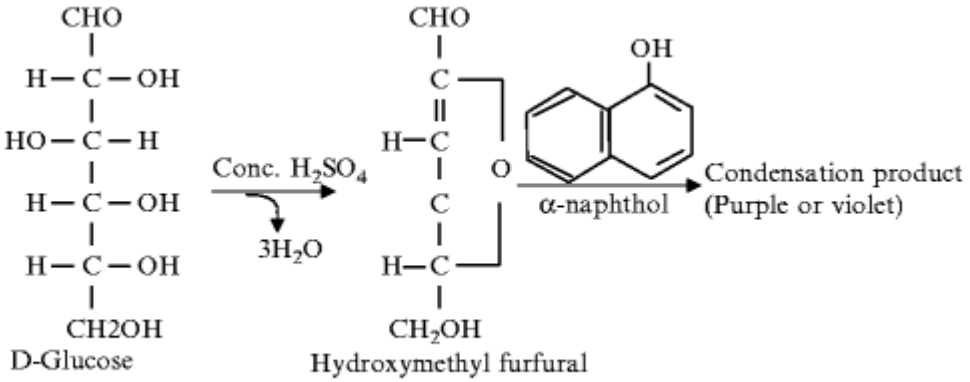
Principle of Molisch test Is a general test for all CHO.Conc.H2SO4 break down the CHO molecules to produce furfural or hydroxyl methyl furfural which react with anaphthol to give violet color complex.

أختبار موليش

تكون حلقة بنفسجية
دليل على وجود السكريات



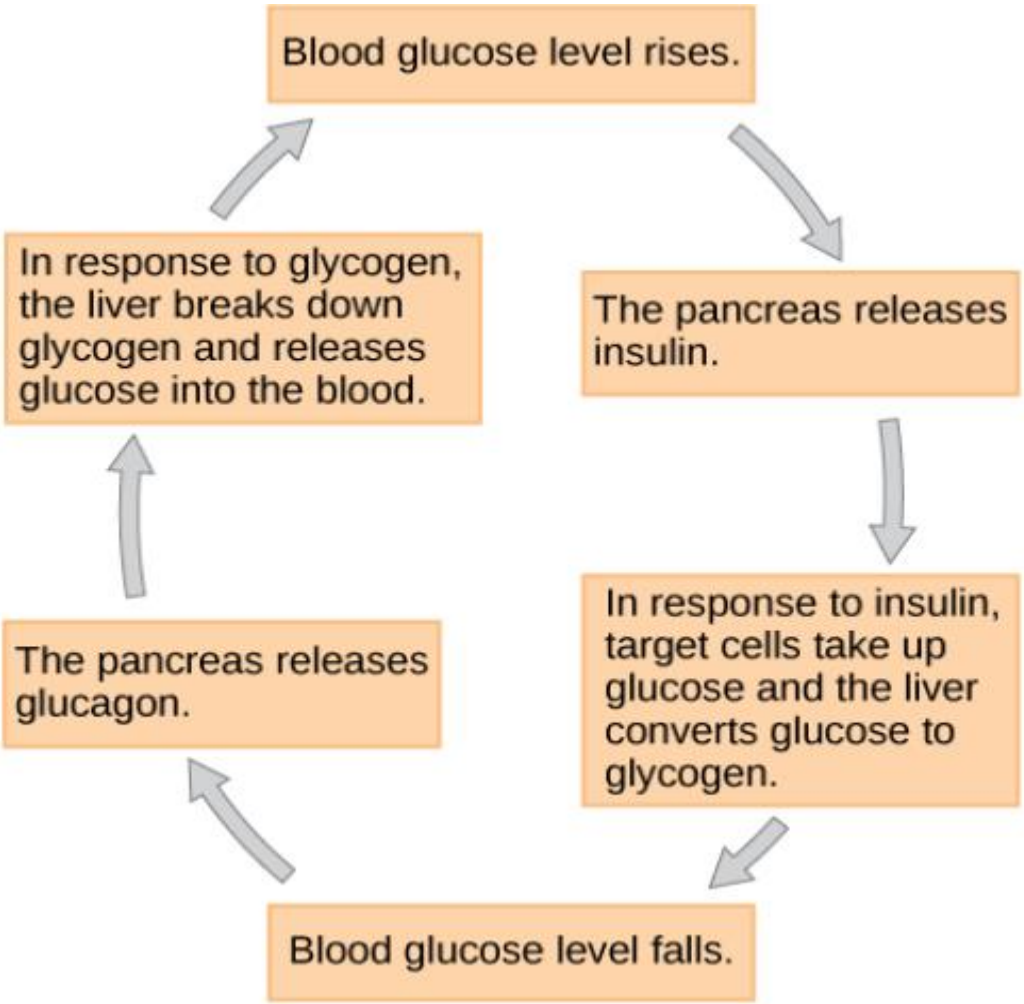
Molisch test

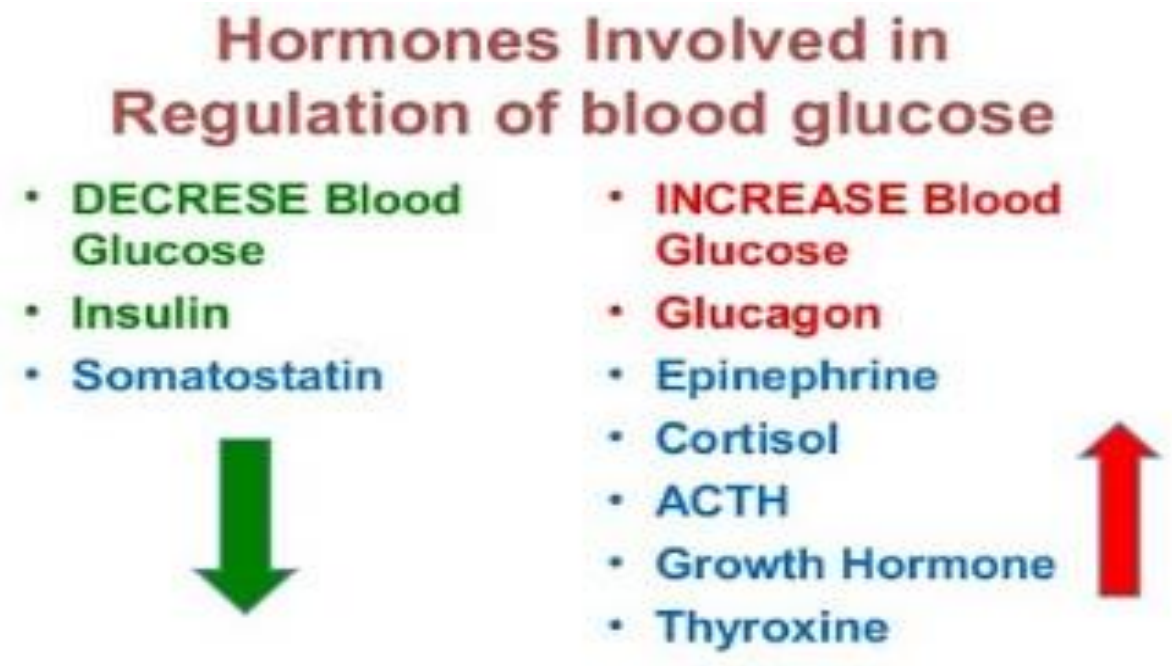


Hormonal regulation of carbohydrate level in the body

And this hormonal regulation of carbohydrate metabolism is mainly occurred by the internal chemical messengers. Hormones like insulin, glucagon, epinephrine, cortisol, TH and GH regulates this metabolism.

(Insulin is a peptide hormone. Secreted by β cells of islets of Langerhans from pancreas.)





Regulation of Blood Glucose Levels by Insulin and Glucagon

Cells of the body require nutrients in order to function, and these nutrients are obtained through feeding.

1- the body uses hormones to moderate energy stores.

2- Insulin is produced by the **beta cells of the pancreas,** which are stimulated to release insulin as blood glucose levels rise (for example, after a meal is consumed).

3- Insulin lowers blood glucose levels by enhancing the rate of glucose uptake and utilization by target cells, which use glucose for ATP production.

4- Insulin also stimulates the liver to convert glucose to glycogen, which is then stored by cells for later use.

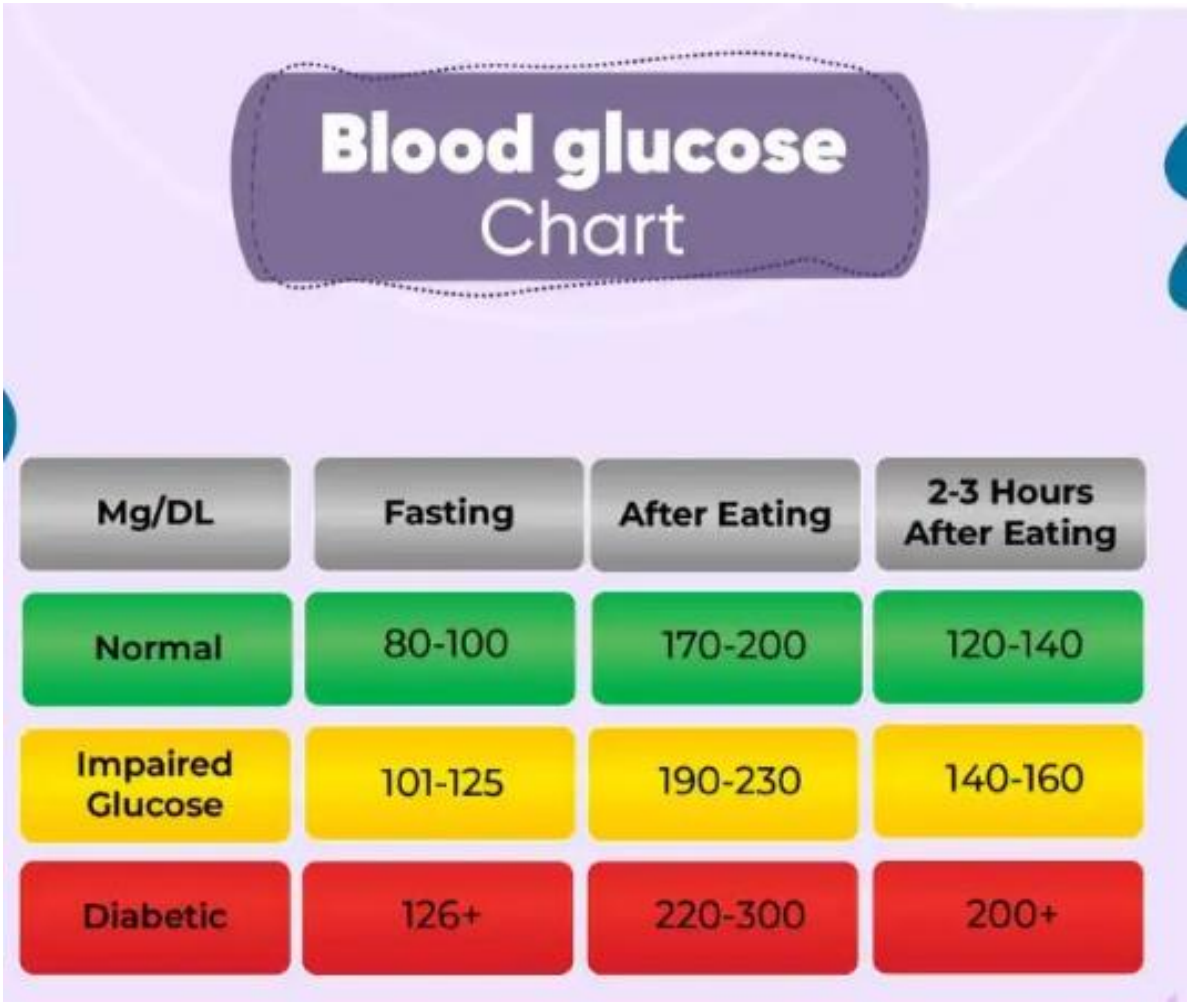
5- Insulin also increases glucose transport into certain cells, such as muscle cells and the liver.

6- Insulin also stimulates the conversion of glucose to fat in adipocytes and the synthesis of proteins.

7-These actions mediated by insulin cause blood glucose concentrations to fall, called a hypoglycemic “low sugar” effect, which inhibits further insulin release from beta cells .

normal plasma glucose level

-The expected values for normal fasting blood glucose concentration are between 70 mg/dL (3.9 mmol/L) and 100 mg/dL (5.6 mmol/L).



Diabetes mellitus (DM)

Diabetes mellitus (DM) is a disease of inadequate control of blood levels of glucose. It has many subclassifications, including :_

1- type 1 diabetes 2- type 2 diabetes

3-maturity-onset diabetes of the young (MODY),

4-gestational diabetes, 5-neonatal diabetes, 6-steroid-induced diabetes.

Diabetes occurs when our bodies are unable to regulate blood sugar levels. There are 3 main types of diabetes.

- Type 1 diabetes, Type 2 diabetes, and gestational diabetes.

- In type, type 1 diabetes, the body's immune system attacks and destroys pancreatic insulin-producing cells. Without insulin, sugar can't enter cells for energy, causing blood sugar levels to rise. It often begins in childhood or adolescence.

-Type 2 diabetes is more common and usually develops later in life. During this condition, the body doesn't use insulin properly; over time, the pancreas can't produce enough insulin to keep up.

- The third type of diabetes i.e. gestational diabetes occurs when the body cannot produce enough insulin to meet the increased demands during pregnancy. This can elevate your blood sugar levels. While it often resolves after childbirth, it increases the risk for both the mother and child to develop type 2 diabetes later in life.

Categories of Blood Sugar Levels

Blood glucose levels are typically categorized into three ranges:

a) Fasting Blood Glucose Levels (mg/dL):

Normal: Less than 100 mg/dL

Impaired Glucose (Prediabetes): 100-125 mg/dL

Diabetic: 126 mg/dL or higher

b) Blood Glucose Levels 1-2 Hours After Eating (Postprandial) (mg/dL):

Normal: Less than 140 mg/dL

Impaired Glucose (Prediabetes): 140-199 mg/dL

Diabetic: 200 mg/dL or higher

c) Blood Glucose Levels 2-3 Hours After Eating (mg/dL):

Normal: Returns to less than 140 mg/dL

Impaired Glucose (Prediabetes): Typically between 140-199 mg/dL

Diabetic: 200 mg/dL or higher

Clinical Significant

Elevated glucose associated with :

1-Pancreatitis 2- pituitary or thyroid dysfunction

3-renal failure 4-liver diseas

Low glucose ass0ciated with:

1-Insulinoma 2-hypopituitarism

3- Neoplasms 4- insulin hypoglycemia.

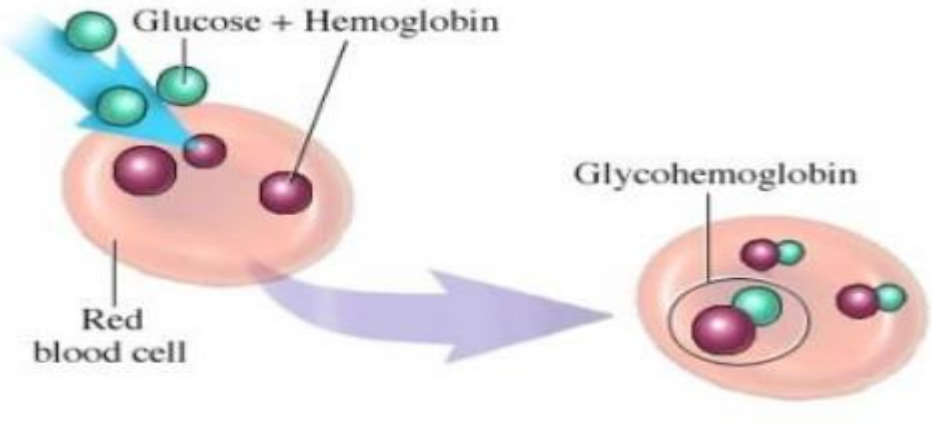
laboratory investigation of diabetes

Tests for type 1 and type 2 diabetes and prediabetes

1-HbA1C test

What is HbA1c?

HbA1c is simply haemoglobin to which circulating glucose has bound.



Glycated haemoglobin : is a form of hemoglobin that is measured primarily to identify the three month average plasma glucose concentration.

• The test is limited to a three month average because the lifespan of a red blood cell is three months (120Days). Different types of hemoglobins:

<u>Different types of hemoglobins</u>:

1. Fetal Hemoglobin – HbF
2. Adult Hemoglobin – HbA
3. Sickle cell disease – HbS
4. Hemoglobinopathies – HbC, HbE
5. Glucose in the blood reacts with the Hemoglobin A to form Glycated Hb.

-The A1C test is a common blood test for diagnosing diabetes. For people living with diabetes, the test checks how well they manage blood sugar levels. The A1C

test also is called the glycated hemoglobin, glycosylated hemoglobin, hemoglobin A1C or HbA1c test. The Hb A1C test measures what percentage of hemoglobin in the blood is coated with sugar, also **called glycated**.

-This blood test, which doesn't require not eating for a period of time (fasting), shows your average blood sugar level for the past 2 to 3 months. It measures the percentage of blood sugar attached to hemoglobin, the oxygen-carrying protein in red blood cells. It's also called a glycated hemoglobin test.

The higher your blood sugar levels, the more hemoglobin you'll have with sugar attached.

- An A1C level of 6.5% or higher on two separate tests means that you have diabetes.
- An A1C between 5.7% and 6.4% means that you have prediabetes.
- Below 5.7% is considered normal.

2-Random blood sugar test. A blood sample will be taken at a random time. No matter when you last ate, a blood sugar level of 200 milligrams per deciliter (mg/dL) — 11.1 millimoles per liter (mmol/L) — or higher suggests diabetes.

Fasting blood sugar test. A blood sample will be taken after you haven't eaten anything the night before (fast).

-A fasting blood sugar level less than 100 mg/dL (5.6 mmol/L) is normal.

-A fasting blood sugar level from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) is considered prediabetes.

-If it's 126 mg/dL (7 mmol/L) or higher on two separate tests, you have diabetes.

3-Glucose tolerance test. For this test, you fast overnight. Then, the fasting blood sugar level is measured. Then you drink a sugary liquid, and blood sugar levels are tested regularly for the next two hours.

-A blood sugar level less than 140 mg/dL (7.8 mmol/L) is normal.

- A reading of more than 200 mg/dL (11.1 mmol/L) after two hours means you have diabetes.

-A reading between 140 and 199 mg/dL (7.8 mmol/L and 11.0 mmol/L) means you have prediabetes.

Lipids

the chief concentrated storage form of energy, besides their role in cellular structure and various other biochemical functions.

Lipids may be as organic substances relatively insoluble in water, soluble in organic solvents (alcohol, ether etc.), actually or potentially related to fatty acids and utilized by the living cells.

lipids are not polymers. Further,lipids are mostly small molecules.

Functions of lipids

Lipids perform several important functions

1. They are the concentrated fuel reserve of

the body (triacylglycerols).

2. Lipids are the constituents of membrane

structure and regulate the membrane

permeability (phospholipids and cholesterol).

3. They serve as a source of fat soluble

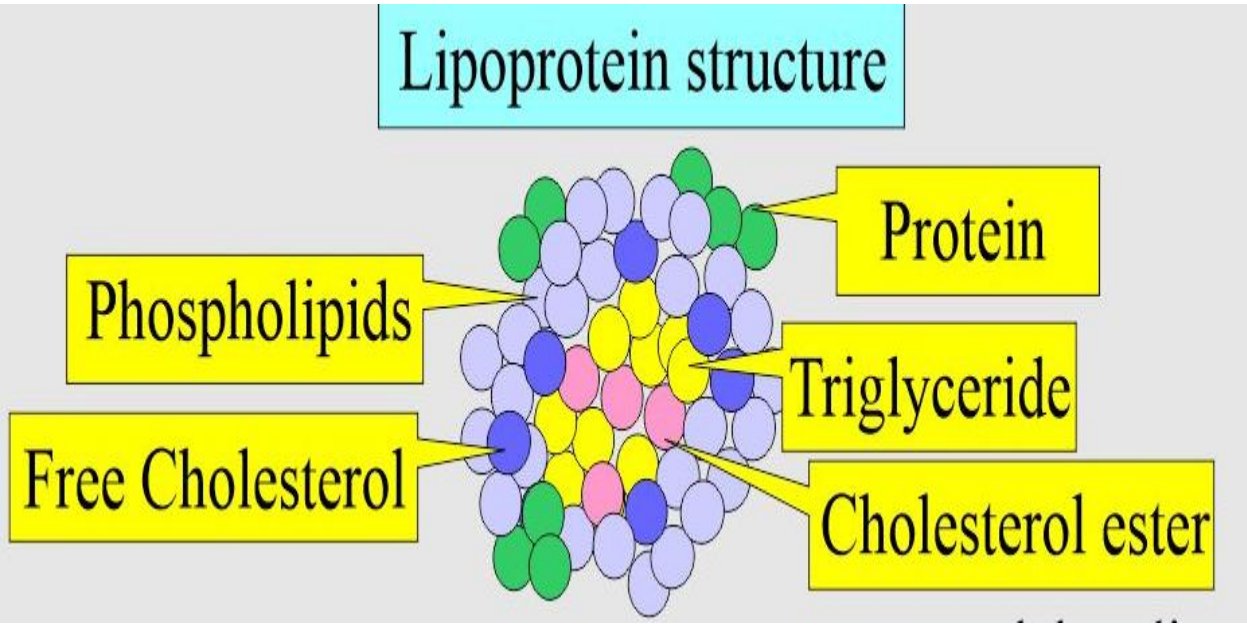
vitamins (A, D, E and K).

4. Lipids are important as cellular metabolic

regulators (steroid hormones and prostaglandins).

General lipoproten

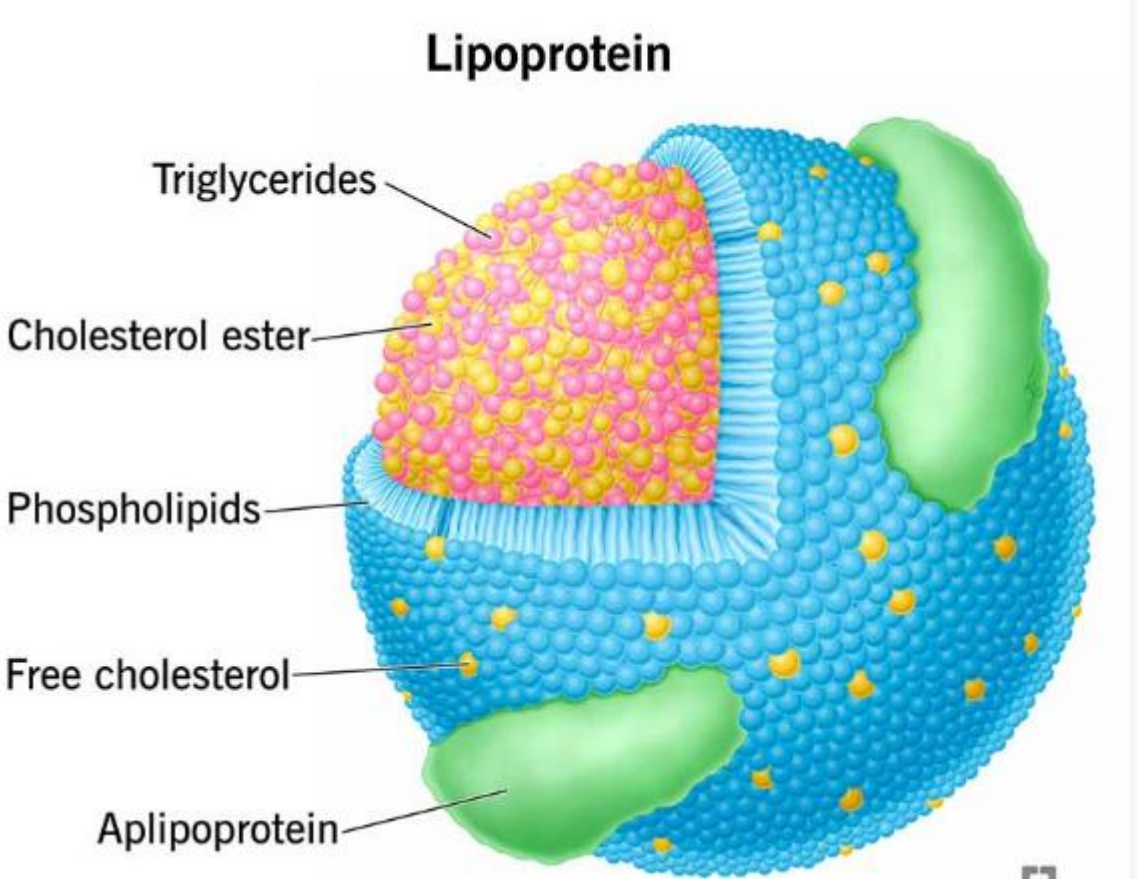
Lipoproteins are macromolecular complexes that consist of discrete particles and are composed of both lipids and proteins. The lipids include cholesterol, phospholipids, and triacylglycerols (TAG).



What are lipoproteins?

Lipoproteins are round particles made of fat (lipids) and proteins that travel in your bloodstream to cells throughout your body. Cholesterol and triglycerides are two types of lipids found in lipoproteins.

Your body makes different types of lipoproteins. High levels of certain lipoproteins can be harmful to your heart. But some lipoproteins have heart-protective benefits.



What are the types of lipoproteins?

There are five main types of lipoproteins:

1-High-density lipoprotein (HDL) is the “good cholesterol.” It carries cholesterol back to your liver to be flushed out of your body. High levels of HDL reduce your risk of cardiovascular (heart) disease.

2-Low-density lipoprotein (LDL) is the “bad cholesterol.” It increases your risk of coronary artery disease, heart attacks and stroke. LDL carries cholesterol that accumulates as plaque inside blood vessels. Plaque buildup can make blood vessels too narrow for blood to flow freely. This condition is atherosclerosis.

3-Very low-density lipoproteins (VLDL) are another type of “bad cholesterol.” VLDLs carry triglycerides — and to a lesser degree, cholesterol — to your tissues.

4-Intermediate-density lipoproteins (IDL) are created when VLDLs give up their fatty acids. They’re then either removed by your liver or converted into LDL.

5-Chylomicrons are very large particles that also transport triglycerides.

What’s the purpose of a lipid blood test?

High cholesterol rarely causes symptoms. Testing is the best way to identify cholesterol issues that affect your heart and blood vessels. use lipid blood tests for:

1-Screenings: The blood test may be part of a routine physical exam.

2-Diagnosis: You may get a cholesterol blood test to diagnose conditions like atherosclerosis.

3-Monitoring: Test results can show if your cholesterol numbers are worsening and need treatment.

lipid associated diseases

What are the diseases associated with lipids?

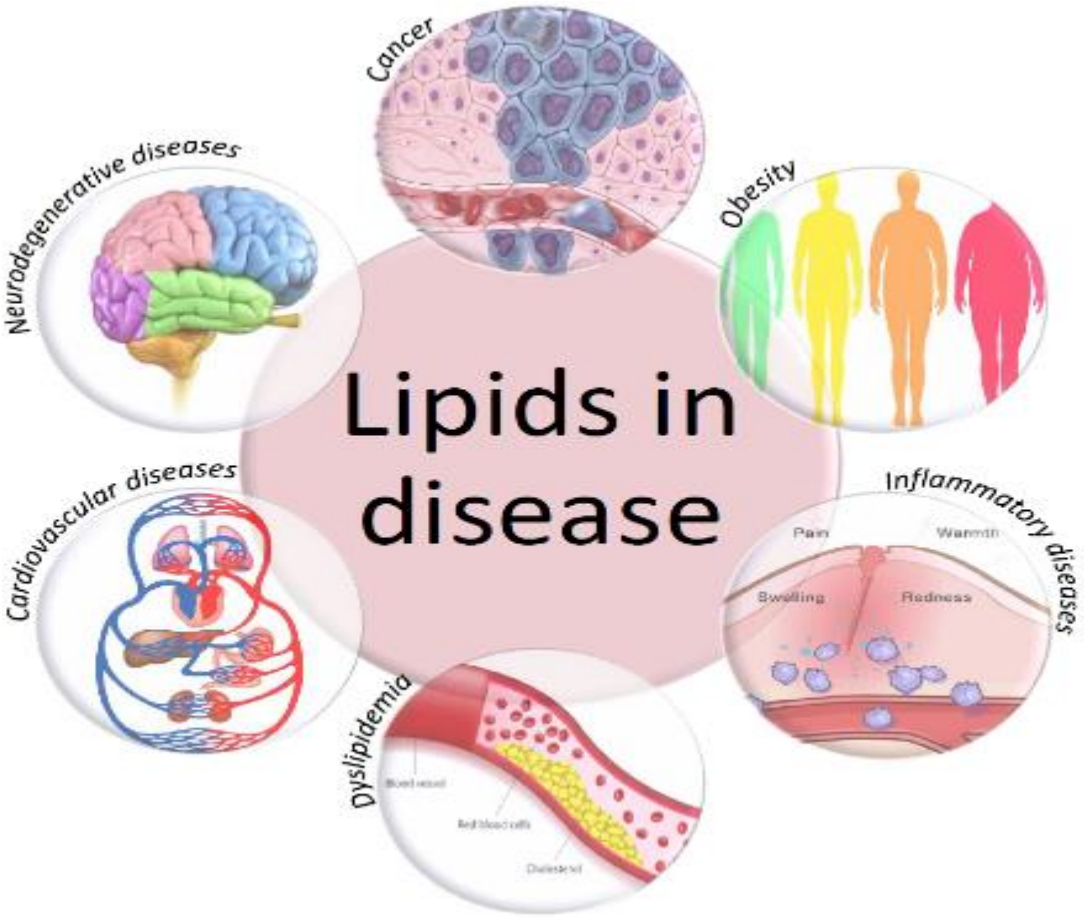
Secondary lipid metabolism abnormalities can cause a variety of illnesses.

1-Diabetes mellitus 2- hypothyroidism (LDL hypercholesterolemia)

3-renal illnesses (hypertriglyceridemia

4-mixed hyperlipoproteinemia 5-lipoprotein elevation)

6- cholestatic liver disorders are the most common clinically.


Lipids in disease
Cancer
Neurodegenerative diseases
Obesity
Cardiovascular diseases
Inflammatory diseases
Pain
Warmth
Swelling
Redness
Dyslipidemia


Coronary Artery Cross-Section
Normal healthy artery
lumen
arterial wall
Plaque build up along the wall of artery
Blockage and narrowing of lumen from plaque

Plasma lipoproteins

Plasma lipoprotein metabolism is regulated and controlled by the specific apolipoprotein (apo-) constituents of the various lipoprotein classes. The major apolipoproteins include apoE, apoB, apoA-I, apoA-II, apoA-IV, apoC-I, apoC-II, and apoC-III. Specific apolipoproteins function in the regulation of lipoprotein metabolism through their involvement in the transport and redistribution of lipids among various cells and tissues, through their role as cofactors for enzymes of lipid metabolism, or through their maintenance of the structure of the lipoprotein particles.

Hormones

living body possesses a remarkable communication system to coordinate its

biological functions. **by two distinctly organized functional systems**.

1. The nervous system coordinates the body functions through the transmission of electrochemical impulses.

2. The endocrine system acts through a wide range of chemical messengers known as hormones.

Hormones are defined as organic substances, produced in small amounts

by specific tissues (endocrine glands), secreted into the blood stream to control the metabolic and biological activities in the target cells. Hormones may be regarded as the chemical messengers involved in the transmission of information from one tissue to another and from cell to cell.

The major endocrine organs in human body are depicted in receptors to which they bind and the signals used to mediate their action.

1. Group I hormones : These hormones bind to intracellular receptors to form receptorhormone complexes (the intracellular messengers) through which their biochemical functions are mediated. Group I hormones are lipophilic in nature and are mostly derivatives of cholesterol (exception—T3 and T4). e.g. estrogens, androgens, glucocorticoids, calcitriol.

2. Group II hormones : These hormones bind to cell surface (plasma membrane) receptors and stimulate the release of certain molecules, namely the second messengers which, in turn, perform the biochemical functions.

Thus, hormones themselves are the first messengers.

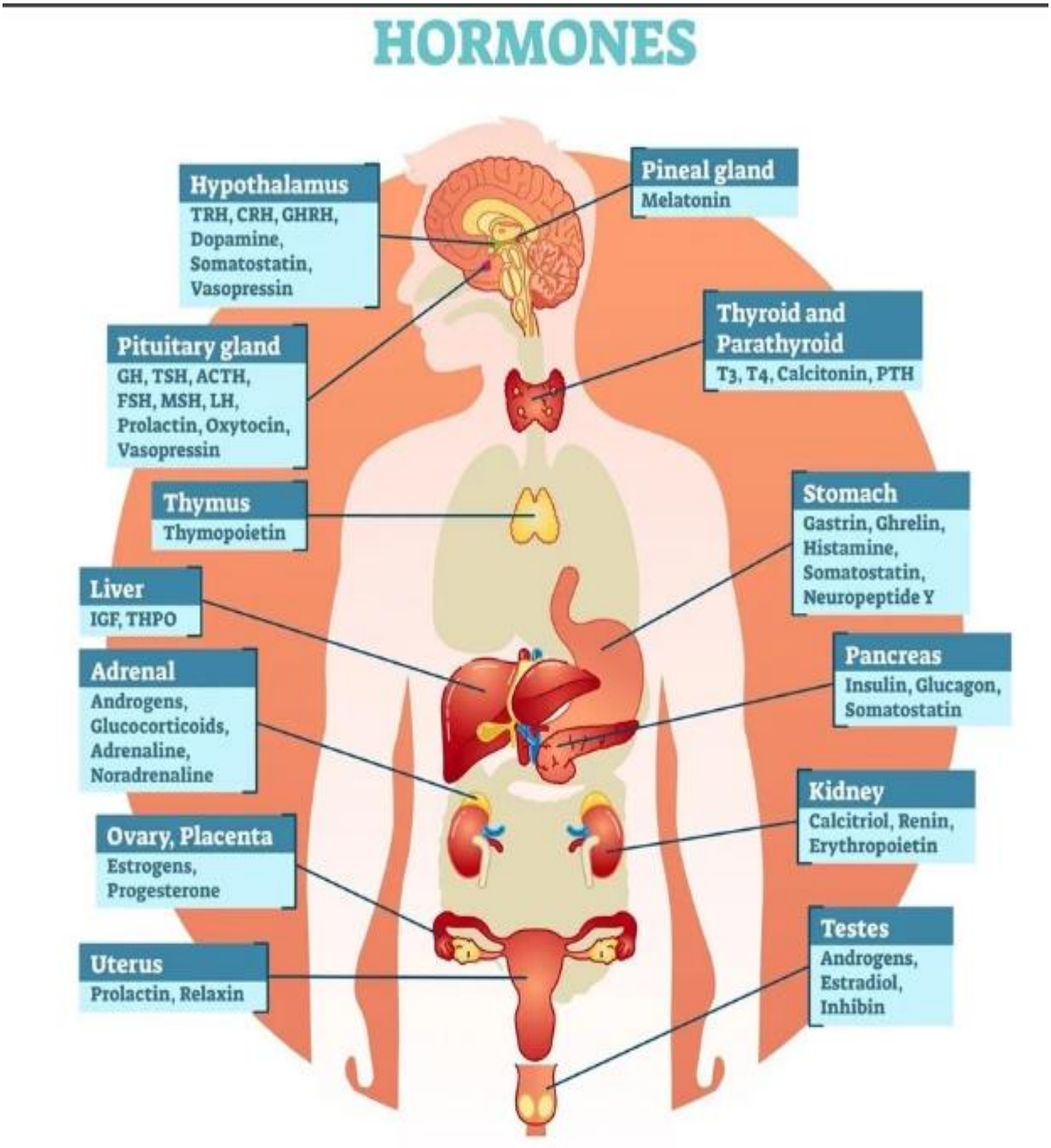
Group II hormones are subdivided into **three categories based** on the chemical nature of the second messengers.

(a) The second messenger is cAMP e.g. ACTH, FSH, LH, PTH, glucagon,

calcitonin.

(b) The second messenger is phosphatidylinositol/calcium e.g. TRH, GnRH, gastrin, CCK.

(c) The second messenger is unknown e.g. growth hormone, insulin, oxytocin, prolactin.



CLASSIFICATION OF HORMONES

Hormones may be classified in many ways based on their characteristics and functions. Two types of classification are discussed here

A. **Based on the chemical nature** The hormones can be categorized into three

groups considering their chemical nature.

1. Protein or peptide hormones e.g. insulin, glucagon, antidiuretic hormone, oxytocin.

2. Steroid hormones e.g. glucocorticoids, mineralocorticoids, sex hormones.

3. Amino acid derivatives e.g. epinephrine, norepinephrine, thyroxine (T4), triiodothyronine (T3).

B. **Based on the mechanism of action** Hormones are classified into two broad

groups (A and B) based on the location of the stimulate the release of certain molecules, namely the second messengers which, in turn, perform the biochemical functions. Thus, hormones themselves are the first messengers.

What are the parts of the hormonal system?

The hormonal system includes many different glands and organs that produce and/or respond to a range of different hormones.

Some examples of hormones that are active in the hormonal system include:

1-**Growth hormone**: This is released from the pituitary gland. It is essential for normal physical growth in children and for some functions in adults, such as maintaining fat and muscle mass.

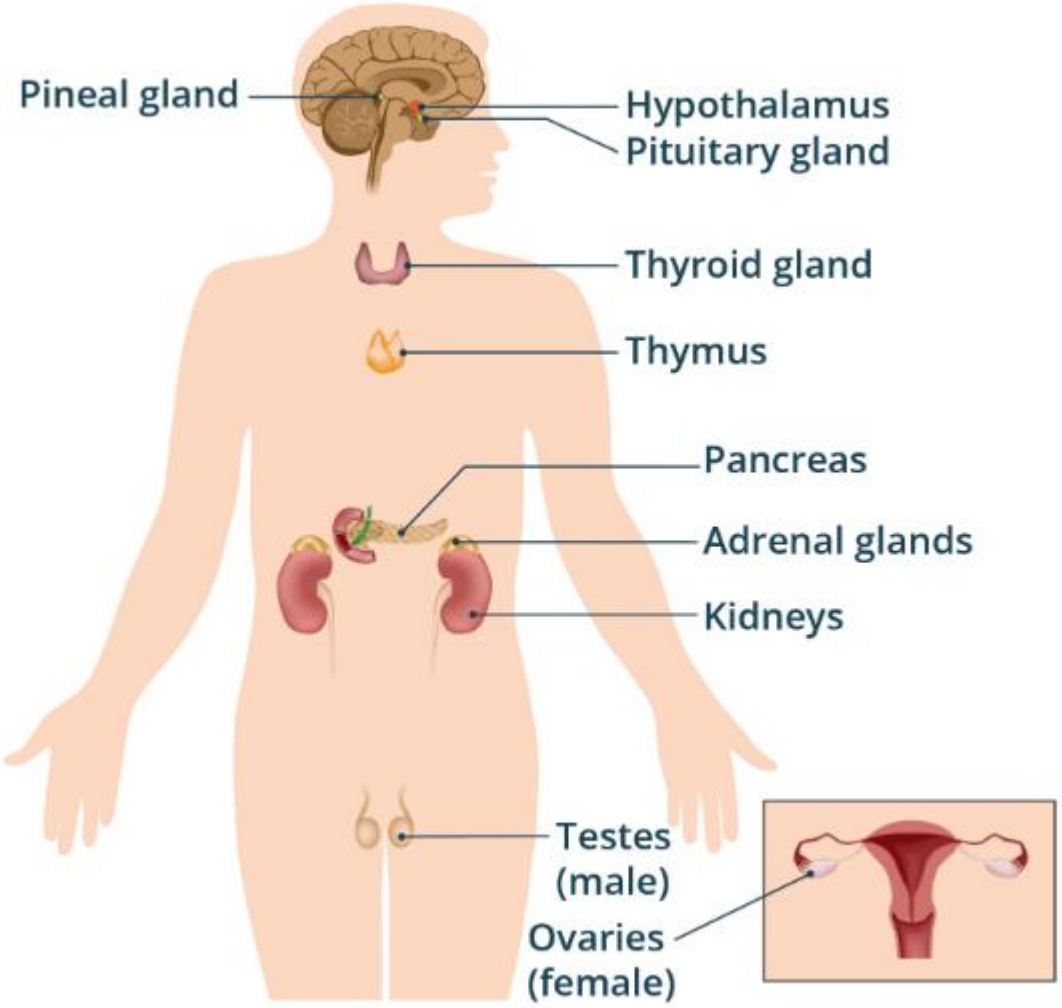
2-**Thyroxine**: The thyroid gland (located in the neck) converts iodine from the diet into thyroxine. This controls many functions of the metabolism, including temperature, heart rate and growth.

3-**Cortisol**: This is released from the adrenal glands (located just above the kidneys). It is important for controlling blood pressure and for stimulating the body's response to stress.

4-**Insulin**: This is produced by islet cells in the pancreas. It helps controls blood sugar levels.

Oestrogen and progesterone: These hormones, released from the ovaries, are responsible for female body characteristics and for storing and releasing eggs.

Testosterone: This is released from the testes. It produces male body characteristics and sperm.



HYPOTHALAMIC HORMONES

Hypothalamus produces at least six releasing factors or hormones.

1. Thyrotropin-releasing hormone (TRH) : It is a tripeptide consisting of glutamate derivative (pyroglutamate), histidine and proline. TRH stimulates anterior pituitary to release thyroidstimulating hormone (TSH or thyrotropin) which,

in turn, stimulates the release of thyroid hormones (T3 and T4).

2. Corticotropin-releasing hormone (CRH) : It stimulates anterior pituitary to release adrenocorticotropic hormone (ACTH) which in turn, acts on adrenal cortex to liberate adrenocorticosteroids. CRH contains 41 amino acids.

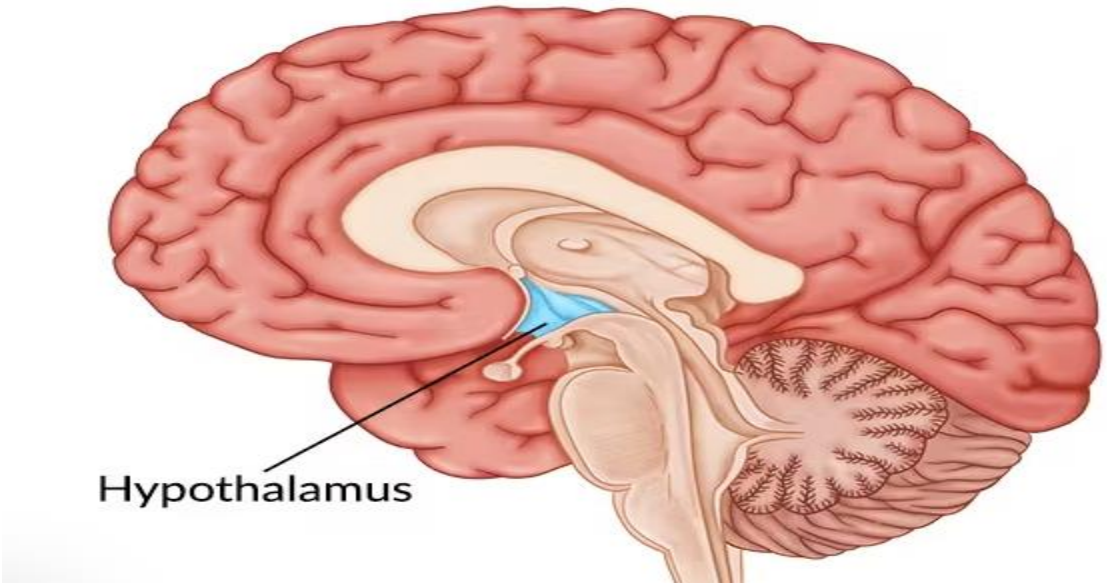
3. Gonadotropin-releasing hormone (GnRH) : It is a decapeptide. GnRH stimulates anterior pituitary to release gonadotropins, namely luteinizing hormone (LH) and follicle stimulating hormone (FSH).

4. Growth hormone-releasing hormone (GRH) with 44 amino acids stimulates the

release of growth hormone (GH or somatotropin) which promotes growth.

5. Growth hormone release-inhibiting hormone (GRIH) : It contains 14 amino acids and is also known as somatostatin. GRIH inhibits the release of growth hormone from the anterior pituitary.

6. Prolactin release-inhibiting hormone (PRIH) : It is believed to be a dopamine and/or a small peptide that inhibits the release of prolactin (PRL) from anterior pituitary.



What Is the Function of the Hypothalamus?

The hypothalamus is a structure located in the center of the brain that serves as the primary link between the central nervous system and the endocrine system. It has a few main functions including:

1-Making hormones, including vasopressin and oxytocin.

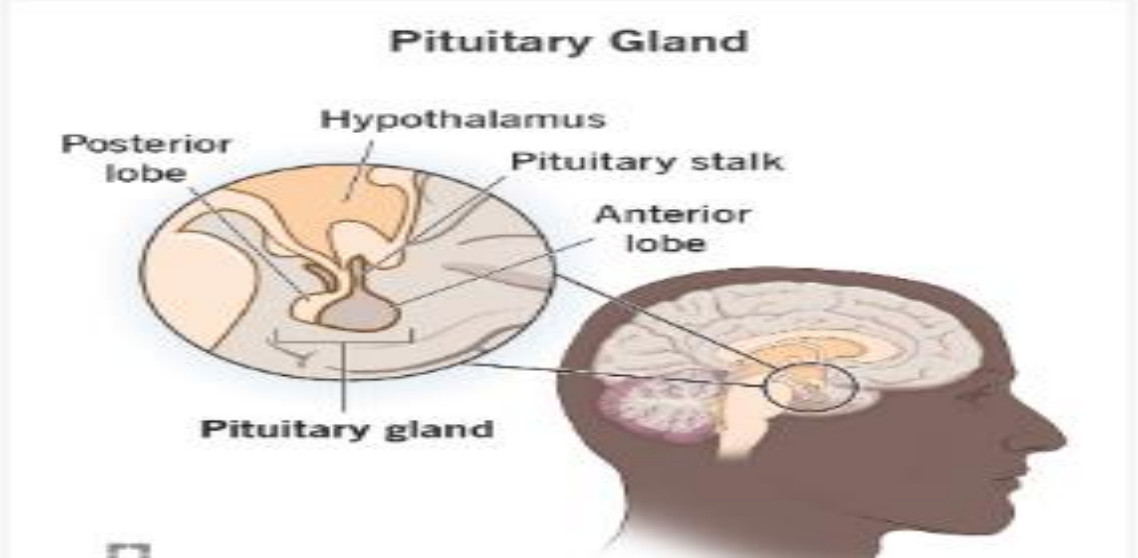
2-Releasing hormones that communicate with the pituitary gland.

3-Regulating basic functions (body temperature, hunger/thirst, sleep/wake cycles, other autonomic life-sustaining functions). These functions are vital to maintaining homeostasis. or the body's internal state of balance.

Pituitary Gland

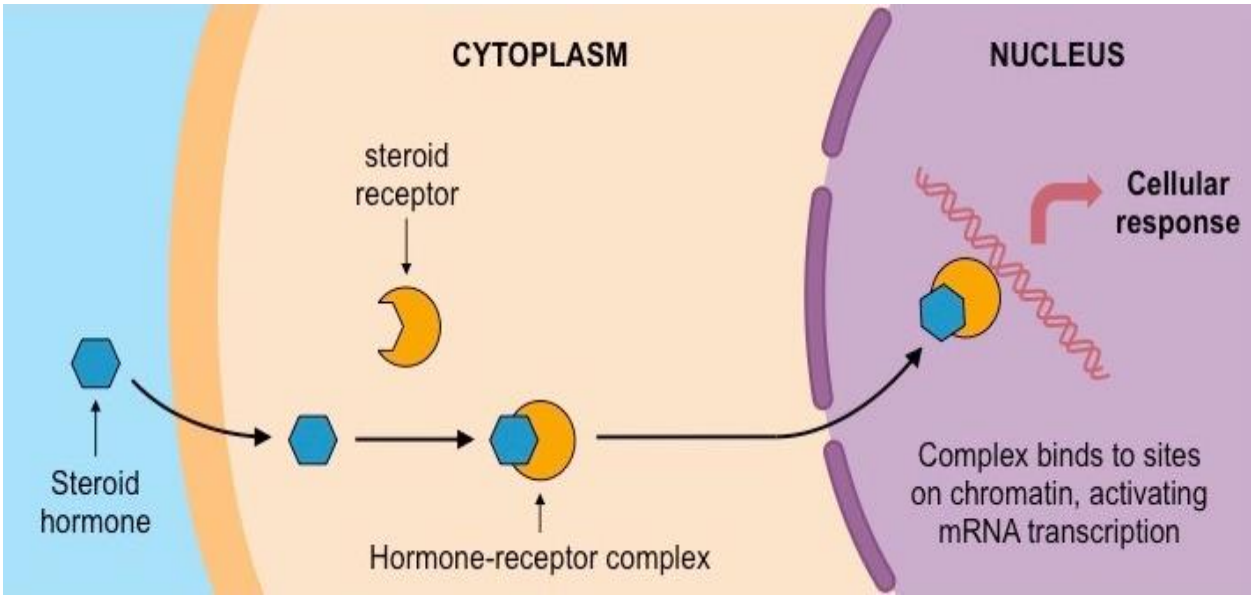
What Is a Pituitary Gland?

The pituitary gland is an endocrine gland about the size of a pea located at the base of the brain. The pituitary gland roughly weighs 0.5 grams in humans, about half-inch in diameter. There is a discrepancy in the pituitary gland size in men and women. During pregnancy, the size of the pituitary gland doubles. The pituitary gland is also known as the "master gland" because it controls the functioning of several other endocrine glands. For example, a stalk of nerves and blood vessels attaches the pituitary gland to the hypothalamus (another endocrine gland). The pituitary gland is responsible for several vital functions in our body.



Steroid Hormones

Steroid Hormones Are Synthesized from Cholesterol ,A variety of steroid hormones are produced in the adrenal cortex, gonads, and placenta. These include: Androgens, including testosterone and dehydroepiandrosterone (DHEA) Estrogens, primarily estradiol.



Steroid Hormones

Steroid hormones are lipophilic (fat-loving) – meaning they can freely diffuse across the plasma membrane of a cell They bind to receptors in either the cytoplasm or nucleus of the target cell, to form an active receptor-hormone complex This activated complex will move into the nucleus and bind directly to DNA, acting as a transcription factor for gene expression Examples of steroid hormones include those produced by the gonads (i.e**. estrogen**, **progesterone** and **testosterone**)

Pregnancy hormones

Hormones during pregnancy are the result of an intricate interaction between hormones generated by different glands and organs. The primary hormones involved comprise human chorionic gonadotropin (hCG), progesterone, estrogen, human placental lactogen (hPL), and oxytocin.

What is HCG Hormone?

HCG hormone (Human Chorionic Gonadotropin) is one of the gestational hormones. Many people may have heard about the HCG test from blood or urine to check whether someone is pregnant or not.

Pancreas

Zollinger-Ellison syndrome (ZES) is a rare digestive disease caused by a tumor (gastrinoma) in the pancreas or small intestine. These tumors, called gastrinomas, release the hormone gastrin, which causes too much acid in the stomach.

Gastrointestinal Diseases

GERD, diarrhea and colorectal cancer are examples of gastrointestinal diseases.

Some of the most common causes of functional GI problems are:

1-Eating a diet low in fiber or high in processed foods

2-Not getting enough exercise

3-Traveling or other changes in your typical routine

4-Stress and anxiety

5-Holding your poop or not going as soon as you need to go

6-Taking certain medicines

7-Hormonal changes (like pregnancy or during menstruation).

8-Food sensitivities or eating something that didn't "agree" with you.

THYROID HORMONES

Thyroid gland (weighs about 30 g in adults) is located on either side of the trachea below the larynx. It produces two principal hormones:-

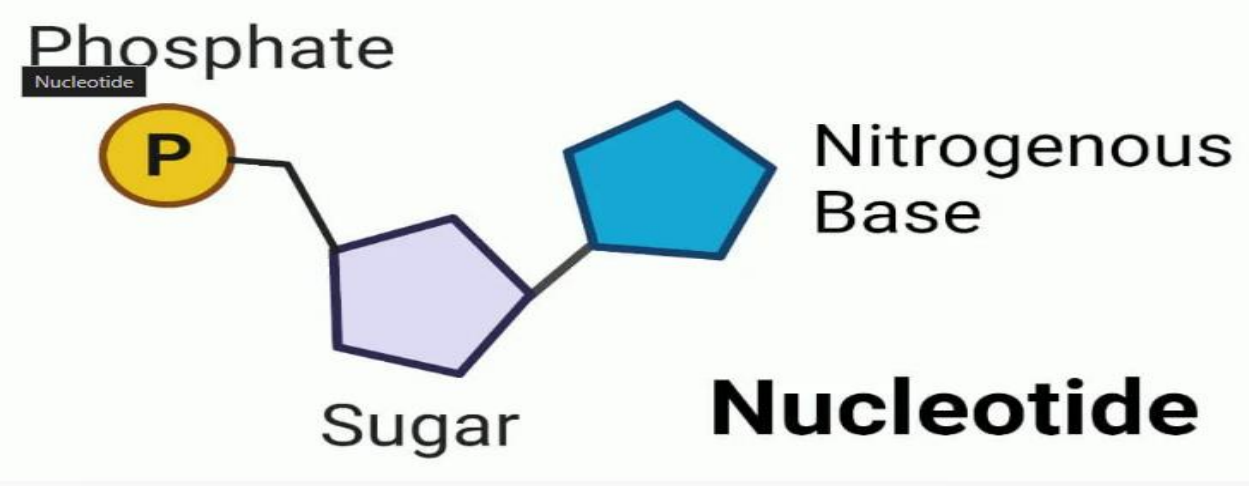
-thyroxine (T4; 3,5,3',5'-tetraiodothyronine) and 3,5,3'-triiodothyronine (T3)

which regulate the metabolic rate of the body. Thyroid gland also secretes calcitonin, a hormone concerned with calcium homeostasis.

Nucleotides

-Nucleotides are organic molecules composed of a nitrogenous base, a pentose sugar and a phosphate. They serve as monomeric units of the nucleic acid polymers – deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), both of which are essential biomolecules within all life-forms on Earth. Nucleotides are obtained in the diet and are also synthesized from common nutrients by the liver.

-Nucleotides are composed of three subunit molecules: **a nucleobase**, a five-**carbon sugar** (ribose or deoxyribose), and **a phosphate group** consisting of one to three phosphates. The four nucleobases in DNA are guanine, adenine, cytosine, and thymine; in RNA, uracil is used in place of thymine.



Difference Between Nucleotides and Nucleosides

Nucleotide names include their nucleoside and the number of phosphate groups they contain.

A nucleoside is essentially a nucleotide minus the phosphate group. A nucleotide has a nitrogenous base, a pentose sugar (ribose or 2'-deoxyribose), and one or more phosphate groups, while a nucleoside consists of the nitrogenous base and pentose sugar. Nucleosides become nucleotides via a process called phosphorylation. Enzymes called kinases perform phosphorylation in cells.

The major nucleosides are adenosine, deoxyadenosine, guanosine, deoxyguanosine, 5-methyluridine, thymidine, uridine, deoxyuridine, cytidine, and deoxycytidine.

Cancer – Cellular differention casingens and cancer therapy

Cancer:- In the normal circumstances, the proliferation of body cells is under strict control. The cells differentiate, divide and die in a sequential manner in a healthy organism. Cancer is characterized by **loss of control of cellular growth** and development leading to **excessive proliferation and spread of cells**. Cancer is derived from a Latin word meaning crab. It is presumed that the word cancer originated from the character of cancerous cells which can migrate and adhere and cause pain (like a crab) to any part of the body.

Neoplasia literally means new growth. Uncontrolled growth of cells results in tumors (a word originally used to represent swelling). Oncology (Greek : oncos tumor) deals with the study of tumors. The tumors are of two types:-

1. **Benign tumors :** They usually grow by expansion and remain encapsulated in a layer of connective tissue. Normally benign tumors are not life-threatening e.g. moles, warts. These types of benign tumors are not considered as cancers.
2. Malignant tumors or cancers : They are characterized by uncontrolled proliferation and spread of cells to various parts of the body, a process

referred to as metastasis. Malignant tumors are invariably life-threatening e.g. lung cancer, leukemia. About 100 different types of human cancers have been recognized. Cancers arising from epithelial cells are referred to as carcinomas while that from connective tissues are known as sarcomas. Methods for the early detection and treatment of cancers have been developed.

Chemical carcinogens

It is estimated that almost 80% of the human cancers are caused by chemical carcinogens in nature. The chemicals may be organic (e.g. dimethylbenzanthracene, benzo (a) pyrene, dimethyl nitrosamine) or inorganic (arsenic, cadmium) in nature. Entry of the chemicals into the body may occur by one of the following mechanisms.

1. Occupation e.g. asbestos, benzene.

2. Diet e.g. aflatoxin B produced by fungus (Aspergillus flavus) contamination of foodstuffs, particularly peanuts.

3. Drugs certain therapeutic drugs can be carcinogenic e.g. diethylstibesterol.

4. Life style e.g. cigarette smoking.

5-Ultraviolet rays, X-rays and J-rays have been proved to be mutagenic in nature causing cancers. These rays damage DNA which is the basic mechanism to explain the carcinogenicity.

- **Cancer :** Free radicals **can damage DNA**, and cause mutagenicity and cytotoxicity, and thus play a key role in carcinogenesis. It is believed that ROS can induce mutations, and inhibit DNA repair process, that results in the inactivation of certain tumor suppressor genes leading to cancer. Further, free radicals promote biochemical and molecular changes for rapid growth of tumor cells.

TUMOR MARKERS

The biochemical indicators employed to detect the presence of cancers are collectively referred to as tumor markers. These are the abnormally produced molecules of tumor cells such as surface antigens, cytoplasmic proteins,

enzymes and hormones. Tumor markers can be measured in serum (or plasma).

Aselected list of tumor markers and the associated cancers are given in Table

A couple of the most commonly used tumor markers are discussed hereunder.

1. Carcinoembryonic antigen (CEA) : This is a complex glycoprotein, normally produced by the embryonic tissue of liver, gut and pancreas.

The presence of CEA in serum is detected in several cancers (colon, pancreas, stomach, lung). In about 67% of the patients with colorectal cancer, CEA can be identified. Unfortunately, serum CEA is also detected in several other disorders such as alcoholic cirrhosis (70%), emphysema (57%) and diabetes mellitus (38%). Due to this, CEA lacks specificity for cancer detection. However, in established cancer patients (particularly of colon and breast), the serum level of CEA is a useful indicator to detect the burden of tumor mass, besides monitoring

the treatment.

Selected tumor markers and associated cancers

Tumor marker	*Associated cancer(s)*
Oncofetal antigens	
Carcinoembryonic antigen (CEA)	Cancers of colon, stomach, lung, pancreas and breast
Alpha fetoprotein (AFP)	Cancer of liver and germ cells of testis
Cancer antigen-125 (CA-125)	Ovarian cancer
Hormones	
Human chorionic gonadotropin (hCG)	Choriocarcinoma
Calcitonin	Carcinoma of medullary thyroid
Catecholamines and their metabolites (mainly vanillyl mandelic acid)	Pheochromocytoma and neuroblastoma
Enzymes	
Prostatic acid phosphatase	Prostate cancer
Neuron specific enolase	Neuroblastoma
Alkaline phosphatase	Bone secondaries

CANCER THERAPY

Chemotherapy, employing certain anticancer drugs, is widely used in the treatment of cancer. In the Table a selected list of the most commonly used drugs, and their mode of action is given.

The effectiveness of anticancer drugs is inversely proportional to the size of the tumor i.e. the number of cancer cells. The major limitation of cancer chemotherapy is that the rapidly dividing normal cells (of hematopoietic system, gastrointestinal tract, hair follicles) are also affected. Thus, the use of anticancer drugs is associated with toxic manifestations.

Cisplatin is used in the treatment of testicular, ovarian and several other cancers (bone, lung).

The side effects of cisplatin include bone marrow depletion, loss of hearing and impairment in kidney function. About 80% of testicular cancer patients survive with a new combination therapy of cisplatin, etoposide, and bleomycin.

A selected list of the most commonly used anticancer drugs and their mode of action

Anticancer drug	*Chemical nature*	*Mode of action*
Methotrexate	Folic acid analogue	Blocks the formatin of tetrahydrofolate (inhibits the enzyme dihydrofolate reductase). THF is required for nucleotide synthesis.
6-Mercaptopurine	Purine analogue	Inhibits the formation of AMP from IMP.
6-Thioguanine	Purine analogue	Blocks thymidylate synthase reaction.
Mitomycin C	Antibiotic	Results in cross bridges between DNA base pairs.
Actinomycin D	Antibiotic	Blocks transcription
Vinblastine and vincristine	Alkaloids	Inhibit cell division and cytoskeleton formation
Cisplatin	Platinum compound	Results in the formation of intrastrand DNA adducts

Free radicals

the supply of oxygen is absolutely essential for the existence of higher organisms. As the saying goes too much of even the best is bad. Very high concentrations of O2 are found to be toxic, and can damage tissues. The present day concept of oxygen toxicity is due to the involvement of **oxygen free radicals** or **reactive oxygen species (ROS)**. In fact, the generation of reactive metabolites of O2 is an integral part of our daily life.

A **free radical** is defined as a molecule or a molecular species that **contains one or more unpaired electrons**, and is **capable of independent existence**.

Types of free radicals

Oxygen is required in many metabolic reactions, particularly for the release of energy. During these processes, molecular O2 is completely reduced, and converted to water. However, if the reduction of O2 is incomplete, a series of reactive radicals are formed, as shown in the next column.

Besides the above (O2 –, H2O2, OH–), the other free radicals and reactive oxygen species of biological importance include singlet oxygen (1O2), hydroperoxy radical (HOO–), lipid peroxide radical (ROO–), nitric oxide (NO–) and peroxynitrite (ONOO–).

The common characteristic features of free radicals are listed

● Highly reactive

● Very short half-life.

* Can generate new radicals by chain reaction.

● Cause damage to biomolecules, cells and tissues.

Sources along with some examples for generation of free radicals

I Cellular metabolism

- Leakage of electrons from the respiratory chain (ETC).
- Production of H_2O_2 or O_2^- by oxidase enzymes (e.g. xanthine oxidase, NADPH oxidase).
- Due to chain reactions of membrane lipid peroxidation.
- Peroxisomal generation of O_2 and H_2O_2.
- During the synthesis of prostaglandins.
- Production of nitric oxide from arginine.
- During the course of phagocytosis (as a part of bactericidal action).
- In the oxidation of heme to bile pigments.
- As a result of auto-oxidation e.g. metal ions [Fe^{2+}, Cu^{2+}]; ascorbic acid, glutathione, flavin coenzymes.

II Environmental effects

- As a result of drug metabolism e.g. paracetamol, halothane, cytochrome P_{450} related reactions.
- Due to damages caused by ionizing radiations (e.g. X-rays) on tissues.
- Photolysis of O_2 by light.
- Photoexcitation of organic molecules
- Cigarette smoke contains free radicals, and trace metals that generate OH^-.
- Alcohol, promoting lipid peroxidation.

Lipid peroxidation

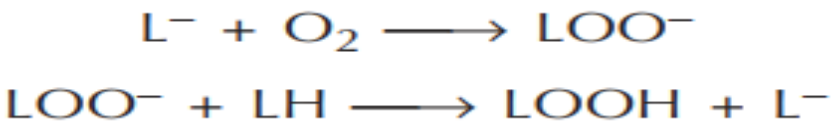
Free radical-induced peroxidation of membrane lipids occurs in three stages- initiation, propagation and termination

Initiation phase : This step involves the removal of hydrogen atom (H) from polyunsaturated fatty acids (LH), caused by hydroxyl radical

$$LH + OH^- \longrightarrow L^- + H_2O$$

Propagation phase : Under aerobic conditions, the fatty acid radical (L–) takes up oxygen to form peroxy radical (LOO–).

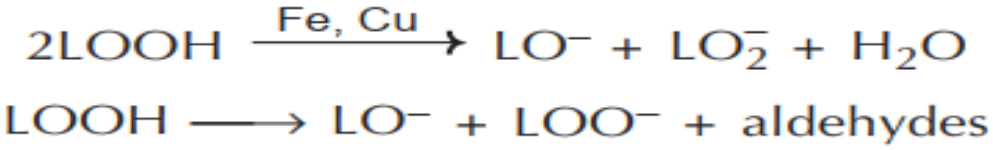
latter, in turn, can remove H-atom from another PUFA (LH) to form lipid hydroperoxide (LOOH).



$$L^- + O_2 \longrightarrow LOO^-$$

$$LOO^- + LH \longrightarrow LOOH + L^-$$

The hydroperoxides are capable of further stimulating lipid peroxidation as they can form alkoxy (LO–) and peroxyl (LOO–) radicals.



$$2LOOH \xrightarrow{Fe,\ Cu} LO^- + LO_2^- + H_2O$$

$$LOOH \longrightarrow LO^- + LOO^- + \text{aldehydes}$$

Termination phase : Lipid peroxidation proceeds as a chain reaction until the available PUFA(Polyunsaturated fatty acids) gets oxidized.

Malondialdehyde (MDA) as a marker for lipid peroxidation

Most of the products of lipid peroxidation are unstable e.g. carbonyls, esters, alkanes, alkenes, 2- alkenal, 2,4-alkadienal, MDA. Of these, malondialdehyde

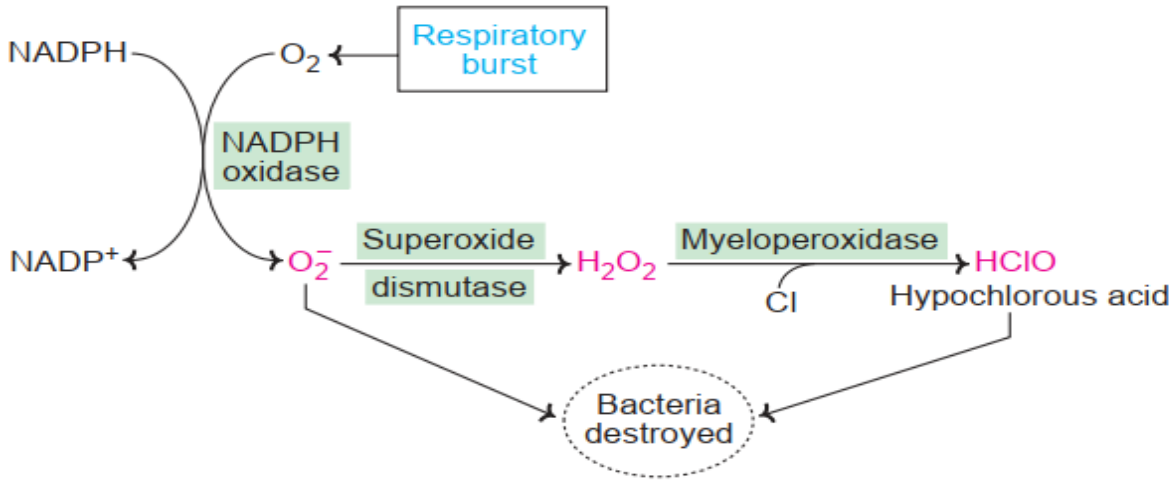
(CHO CH2 CHO) is the most extensively studied, and is used as a biochemical

marker for the assessment of lipid peroxidation. MDA and other aldehydes react with thiobarbituric acid and produce red-coloured products namely thiobarbituric acid reactive substances (TBARS) which can be measured colorimetrically. The estimation of serum MDA is often used to assess oxidative stress, and free radical damage to the body.

- **Nuclear accidents** explosions result in ionizing radiations. This causes oxidative damage to DNA and mutations which may lead to cancers.

Generation of ROS by macrophages

During the course of phagocytosis, macrophages produce superoxide (O^{-2}), by a reaction catalysed by NADPH oxidase . This O^{-2} radical gets converted to H2O2, and then to hypochlorous acid (HClO). The superoxide radical along with hypochlorous ions brings about bactericidal action. This truly represents the beneficial affects of the free radicals generated by the body. A large amount of O2 is consumed by macrophages during their bactericidal function, a phenomenon referred to as respiratory burst. It is estimated that about 10% of the O2 taken up by macrophages is utilized for the generation of free radicals.



Generation of free radicals by macrophages and respiratory burst.

Vitamins and Minerals

-Vitamins are organic substances, which means they're made by plants or animals.
-Minerals are inorganic elements that come from soil and water, and are absorbed by plants or eaten by animals.

-Vitamins may be regarded as organic compounds required in the diet in small amounts to perform specific biological functions for normal maintenance of optimum growth and health of the organism. Hence, the higher organisms have to obtain them from diet. The vitamins are required in small amounts, since their degradation is relatively slow.

What do minerals do in the body?

Minerals are important for your body to stay healthy. Your body uses minerals for many different jobs, including keeping your bones, muscles, heart, and brain working properly. Minerals are also important for making enzymes and hormones.

Types of minerals and their functions

There are hundreds of minerals – they are usually classified as either major or trace minerals. Although the amount you need differs between minerals, major (or macrominerals) are generally required in larger amounts. Some examples include calcium, phosphorus, potassium, sulphur, sodium, chloride, magnesium.

Trace minerals (microminerals), although equally important to bodily functions are required in smaller amounts. Examples include iron, zinc, copper, manganese, and iodine selenium. Some of the important minerals to keep us healthy are listed below.

1-Calcium

Calcium is vital to keep our bones strong and healthy. If you don’t get enough calcium, your bones will eventually become weak and brittle and can lead to conditions like osteoporosis. Calcium helps:

A-strengthen bones and teeth B -regulate muscle and heart function

C-blood clotting D-transmission of nervous system messages

E-enzyme function. F-Food sources of calcium

At different life stages, our calcium needs vary. It is better to get calcium from foods than from calcium supplements.

Good sources of calcium include dairy foods like milk, yoghurt and cheese

Other sources of calcium include almonds

2-Iodine

Iodine is essential to make thyroid hormones. These hormones control your metabolic rate (the rate your body uses energy when it is resting). They also help your brain and body grow and develop.

- Food sources of iodine

We only need a very small amount of iodine in our diet. Iodine is found naturally in foods such as:

-dairy products - seafood -seaweed (kelp)

- eggs -some vegetables.

-Iodine can also be found in iodised salt.

You are likely to be getting enough iodine through your diet. However, if you are deficient and need to take a supplement, be guided by your doctor. Too much iodine can be harmful, especially if you have an underlying thyroid disorder.

3-Iron

Iron is an important mineral that is involved in various bodily functions, including the transport of oxygen in the blood the provision of energy to cells. It also vital to help our immune system function effectively to fight infection.

Food sources of iron:- Iron can be found in animal and plant foods including:

-red meat and offal -fish -poultry

-legumes -eggs

Iron deficiency:- Iron deficiency is common and can affect adults and children. Around one in 8 people do not consume enough iron to meet their needs.

Some factors such as certain foods and drinks can affect how much iron your body absorbs. Also, some groups are more at risk of iron deficiency, such as babies and young children, teenage girls, women with heavy periods, vegans and vegetarians and people with chronic conditions.

4-Zinc

Zinc is an important mineral involved in various bodily functions – growth and development as well as immune function.

Zinc also helps to produce the active form of vitamin A and transports it around the body.

Food sources of zinc:- Zinc is highest in protein-rich foods but may also be found in some plant foods. Dietary sources include:

- red meat -shellfish -poultry
- milk and cheese -whole grains - cereals with added zinc.

5-Magnesium

Magnesium is important due to its many functions in the body – including maintaining bone health and using glucose for energy.

Magnesium also supports immune function and helps regulate blood pressure and lung function.

Food sources of magnesium :-Dietary sources include:

- nuts (such as cashews) -legumes -dark green vegetables
- seafood -whole grains -chocolate and cocoa.

6-Potassium

Potassium is important for the nerves, muscles and heart to work properly. It also helps lower blood pressure.

Food sources of potassium :-Our bodies are designed for a high-potassium diet, not a high-salt diet. Food processing tends to lower the potassium levels in many foods while increasing the sodium content.

It is much better to eat unprocessed foods – such as fruit, vegetables and lean meats, eggs, fish and other healthy, everyday foods.

Foods high in potassium include:

- bananas and apricots -mushrooms and spinach - nuts and seeds.

Be guided by your doctor, some people with kidney disease, or who are taking some medications, need to be careful not to get too much potassium in their diet.

7-Sodium

A small amount of sodium is important for good health as it helps to maintain the correct volume of circulating blood and tissue fluids in the body.

Most of us are consuming far more sodium than we need. In fact, many Australians are consuming almost double the amount required.

Too much sodium can lead to high blood pressure (hypertension) and other health conditions.

Food sources of sodium:- Salt is the main source of sodium in our diet. It is a chemical compound (electrolyte) made up of sodium and chloride.

Many foods – wholegrains, meat and dairy products – naturally contain small amounts of sodium, while highly processed foods usually contain large amounts.

energy requirements for vitamins and minerals

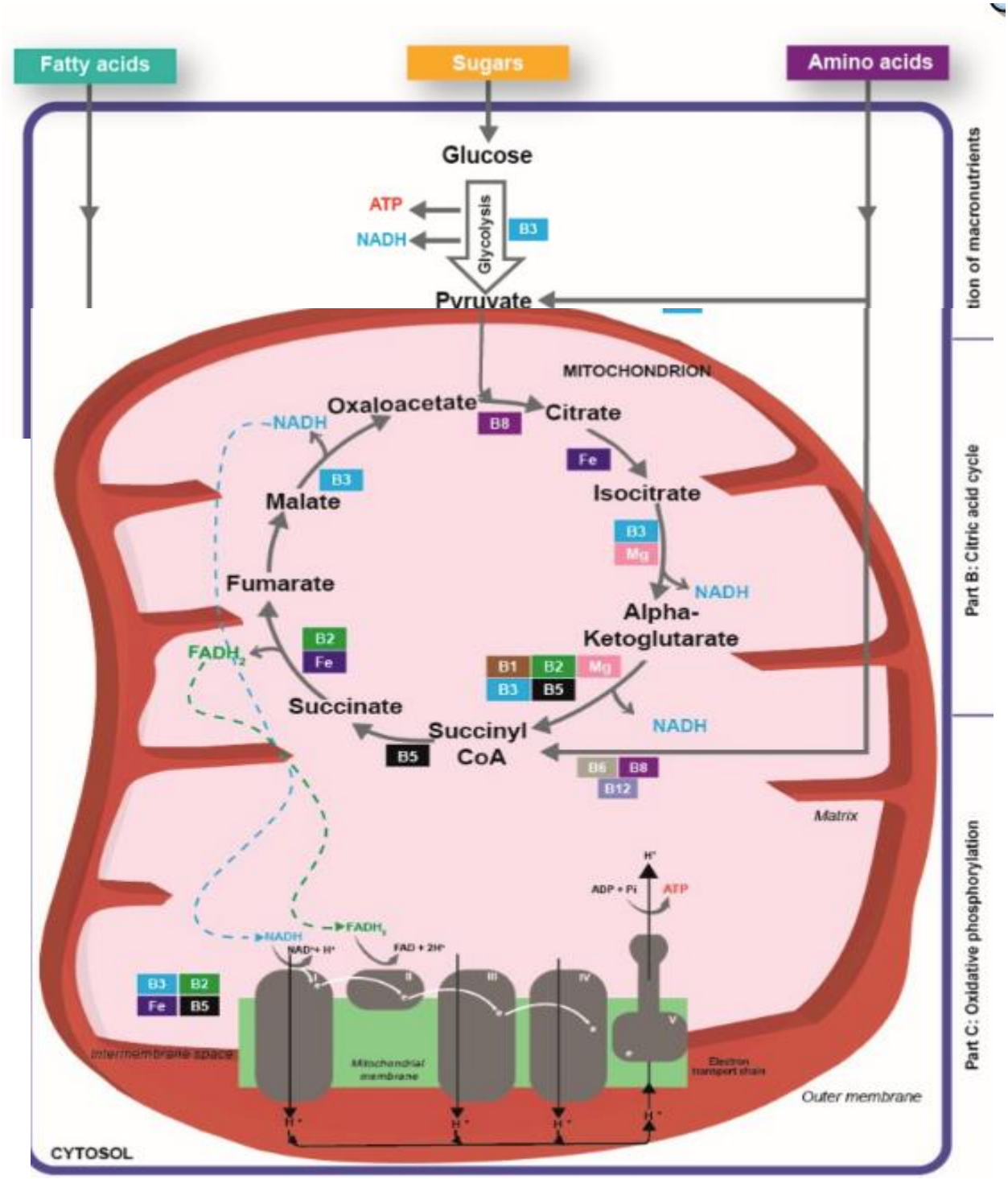
Vitamins and minerals are essential to humans as they play essential roles in a variety of basic metabolic pathways that support fundamental cellular functions. In particular, their involvement in energy-yielding metabolism, DNA synthesis, oxygen transport, and neuronal functions makes them critical for brain and muscular function. These, in turn, translate into effects on cognitive and psychological processes, including mental and physical fatigue.

Vitamins and Minerals Have Critical Roles in Cellular Energy Production

In humans, dietary macronutrients provide the fuel required to maintain the biochemical and structural integrity of the body, to perform physical activity and

to enable new tissue deposition [43]. Ingested food is digested by enzymes that break down carbohydrates into monomeric sugars (monosaccharides), lipids into fatty acids and proteins into amino acids. Sugars, fatty acids and amino acids enter the cell, where a gradual oxidation occurs, first in the cytosol, then in the mitochondria. The energy-generation process can be broken down into the three steps described below, that ultimately produce chemical energy as ATP that can be easily used elsewhere in the cell.

Oxidation of macronutrients into acetyl co-enzyme (acetyl-CoA, Figure)



Overview of the involvement of vitamins and minerals in the major pathways of cellular energy production. This figure displays a simplified scheme of energy metabolism. Briefly, macronutrients are oxidized (part A) into acetyl-CoA through several pathways including glycolysis, which produces pyruvate from glucose, and vitamins B1, B2, B3, B5 and C play important roles Then acetyl-CoA enters the citric acid cycle (part B), which generates energy as NADH and FADH2 through a series of eight oxidations that involve vitamins B1, B2, B3, B5, B6, B8 and B12 as well as iron and magnesium. Finally, the electrons of NADH and FADH2 are transferred to the electron transport chain (part C), where they provide energy used to generate ATP molecules; this step needs the input of vitamins B2, B3, B5 and of iron.

Acetyl-CoA is an activated carrier molecule that is derived from pyruvate that is itself issued from glucose during glycolysis, from fatty acids through beta-oxidation, and from certain amino acids (although they are preferably spared for protein synthesis)

Synthesis of vitamins by intestinal bacteria

Vitamins, as per the definition, are not synthesized in the body. However, the bacteria of the gut can produce some of the vitamins, required by man and animals. The bacteria mainly live and synthesize vitamins in the colon region, where the absorption is relatively poor.

Classification of vitamins

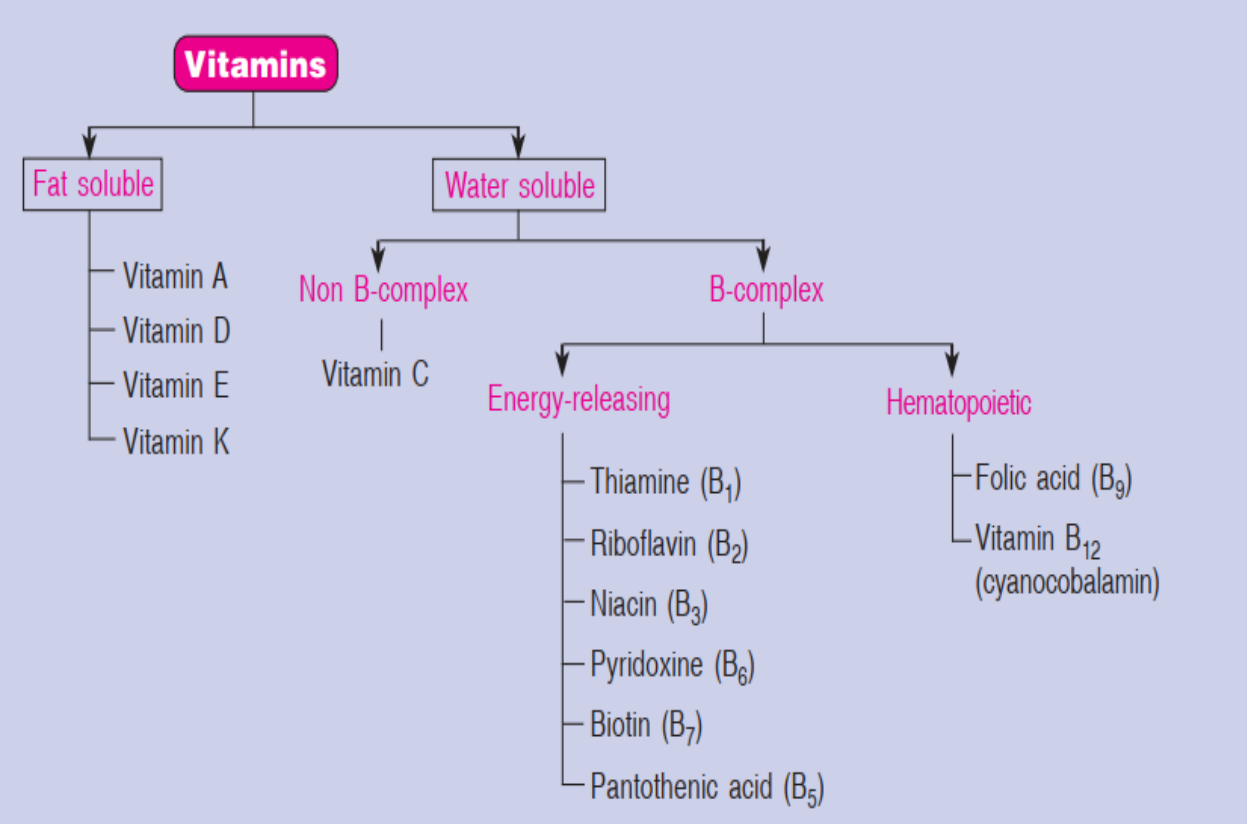
There are about 15 vitamins, essential for humans. They are classified as fat soluble (A, D, E and K) and water soluble (C and B-group) vitamins as shown in the Table , The B-complex vitamins may be sub-divided into energy-releasing (B1, B2, B6, biotin etc.).

hematopoietic (folic acid and B12). Most of the water soluble vitamins exert the functions through their respective coenzymes while only one fat soluble vitamin (K) has been identified to function as a coenzyme.

As far as humans are concerned, it is believed that the normal intestinal **bacterial synthesis**, and absorption of **vitamin K** and **biotin may be sufficient** to meet the body requirements. For other B-complex vitamins, the synthesis and absorption are

relatively less. Administration of anitibiotics often kills the vitamin synthesizing bacteria present in the gut, hence additional consumption of vitamins is recommended.

Classification of vitamins



Malnutrition risk

What are the consequences of malnutrition?

Malnutrition affects every system in the body and results in increased vulnerability to illness, increased complications and in extreme cases even death.

1-Immune system Reduced ability to fight infection.

2-Muscles :Inactivity and reduced ability to work, shop, cook and self-care.

3- Inactivity may also lead to pressure ulcers and blood clots.

4-Heart failure.

5- Impaired wound healing.

6- Kidneys :Inability to regulate salt and fluid can lead to over-hydration or dehydration.

7- Brain : Malnutrition causes apathy, depression, introversion, self-neglect and deterioration in social interactions.

8- Reproduction: Malnutrition reduces fertility and if present during pregnancy can predispose to problems with diabetes, heart disease and stroke in the baby in later life.

9- Impaired temperature regulation :-This can lead to hypothermia.

Obesity

Obesity is a complex disease involving having too much body fat. Obesity isn't just a cosmetic concern. It's a medical problem that increases the risk of many other diseases and health problems. These can include heart disease, diabetes, high blood pressure, high cholesterol, liver disease, sleep apnea and certain cancers.

-There are many reasons why some people have trouble losing weight. Often, obesity results from inherited, physiological and environmental factors, combined with diet, physical activity and exercise choices.

Symptoms

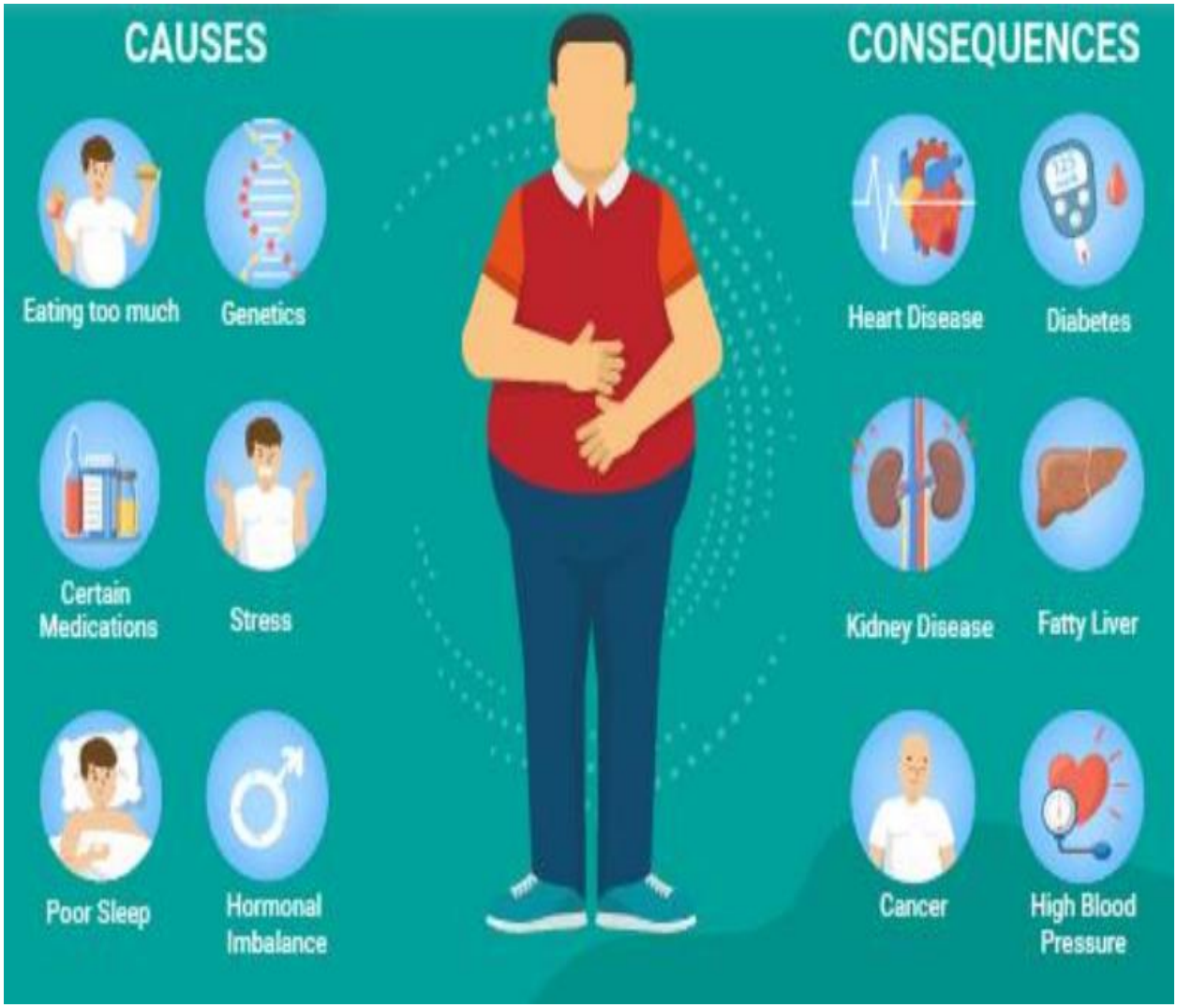
Body mass index, known as BMI, is often used to diagnose obesity. To calculate BMI, multiply weight in pounds by 703, divide by height in inches and then divide again by height in inches. Or divide weight in kilograms by height in meters squared. There are several online calculators available that help calculate BMI.

BMI	Weight status
Below 18.5	Underweight
18.5-24.9	Healthy
25.0-29.9	Overweight
30.0 and higher	Obesity

-For most people, BMI provides a reasonable estimate of body fat. However, BMI doesn't directly measure body fat. Some people, such as muscular athletes, may have a BMI in the obesity category even though they don't have excess body fat.

- Many health care professionals also measure around a person's waist to help guide treatment decisions. This measurement is called a waist circumference. Weight-related health problems are more common in men with a waist circumference over 40 inches (102 centimeters). They're more common in women with a waist measurement over 35 inches (89 centimeters). Body fat percentage is another measurement that may be used during a weight loss program to track progress.

Causes:- Although there are genetic, behavioral, metabolic and hormonal influences on body weight, obesity occurs when you take in more calories than you burn through typical daily activities and exercise. Your body stores these excess calories as fat.



Glycemic index (GI)

Glycemic index (GI) is a measure of how quickly a food can make your blood sugar (glucose) rise. Only foods that contain carbohydrates have a GI. Foods such as oils, fats, and meats do not have a GI, though in people with diabetes, they can affect the blood sugar.

What is the glycaemic index (GI)?

The glycaemic index (GI) is a rating system for foods containing carbohydrates and shows us how quickly each food affects your blood sugar (glucose) level when that food is eaten on its own.

Dr. David Jenkins originally created the GI to rank carbohydrates for people with diabetes. Instead of categorising carbohydrates as simple or complex, the GI ranks foods on a scale from 0 to 100.

Glycemic Index

Low GI (<55), Medium GI (56-69) and High GI (70>)

Grains / Starchs		Vegetables		Fruits		Dairy		Proteins	
Rice Bran	27	Asparagus	15	Grapefruit	25	Low-Fat Yogurt	14	Peanuts	21
Bran Cereal	42	Broccoli	15	Apple	38	Plain Yogurt	14	Beans, Dried	40
Spaghetti	42	Celery	15	Peach	42	Whole Milk	27	Lentils	41
Corn, sweet	54	Cucumber	15	Orange	44	Soy Milk	30	Kidney Beans	41
Wild Rice	57	Lettuce	15	Grape	46	Fat-Free Milk	32	Split Peas	45
Sweet Potatoes	61	Peppers	15	Banana	54	Skim Milk	32	Lima Beans	46
White Rice	64	Spinach	15	Mango	56	Chocolate Milk	35	Chickpeas	47
Cous Cous	65	Tomatoes	15	Pineapple	66	Fruit Yogurt	36	Pinto Beans	55
Whole Wheat Bread	71	Chickpeas	33	Watermelon	72	Ice Cream	61	Black-Eyed Beans	59
		Cooked Carrots	39						
Muesli	80								
Baked Potatoes	85								
Oatmeal	87								
Taco Shells	97								
White Bread	100								
Bagel, White	103								

Toxic substances in foods

Toxic substances in foods refer to chemicals that can harm human health. These substances can often be found in environmental pollution, pesticides, food processing methods, and even naturally in some foods.

-Toxic foods contain additives, genetically modified food (RED 40) and chemicals (MSG and aspartame). Therefore, you should stop yourself before buying or getting these foods.

-Another source of toxins is alcohol. Beverages containing alcohol contain sulfites, which can be considered toxic. We can also get toxins from vegetables and fruits that have been exposed to pesticides and grown based on conventional agriculture.

-One of the current toxin debates is mercury, which is found in foods and that we consume with some foods. High levels of mercury can cause illness and even death. Stay away from processed foods to avoid the effects of toxins.

What is a Toxic Substance?

It is important to know what the toxic substance is rather than common foods that contain toxins. Toxic substances are chemicals that disrupt normal physiological and biochemical mechanisms and kill many organisms when they invade the mouth, respiratory, skin, and infectious organisms. Toxic substances can exist in the form of solids, liquids, gasses or sprays. These substances can cause serious organ damage, dysfunction and inflammation in the long term.

Substances or drugs that are harmless or even beneficial to one person may have harmful or toxic effects on another. For example, aspirin alone has a good effect, but an overdose can be fatal. Medicines (including vitamins and supplements), detergents, pesticides, insecticides, chemicals used on plants, animals and food contain toxic substances.