Northern Technical University
Kirkuk Technical Institute
Department of Community Health Technologies

Clinical chemistry

First Stage

Dr. Layla A. S Laylani
&
MSc. Israa N. Q Al.attar

Introduction to Clinical Chemistry

Introduction

* It is a science which interest in study of changes in the chemical substances in patient's body because of disease.

* The main role of clinical biochemistry also refers to study and measure the biochemical abnormalities of substances in human diseases

* **Clinical chemistry:** is the area of clinical pathology that is generally concerned with analysis of bodily fluids.

Techniques

Techniques are used in clinical laboratory such as spectrophotometry, immunoassays, and electrophoresis to measure the concentration of substances such as glucose, lipids, enzymes, electrolytes, hormones, proteins, and other metabolic products present in human blood and urine.

Normal range

Set of values that use to interpret a patient's test results.

The normal range for a given test is based on the results that are seen in 95% of the healthy population. The normal range for a test may be different for different groups of people (for example, men and women). Also, it called reference range, or reference values

Types of specimens in clinical analysis

1. Whole blood
2. Serum
3. Plasma
4. Urine
5. Cerebrospinal fluid (CSF)
6. Saliva

Body Fluids
Blood

Body Fluids

* Body fluids are the fluids such as blood, lymph, milk and saliva which are produced in the body

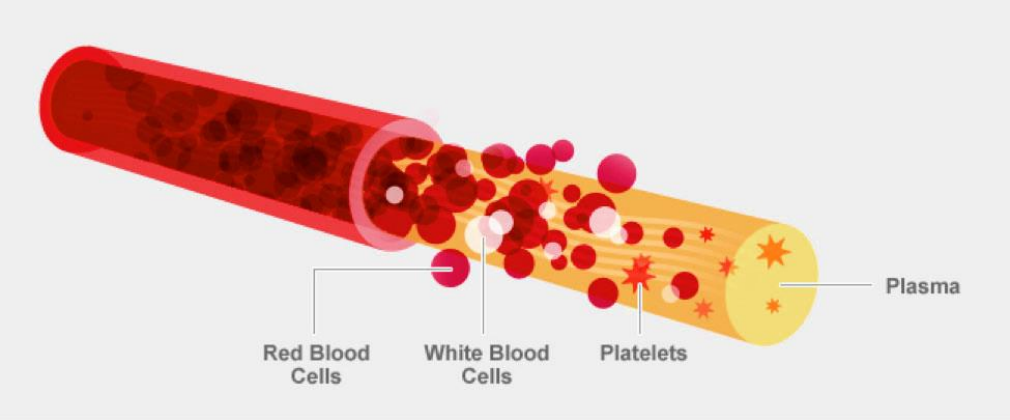
* Blood and lymph are the two most important body fluids in the human body.

Lymph

- is a colorless fluid present in the interstitial tissues.
- It circulates throughout the lymphatic system. It can be defined as blood without RBCs.
- The exchange of nutrients, hormones, and gases occurs through this fluid.
- It consists of lymphocytes that play a major function in the immune responses of the body.

Blood

* Is a fluid connective tissue that consists of plasma, blood cells and platelets.
* It circulates throughout our body delivering oxygen and nutrients to various cells and tissues.
* It makes up **8%** of our body weight.
* An average adult possesses around **5-6 liters** of blood.



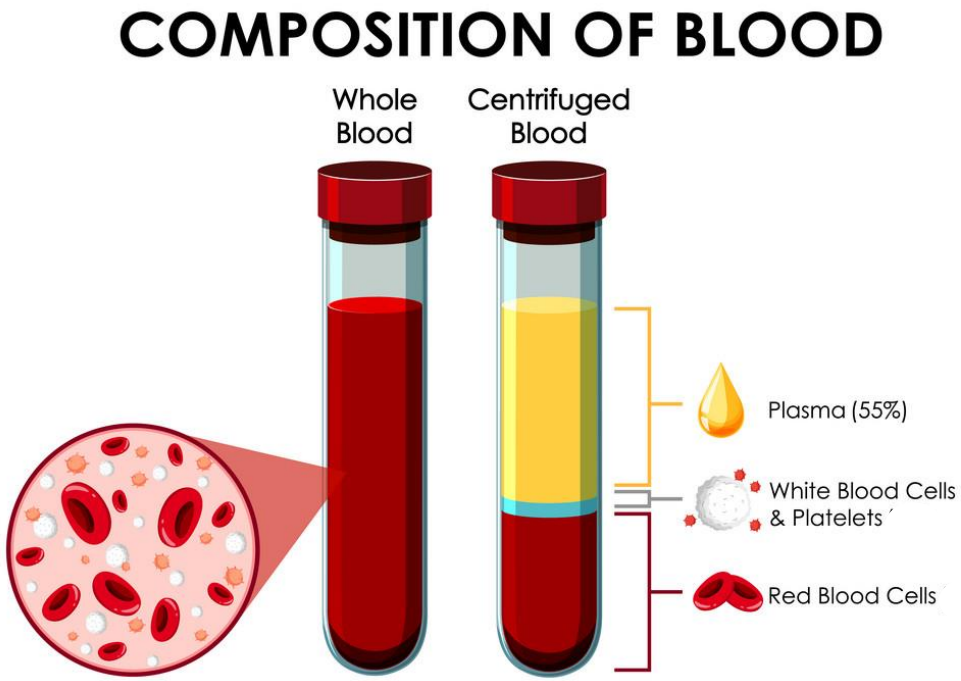
Whole Blood: the blood that flows through vein and arteries is called whole blood.

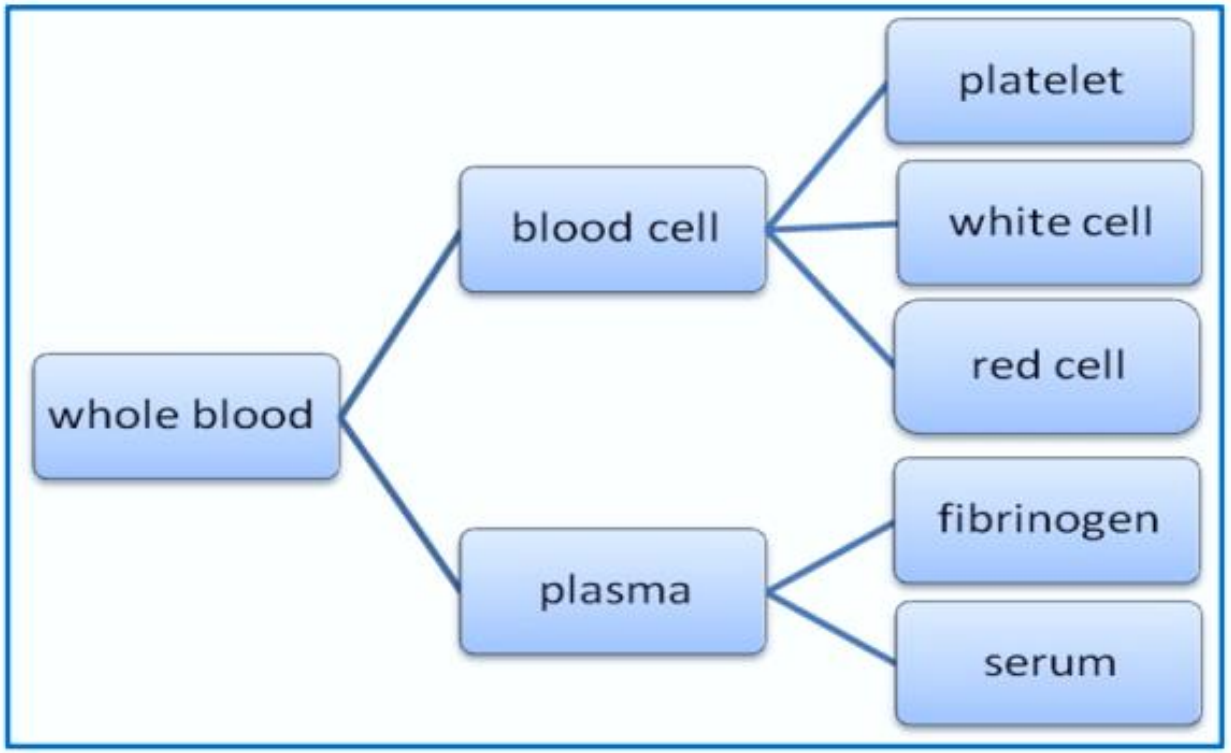
Composition of blood:

1- Plasma (55%)

2- White blood cells WBCs & Platelets (1%)

3- Red blood cells RBCs (44%)



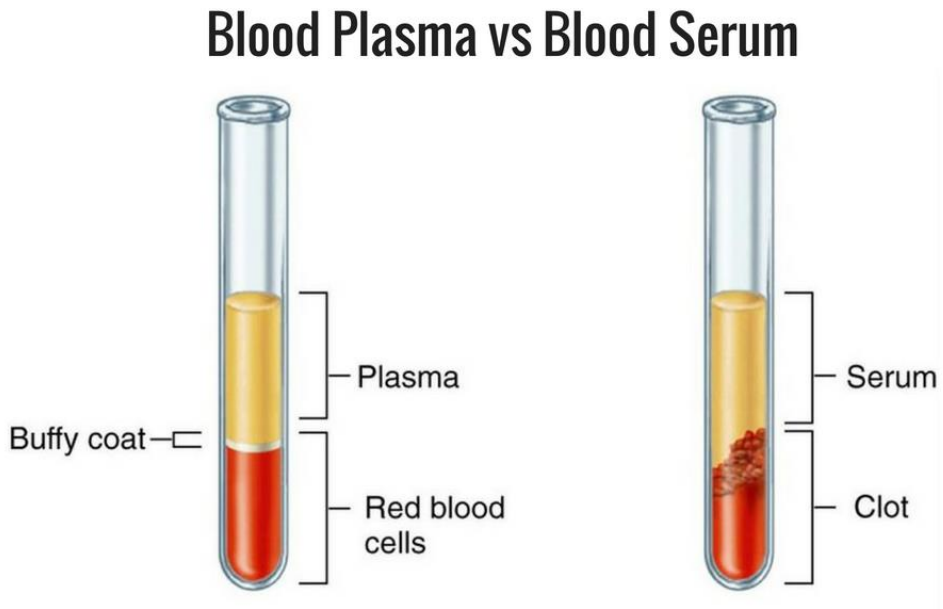

whole blood
blood cell
plasma
platelet
white cell
red cell
fibrinogen
serum

Plasma: is a pale yellow colored liquid component of a blood that holds the cellular elements of blood in suspension

Consist of ⟶ (water + electrolytes + proteins)

Serum: the fluid separates from clotted blood or blood plasma.

- It similar in composition to plasma but lacks fibrinogen and other substances that are used in the coagulation process.



The difference between plasma & serum

Plasma produced when centrifuge blood with anticoagulant.

Whole blood + anticoagulant

↓ Centrifuged

Plasma + Blood cells

Serum produced when centrifuge blood after clotting.

Whole blood → Clot formation

↓ Centrifuged

Clot + Serum

plasma proteins can divided in to:

Albumin : these help to regulate water potential by maintaining normal blood volume and pressure .They are the most common plasma proteins.

Immunoglobins (antibodies): these are very large proteins that target infection, together with the WBC they form the immune system.

Fibrinogen: to form a blood clot.

Major Types:

Albumin *(60%)*

Major component of osmotic pressure of plasma

Globulins *(35%)*

Antibodies (immunoglobulin) and transport proteins

Fibrinogens *(4%)*

Functions in blood clotting

Other *(<1%)*

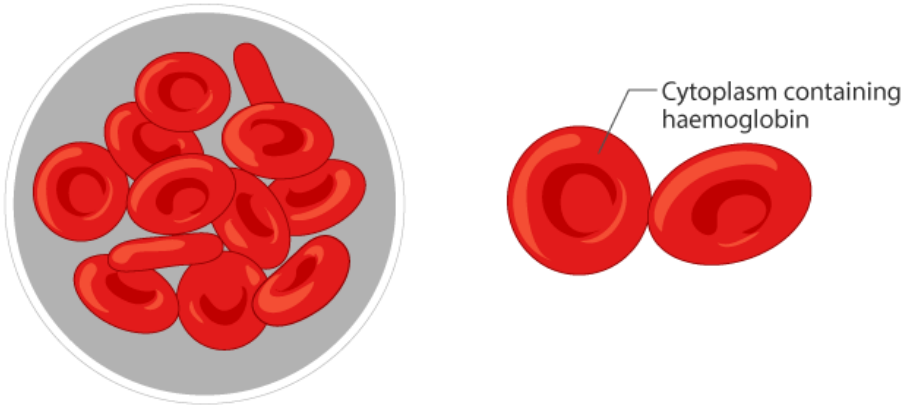
Various roles (α-1-antitrypsin, coagulation factors, etc.)

Blood cells

composed of red blood cell ,white blood cell and Platelets together they make up the 45% of blood.

1-Red blood cells (RBC)

* They are produced from stem cells in the bone marrow ,are full of hemoglobin
* Have no nucleus or mitochondria.
* Their function is to transport respiratory gases.
* It stay in circulation for about 120 days before they are destroyed in liver and spleen.

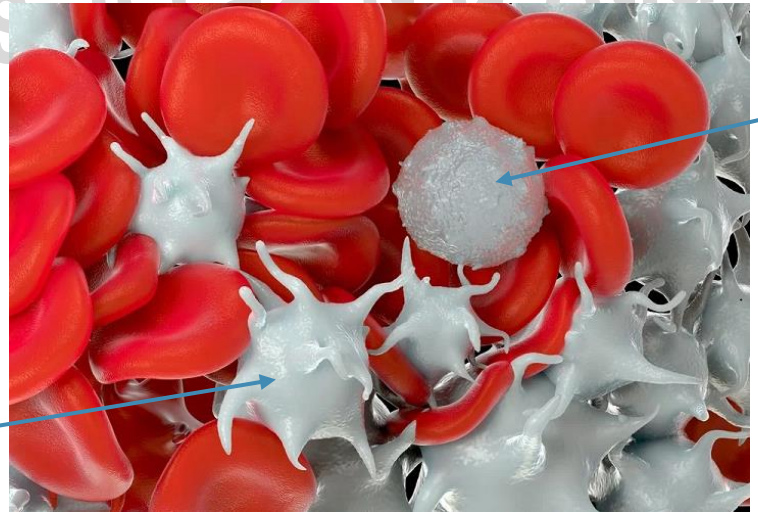


2- White blood cells (WBC)

* They are larger than RBC ,almost colorless.
* have a nucleus and do not contain hemoglobin .
* It live for a few days ,others can live for many months or years .
* They protect us from the infection and invasion by the foreign bodies.

3- Platelets

* Are not true cells; they are tiny fragments of other cells , that were formed in the bone marrow.
* their life-span is 7-11 days.
* Platelets play an important role in blood clotting.



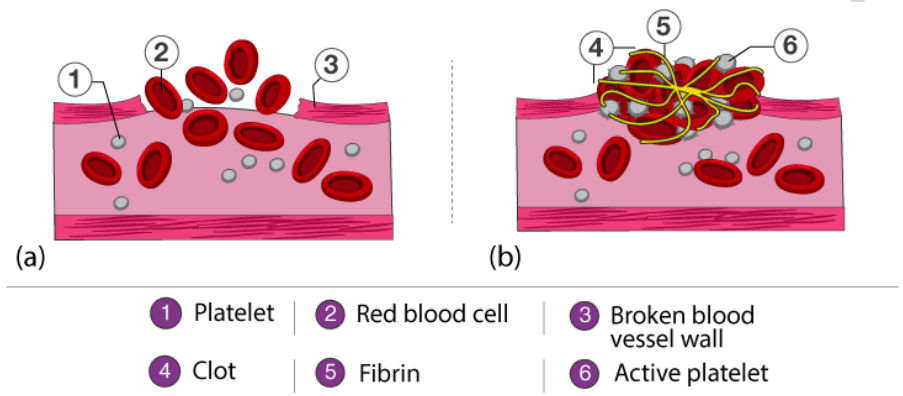
General properties of blood

1- Oxygenated blood has a characterized bright red color while deoxygenated blood has a dark publish color.
2- Specific gravity ranged between **1.054-1.060** .
3- PH of blood ranged between **7.35 - 7.45** .
4- The viscosity of blood approximately **4.5** times of water .

Function of blood

1- It carries oxygen , minerals and food to cells and it carries carbon dioxide (C_{02}) and others products away from cells.
2- Transport hormones ,enzymes and blood cells.
3- Regulate body temperature.
4- Maintenance of acid-base balance.
5- Contain clotting system (anticoagulants).
6- Blood play a role in defending the body against disease and protect us from the infections.

Clotting Factor: reaction which begins with chemicals released by injured cells and ends with a sticky meshwork of fibrin stop bleeding by producing a clot.



Mechanism of Clotting :

Prothrombin —(Thromboplastin)→ **Thrombin**

Fibrinogen —(Thrombin)→ **Fibrin**

(dissolved protein in plasma) ***(insoluble protein)***

Anticoagulant: A substance which prevents the coagulation of blood

Blood anticoagulants are:

1- Heparin: preventing transformation of prothrombin into thrombin and these prevented formation fibrin from fibrinogen .

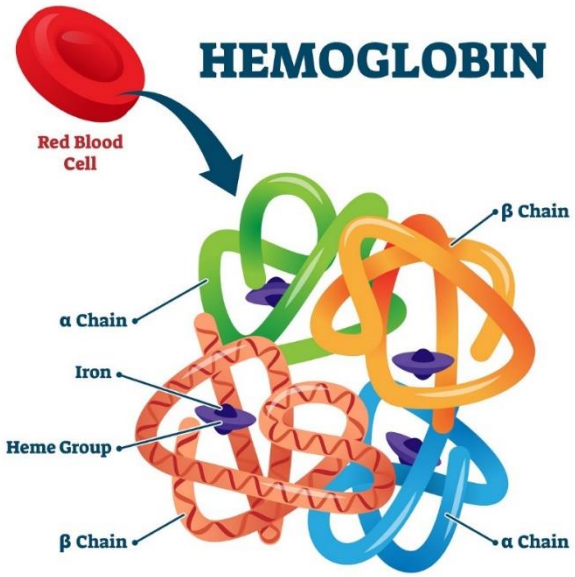
2- Oxalates (Na , Li , NH_4): to make on sedimentation of the Ca^{+2} in sample therefore don't to use in determination of test the Ca^{+2}

3- Sodium Fluoride: effective on enzymes (Inhibited of enzyme), don't to use in determination of test the enzymes .

4- Ethylene Diamine Tetra Acetic Acid (EDTA):

Hemoglobin

* Hemoglobin is the red pigments of blood, it is a conjugated protein.
* Hemoglobin = Globin(protein portion) + Hem group
* Hemoglobin consists of four polypeptide chains; each of them contains a hem group.
* Each hem group is composed of a porphyrin ring with an iron atom at its center.
* The iron atoms each bind to an oxygen molecule. They can also bind to carbon monoxide.



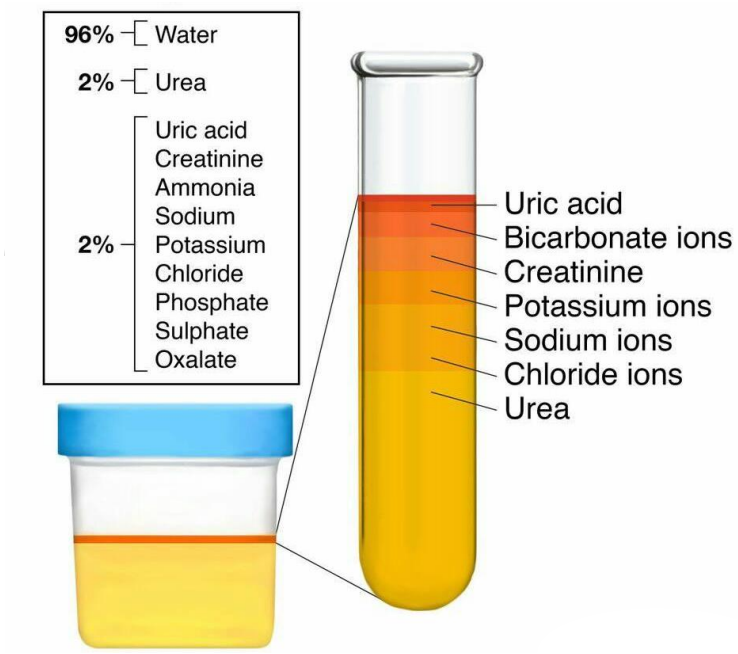
Body Fluids
Urine

Urine

Urine: is the fluid ; a complex aqueous solution of inorganic salts and organic compounds waste products of body metabolism excreted by the kidneys.

composition of normal urine:

In general, urine consists of urea (2%) , organic and inorganic chemicals (2%) dissolved in water (96%)



* The concentration of these substances can be affected by various factors such as:

1. Dietary intake,
2. Physical activity,
3. Body metabolism,

Urine formation process occur in 3 step :

1- glomerular filtration.

This takes place through the semipermeable wall of glomerulus and glomerular capsule, water and small molecules move from the glomerulus to the inside of the glomerular capsule.

2- tubular reabsorption.

many molecules are reabsorbed from the nephron into the capillary (diffusion, facilitated diffusion, osmosis, and active transport)i.e.
Glucose is actively reabsorbed with transport carriers.
If the carriers are overwhelmed glucose appears in the urine indicating diabetes

3- tubular excretion.

Substances are actively removed from blood and added to tubular fluid (active transport)
H+, creatinine, and some drugs are moved by active transport from the blood into the distal convoluted tubule

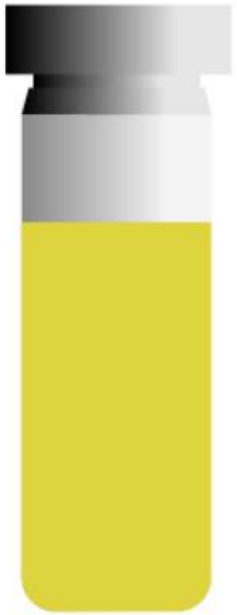
Constituents of chemicals solutes (organic & inorganic) in urine:

1- Organic

- Urea 2%
- Uric acid 0.03%
- Creatinine 0.1%

2- Inorganic

- Chloride
- Sulphate
- Calcium
- Sodium
- Phosphate
- Potassium
- Magnesium



Urine

0.05% Ammonia	0.18% Sulphate
0.12% Phosphate	0.6% Chloride
0.01% Magnesium	0.015% Calcium
0.6% Potassium	0.1% Sodium
0.1% Creatinine	0.03% Uric acid
2% Urea	

95% Water

Urinalysis

* Other names for it are **urine test** and **urine analysis**.

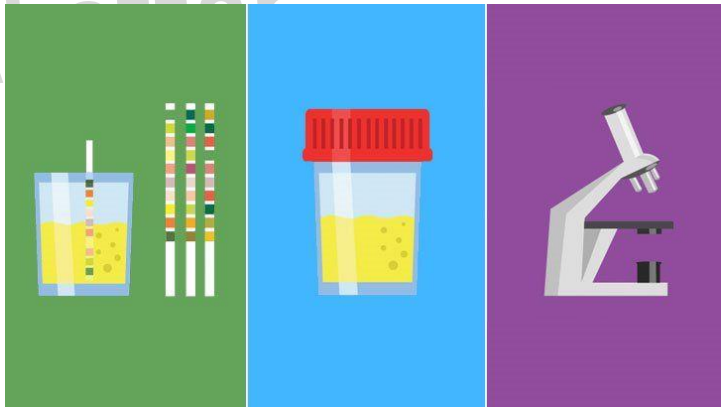
* it is a laboratory test done to detect problems with body that can appear in urine.

Urinalysis consist of:

1- Physical Examination:
Volume, Specific gravity, Color, Appearance, odor, pH.

2- Chemical Examination :
- For Normal Constituents
- **Organic:** Urea, Uric acid, Creatinine.
- **Inorganic:** Chloride, Phosphate, Bicarbonate, Sulphate, Ammonia, Oxalates

- For Abnormal Constituents-
- Proteins, Sugar (Glucose), Ketone bodies, Bilirubin, Bile salts & Blood



3- Microscopic examination

Urine properties

1- Volume

* Normally **1.5 -2** litters/**24** hours per normal adult.
* The actual quantity per person, per day affected by factors such as: recent fluid intake, diet, temperature and blood pressure

-If more than **2** liters/day named as Polyuria
-If less than **1** liter/day named as oliguria

* Polyuria : an increase in urine amount (in diabetic mellitus)
* Oliguria: decrease in urine amount (in dehydration Nephritis)
* Anuria: the complete absence of urine (in kidney failure)

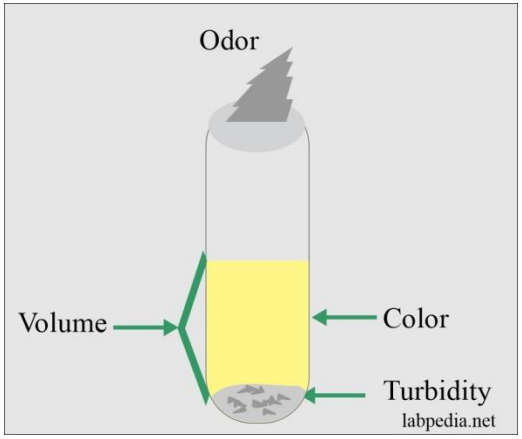
Normally	• **1.5 -2 litters/day**
Polyuria	• **more than 2 liters/day**
Oliguria	• **less than 1 liter/day**

2- Color

- Normal color is yellow or amber yellow.
- Abnormal colors: Colorless (polyuria).
- Orange (due to antibiotic intake or eating certain foods)
- Brownish or greenish (Bilirubin >2mg/dl in blood).
- Reddish (RBC's due to stone or blood mesentration).
- Milky (usually in male due to sperms in urine).
- Cloudy with offensive odor (due to pus, crystals or epithelial cells).

3- Odor

- Normally with aromatic odor.
- Abnormally: - Offensive odor due to pus increases.
- Acetone odor: - due to ketones increase (Ketonuria).



Abnormal Urinalysis

* For detecting the presence of abnormal constituents, urine reagent strip will be used.

* Reagent strips provide a means of rapidly screening large numbers of urine specimens in a short time:- pH, protein, glucose, ketones, blood, bilirubin, urobilinogen, nitrite.

In addition, SG and ascorbic acid may also be screened.

* A reagent strip is an inert plastic strip onto which reagent test are bonded.

* Chemical reactions take place when the strip is wetted in a urine sample

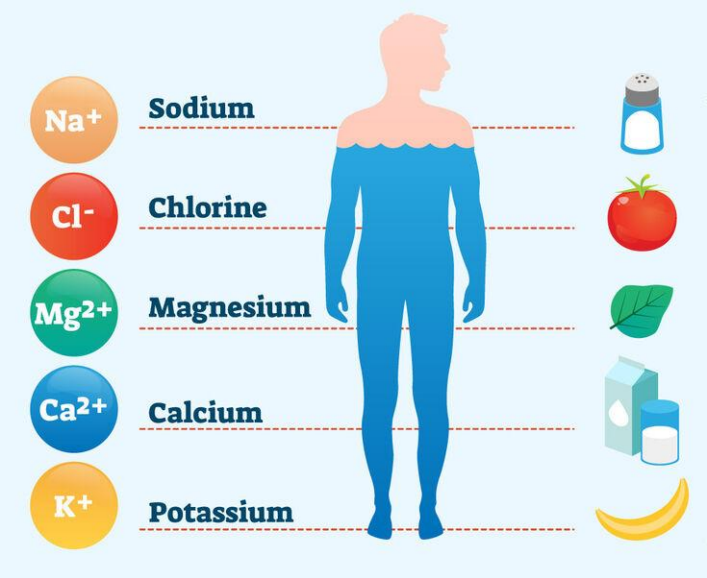
Disorder of electrolyte

electrolyte imbalance

An electrolyte imbalance occurs when you have too much or not enough of certain minerals in your body. This imbalance may be a sign of a problem.

Electrolytes: are minerals that give off an electrical charge when they dissolve in fluids like blood and urine.

Sodium → Na^+
Potassium → K^+
Chloride → Cl^-
Calcium → Ca^{2+}
Magnesium → Mg^{2+}
Phosphate → PO_4^{3-}



High electrolyte imbalances include:

Sodium: Hypernatremia.
Potassium: Hyperkalemia.
Calcium: Hypercalcemia.
Chloride: Hyperchloremia.
Magnesium: Hypermagnesemia.
Phosphate: Hyperphosphatemia.

Low electrolytes or electrolyte deficiencies include:

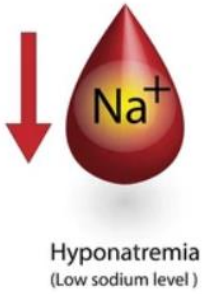
Sodium: Hyponatremia.
Potassium: Hypokalemia.
Calcium: Hypocalcemia.
Chloride: Hypochloremia.
Magnesium: Hypomagnesemia.
Phosphate: Hypophosphatemia.

Sodium

The normal sodium level in blood is 135-145 mEq/L

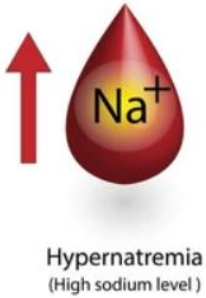
Hyponatremia

- Kidney failure
- Congestive heart failure
- Diuretics (water pills)
- Antidepressants and pain medication
- Severe vomiting or diarrhea
- Excessive thirst



Hypernatremia

- dehydration
- vomiting
- kidney disease
- diabetes insipid us
- extreme diarrhea
- Taking certain medications
- having large areas of burned skin can also lead to too much sodium in the blood.



Calcium

The normal calcium level in blood is 8.5-10.2 mg/dl (2.13 - 2.55 mmol/L)

Factors regulating blood calcium level

1- Vitamin D
2- Parathyroid hormone (PTH)
3- Calcitonin

Causes of Hypocalcemia and Hypercalcemia

Hypocalcemia

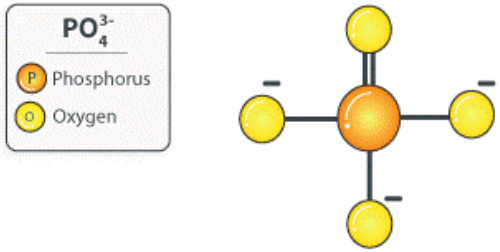
- Inadequate intake of calcium-rich food
- Medications intake that decreases calcium
- Hormonal changes in women
- Genetic factors
- Hypoparathyroidism
- Renal diseases leading to vitamin D
- inadequacy
- Abnormal blood magnesium levels

Hypercalcemia

- Hyperparathyroidism
- Cancer
- Heredity
- Severe dehydration
- Medications that increase the release of parathyroid hormone
- Intake of calcium and vitamin d supplement

Phosphate

Normal values range from:
- Adults: 2.8 to 4.5 mg/dL
- Children: 4.0 to 7.0 mg/dL



hypophosphatemia

- Alcoholism
- Hypercalcemia (too much calcium in the body)
- Primary hyperparathyroidism
- Too little dietary intake of phosphate
- Very poor nutrition
- Too little vitamin D

hyperphosphatemia

- Diabetic ketoacidosis
- Hypoparathyroidism (parathyroid glands do not make enough of their hormone)
- Kidney failure
- Liver disease
- Too much vitamin D
- Too much phosphate in diet
- Use of certain medicines such as laxatives that have phosphate in them

Iron

Normal results of iron

- 70 to 175 mcg/dL for men
- 50 to 170 mcg/dL for women
- 50 to 120 mcg/dL for children

*** following tests to check iron levels**

- Serum iron
- Hemoglobin
- Transferrin
- Ferritin

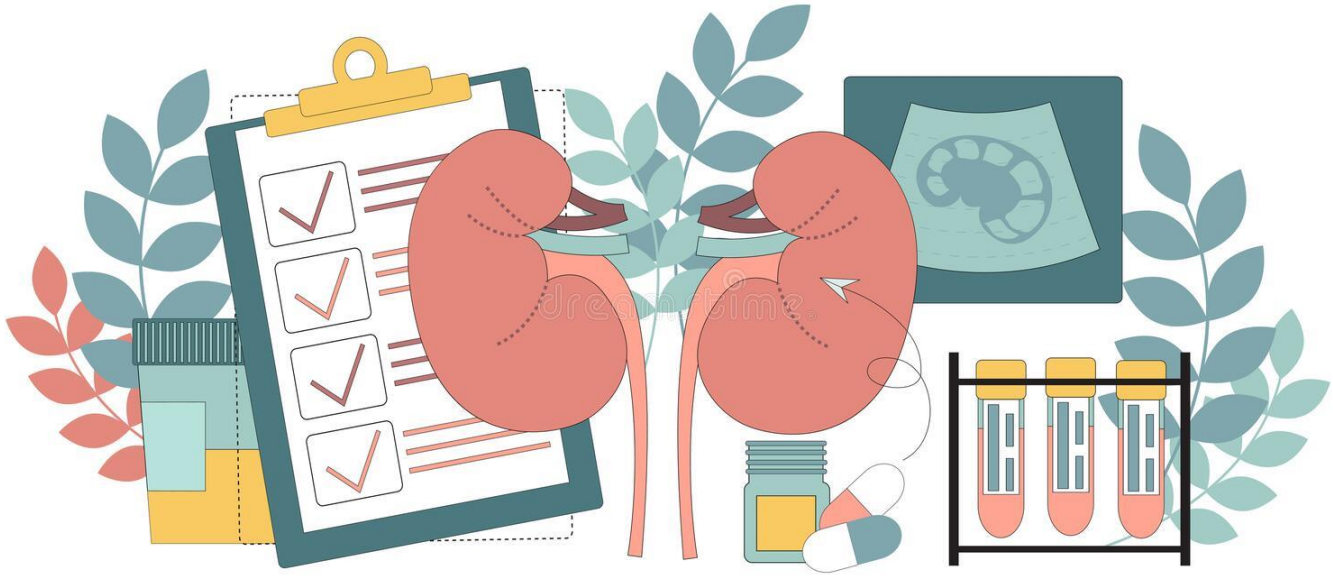
* Lower iron levels can be caused by conditions such as:

- Long-term digestive tract bleeding
- Intestinal conditions that cause poor absorption of iron
- Not enough iron in the diet
- Pregnancy

* High iron levels can be caused by conditions such as:

- Hemochromatosis
- Hemolytic anemia
- Hepatitis
- Iron poisoning
- Frequent blood transfusions

Kidney functions test (KFTs)



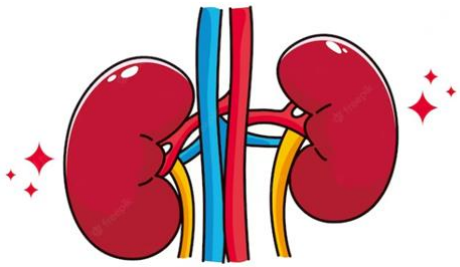
Kidney functions

Kidneys, the body's natural filtration system, perform many vital functions.

Including very important physiological roles:

A- Excretory Function (Filtration and excretion) Removal

1. End products of metabolism,
2. Excess inorganic ions ingested in the diet,
3. Drugs and toxins from the body through urine formation.



B- Regulatory Function:

1. Maintaining proper acid base balance
2. Maintain of homeostasis (regulation of water , electrolyte , acid base balance , pH).

C- Endocrine Function:

The kidney can be regarded as an endocrine organ that produces certain hormones and is also responsible for activation of several hormones

*** Hormonal functions (secretion).**

a- Erythropoietin: stimulates hemoglobin synthesis and formation of erythrocytes.

b- Calcitriol: active of Vitamin D and regulate calcium absorption from the gut.

c- Renin: proteolytic enzyme and formation of angiotensin ll , aldosterone production .

kidneys work:

Each of kidneys is made up of about a million filtering units called nephrons.
Each nephron includes a filter, called the glomerulus, and a tubule.

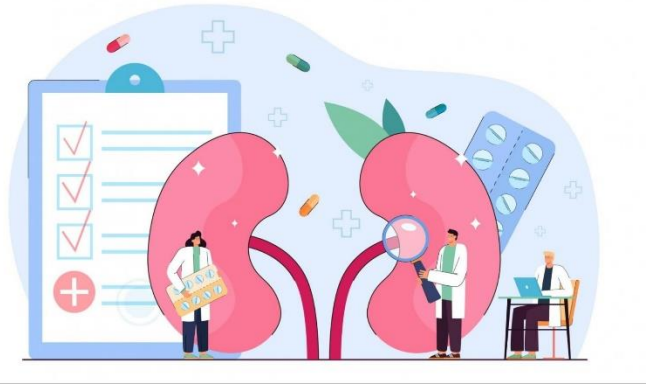
The nephrons work through a two-step process: the glomerulus filters blood, and the tubule returns needed substances to blood and removes wastes.

Kidney function tests is a group of blood tests that are done

1- To measure the levels of substances normally regulated by the kidneys
2- To help determine the cause of kidney dysfunction.
3- Early detection of possible renal impairment.
4- Monitor response to treatment.
5- Monitor the safe and effective use of drugs which are excreted in the urine.

The usual blood test which checks that the kidneys are working properly measures the level of :-

1- Blood urea nitrogen (BUN)
2- Creatinine
3- Creatinine Clearance Test
4- Uric acid.
5- Dissolved salts

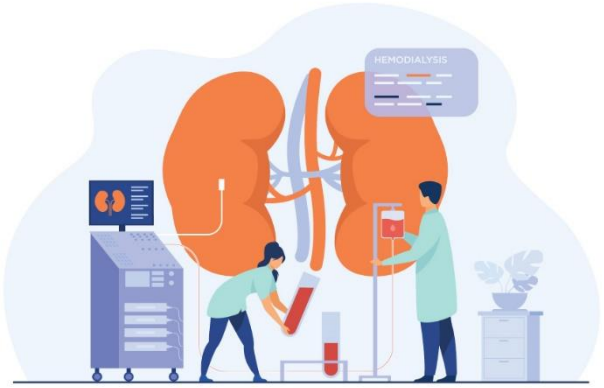


Blood supply to kidneys – relatively large.

1- Average **1200** ml of blood (650 ml plasma) passes through the kidney every minute.
2- Average **120-125** ml is filtered per minute by the kidneys.

glomerular filtration rate (GFR)

1- Normal filtrate formed in an adult is about **175-180** liters /day.
2- Only **1.5** liters is excreted urine
More than **99%** of the glomerular filtrate is reabsorbed by the kidneys



Causes of renal disease :

1- Pre-renal
- Any condition that results in reduced blood flow to kidneys.
- Severe blood loss.
- Hemolysis.

2- Renal
- Damage to renal tissue, glomerular basement membrane or tubules.
- Diabetic or hypertensive nephropathy.
- Tubular damage due to toxic substances.
- Glomerulonephritis

3- Post Renal
- Obstruction to urine outflow.
- Ureteric or urethral stone.
- Prostatic cancer.

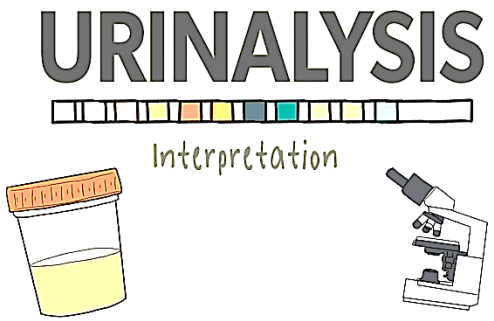
Some common kidney function tests:

1- Urinalysis

* A urinalysis (also known as a urine test) is a test that examines the visual, chemical and microscopic aspects of urine .
* It can include a variety of tests that detect and measure various compounds that pass through your urine using a single sample of urine

* Use urinalysis to screen for or monitor certain common health conditions, such as liver disease, kidney disease and diabetes, and to diagnose urinary tract infections (UTIs).

* Tests are included in urinalysis
- Color and appearance.
- Chemical findings.
- Microscopic findings.



2- Blood/serum analysis:

- Estimation of serum urea,
- Blood urea nitrogen
- Serum creatinine
- Protein and electrolyte

3- Glomerular function tests: Clearance test

a- Urea clearance
b- Creatinine clearance rate
c- Inulin clearance

4- Tubular function tests:

a- Urine concentration
b- Dilution test
c- urine acidification test

A-Serum urea

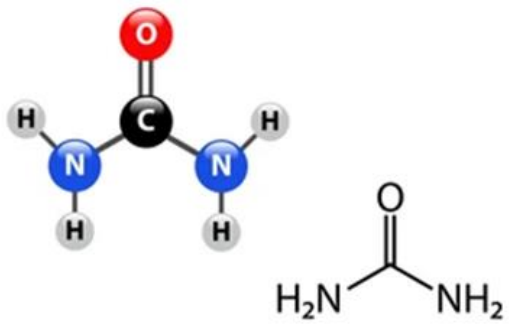
Urea: is the end product of protein catabolism. The urea is produced from the amino group of the amino acids and is produced in the liver by means of the Urea cycle.

* Urea undergoes filtrations at the glomerulus as well as secretion and re absorption at the tubular level.

* The rise in the level of serum urea is generally seen as a marker of renal dysfunction specially glomerular dysfunction.

* Urea level only rises when the glomerular function is reduced below **50%**.

* The normal serum urea level is between **20-45 mg/dl**. But the level may also be affected by diet as well as certain non kidney related disorders.



Urea
CH_4N_2O

increase the blood urea level

A high protein diet.

hyper metabolic conditions, starvation.

decrease the blood urea level

a low protein diet , in case of hepatic injury.

* So even though blood urea is not an excellent marker of renal dysfunction as it rises quite late in the dysfunction and its rise is also not exclusive to kidney dysfunction, but for practical purposes serum urea level is still one of the most ordered test and forms an important part of the kidney function test.

Urea cycle

The urea cycle is a filtering process to remove toxic substances from your body and keep other substances that are good for moving throughout your body.

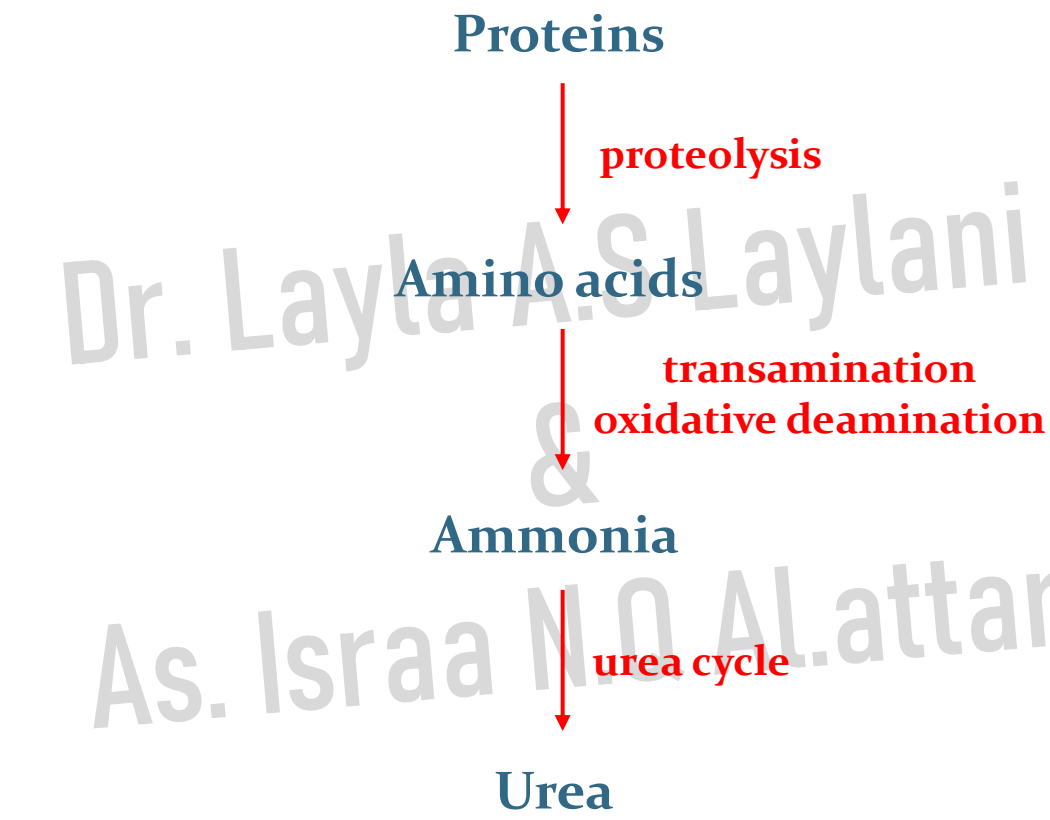
* The urea cycle begins when you eat

1- body breaks down (metabolizes) **protein** that comes from food in your diet and turns it into **amino acids** (which are the building blocks of proteins).

2- Digestion of **proteins** leads to waste products that turn into **ammonia** (Ammonia is toxic to body).

3- To remove ammonia, enzymes (which are proteins that produce chemical reactions) convert **ammonia** into **urea**

* Enzymes move urea through your blood and kidneys.
* The final step of the urea process is to pass (excrete) urea from body in urine.

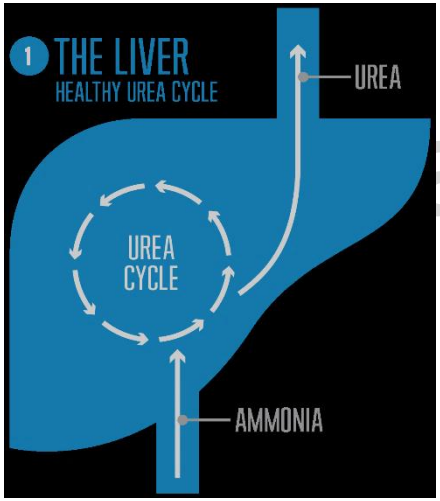


Relationships among some nitrogen compounds

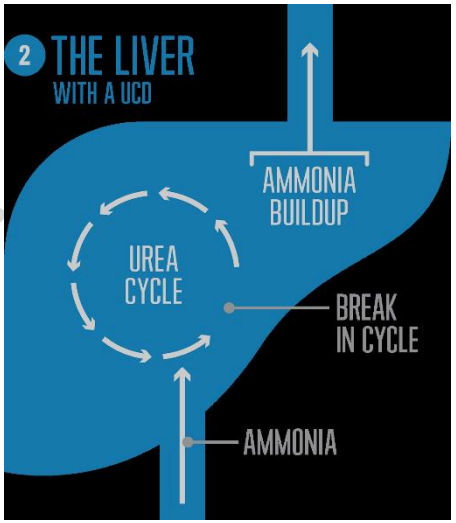
Urea cycle disorder (UCD)

Urea cycle disorder: is a genetic condition, also known as an inborn error of metabolism that causes ammonia to build up in your blood

* In someone with a UCD, the enzyme is missing or is not working correctly. because of this, ammonia builds up in the blood and it can be harmful.



Healthy Urea Cycle



Urea Cycle Disorder

B- Blood urea nitrogen (BUN)

The blood urea nitrogen (BUN) test reveals important information about how well the kidneys and liver are working.

* **Urea nitrogen** a waste product made as the body breaks down protein.

* High urea levels suggest decreased kidney function.

* BUN tests measure the amount of nitrogen in the blood.
However, not all elevated BUN tests are due to kidney damage.
Common medications can also increase BUN.

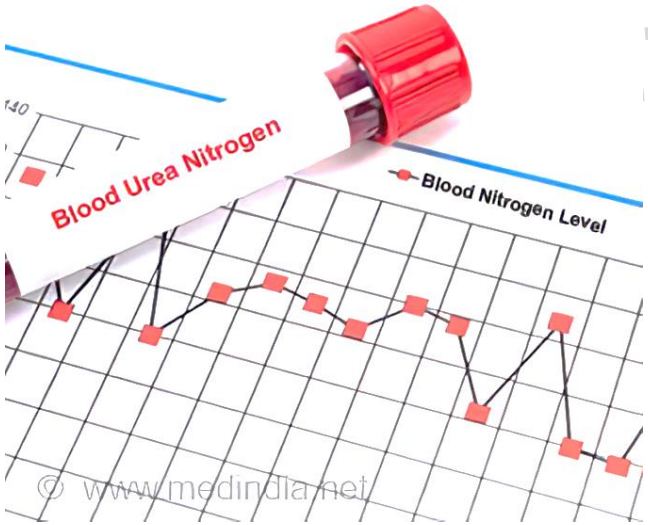
* Normal range of urea in blood **7- 20 mg/dL**.

*** Clinical significance :-**

a- Hyperuremia caused by (**Obstruction of urinary tract, Dehydration**).
b- Hypouremia (**severe liver disease or malnutrition**).

Blood urea nitrogen (BUN)

Sometimes the Serum urea level is expressed as blood urea nitrogen.
BUN can be easily calculated from the serum urea level. The molecular weight of urea is **60** and it contains two nitrogen atoms of combined atomic weight of **28**.
Hence the contribution of nitrogen to the total weight of urea in serum is **28/60** that is equal to **0.47**.
Hence the serum urea levels can be easily converted to BUN by multiplying it by **0.47**.
A rise in blood nitrogen level is known as azotemia.



C- Creatinine

* Creatinine is the waste product of creatine, which the muscles use to make energy.
* Creatinine is a nitrogenous compound it is produced from creatine in muscle at a rate dependent on muscle mass.
* It is usually removed from the blood by the kidneys and passes out in the urine.
* Creatinine varies with

1- Age
2- Gender
3- Body weight

* Creatinine is usually a more accurate marker of kidney function than urea. Because creatinine is less affected by diet and more suitable as an indicator of renal function.
* Creatinine should be

1- For males **0.8–1.2** mg/**100** ml
2- For females **0.6–0.9** mg/**100** ml.

* Clinical sig. chronic kidney debase & kidney obstruction.

D- Creatinine Clearance Test

* Creatinine clearance may be defined as the volume (ml) of plasma that would be completely cleared of creatinine per minute.

* This test evaluates how efficiently the kidneys clear creatinine from the blood.

* The body does not recycle creatinine, so all creatinine filtered by the kidneys in a given amount of time is excreted in the urine.

* That making creatinine clearance a very specific measurement of kidney function than other tests.

* Normal values

a. In male **107** to **139** mL/min

b. In female **87** to **107** mL/min

Creatinine Clearance (c)

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

C_{cr} = creatinine clearance
U_{cr} = conc. Of creatinine in urea
P_{cr} = creatinine conc. In plasma
V = urine volume in min. (urine flow rate)

Example

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

$$C_{cr} = \frac{1.25 \text{ mg/mL} \times \frac{60 \text{ mL}}{60 \text{ min}}}{0.01 \text{ mg/mL}}$$

$$= \frac{1.25 \text{ mg/mL} \times 1 \text{ mL/min}}{0.01 \text{ mg/mL}} = \frac{1.25 \text{ mg/min}}{0.01 \text{ mg/mL}} = 125 \text{ mL/min}$$

E- Uric Acid

- This test measures the amount of uric acid in a sample.
- Uric acid is a normal waste product that body makes when it breaks down chemicals called purines.
- Purines come from cells when they die.
  Purines are also found in many foods and beverages.
- Most uric acid dissolves in blood.
- kidneys filter the uric acid out of blood and it leaves body in urine.
- If uric acid builds up in blood, it can form needle-shaped crystals in and around joints this condition is called gout.

- High uric acid levels can also cause kidney stones, or kidney failure.
  But not everyone with high levels of uric acid will have these problems.

Other names: serum urate, UA, uric acid serum and urine

Normal values in blood 3.5 to 7.2 (mg/dL).
Normal values in urine 250 to 750 mg/24 hours.

used for:

A uric acid blood test may be used to:

- Help diagnose gout
- Monitor uric acid levels in people who are having cancer chemotherapy or certain other cancer treatments.

A uric acid urine test may be used to:

- Help find out whether high levels of uric acid are causing kidney stones

High uric acid levels in a blood test may happen if:

1- body makes too much uric acid
2- kidneys can't remove uric acid from blood
3- are eating too many foods that cause high levels of purines such as:

- Red meat and organ meats, including liver and kidney
- Certain kinds of seafood, including shellfish, sardines and tuna
- Alcohol (all types)
- High fructose corn syrup in soda and sweets

High levels of uric acid may be related to many conditions, including:

- Gout
- Kidney disease
- Leukemia or cancer that has spread in body (metastatic cancer)
- Side effects from certain cancer treatments.
- Alcohol use disorder.
- Preeclampsia, a condition that can cause dangerously high blood pressure in pregnant women.

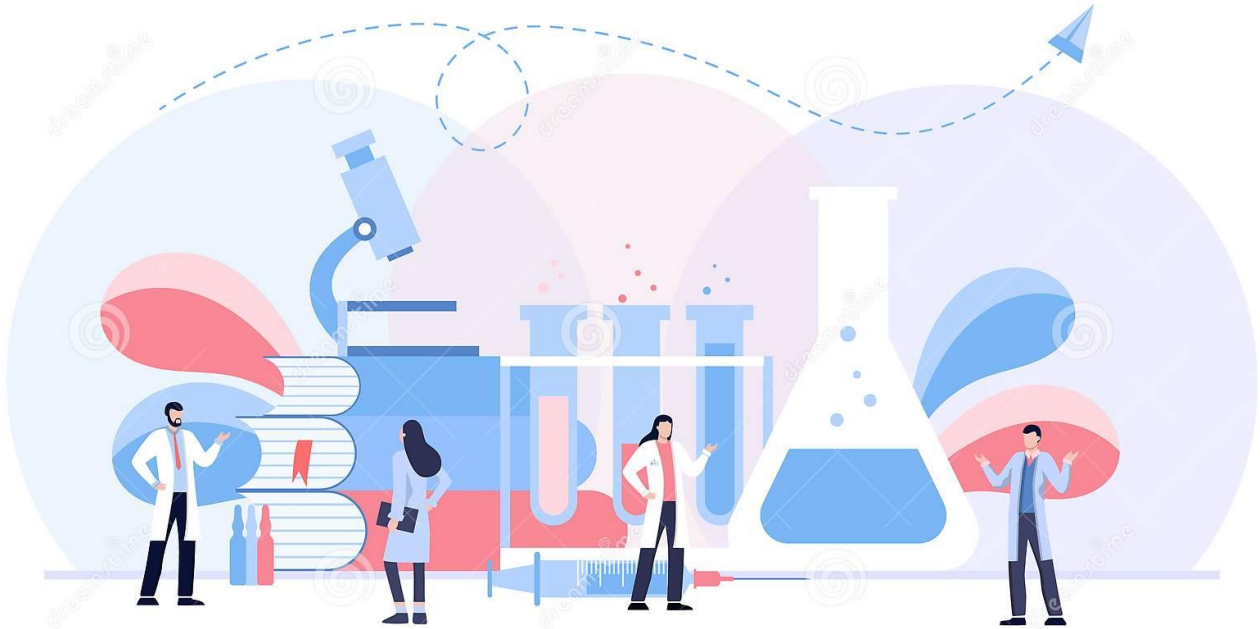
* Low levels of uric acid in blood are uncommon and usually don't cause health problems. Health conditions that are related to low uric acid levels are usually diagnosed using other tests.

High uric levels in urine, may be related to:

- Kidney stones or having a high risk for kidney stones
- An inherited genetic condition

* Low levels of uric acid in urine may be related to kidney disease, lead poisoning, or alcohol use disorder.

Plasma protein



Plasma protein

* Blood proteins, also termed plasma proteins, are proteins present in blood plasma.
* They serve many different functions, including transport of lipids, hormones, vitamins and minerals in activity and functioning of the immune system.
* Plasma contains >300 different proteins
* Many pathological conditions affect level of plasma proteins
* Mostly synthesized in the liver some are produced in other sites
* A normal adult contains 70 g/L of pps
* Contrary to popular belief, hemoglobin is not a blood protein, as it is carried within red blood cells, rather than in the blood serum.

Types of Plasma Proteins

The three significant plasma protein fractions are:
albumin, globulin, and fibrinogen.

Serum albumin: accounts for **60%** of blood proteins
is a major contributor to maintaining the oncotic pressure of plasma and assists as a carrier in the transport of lipids and steroid hormones.

Globulins: make up **35%** of blood proteins and transport ions, hormones, and lipids assisting in immune function.

Fibrinogen: comprises **4%** of blood proteins; conversion of fibrinogen to insoluble fibrin is essential for blood clotting.

* The remainder of the plasma proteins **1%** are regulatory proteins, such as enzymes, proenzymes, and hormones.

* All blood proteins are synthesized in liver except for the gamma globulins.

Major Types:

- **Albumin** *(60%)*
  Major component of osmotic pressure of plasma
- **Globulins** *(35%)*
  Antibodies (immunoglobulin) and transport proteins
- **Fibrinogens** *(4%)*
  Functions in blood clotting
- **Other** *(<1%)*
  Various roles (α-1-antitrypsin, coagulation factors, etc.)

Blood protein	Normal level	%	Function
Albumins	3.5-5.0 g/dl	60%	create and maintain osmotic pressure; transport insoluble molecules
Globulins	2.0-2.5 g/dl	35%	participate in immune system
Fibrinogen	0.2-0.45 g/dl	4%	Blood coagulation
Regulatory proteins		<1%	Regulation of gene expression
Clotting factors		<1%	Conversion of fibrinogen into fibrin

Hypoproteinemia

Hypoproteinemia is a clinical condition that involves low protein levels in the person's blood

Causes

- Malnutrition and undereating
- Liver disorders
- Kidney problems
- Celiac disease
- Inflammatory bowel disease

Diagnosis

- A blood test can reveal whether a person has enough protein in the body.
- perform a set of blood tests known as a total protein, albumin, and albumin/globulin (A/G) ratio.
- This test can reveal whether total protein levels are low and if albumin and globulin proteins are at optimal levels.
- If these two proteins are out of balance, it may signal a medical problem.

Non-protein nitrogen compounds

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

Low-molecular weight nitrogen compound	Source	Clinical and biochemical significance
Amino acids	Proteins	• Liver disease • Renal disease • Inborn errors of amino-acid metabolism
Ammonia	Amino acids	• Liver disease • Renal disease • Inborn errors of enzymes of the urea cycle
Urea	Ammonia	• Liver disease • Renal disease
Creatinine	Creatine	• Renal disease
Uric acid	Purine nucleotides	• Purine metabolism disorders • Excessive cell lysis

clinical enzymology

clinical enzymology

* Enzymes are catalysts that increase the rate of physiologic reactions.
* Each and every reaction in our body catalyzed by enzyme.
* 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.
* Thus clinical enzymology refers to measurement of enzyme activity for the diagnosis and treatment of diseases
* Since the tight control of enzyme activity is essential for homeostasis, any malfunction of a single critical enzyme (mutation, overproduction, underproduction or deletion) can lead to a genetic disease - commonly called inborn errors of metabolism.

Enzymes present in plasma can be classified into 2 types, they are
1- Functional Plasma enzymes.
2- Non-functional plasma enzymes.

Functional Plasma enzymes	Non-functional plasma enzymes
Present in plasma at higher concentration than tissues	Present in plasma at lower concentration than tissues
They function in plasma	Do not have any function in plasma
Mostly synthesized by the liver	Mostly synthesized by liver, skeletal muscle, heart, brain etc.
Usually decreased in disease conditions	Usually increased in disease conditions
Eg. Clotting enzymes, lipoprotein lipase	Eg. Creatine kinase, Alanine transaminase etc

* Measurement of these enzymes in plasma can be used to assess cell damage and proliferation (diagnosis of disease)

Distribution and application of clinically important enzymes

Enzymes	Tissues	Clinical applications
Alanineamino transferase	Liver	Hepato parenchymal diseases
Aspartate amino transferase	Liver Skeletal muscle Heart, Erythrocytes	Hepatic parenchymal disease, Muscle disease
Alkaline phosphatase	Liver, bone, Placenta	Liver and bone diseases
Amylase	Salivary glands Pancreas	Pancreatic diseases
Lipase	Pancreas	Pancreatic diseases

1- Liver enzymes

1- alanine transaminase (ALT)

- Test is a blood test that checks for liver damage.
- This enzyme is found mainly in your liver. Smaller amounts of ALT are in kidneys and other organs, too.
- body uses ALT to break down food into energy.
- Normally, ALT levels in the blood are low if liver is damaged, it will release more ALT into your blood and levels will rise.
- Doctors often give the ALT test along with other liver tests.

- The normal range is 7 to 55 U/L.

Other names for this Test:

- Alanine Aminotransferase Blood Test.
- Glutamic-Pyruvic Transaminase (GPT) Blood Test.
- Serum Glutamic-Pyruvic Transaminase (SGPT) Blood Test.

Why would doctor order this test?

if have symptoms of liver disease or damage, such as:

- Stomach pain or swelling
- Nausea
- Vomiting
- Yellow skin or eyes (a condition called jaundice)
- Weakness
- Extreme tiredness (fatigue)
- Dark-colored urine
- Itchy skin

Here are some reasons:

- been exposed to the hepatitis virus.
- drink a lot of alcohol.
- have a family history of liver disease.
- take medicine that's known to cause liver damage.

2- Aspartate Transaminase (AST)

- is an enzyme that is found mostly in the liver, but it's also in muscles and other organs in body.
- When cells that contain AST are damaged, they release the AST into blood.
- An AST blood test measures the amount of AST in your blood. The test is commonly used to help diagnose liver damage or disease.

Other names for this Test:

- SGOT test.
- serum glutamic oxaloacetic transaminase test.
- aspartate transaminase test.

Used for:

- An AST blood test is often part of a routine blood screening to check the health of liver.
- The test may help diagnose or monitor liver problems.
- It may also help diagnose other health conditions.

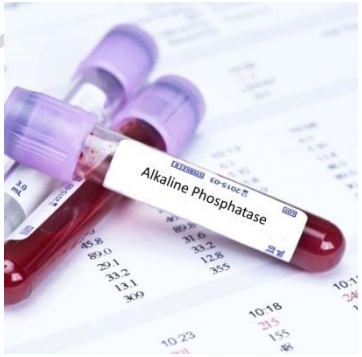
- The normal range is 8 to 48 U/L.

3- Alkaline phosphatase (ALP)

- test measures the amount of ALP in blood.
- ALP is an enzyme found in many parts of body.
- Each part of your body produces a different type of ALP.
- Most ALP is found in your liver, bones, kidneys, and digestive system.

- Abnormal levels of ALP in blood may be a sign of a wide range of health conditions, including liver disease, bone disorders, and chronic kidney disease.
- But an alkaline phosphatase test alone can't identify the source of ALP in blood, so other tests are usually needed to make a diagnosis.

Other names for this Test:
ALK, PHOS



used for:
- an alkaline phosphatase test is often used to screen for or help diagnose diseases of the liver or bones.
- The test may also help diagnose or monitor other health conditions.

- The normal range is 45 to 115 U/L.

2- Pancreatic enzymes

a-Amylase (AML)

* is an enzyme belonging to the class of hydrolases that catalyze the breakdown of starch and glycogen.

* Starch consists of both amylose and amylopectin.
amylase is therefore an important enzyme in the physiologic digestion of starches.

* amylase requires calcium and chloride ions for its activation .

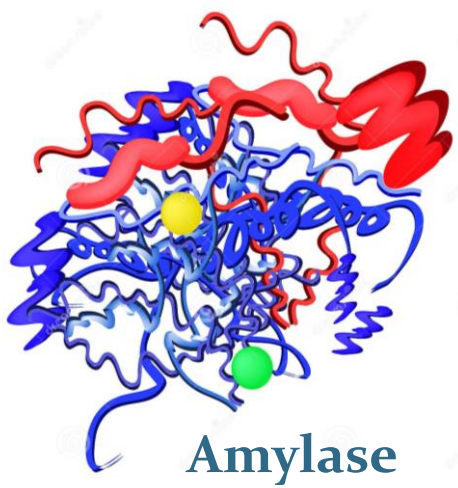
* The acinar cells of the pancreas and the salivary glands are the major tissue sources of serum AMS.

* Lesser concentrations are found in skeletal muscle and the small intestine and fallopian tubes.

* AMS is the smallest enzyme, with a molecular weight of (54 to 62 kDa) Because of its small size, it is readily filtered by the renal glomerulus and also appears in the urine.

* - Digestion of starches begins in the mouth with the hydrolytic action of salivary AMS.
  - Salivary AMS activity, however, is of short duration because, on swallowing, it is inactivated by the acidity of the gastric contents.
  - Pancreatic AMS then performs the major digestive action of starches once the polysaccharides reach the intestine.

* Normal values of amylase
  Serum ⟶ **40** to **140** units per liter (U/L) or **0.38** to **1.42** microkat/L (µkat/L).
  Urine ⟶ **1–15** U/h



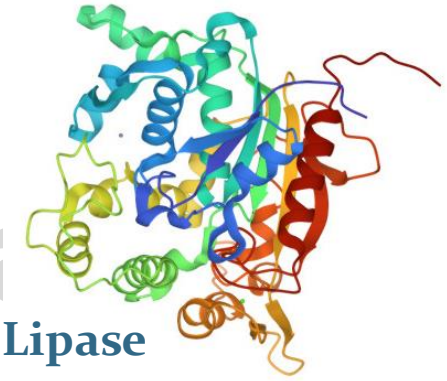
Amylase

Diagnostic Significance :

The diagnostic significance of serum and urine AMS measurements is in the diagnosis of acute pancreatitis.

High amylase levels	Low amylase levels
Acute pancreatitis	Chronic pancreatitis
Pancreatic cancer	Liver disease
Swollen salivary glands	Kidney disease
Cholecystitis	Cystic fibrosis
Gastroenteritis	Preeclampsia

b-Lipase (LPS)



Lipase

* Lipase is an enzyme that is made by pancreas also made in salivary glands and in stomach.
* It helps body digest fats.
* with molecular weight of 48 kDa.
* Higher levels of lipase may have a problem with your pancreas (acute pancreatitis, or sudden inflammation of the pancreas).
* normal value are 0 to 160 units per liter (U/L) or 0 to 2.67 microkat/L (µkat/L).
* 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.
* Lipase is not normally detected in urine samples.

Liver function test

liver

* The liver is the largest organ in the body. It is located below the diaphragm in the right upper quadrant of the abdominal cavity.

* An adult's liver weighs approximately The human liver weighs approximately **1500 g** and comprises **~2%** of total BW, and extends approximately from the right 5th rib to the lower border of the rib cage.

* The liver is separated into a right and left lobe, separated by the falciform ligament.

* The right lobe is much larger than the left lobe.

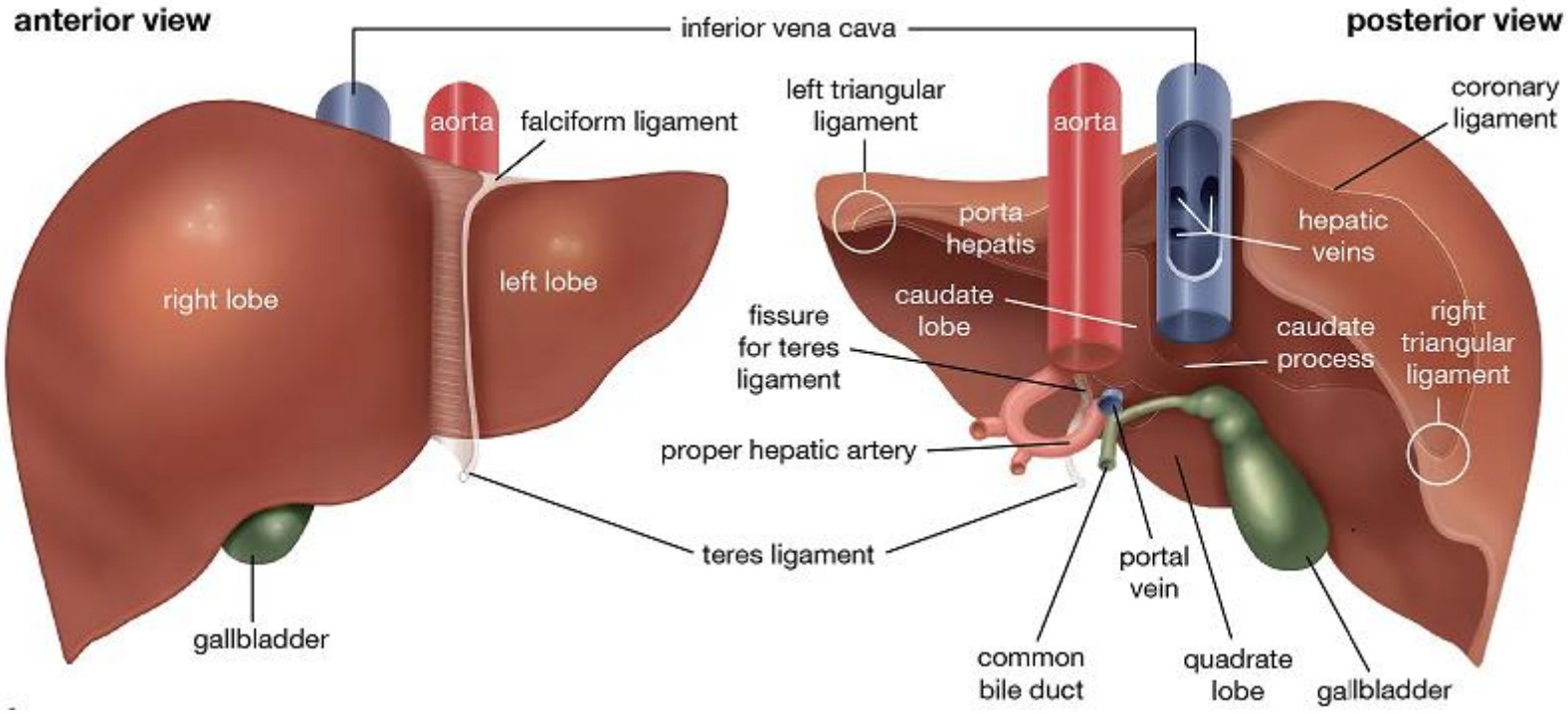
* The working cells of the liver are known as hepatocytes. Hepatocytes have a unique capacity to reproduce in response to liver injury.

* Liver regeneration can occur after surgical removal of a portion of the liver or after injuries that destroy parts of the liver. Although the liver's ability to react to damage and repair itself is remarkable, repetitive insults can produce liver failure and death.

Functions of the liver

The primary functions of the liver are:

1- Production of bile
2- Production of certain proteins for blood plasma
3- Production of cholesterol and special proteins to help carry fats through the body Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy) and to balance and make glucose as needed
4- Regulation of blood levels of amino acids
5- Processing of hemoglobin for use of its iron content
6- Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)
7- Clearing the blood of drugs and other poisonous substances
8- Regulating blood clotting
9- Resisting infections by making immune factors and removing bacteria from the bloodstream
10- Clearance of bilirubin, also from red blood cells. If there is an accumulation of bilirubin, the skin and eyes turn yellow.


anterior view
inferior vena cava
posterior view
aorta
falciform ligament
left triangular ligament
aorta
coronary ligament
porta hepatis
hepatic veins
right lobe
left lobe
caudate lobe
fissure for teres ligament
caudate process
right triangular ligament
proper hepatic artery
teres ligament
portal vein
gallbladder
common bile duct
quadrate lobe
gallbladder

Liver function tests (LFTs)

* Liver function tests are a group of tests done to assess the functional capacity of the liver as well as any cellular damage to the liver cells.

* To assess all functional capabilities of the liver such as:

A- Its Synthetic ability: By measuring the various plasma proteins such as albumin and prothrombin that are synthesized by the liver.
Also lipids which are also synthesized in the liver.

B- Its secretory/excretory abilities: By measuring the serum billirubin level.

1- Serum Bilirubin

* A bilirubin blood test measures the levels of bilirubin in blood.

* Bilirubin is a yellowish substance made during your body's normal process of breaking down old red blood cells.

Bilirubin is found in bile, a fluid your liver makes that helps you digest food.

* This test is used to find out how well liver is working.

* A small amount of bilirubin in your blood is normal, but a high level may be a sign of liver disease.

* If liver is damaged, bilirubin can leak out of liver and into blood.
when too much bilirubin gets into the blood stream, it can cause jaundice, a condition that causes skin and eyes to turn yellow.

* The common method of measuring serum bilirubin level is the Diazo method

* Bilirubin mainly exists in two forms in the blood.
Initially, bilirubin is "unconjugated" and water-insoluble.
unconjugated bilirubin is attached to albumin, the main protein in blood that carries substances to the liver.

* In the liver, bilirubin undergoes a process called conjugation with a substance called glucuronide; bilirubin becomes water-soluble and ready to be excreted into the bile.

* A total blood test includes unconjugated and conjugated bilirubin.

Total bilirubin: 0.2 to 1.2 mg/dL
Direct (conjugated) bilirubin: less than 0.3 mg/dL
Indirect (unconjugated) bilirubin: about 0.2 to 1.2 mg/dL

Liver Function Test

2- Total serum protein

* Protein in the blood consists of two main components: albumin and globulin.

* Albumin: produced by the liver
  Globulin: Some globulins are made by the liver others are made by the immune system, there are different types of globulins called alpha, beta, and gamma globulins

* Proteins are the essential building blocks of body tissues and cells, they are responsible for the production of hormones and enzymes in the body

* The total protein test is performed by measuring the amount of albumin and globulin in the blood serum.

* The normal range is 6.4 to 8.3 g/dL

* To measure the total protein content of the sample the biuret method it used.

Albumin/Globulin (A/G) Ratio

The albumin/globulin ratio in a total protein test is the ratio of the concentrations of two proteins albumin and globulin obtained by direct measurement of blood concentrations.

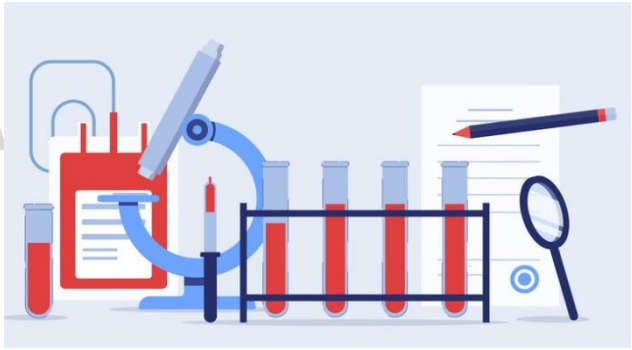
A/G Ratio = Albumin / (Total protein – Albumin)
Where both Albumin and Total protein are given in g/dL

Total protein → **6.4 to 8.3 g/dL**

Albumin → **3.4 to 5.4 g/dL**

Globulins → **2 to 3.5 g/dL**

A/G ratio → **1.5 to 2.5 g/dL**



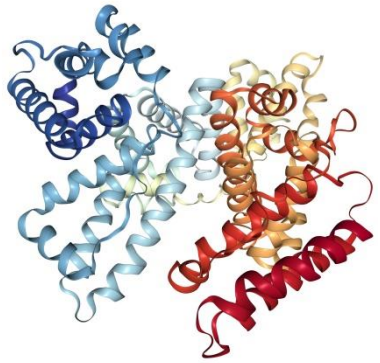
3- SERUM ALBUMIN (ALB)

* Albumin is the most common protein found in blood plasma. It helps to ensure blood stays in arteries and veins, and helps carry hormones, vitamins, and enzymes throughout the body.

* Albumin is made in the liver and quickly carried to the bloodstream

* The normal range is 3.4 to 5.4 g/dL.

* Lower-than-normal level of serum albumin may be a sign of:
1- Kidney diseases
2- Liver disease
3- Thyroid disease



Albumin

* High-than-normal level of serum albumin may be a sign of:
1- Dehydration
2- High protein diet

* To measure serum albumin the Bromocresol green method is used.

4- prothrombin time (PT/INR)

* A prothrombin time (PT) test measures how long it takes for a clot to form in a blood sample.

* An INR (international normalized ratio) is a type of calculation based on PT test results.

* Prothrombin is a protein made by the liver.

* It is one of several substances known as clotting factors (coagulation).

* When get a cut or other injury that causes bleeding, clotting factors work together to form a blood clot, how fast blood clots depends on the amount of clotting factors in blood and whether they're working correctly.

* If blood clots too slowly, you may bleed too much after an injury.

* If blood clots too fast, dangerous clots may form in arteries or veins.

PT/INR test is most often used to:

1- See how well warfarin is working.
Warfarin: is a blood-thinning medicine that's used to treat and prevent dangerous blood clots. (Coumadin is a common brand name for warfarin.)
2- Find out the reason for abnormal blood clots
3- Find out the reason for unusual bleeding
4- Check clotting function before surgery
5- Check for liver problems

* Are INR or prothrombin time results were not normal, it may mean one of the following conditions:

1- A bleeding disorder, a condition in which the body can't clot blood properly, causing excessive bleeding
2- A clotting disorder, a condition in which the body forms excessive clots in arteries or veins
3- Liver disease
4- Vitamin K deficiency. Vitamin K plays an important role in blood clotting.

* A normal PT/INR range

- 11 to 13.5 seconds
- INR of 0.8 to 1.1
- INR of 2.0 to 3.0 is a general therapeutic range for people taking warfarin.

* Prothrombin time calculation:

$$INR = \left\{ \frac{PT\ (pat)}{PT\ (n)} \right\}^{ISI}$$

PT (pat) = Patients prothrombin
PT (n) = Normal reference range
ISI = International sensitivity index (the optimal ISI is 1.3 to 1.5)

Carbohydrate

1- Glycaemia

* also known as blood sugar , blood sugar concentration, or blood glucose.

* Glucose (sugar) mainly comes from carbohydrates in the food and drinks consume. It's body's main source of energy, blood carries glucose to all of body's cells to use for energy.

* Insulin, a hormone pancreas makes, is the most significant contributor to maintaining healthy blood sugar.

* is a blood test that mainly screens for diabetes by measuring the level of glucose (sugar) in your blood.

* There are two main types of blood glucose tests:
  1- Capillary blood glucose test.
  2- Venous (plasma) blood glucose test.

* Normal range 70-100 mg/dL

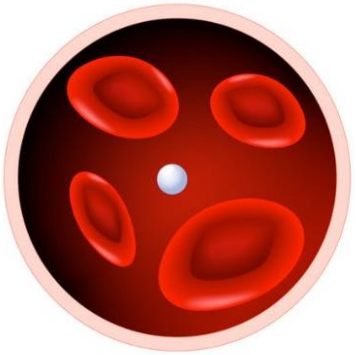
Hypoglycemia

* is a condition in which blood sugar (glucose) level is lower than the standard range.

* also called low blood glucose (sugar) , occurs when the level of glucose in blood drops below what is healthy .

* causes of hypoglycemia include:
  - not eating enough.
  - skipping meals.
  - drinking alcohol.
  - taking too much insulin.

* hypoglycemia signs and symptoms can include:
  - Dizziness, Fatigue, Shakiness, Sweating, Hunger, Headache
  - Fast heartbeat.
  - Inability to concentrate.
  - Irritability or anxiety

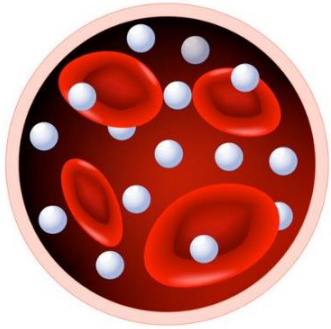


HYPOGLYCEMIA
(low blood sugar)

Hyperglycemia

* Hyperglycemia is a condition in which an excessive amount of glucose circulates in the blood plasma

* blood glucose levels rise either because there is an insufficient amount of insulin in the body or because the body cannot use insulin well.



HYPERGLYCEMIA
(high blood sugar)

* There are two main kinds:

1- Fasting hyperglycemia
This is blood sugar for patients who have diabetes that's higher than 130 mg/dL after not eating or drinking for at least 8 hours.

2- after-meal hyperglycemia. This is blood sugar that's higher than 180 mg/dL 2 hours after eat

* A number of medical conditions can cause hyperglycemia, but the most common by far is diabetes mellitus

What causes hyperglycemia other than diabetes?

- Pancreatic Diseases [Pancreatitis, Cancer, or Cystic Fibrosis]
- Obesity and Weight Factors.
- Lack of Physical Activity [Not Using Energy Stores].
- Polycystic Ovarian Syndrome [PCOS].

Symptoms of hyperglycemia include:

- increased thirst and a dry mouth
- needing to pee frequently
- tiredness
- blurred vision
- unintentional weight loss
- recurrent infections, such as thrush, bladder
- infections (cystitis) and skin infections

* Hyperglycemia can affect people with type 1 diabetes and type 2 diabetes, as well as pregnant women with gestational diabetes.

* It can occasionally affect people who don't have diabetes, but usually only people who are seriously ill, such as those who have recently had a stroke or heart attack, or have a severe infection.

Two major methods have been used to measure glucose:

1- is a chemical method.

2- using enzymes specific to glucose, the two most common employed enzymes are glucose oxidase and hexokinase.

* measurements are performed in a medical laboratory, using hexokinase, glucose oxidase or glucose dehydrogenase enzymes.

Blood glucose laboratory tests

1. Fasting blood sugar (glucose) test (FBS)
2. Random blood sugar (RBS)
3. Average blood glucose may be estimated by measuring glycated hemoglobin (HbA1c)

Hormonal regulation of carbohydrate metabolism

The normal glucose concentration: 70 to 100 mg/dL a slight variation of this normal level leads to hyperglycemia or hypoglycemia, the level of glucose is regulated by various hormones.

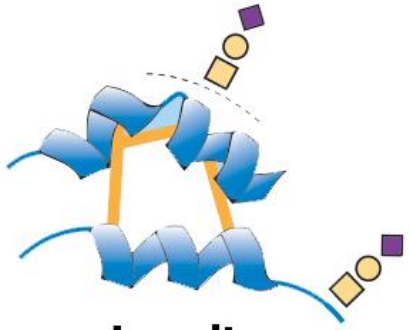
* There are two types of mutually antagonistic metabolic hormones affecting blood glucose levels:

1- catabolic hormones (such as glucagon, cortisol and catecholamines) which increase blood glucose

2- anabolic hormone (insulin), which decreases blood glucose

Insulin

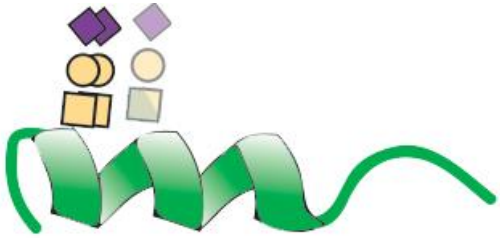
- Insulin is a peptide hormone secreted by β cells of islets of Langerhans from pancreas.
- Elevated blood glucose level leads to insulin secretion.
- The secreted insulin carries various anabolic functions.
- Thus, maintain high blood glucose in normal range.



Insulin

Glucagon

- Glucagon is also a peptide hormone secreted by α cells of islets of Langerhans from pancreas.
- It is an antagonist of insulin which shows the catabolic activities.
- It is secreted when there is fall in blood glucose level from normal range.
- Thus, it stops insulin secretion during low blood glucose level.
- It increases blood glucose mainly by breaking down of stored glycogen and triglycerides.



Glucagon

Lipids

lipid disorder

The term “lipid disorder” covers a range of conditions that can cause abnormal levels of lipids, in the blood.

Types of lipid disorders

- Familial combined hyperlipidemia (FCHL)
- Familial defective apolipoprotein B-100
- Familial dysbetalipoproteinemia (type 3 hyperlipoproteinemia)
- Familial hypertriglyceridemia
- Heterozygous familial hypercholesterolemia

Causes of lipid disorder

- Genetic factors
- Diet and lifestyle factors
- Medical conditions

Diagnosis of lipid disorder

can run a blood test called a lipid profile or lipid panel to initially diagnose a lipid disorder, this measures levels of total cholesterol, LDLs, HDLs, and triglycerides.

Disorders associated with lipids and lipoproteins

Obesity, the metabolic syndrome and diabetes are commonly associated with disorders of lipid and lipoprotein metabolism.

Common symptoms of these conditions include:

- leg pain, especially when walking or standing.
- chest pain.
- tightness or pressure in the chest and shortness of breath.
- pain, tightness, and pressure in the neck, jaw, shoulders, and back.
- indigestion and heartburn.
- sleep problems and daytime exhaustion.
- dizziness.
- heart palpitations.

How can lipid disorders be prevented?

- Lifestyle Modifications for Lipid Disorders.
- Exercise Regularly.
- Maintain a Healthy Weight.
- Consume Omega-3 Fatty Acids.
- Avoid Alcohol.

Secondary disorders of lipid metabolism?

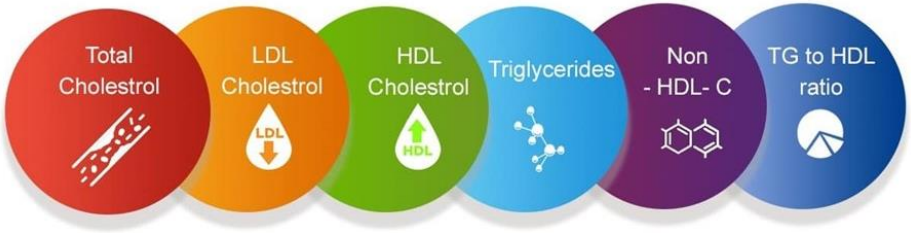
- Hypothyroidism (LDL hypercholesterolemia).
- Renal illnesses
  (hypertriglyceridemia, mixed hyperlipoproteinemia , lipoprotein elevation).
- Cholestasis liver disorders are the most common clinical.

What causes abnormal lipid metabolism?

Abnormal levels of blood lipids cause fat deposits in artery walls, which initiates complications inside the blood vessels. Causes for high lipid levels include diabetes, alcoholism, kidney disease, hypothyroidism, liver disease, and stress.

Lipid profile includes:

1. Total cholesterol (TC).
2. High-density lipoprotein cholesterol (HDL)
3. Triglyceride (TG).
4. Calculated Low-density lipoprotein (LDL).
5. Calculated very Low Density Lipoproteins (VLDL).

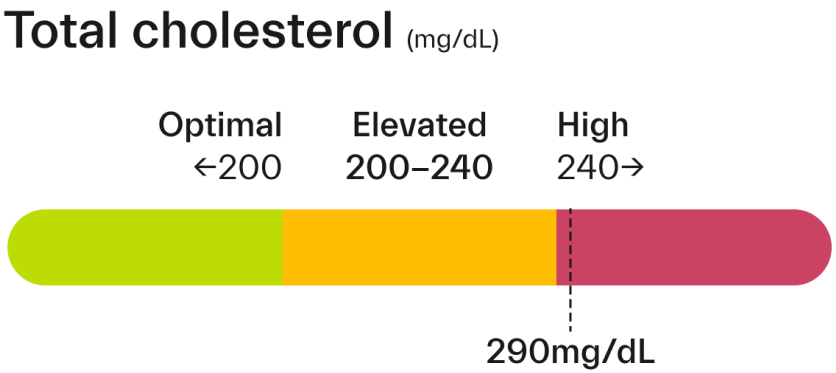


Total cholesterol (TC)

- Cholesterol is a waxy, fat-like substance that plays many roles in the body, including synthesizing hormones and vitamin D. It also assists in the transporting of lipids.
- Cholesterol is found in the foods eat, but it is also made by the liver.
- Cholesterol circulating in the blood is carried by special particles called lipoproteins.
- The two major cholesterol-carrying lipoproteins are low-density lipoprotein (**LDL**) and high-density lipoprotein (**HDL**).

* Total cholesterol level is a combination of LDL cholesterol and HDL cholesterol.

- Normal value of total cholesterol **150 - 200** mg/dl



Hypocholesterolemia

Possible causes of low cholesterol are

- hyperthyroidism, or an overactive thyroid gland
- adrenal insufficiency
- liver disease
- malabsorption
- malnutrition
- abetalipoproteinemia
- hypobetalipoproteinemia
- manganese deficiency
- leukemia and other hematological diseases

hypercholesterolemia

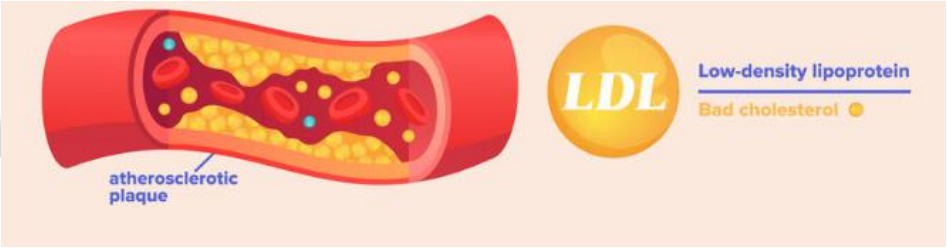
- genes (pure or familial hypercholesterolemia).
- A diet that includes a lot of saturated.
- A lack of exercise.
- Tobacco products.
- Obstructive liver disease.
- Diabetes.
- Hypothyroidism.
- Chronic kidney failure.
- Nephrotic syndrome.

Low-density lipoprotein (LDL)

- It is sometimes called the "**bad**" cholesterol because a high LDL level leads to a buildup of cholesterol in your arteries.
- Is type of lipoproteins.
- Are a combination of fat (lipid) and protein.
- The lipids need to be attached to the proteins so they can move through the blood.

Risks of High LDL Cholesterol

- coronary heart disease
- atherosclerosis
- angina, or chest pain
- heart attack
- stroke
- carotid artery disease



- Normal value of LDL **70 - 130** mg/dl

High-density lipoprotein (HDL)

- HDL is known as the "**good**" cholesterol because it carries LDL, triglycerides, and harmful fats and returns them to liver for processing.
- When HDL reaches liver, the liver breaks down the LDL, turns it into bile, and removes it from body.
- Is type of lipoproteins.

* Having low levels of HDL cholesterol can be of more concern, as it can indicate that the person is at risk of developing heart disease.

Low levels can occur due to:

- genetic factors
- type 2 diabetes
- smoking
- obesity

- Normal value of LDL **40 - 60** mg/dl

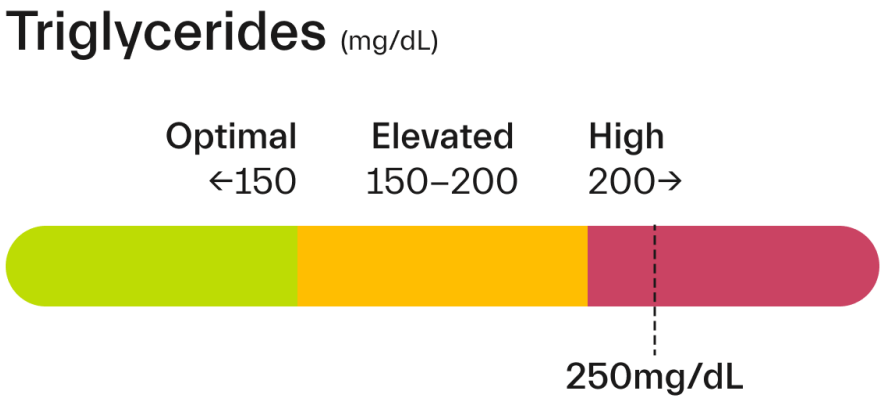
Triglycerides

- A triglycerides test measures the amount of triglycerides in the blood through a blood sample.
- Other names for a triglycerides test: **TG**, **TRIG**
- **Hypertriglyceridemia** is the medical term for elevated triglycerides in the blood.
- If your triglyceride levels are high, your cholesterol may also be high. This condition is known as **hyperlipidemia**.

- Normal value of triglycerides **10 - 150** mg/dl

A low triglyceride level may be due to:

- a low-fat diet
- hyperthyroidism
- malabsorption syndrome
- malnutrition



*** There are many reasons why triglyceride level may be high.**

Some of them are due to lifestyle habits these include:

- smoking
- being overweight or obese
- increasing alcohol consumption
- eating a diet low in protein and high in carbohydrates

There are also medical conditions including:

- cirrhosis
- diabetes, especially if it's not well
- controlled
- genetic factors
- hyperlipidemia
- hypothyroidism
- kidney disease
- pancreatitis

Vitamin

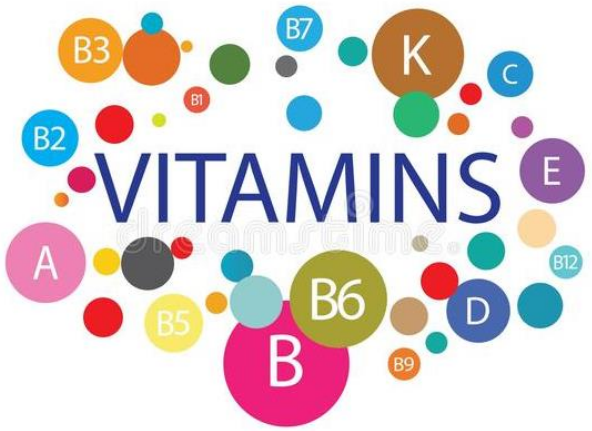
Vitamin

- The term “vitamin” is used to describe certain organic compounds that are needed by the body but that cannot be manufactured by the body.
- The amounts of vitamins required are very small, perhaps hundredths of grams.
- Vitamins are mainly obtained from our foods.

Classification of vitamins

- Based on solubility Vitamins are classified
- as either fat-soluble (lipid soluble) or water-soluble.

- Vitamins A, D, E and K are fat-soluble.
- B1 (thiamine), B2(riboflavin), B3(niacin), B5(pantothenic acid), B6(Pyridoxine) B7(Biotin), B9(Folic acid), B12(cobalamin) and Vitamin C are water-soluble.



Vitamin D

Vitamin D testing measures the level of this essential substance in blood, it is used to diagnose vitamin D deficiencies.

The main function of vitamin D

- is to aid in the absorption of calcium during bone formation.
- Maintaining adequate levels of vitamin D supports healthy bones.
- In addition, vitamin D has anti-inflammatory and other properties that play a role in maintaining normal muscle, immune, and nervous system functions.

There are two major forms of Vitamin D:

- Vitamin D2 (ergocalciferol): This is created in plants
- Vitamin D3(cholecalciferol): This is generated in the skin when it is exposed to sunlight.

Both vitamin D2 and D3 need to go through chemical changes before being able to be used by the body.
These changes occur in the liver and the kidneys and convert vitamin D into measurable substances called 25-hydroxyvitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)2D].

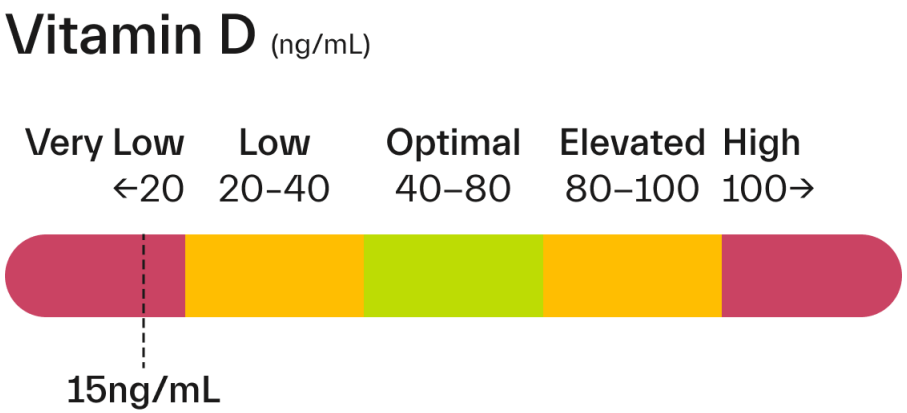
hypovitaminosis D

- Not enough exposure to sunlight.
- Darker skin pigment.
- Malnutrition.
- Kidney or liver failure.
- Certain medications.
- Certain types of cancer, such as lymphoma.
- A family history of vitamin D deficiency or childhood rickets.

hypervitaminosis D

- take vitamin D supplements.
- kidney disease.
- liver disease.
- tuberculosis.
- hyperparathyroidism.

- Normal value of vitamin D
  40 - 80 ng/ml



Vitamin E

- A vitamin E test measures the amount of vitamin E in blood.
- Vitamin E (also known as tocopherol or alpha-tocopherol)
- Is a nutrient that is found in every cell of body.
- It boosts immune functions and helps clear harmful antigens from the body.
- It also helps in the maintenance of RBCs production and blood clotting.
- Vitamin E is a type of antioxidant, which means that it protects cells from damage.

- **Other names:** tocopherol test, alpha-tocopherol test, vitamin E serum.

Vitamin E deficiency most of the time, it's caused by conditions that prevent body from properly absorbing vitamin E, including:

- Liver disease
- Cystic fibrosis
- Celiac disease
- Pancreatitis
- Certain genetic disorders
- Eating an extremely low-fat diet can also lead to a vitamin E deficiency.

Vitamin E excess is also uncommon.

- It usually happens from taking too many vitamin E supplements.
- Too much vitamin E can increase your risk of bleeding, including bleeding in the brain, called a hemorrhagic stroke.

- Normal value of vitamin E **5.5 - 17** µg/mL

Vitamin B_{12}

- The vitamin B12 blood test measures the amount of vitamin B12 in blood.
- Vitamin B12 is one of the B group of vitamins.
- It is also known as cobalamin.
- It is vital for making red blood cells and for cell and tissue repair.
- Vitamin B12 also helps with nerve health.
- Vitamin B12 and folate work together to help with cell functioning.

Low Levels of vitamin B12 this result suggests a vitamin B-12 deficiency, pernicious anemia, or an overactive thyroid.

- People with low vitamin B12 levels often experience neurological symptoms as well as fatigue and weight loss.

high vitamin B12 this result may suggest liver or kidney problems, diabetes, or certain forms of leukemia.

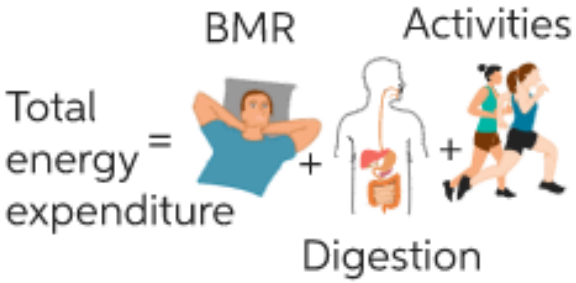
- Normal value of vitamin B12 **160 - 950** pg/mL

Energy requirement

is the amount of food energy needed to balance energy expenditure in order to maintain body size, body composition and a level of necessary and desirable physical activity consistent with long-term good health.
This includes the energy needed for the optimal growth and development of children, for the deposition of tissues during pregnancy, and for the secretion of milk during lactation consistent with the good health of mother and child.

- Energy requirements differ among people based on age groups, activity level.

- The energy expenditure is the total basal metabolic rate (BMR), the effect of food after digestion, activity level, and the energy used in tissues.



Malnutrition

is a serious condition that happens when your diet does not contain the right amount of nutrients.

- It means "poor nutrition" and can refer to:
  undernutrition – not getting enough nutrients
  overnutrition – getting more nutrients than needed

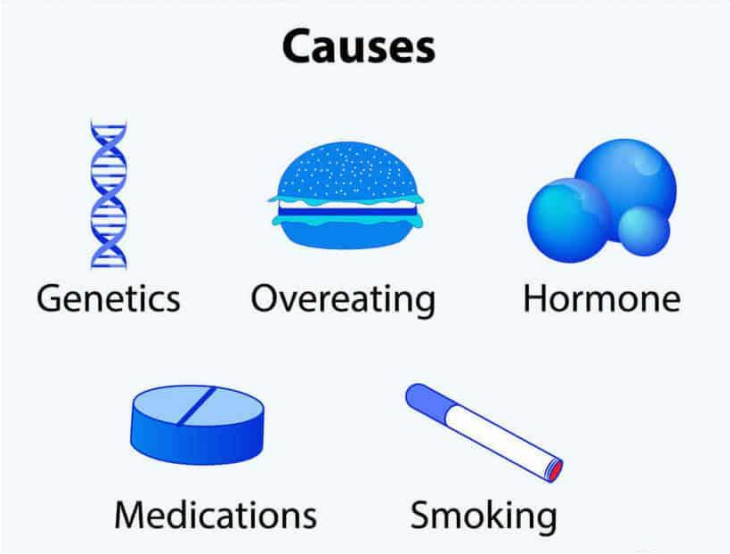
Common signs of malnutrition include:

- unintentional weight loss – losing 5% to 10% or more of weight over 3 to 6 months is one of the main signs of malnutrition
- a low body weight – people with a body mass index (BMI) under 18.5 are at risk of being malnourished
- a lack of interest in eating and drinking
- feeling tired all the time
- feeling weak
- getting ill often and taking a long time to recover
- in children, not growing or not putting on weight at the expected rate

Obesity

- Obesity is a complex disease involving an excessive amount of body fat.
- Obesity isn't just a cosmetic concern.
- It's a medical problem that increases the risk of other diseases and health problems, such as heart disease, diabetes, high blood pressure and certain cancers.

* Obesity is generally caused by eating too much and moving too little. if you consume high amounts of energy, particularly fat and sugars, but do not burn off the energy through exercise and physical activity, much of the surplus energy will be stored by the body as fat.



Glycemic index (GI)

- Is a value assigned to foods based on how quickly and how high those foods cause increases in blood glucose levels.
- Foods low on the glycemic index (GI) scale tend to release glucose slowly and steadily.
- Foods high on the glycemic index release glucose rapidly.

The best low GI foods

A healthy, low glycemic diet should comprise mostly low GI foods, such as:

- **Fruits:** apples, berries, oranges, lemons, limes, grapefruit.
- **Non-starchy vegetables:** broccoli, cauliflower, carrots, spinach, tomatoes.
- **Whole grains:** barley, buckwheat, oats.

Natural toxic substances in foodstuffs

- Natural toxins are toxic compounds that are naturally produced by living organisms.
- These toxins are not harmful to the organisms themselves but they may be toxic to other creatures, including humans, when eaten.
- These chemical compounds have diverse structures and differ in biological function and toxicity.

Some of the most commonly found natural toxins:

- **Aquatic biotoxins**

- **Cyanogenic glycosides**

cyanogenic glycosides are phytotoxins (toxic chemicals produced by plants) cassava, sorghum, stone fruits, bamboo roots and almonds are especially important foods containing cyanogenic glycosides.

- **Furocoumarins**

these toxins are present in many plants such as parsnips, celery roots, citrus plants and some medicinal plants.

- **Lectins**
  many types of beans contain toxins called lectins

- **Mycotoxins**
  mycotoxins are naturally occurring toxic compounds produced by certain types of moulds.

- **Solanines and chaconine**
  which include tomatoes, potatoes, and eggplants
  higher concentrations are found in potato sprouts and bitter-tasting peel and green parts, as well as in green tomatoes.

- **Poisonous mushrooms**
  wild mushrooms may contain several toxins, such as muscimol and muscarine.

Cancer

Cancer

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.

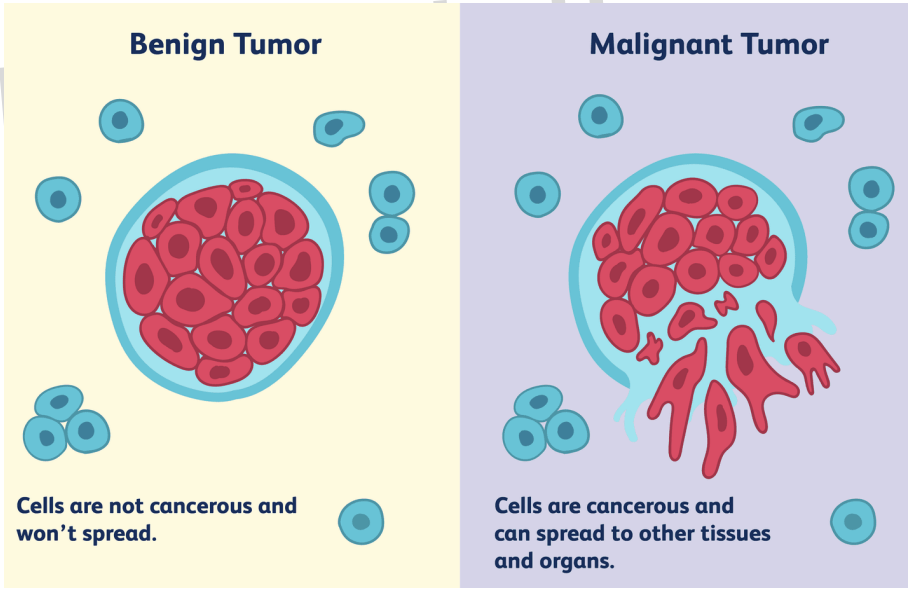
- Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place.

- Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't.
- These cells may form tumors, which are lumps of tissue.
- Tumors can be cancerous or not cancerous (benign).

Cancerous ⟶ Malignant tumors
Not cancerous ⟶ Benign tumors

Malignant tumors spread into, or invade, nearby tissues and can travel to distant places in the body to form new tumors (a process called metastasis).
- Many cancers form solid tumors, but cancers of the blood, such as leukemia's, generally do not.

Benign tumors do not spread into, or invade, nearby tissues.
When removed, benign tumors usually don't grow back, whereas cancerous tumors sometimes do.
- Benign tumors can sometimes be quite large, however.
- Some can cause serious symptoms or be life threatening, such as benign tumors in the brain.



Differences between Cancer Cells and Normal Cells

- grow in the absence of signals telling them to grow.
- normal cells only grow when they receive such signals.

- ignore signals that normally tell cells to stop dividing or to die (a process known as programmed cell death, or apoptosis).

- invade into nearby areas and spread to other areas of the body.
- normal cells stop growing when they encounter other cells, and most normal cells do not move around the body.

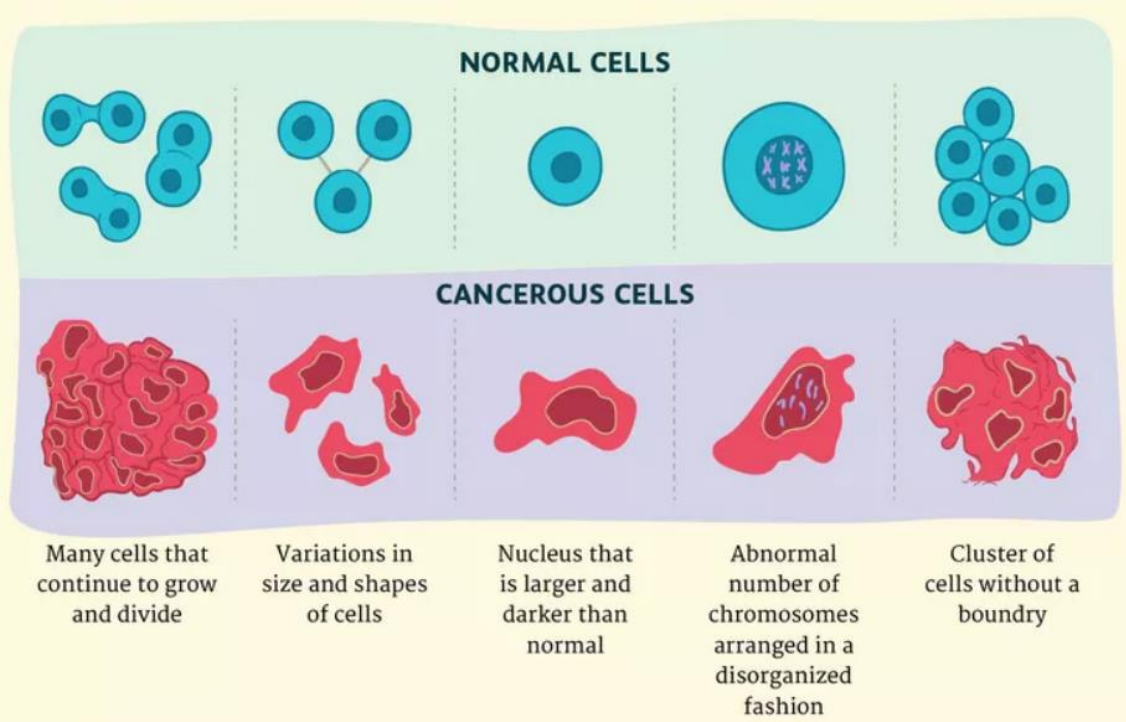
- tell blood vessels to grow toward tumors.
- these blood vessels supply tumors with oxygen and nutrients and remove waste products from tumors.

- hide from the immune system. The immune system normally eliminates damaged or abnormal cells.

- trick the immune system into helping cancer cells stay alive and grow.
- For instance, some cancer cells convince immune cells to protect the tumor instead of attacking it.

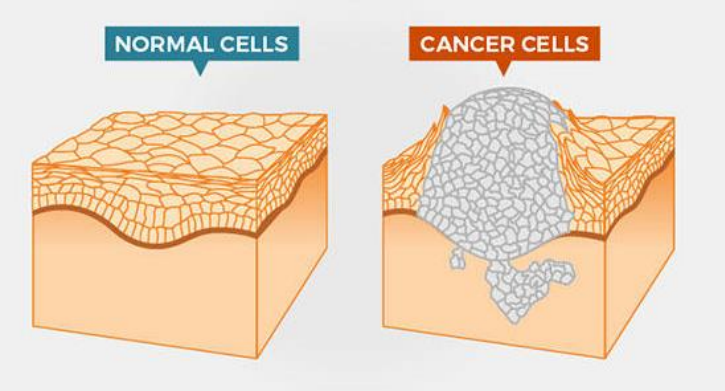
- accumulate multiple changes in their chromosomes, such as duplications and deletions of chromosome parts. Some cancer cells have double the normal number of chromosomes.

- rely on different kinds of nutrients than normal cells. In addition, some cancer cells make energy from nutrients in a different way than most normal cells. this lets cancer cells grow more quickly.



How does cancer form?

cancer is a disease caused when cells divide uncontrollably and spread into surrounding tissues.

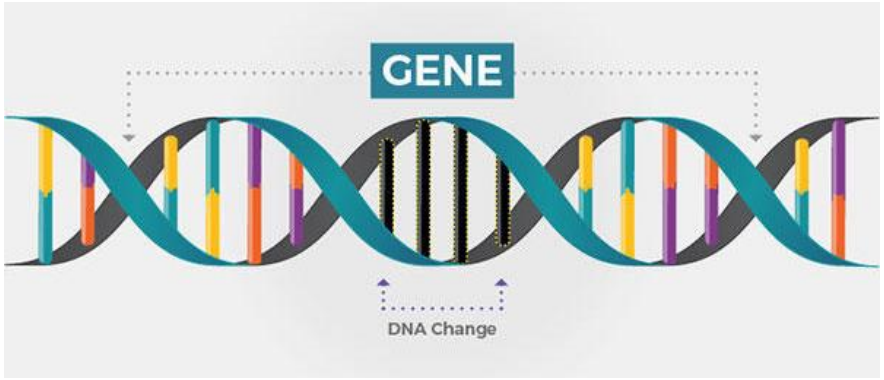


What causes cancer?

Cancer is caused by changes to DNA.

Most cancer-causing DNA changes occur in sections of DNA called genes.

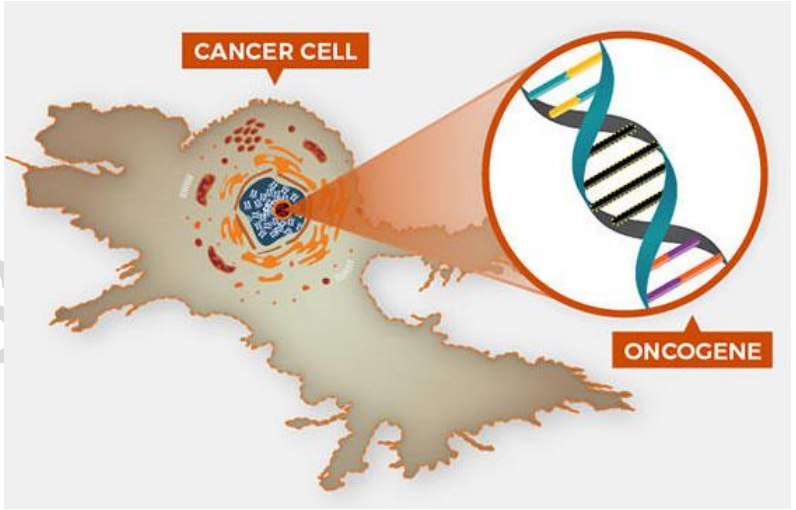
These changes are also called genetic changes.



What are oncogenes?

A DNA change can cause genes involved in normal cell growth to become oncogenes.

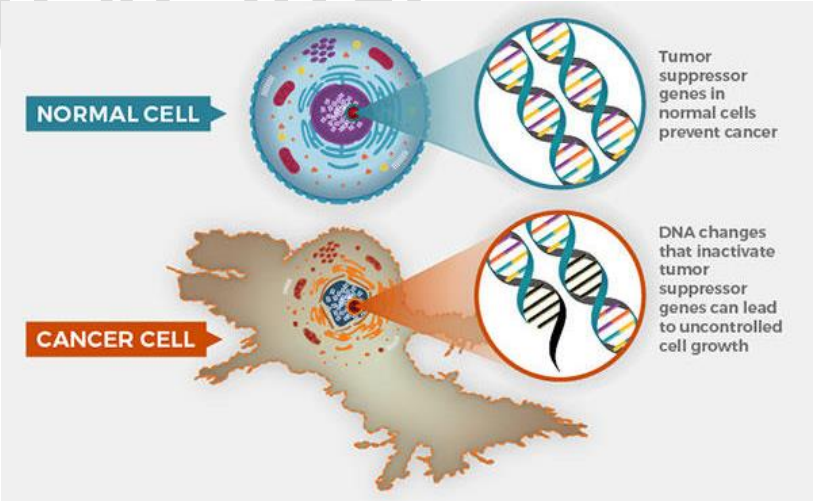
Unlike normal genes, oncogenes cannot be turned off, so they cause uncontrolled cell growth.



What are tumor suppressor genes?

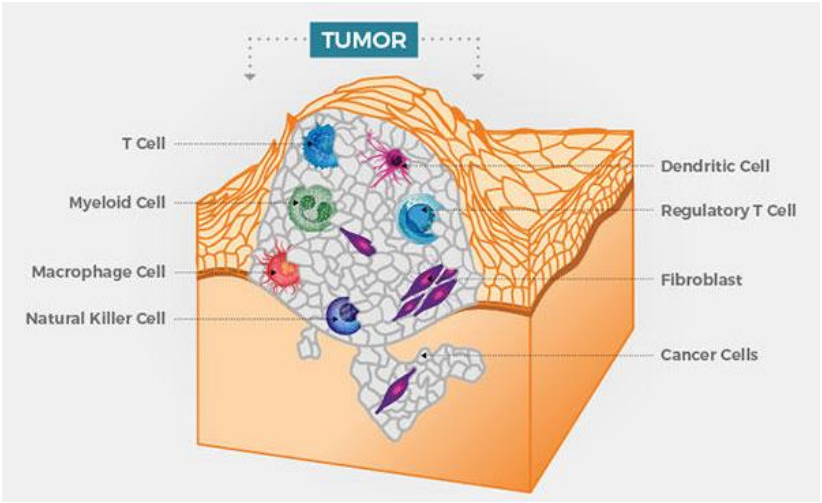
In normal cells, tumor suppressor genes prevent cancer by slowing or stopping cell growth.

DNA changes that inactivate tumor suppressor genes can lead to uncontrolled cell growth and cancer.



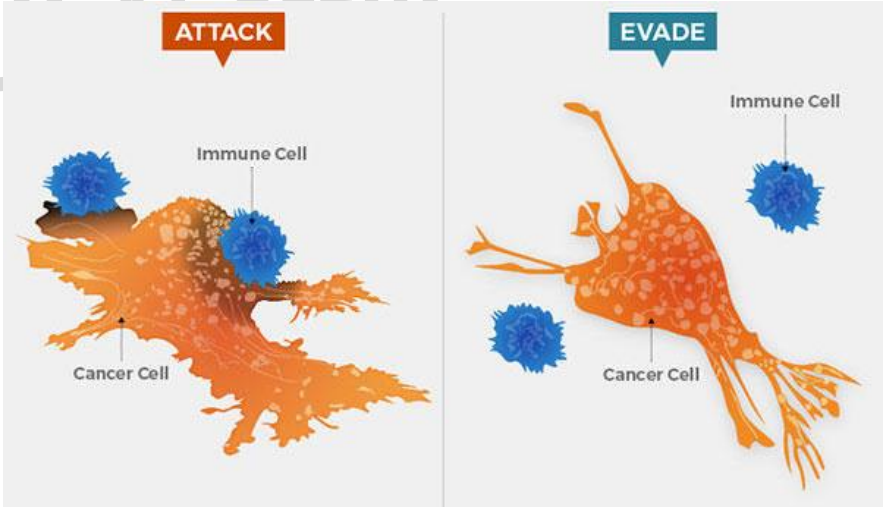
What is the tumor microenvironment?

Within a tumor, cancer cells are surrounded by a variety of immune cells, fibroblasts, molecules, and blood vessels-what's known as the tumor microenvironment. Cancer cells can change the microenvironment, which in turn can affect how cancer grows and spreads.



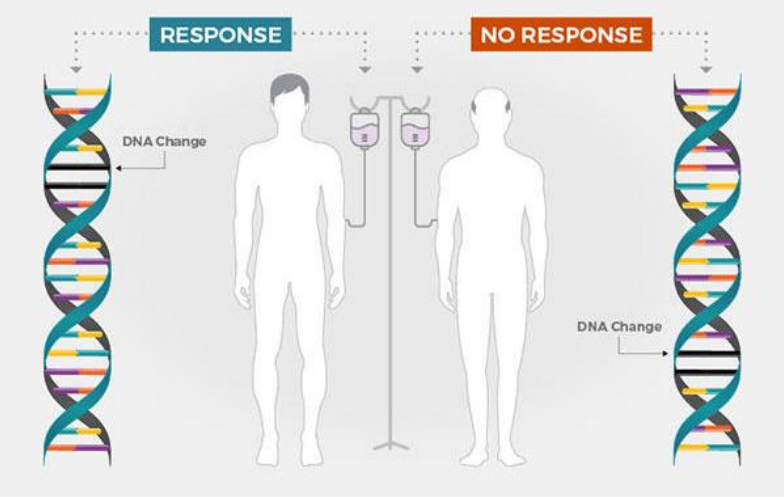
How dose the immune system interact with cancer?

Immune system cells can detect and attack cancer cells. But some cancer cells can avoid detection or thwart an attack. Some cancer treatments can help the immune system better detect and kill cancer cells.



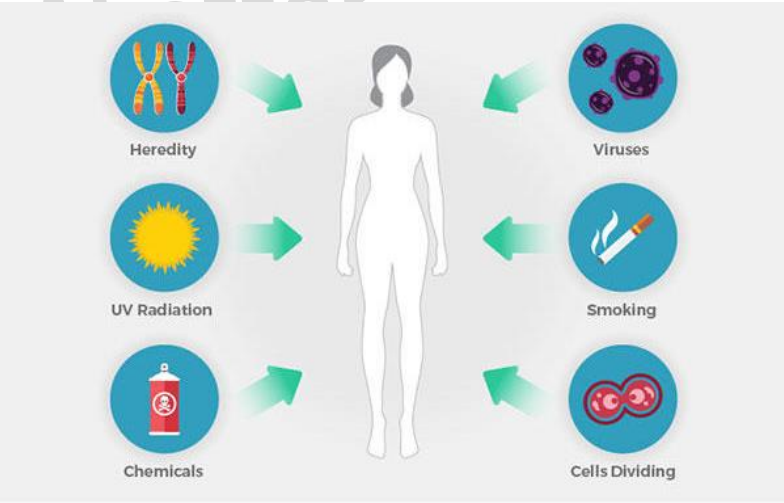
How do genetic changes affect cancer treatment?

Each person's cancer has a unique combination of genetic changes.
Specific genetic changes may make a person's cancer more or less likely to respond to certain treatments.



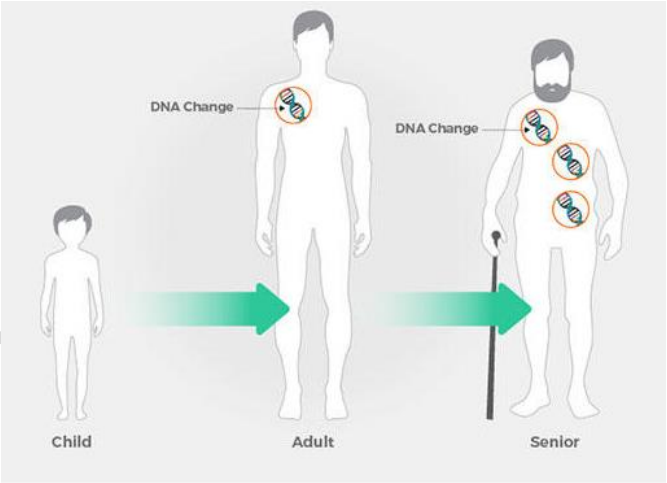
What causes genetic changes?

Genetic changes that cause cancer can be inherited or arise from certain environmental exposures.
Genetic changes can also happen because of errors that occur as cells divide.



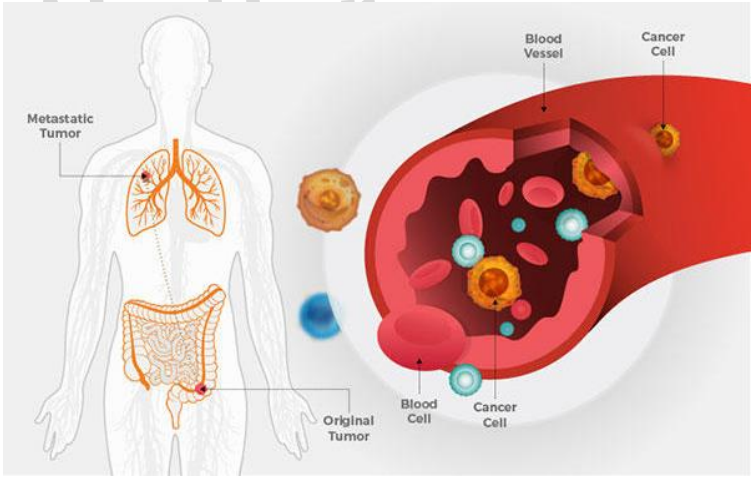
How dose age relate to cancer?

Most often, cancer-causing genetic changes accumulate slowly as a person ages, leading to a higher risk of cancer later in life.



What is metastasis?

Cancer cells can break away from the original tumor and travel through the blood or lymph system to distant locations in the body, where they exit the vessels to form additional tumors. This is called metastasis.



Types of Genes that Cause Cancer

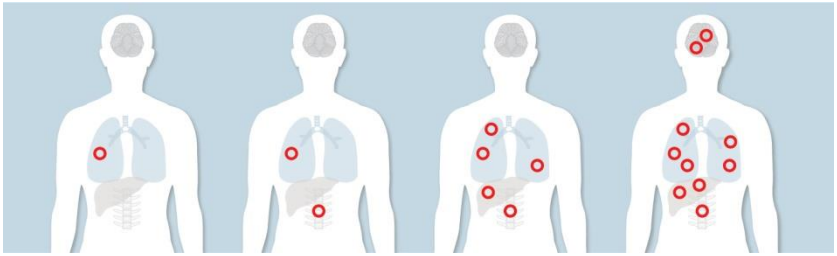
The genetic changes that contribute to cancer tend to affect three main types of genes:

- Proto-oncogenes
- Tumor suppressor genes
- DNA repair genes.

When Cancer Spreads

- A cancer that has spread from the place where it first formed to another place in the body is called metastatic cancer.
- The process by which cancer cells spread to other parts of the body is called metastasis.

- Metastatic cancer has the same name and the same type of cancer cells as the original, or primary, cancer. For example, breast cancer that forms a metastatic tumor in the lung is metastatic breast cancer, not lung cancer.



Applications of Tumor Markers

1- Diagnosis (D) to help to establish the diagnosis
2- Screening (S) to identify patients with early cancer
3- Prognosis (P) to assess the aggressiveness
4- Monitoring (M)
- Evaluate the Response to Treatment (RT)
- Detection of Recurrence (R)

5- Determination of Risk

Methods for detection of cancer

Immunoassay is the most common measurement method.

Some common types of lab tests used to help diagnose cancer:

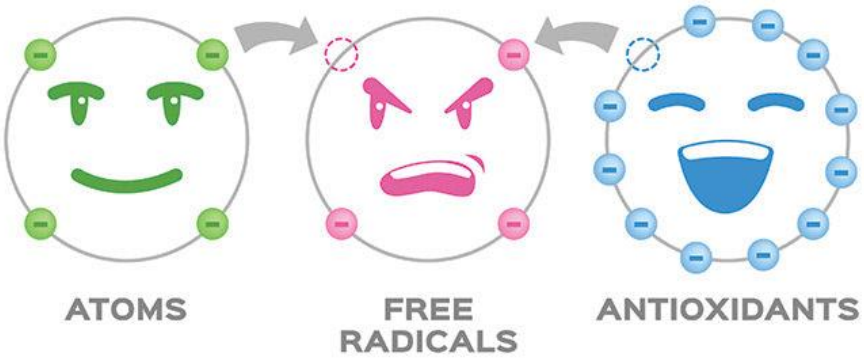
- Blood chemistry test
- Complete blood count (CBC)
- Cytogenetic analysis
- Immunophenotyping
- Liquid biopsy
- Tumor marker tests

Free radical

- A free radical is termed as a molecular species which can contain an unpaired electron in its atomic orbital and can exist independently.
- All the radicals share some common properties due to the unpaired electron.

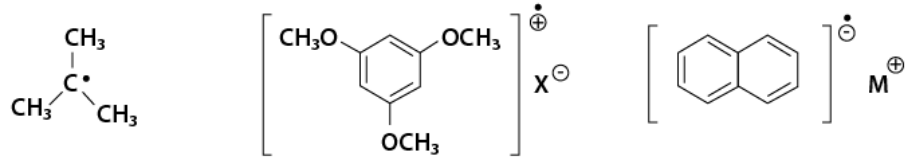
Properties of Free Radicals

- Free radicals are unique and rare species and are present only under special and limited conditions.
- Molecular oxygen is a typical free radical
- Nitrogen monoxide and nitrogen dioxide are also stable, free radical species.
- free radicals are very familiar to us in our lives and are very important chemicals.
- Free radicals are highly reactive and very unstable. They can donate an electron or accept an electron from other molecules, therefore, can behave as oxidants or reluctant.



Types of Free Radicals

Most organic radicals are quite unstable and very reactive. There are two kinds of radicals, neutral radicals and charged radicals as shown below.



Neutral radical | cation radical | anion radical

What causes free radicals?

Free radicals are highly reactive and unstable molecules that are produced in the body naturally as a byproduct of normal metabolism, or by exposure to toxins in the environment such as tobacco smoke and ultraviolet light

Antioxidants and Free Radicals

- Many of the plant chemicals (phytochemicals) in our foods are antioxidants.
- These nutrients stop the formation of free radicals and may reduce the damage they would cause in the body.
- The power of antioxidants to fight free radicals is one reason why a diet rich in vegetables and fruits has been linked with a lower risk of many diseases.


تمّت
بحمد الله