

تفریغ ڪلینکال



المحاضرة: Hematology

الصيدلانية: ياسمين خليل



لجان التّفعّلات

اللهم علمنا ما ينفعنا وانفعنا بما علمنا و زدنا علما

Hematology

علم دراسة الدم وكيفية تحطّنه ومحوّلاته ووظائفه وأمراضه

اللهم ارحم أيهم واغفر له وعافه وأعف عنه ومعه
وأهله والمسلمين في الجنة

Hematology

Hematology is defined as the science that deals with the: formation, composition, functions and diseases of the blood.

What is Blood? \rightarrow
 نسج سائل
 فيه خلايا معلقة في مادة زرقاء تسمى بروتين جسم الإنسان

- Blood is a fluid tissue containing many suspended cells and is found in the circulatory system transporting substances.
ويحمل على نقل مكونات
الجسم ، ولذلك
- These substances may include the digested food substances like amino acids and glucose, excretory products of the body and tissues and oxygen and carbon dioxide for respiration.
ناقل غذاءات ومشهول عن تنفس
- Blood also serves to protect the body against pathogens.
WBs

Blood Composition

Plasma

RBCs

White Blood Cells

(immune system)

Blood Platelets to prevent blood loss

OTHER SOLUTES

Electrolytes

Normal extracellular fluid ion composition essential for vital cellular activities. Ions contribute to osmotic pressure of body fluids. Major plasma electrolytes are Na^+ , K^+ , Ca^{2+} , Mg^{2+} , Cl^- , HCO_3^- , HPO_4^{2-} , SO_4^{2-}

Organic nutrients

Used for ATP production, growth, and maintenance of cells; include lipids (fatty acids, cholesterol, glycerides), carbohydrates (primarily glucose), and amino acids

Organic wastes

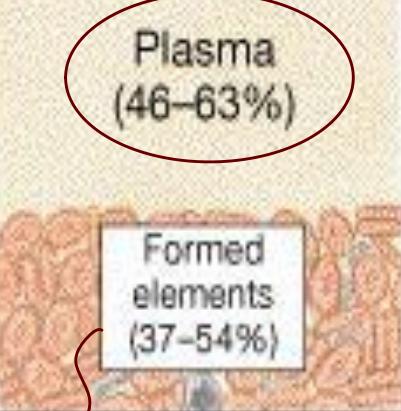
Carried to sites of breakdown or excretion; include urea, uric acid, creatinine, bilirubin, ammonium ions



الدم
Sample of whole blood

Contains

Plasma (46–63%)



الخلايا المكونة
الخلايا المعلقة

PLASMA COMPOSITION	
Plasma proteins	7%
Other solutes	1%
Water	92%
① Transports organic and inorganic molecules, formed elements, and heat	
②	
③	

Fibrinogen converts
to Fibrin
platelet 20
وغيره

FORMED ELEMENTS	
Platelets	0.1%
White blood cells (WBCs)	immune system
Red blood cells	99.9% O_2 , CO_2 transporter (RBCs)

الخلايا المكونة
الخلايا المعلقة

PLASMA PROTEINS

Albumins

60%
كبير في حافظ
الدورة الدموية وتنقية
الدماء وتأديب الماء

Globulins

35%

Fibrinogen

4%

clotting

Regulatory proteins

<1%

PLASMA PROTEINS

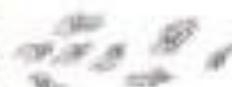
Major contributors to osmotic concentration of plasma; transport lipids, steroid hormones

Transport ions, hormones, lipids; immune function

Essential component of clotting system; can be converted to insoluble fibrin

Enzymes, proenzymes, hormones
مثبط (أكتيفاتور) بروتيغان

PLATELETS



WHITE BLOOD CELLS



Neutrophils (50–70%)

Eosinophils (2–4%)

Basophils (<1%)

Lymphocytes (20–30%)

Monocytes (2–8%)

μm 0 5 10 15

Monocytes (2–8%)

Blood components

معلومات علمية
لـ خواص بـ نبات

□ **Plasma** is a pale yellowish fluid with a total volume of 2-3 liters in a normal adult.

□ Its contents are :

□ Water 90.0%

اللهم صل وسلام وبارك

□ Protein 8.0%

على محمد

□ Inorganic Ions 0.9%: Sodium, potassium, calcium, chloride, hydrogen, carbonate and phosphate

□ Organic Substances 1.1%

□ **Serum Albumin** composed of 60% of the total plasma protein.

□ **Serum Globulins** make up 36% of the total plasma protein. Globulins aid in the inflammatory response of the body.

الـ مـ حـ اـ مـ اـ

□ **Fibrinogen** and **prothrombin** are important in the clotting process of blood.

Blood components

plasma

Protein Functions Include:

- ❑ Transportation of insoluble substances around the body by allowing them to bind to protein molecules تَبَلُّغُ الْمَوَادِ عَنْ إِذَانَةٍ فِي الْمَمْ (الْمَاءِ) عَنْهُ تَقْدِيرُ مُتَشَبِّهٍ فِي الْمَمْ وَتَرْجُحُ الْمُتَكَاهِ إِلَيْهَا إِيَّاهَا

- Blood clotting
- Responses in accordance to disease (inflammatory response)
- Protection from infection (the **gamma** globulins function)

Balance for the pH of the blood = 7.4 by hemoglobin which works inside RBCs and albumin that works outside RBCs

Substances

- ❑ Blood plasma carry organic substances such as nutrients (digested food substances like glucose, amino acids, glycerol, triglycerides, cholesterol and vitamins).
- ❑ Waste products of the body (urea and cellular waste that will be excreted out of the body).
- ❑ Hormones, such as cortisol and thyroxine are also transported around the body in plasma attached to plasma proteins.
- ❑ Medicine and drugs also circulate within the plasma.

Blood components

platelets, WBCs, $\text{RBCs} = 1\%$ و $\text{RBCs} = 99\%$ لما ينفعه في دم من 40-50 لتر

① Red Blood Cells (RBC) (Erythrocytes)

- Red blood cells are the most common cells found in blood.
فـ لو تقيـس لـ كـلـيـة دـمـيـة أـكـثـر مـنـ 3ـ 4ـ لـ تـرـ مـلـ كـبـيرـ
- There are about 5 million RBC in each cubic millimeter of blood
- This number varies with individuals in accordance to heredity, gender and state of health.
males > females
عـاءـيـةـ لـ اـنـصـرـ
الـ كـلـيـةـ اـنـعـيـ
Hb 13
لـ كـلـيـةـ كـلـيـةـ مـوـرـيـ
hemoglobin in
- These cells are produced by the bone marrow and have a lifespan of 3-4 months. When they die, they are destroyed by macrophages in the liver and spleen.
نـوـجـ مـنـ لـ تـرـ وـ بـلـيـنـ بـلـيـنـ
apoptosis + iron reuse
WBCs
- This process releases iron to be stored in the liver, to be recycled and bile pigments to be excreted.

Blood components

Structure of A Red Blood Cell

حَلْةٌ دَمْرَعَزْ تَبَعَّدُ مَعَتَرَلَدْ دَفَلْ

- Red blood cells have a bi-concave shape with a flattened center.
- It has a diameter less than 0.01 millimeters and do not have a nucleus.
RBCs خَلْلَنَادْ صَلَنِهَا فَوَاهَ وَغَلَوْ مَنَهَا نُوكُو
- Haemoglobin gives RBC its red color and Haemoglobin that contains iron, can easily transport gases such as O_2 and CO_2 .
عَلَاهَ تَقْدِرُ تَغْيِيرَهُنْ (لَهُنْ) بَلْ دَمْهُوا رَضِيقَة
- RBCs are highly elastic, rendering it able to squeeze through capillary walls

Functions of Red Blood Cells

- Are important in the process of respiration in carrying O_2 and CO_2



② White Blood Cells (Leucocytes)

صهارز دنایی

- White blood cells (WBCs) are responsible for the defense system in the body.
WBCs و دمجه ایمپریاں = RBCs ویکس
- There are approximately 6,000 white blood cells per millimeter of blood
- WBCs fight infections and protect our body from foreign particles, which includes harmful germs and bacteria.
- WBCs are formed from the stem cell of the bone marrow.
RBCs ایمپریاں نکر دنیا bone marrow میں تیج میں
- It has a life-span of a couple of days and when they die, they are destroyed by surrounding white blood cells and replaced with new ones.
by marophages

Structure of White Blood Cells

- ❑ WBCs are colorless, because they contain no haemoglobin.
مکارها ری ملا می باشند
- ❑ It contains a nucleus and has an irregular shape.
- ❑ Though there are fewer WBCs than RBCs, they are much bigger in size.
- ❑ They can change their shape easily and this allows them to squeeze through walls of the blood vessels into the inter-cellular spaces

WBCs have nucleus but platelets and RBCs do not
WBCs have 5 types but " " " " "

White Blood Cells (Leucocytes)

Unlike the Red blood cells or platelets, there are **5 different types** of white blood cells, each serving a different purpose in our body's immune system.

Neutrophils

The largest

- Neutrophils make up 55%-70% of the total white blood count in the blood stream.
- Neutrophils can be most commonly found **near sites of infection or injury** where they will stick to the walls of the blood vessels and engulf any foreign particles that try to enter the bloodstream.
- They can also be found in the **pus of wounds**.

*الليمف أو إلبي ينبع من سائل تكوب تحوى
كتام و 81 فين غريب ينبع من الجرح*

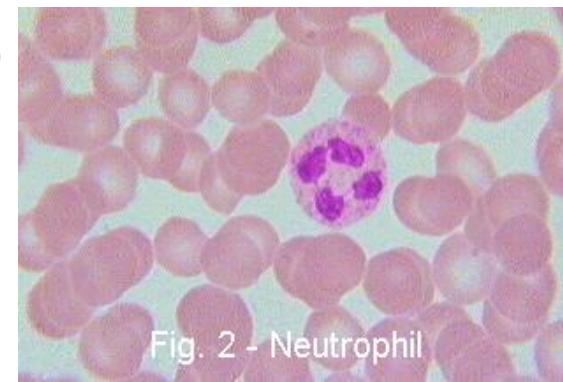


Fig. 2 - Neutrophil

White Blood Cells (Leucocytes)

Eosinophils

- ✓ Eosinophils make up 2%-5% of the total blood count and mainly attacks **parasites** and **antigen complexes**.
- ✓ These cells are also responsible for **allergic response** within the blood.

عزم خلايا بين مع
صائم في الـ تفاعـلـ التـسـعـيـة

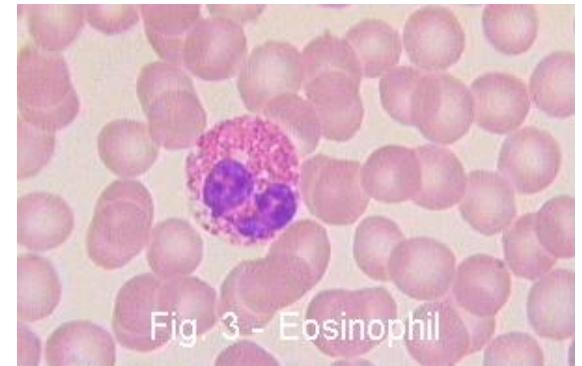


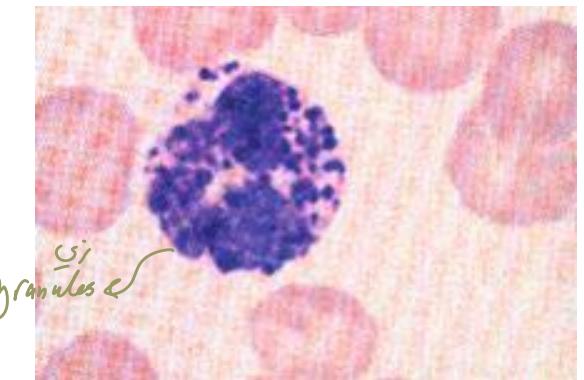
Fig. 3 - Eosinophil

Basophiles

صـائـمـ عـنـ الـتـجـاـبـ
Eosinophil اـنـتـسـعـيـةـ اـخـتـرـقـ

- ✓ Basophiles make up less than 1% of the total white blood count.
- ✓ Upon stimulation, a **massive release of granule** contents. Chemicals released include: heparin, histamine, and other substances which mediate hypersensitivity reactions within the blood.

الـ تـجـاـبـ مـنـ طـالـلـ :
① vaso dilatation
② increase vessels' permeability
فـ بـ تـجـاـبـ اـنـتـسـعـيـةـ حـرـادـ وـ كـارـتـرـهـاـ تـالـهـ



White Blood Cells (Leucocytes)

Monocytes

أجبر نوع حمّى من أنواع WBCs

- Monocytes 5%-8% of the total white blood count
- Are the largest of the 5 types of white blood cells.
- They act as tissue macrophages and **remove foreign particles** and prevent the invasion of germs which cannot be effectively dealt with by the neutrophils.

يشتمل على مكابح اجح مع الم

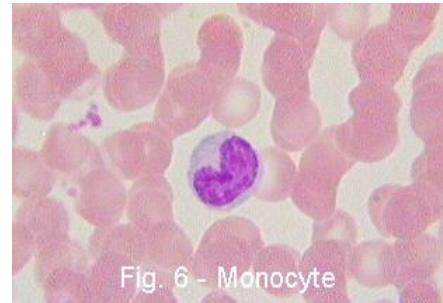


Fig. 6 - Monocyte

Lymphocytes

يُرسنوا مثلاً في العروق الدموية

- Lymphocytes **produce antibodies** against toxins secreted by bacteria and infecting germs.
- These antibodies will be excreted into plasma to kill bacteria in the blood as well as act antitoxins. In addition, they cause the foreign particles to cluster to be engulfed by phagocytes.
- The nature of lymphocytes is **highly specific** and they can only recognize certain antigens.

عند ملتقى الالتحام بينها من خارج دم أو بكتيريا طلوع بابي
لهم يسمى بجهة العروق إنها عزيز ببر بالغاني

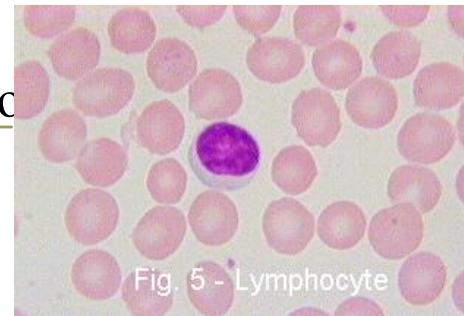


Fig. 5 - Lymphocyte

③

Blood Platelets

- Blood Platelets are granular **non-nucleated** fragments of cytoplasm in the form of oval discs.
- A platelet consists of two parts, a clear outer ground substance occupying the greater part of the platelet and a central part that contains **granules**.
أ جزء، الباقي الغارق هو انعكاس
وزو، افقي دهني ومسطحة منها انوار ابي سادة platelets تتجه مع دفعه ديلوك clot

Functions of Blood Platelets

هو العامل المسؤول عن تثبيط النزيف *Septotonin*
وتحت خلايا داخل clot التي جعلتها ان تكون ملتهبة وتحتاج لبعض الماء
الجرع

- They secrete a hormone called **serotonin** which contract blood vessels.
- Have a major role in accumulating at sites of injury sticking together to plug gaps in **broken blood vessels**.
- They are rich in activators for some proteins, these proteins form a fibers as network → helping in forming the clot → bleeding will be stopped.



Laboratory evaluation

for immature RBCs

by using microscope

- CBC, including RBC indices, a reticulocyte index, examination of a peripheral blood smear
كـ حـجـمـهـا أـكـبـرـهـا

أمم وآباء لا ينحدر أكلها لا يرى قد يرى ما قد يرى حبها؟ وكون سكانها؟

① Complete Blood Count (CBC)

- The Complete Blood Count (CBC) test is an automated count of the cells in the blood.
- It provides information about the white blood cell (WBC), red blood cell (RBC), and platelet populations present.

- This information includes the number, type, size, shape, and some of the physical characteristics of the cells. Any abnormalities found are noted.
(reticulocyte) immature RBCs > normal RBCs > mature WBCs > platelets
↑ in anemia & RBCs < normal
↓ in reticulocytosis & platelets < normal

Hemoglobin (Hgb): $\text{Hb} = \text{Hemoglobin}$

- Very rough estimate of the oxygen-carrying capacity of blood hemoglobin is found within the biconcave red blood cells.
- The normal haemoglobin count is 12-16 g/dl of blood in females and 13-18 g/dl in males.

③ **Hematocrit (Hct):** $= \frac{\text{Red cell volume}}{\text{Total blood volume}} \times 100$

- PCV is the actual volume of RBCs in a unit volume of whole blood
- It is about three times the Hgb value
- Low Hct indicates a reduction in either the number or size of RBCs, or an increase in plasma volume

Laboratory evaluation

④ RBC count:

الزمه هو انه يتوفى العدد من دون الحجم

- It is an actual count of RBCs per unit of blood
- RBCs are normally all the same size and shape
- Variations can occur with vitamin B12 and folate
variety of other conditions.

⑤ RBC indices:

لتو صف الحجم و مقدار الاهيئه في حرب ماء، لم الجراد

- Wintrobe indices describe the size and Hgb content of the RBCs and are calculated from Hgb, Hct and RBC count *میزان گلبین و همت*
- MCV, MCH and MCHC

Mean corpuscular volume (MCV)

□ Hct/RBC count $\frac{Hct}{RBCs\ Count} =$ حمّة بخونه / أ�数ه
قدره حمّة بخونه الراوحة

Mean The average volume of RBCs
أكبر من الطبيعي Micro-, normo- and macrocyt
أصغر من الطبيعي Reticulocytosis \rightarrow اضطراب في إنتاج كريات حمراء

Mean corpuscular hemoglobin (MCH)

$$\text{Heme} \xrightarrow{\text{محتوى}} \text{Hgb/RBC} \xrightarrow{\text{محتوى}} \text{count} = \frac{\text{Hgb}}{\text{RBC count}} = \frac{\text{محتوى حمّى}}{\text{محتوى كريات الدم الحمراء}}$$

The percent volume of Hgb in an RBC

□ Microcytosis or hypochromia causes

□ Elevated MCH is macrocytosis حجمها اكبر من المعدل الطبيعي فاتجحوى

حَمْرَهَا أَكْبَرُ مِنَ الْهَمْبِعِينَ فَاتَّحَوْيَ

e MCH → iron deficiency

Low HbA_{1c} (≤ 90)

مُرْصَدٌ لِلْكَوْرَدِ إِنْ دَاعِمُنَا لِنُرْجِعَ إِلَيْهِ
هو HbA_1 ونوع Hbf و HbA_2 ونوع Hb

و مكتبة لـ تكنولوجيا HbA_{1c} < 90 ملغم

Laboratory evaluation

* حكينا ماتكلروه MCH كايلحة يعني ضيارة ① دم صغير وعدد ضئيل
② دم ضيق كايلحة غير عادي ضئيل

طبعاً كفي بي أيه اذا كتلة دم النوى لو اثنانية

C Mean corpuscular hemoglobin concentration (MCHC)

مقدار لا يعتمد على الحجم (Volume) يعني بلوغ مقداريات الدم المطلوب نفس قدرية فيها hemoglobin مقدار دم ميزة مقدار مقدار نصفه (MCHC) يعني تفاصيل دم به إنتشار متساوٍ بالحجم (الارتفاع) يعني Hemo كافية

Hgb/Hct

- The weight of Hgb per volume of cells
بلوچ نسبتنا العجم فو سواه عيشه جواهه هنرمه كز عيشه ما ساجعني
- It is independent of cell size
- It can differentiate between microcytosis and hypochromia
صريح فلما عرفنا استثناء نازل في الاول في الثانية.
- A low MCHC always indicates hypochromia

شو استخدنا ؟ إنه ماتخلو MCH نازل يعني ضيارة في سايي ، يعني بروح أقصى MCHC دا داينه بروح نازل يعنيها استثناء hypochromic دا داينه طبعاً في استثناء microcytic

الله ارحم والدينا

Total reticulocyte count:

- Indicates new RBC production
- Normal is 1%

اما دا كتر من ١٪

يعني ينبع من immature RBCs
أو reticulocyte

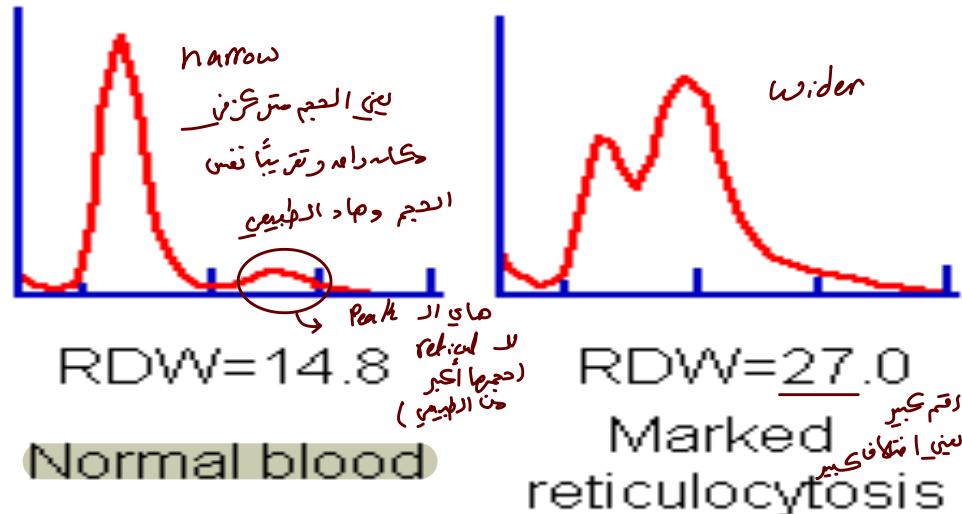
Laboratory evaluation

- RBC distribution width (RDW)
نسبة مشار دلاتا = 14.8
- RDW = (Standard deviation of red cell volume ÷ mean cell volume) x 100

- The higher the RDW, the more variable the size of RBCs
هاده نسبة اتنى متحركة
- Helpful in the diagnosis of mixed anemia

تحتوى على كل النحوين، سامة

iron deficiency + folate deficiency
or
iron defici + B_{12} defici
or iron + B_{12} + folate defici



□ Peripheral smear:

عنصر فيه افطعه اسماك عينيه اسماك سلايم وتحتها اسماك بوكب

- Complements other clinical data
- It provide information on the variation in cell size and shape



myoglobin

ڪو ۽ اسٽي نا ڦڳڻا، بُرُو ٻئانَ

لهم عندي

ف لازم تنبه لخزونه الحدي

Iron

نحو جسم الكتاب (مجرى)
 ٤٩ جسم $\frac{2}{3}$: هميوكتوبين
 ٥٠ $\frac{1}{4}$: حزاره
 ٥١ يفتح : $\frac{1}{4}$ on the free

- The total iron content of the adult body is approximately 4g (70mmol), of which some two-thirds is in haemoglobin. **Iron stores** (mainly spleen, liver and bone marrow) contain about one-quarter of the body's iron.
محتوى احدي اربعين في المائة ينتمي الى احتياطات الحديد، بينما الباقي مابعد ذلك ينتمي الى احتياطات الحديد
- Most of the remainder is in myoglobin and other haemoproteins; only 0.1% of the total body iron in the plasma where it is almost all bound to a transport protein, **transferrin**.
الباقي من احتياطات الحديد ينتمي الى احدي اربعين في المائة ينتمي الى احتياطات الحديد، بينما الباقي مابعد ذلك ينتمي الى احتياطات الحديد
- The mean daily intake of iron is about 20 mg but less than 10% of this is absorbed.
متوسط ادخال الحديد في اليوم الواحد ينحو 20 ملجم، حيث ان اقل من 10% من ادخال الحديد ينتمي الى احتياطات الحديد
- Iron absorption is determined by the state of the body's iron stores, being increased when they are depleted and decreased when they are adequate. It is also increased when erythropoiesis is increased (irrespective of the state of iron stores).
محتوى احتياطات الحديد ينحدر الى اعلى اذ ان احتمال امداد اوكسجين الى الخلايا ينحدر
- Iron is more readily absorbed in the Fe^{2+} form but dietary iron is mainly in the Fe^{3+} form. **Gastric secretions** are important in iron absorption in that they liberate iron from food (although haem can be absorbed intact) and promote the conversion of Fe^{3+} ions to Fe^{2+} .
المحتوى من الطعام موجود على شكل Fe^{3+} في نصف منه Fe^{2+} من من المحتوى

في المجموع دلائل اتجاه اكسي ايونية بجزء الكهيل بجعل Fe^{2+} (ferrous) اما المقدرات دور مراتب منها بعنصر Fe^{3+} (ferric)

Iron

Ferric Ascorbic acid → Ferrous

بروتينات
بروتينات
بروتينات

→ vit C

□ **Ascorbic acid** and other reducing substances facilitate iron absorption while **phytic acid** (in cereals), **phosphates and oxalates** form insoluble complexes with iron and decrease its absorption.

صيغة يقللها
صيغة يقللها
صيغة يقللها

insoluble compound

□ Once absorbed into the **intestinal mucosal cells**, iron is either transported directly into the **blood stream**, or else combines with **apoferitin**, a complex iron-binding protein, to form **ferritin**. This iron is lost into the lumen of the gut when **mucosal cells are shed**. In iron deficiency, the **apoferitin content of mucosal cells decreases** and **a greater proportion of absorbed iron reaches the blood stream**.

دالاً ماء، فالامتنان السليم صاد بذدي إلى نفحة صفراء الحديبة تكون منها حفارة العدبة فـ تأكله إلـ وـ نـ هـاـ بـ نـ هـاـ

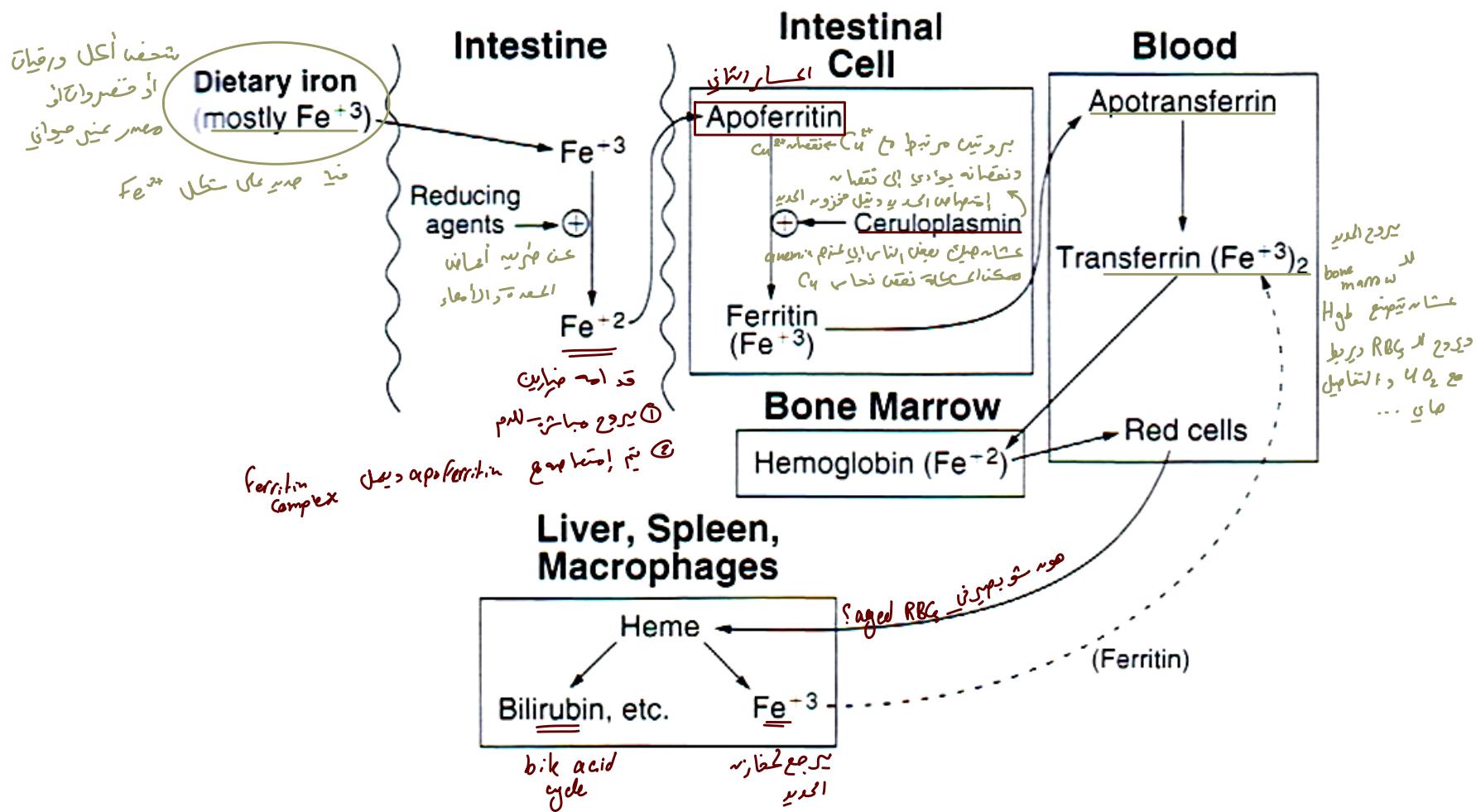
□ In the blood, iron is transported bound mainly to **transferrin**. **Transferrin** is normally about one-third saturated with iron. In tissues, iron is bound in **ferritin** and **haemosiderin**. **Free iron is very toxic and protein binding allows iron to be transported and stored in a non-toxic form**

□ It is **rarely** necessary to use biochemical tests merely to substantiate a diagnosis of iron deficiency, since this **by far the commonest cause of microcytic** (any anaemia in which the average size of circulating erythrocytes is smaller than normal), **hypochromic** anaemia, and the diagnosis is confirmed by a response to iron therapy.

دـ حـ وـ تـ حـ سـ تـ لـ سـ هـ إـ زـ اـ مـ اـ تـ حـ سـ تـ دـ حـ أـ نـ هـ بـ حـ ، دـ حـ وـ تـ حـ سـ تـ بـ لـ كـ لـ اـ سـ هـ بـ حـ عـ زـ نـ هـ صـ بـ حـ ، أـ مـ اـ لـ وـ مـ اـ تـ حـ سـ تـ بـ لـ كـ لـ اـ سـ هـ بـ حـ اـ سـ هـ لـ زـ :

لـ حـ يـ عـ كـ اـ فـ حـ خـ صـ بـ حـ

Transport of iron



Free iron

Plasma iron

٢٤

۴- استخدم لتصحيحه نفعاً، لغيره كنفعاً، لآخرين كنعيلاً، لآخرين كنعيلاً

- The plasma iron concentration is of little value in the investigation of iron metabolism, except in relation to **haemochromatosis** and in the diagnosis and management of **iron poisoning**.
لتشخيص امراض ادوية معدية (لقصور)
← يقل نسبتاً الماء على يمين المخاوف المائية شبه حبر
- A fall in plasma iron concentration is a late feature of iron deficiency, although a raised plasma iron is usually present in iron overload. *Toxic doses*
- The concentration of iron in the plasma of normal individuals fluctuates considerably; differences of more than 20% can occur within a few minutes, and of 100% from one day to the next. → *fluctuation* ①

و^و يُشكّل $\frac{1}{n}$ صناعته من كل العجائب

عُتَّابِهِمْ كَمَا يُعَتَّبُ عَلَيْهِ خَلِفَهُمْ مَسْوِيٌّ وَنَعْلَمُ أَكْثَرَهُمْ

Plasma ferritin

فنازنه حدید

less than 20 mg/L \rightarrow iron depletion
and empty stoma if it's less than 12 mg/L

فَتَاهَ أَمْبَعُوا إِنَّمَا الْمُنْذَرُ مِنَ الْمُنْذَرِ

- Although plasma ferritin concentration is more difficult to measure than iron or iron-binding capacity, it is by far superior to them for the assessment of body iron stores.
- **The only known cause of low plasma ferritin concentration is a decrease in body iron stores;** concentration below 20 µg/L indicate depletion, and below 12 µg/L suggests a complete absence of stored iron.

يُزداد في حادث الحريق $inflammable$ يختلف المقام تبعًا حسب النوع المهني للشخص

Fluctuation اضطراب

- However, ferritin is an **acute phase protein** and patients with iron deficiency may have plasma ferritin concentrations within the reference range when they are acutely ill.

دفعت **plasma ferritin** بحسب مقدار **plasma** في ملليلتر **كاملة** و **أقصى قيمها** بين **100** و **150** **أونتها** **أو** **ترتفع** **الستة**

Iron overload

- This can occur with increased intestinal absorption of iron: either acutely, as in iron poisoning, or chronically, as is seen in people who traditionally cook their food in iron pots.

عن طريق أقتن سبيكة زيادة إلزامياً، غالباً كأكواب أو أطباق قد اصطبوا في الماء. ② المطبخ من أواني صناعية
وتحمّل الماء داخلها من معينات وعذتها
وتحمّل الماء بعثبات كبيرة
- Increased parenteral iron administration occurs unavoidably in patients given repeated blood transfusions for the treatment of refractory anaemias and can also lead to overloading of the body's iron stores (**haemosiderosis** or **acquired haemochromatosis**).

مرضى لا بد من تناوله من أطباق B12 وD5000 وD5000 دينير ما على تحمل supplements بل يوم حنة
سواء بآف infusion دفعه اعطال بغير عنده من overloading أكثر وأسرع كثيـر دايركتيان ↑ بحد عـيـنـ
- The excess iron is deposited mainly as haemosiderin in reticuloendothelial cells in the liver and spleen where it is relatively innocuous, but with time parenchymal deposition may lead to hepatic fibrosis and myocardial damage.

حـكـار صـوـتـه يـوـجـدـه إـلـيـه مـلـكـاتـه مـلـكـاتـه

Tests for Iron

- Serum iron: is the concentration of iron bound to transferrin
- Total iron binding capacity (TIBC)
- Percentage transferrin saturation
- % Transferrin saturation = $(\text{Serum iron} / \text{TIBC}) \times 100$

وعلـاـجـاـزـاـتـهـ المـلـكـاتـهـ TIBC علىـاـجـاـزـاـتـهـ نـسـبـةـ اـبـرـدـتـهـ (ـعـلـةـ مـعـكـيـةـ).

يتحول دافل الجم إلى folate ويشتمل على مادة إنه لايبي اوكيل metabolism لاثني وعدين

وَالْمَتَاجِنَّلُ حَوْلَ بَرْزَنَةِ وَاهِهِ مَنْقُوا مِنْ مَكَانٍ لَا يُرَى فِي هَذِهِ الْأَرْضِ
وَمَوْجُودٌ فِي الْوَرَقَيَّاتِ
نَفْسُهُ نَادِرٌ¹ مَا يَدْعُونَ
وَهُوَ Co-energy

Folic acid

- Folate coenzymes are essential for the transfer of a single carbon units. A derivative of folic acid is vital to **purine and pyrimidine** (and hence nucleic acid) synthesis. *→ RBCs have no DNA but WBCs have (reticulocytes) immature RBCs have DNA now* $\hookrightarrow \text{DNA}$
- Folate is absorbed from dietary sources such as green leafy vegetable. *مخزون 5 مللي اسوم يستخدم في 13 يوماً مأخذنا 50 مللي اسوم بذرة (نادرًاً يمتص)*
- Dietary sources provide approximately 500 μg of folate per day. The human daily requirement for folate is approximately 50 μg . Body stores of folate amount approximately 5 mg. Interruption of absorption of folate may therefore result in deficiency within a few months. $\frac{5000 \text{ mg}}{50 \text{ mg}} = 100 \text{ days} \approx 3 \text{ months}$
- Folic acid deficiency is relatively common; its manifestation is as a **macrocytic anaemia**: *مكروه حجم اسوي عان من المطبوخ* *فرماد 1472 سنت اسماخ فوليك*
- Inadequate intake, decreased absorption, hyperutilization (during pregnancy, ^①malignancy), and inadequate utilization
- It is destroyed by cooking or processing.

يُفسد H_2O أو الأكاليل المُعلَّب من H_2O فاصد

Vitamin B₁₂

احتياجنا من 500 μg
دورة B₁₂ فيها 500 000 μg
مع تناولنا نحصل على مرتين
لعين حامة 2000 يوم ($\frac{1000 \text{ kg}}{0.5 \text{ kg}}$)

- Vitamin B₁₂ refers to a group of physiologically active substances chemically classified as cobalamins. *Some as v.t B₁₂*
- In humans, the daily requirement is 0.5 μg . The only significant dietary sources of vitamin B₁₂ are meat, milk or milk products and eggs.
*احتياج ادمي رفقاء تفضل
احتياج انسان يومي*
- It is stored within the liver and released to plasma to meet physiological demands. If the quantity of vitamin B₁₂ exceeds the capacity of hepatocyte receptors, most of the excess is excreted by the kidneys. Normally, approximately 1 mg of vitamin B₁₂ is stored in the liver, a quantity equivalent to the daily metabolic requirement for 2000 days; **thus dietary deficiency or impaired absorption of vitamin B₁₂ does not become evident for 5 years or more.**
نحتاج 5 سنوات من متاعل! مثلاً ماء بين نفخ B₁₂ ونفخ بـ 18
- In the stomach, vitamin B₁₂ forms a complex with intrinsic factor (IF). When the vitamin B₁₂-IF complex reaches the distal ileum, it is bound by receptors on the surface of mucosal epithelial cells and then enters the cells. Within the mucosal epithelial cells, the vitamin B₁₂-IF complex is dissociated, and the vitamin then passes into the plasma. The gastric secretion of IF is stimulated by food, histamine and gastrin; it is inhibited by vagal blockade.
*نفع IF يعود إلى تناول B₁₂ ونفع انتهاج بـ IF ، تناول انتهاج
انتعال ، تناول صلبيين وسبابك في درجة
stress / vagal block درجة*

Vitamin B₁₂

Huge RBCs

size

↑ size
↑ size
↑ size

- The deficiency of vitamin B₁₂ in humans is associated with **megaloblastic anaemia**.

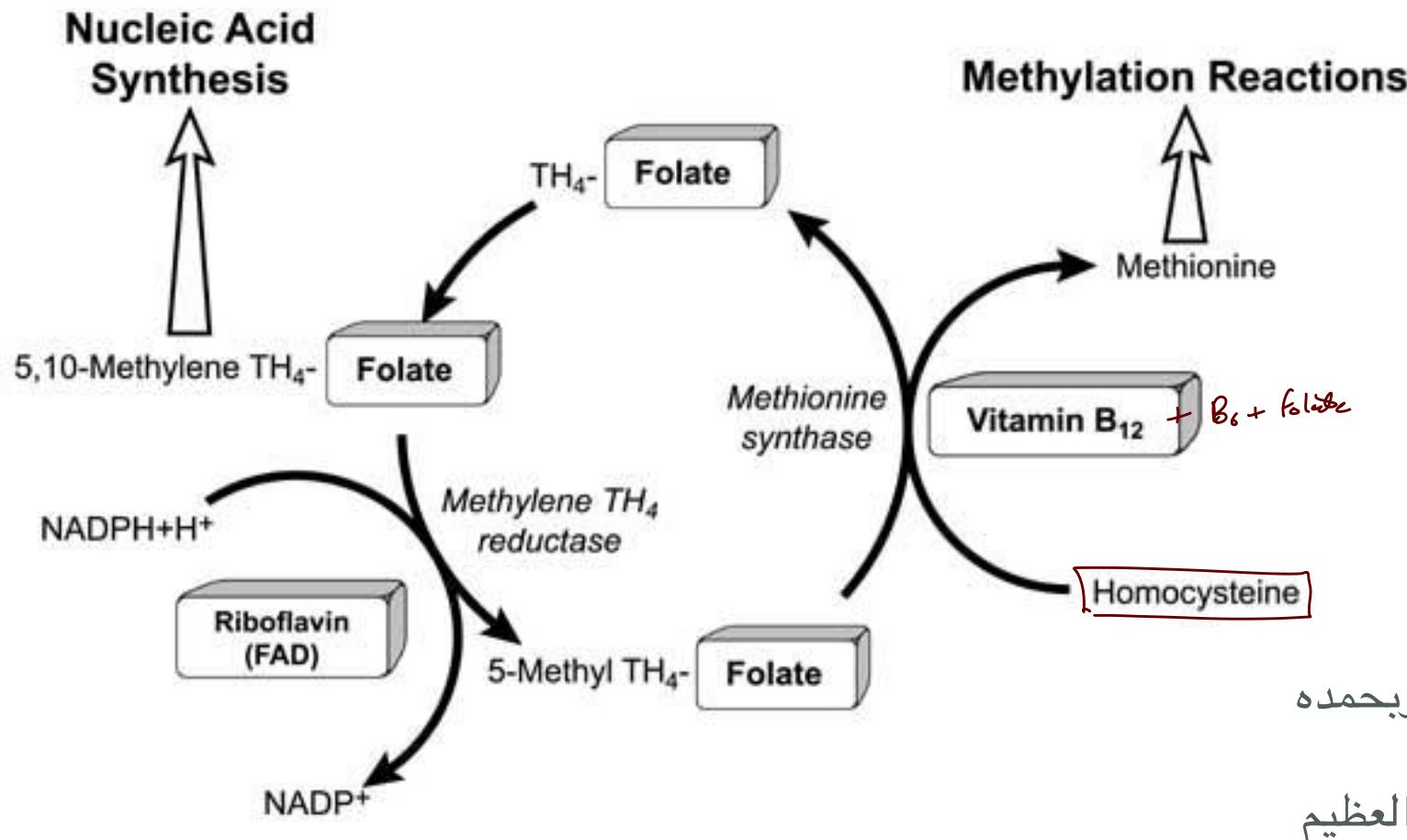
نقص فيitamin B₁₂ يسبب انماضياً (macrocytic anaemia)

- Pernicious anaemia:** the most important disorder of vitamin B₁₂ metabolism, is due to decreased secretion of **IF**. It is an **autoimmune disease**. Deficiency of vitamin B₁₂ causes serious and often irreversible neurological disorders such as burning pain or loss of sensation in the extremities, weakness, spasticity and paralysis, confusion, disorientation and dementia.

↑ time of onset
↑ time of onset

Tests for vitamin B₁₂

- Vitamin B12: serum values are maintained at the expense of vitamin B₁₂ tissue stores.
- Homocysteine:** vitamin B₁₂ and folate are required for conversion of homocysteine to methionine. It can be also elevated in B₆ deficiency.
Produced by amino acids metabolism then converted to methionine by B₆, B₁₂
- Methylmalonic acid (MMA):** a vitamin B₁₂coenzyme is needed to convert methylmalonyl coA to succinyl coA. Increased urinary excretion of MMA is a more specific marker of vitamin B₁₂ deficiency.
ذئب تنصير في فحص دم المريض

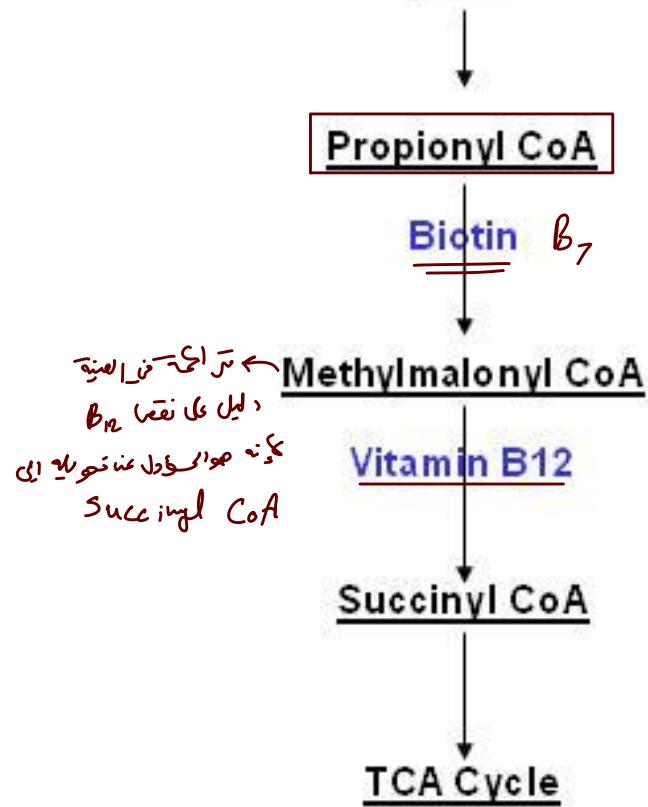


سبحان الله وبحمده

سبحان الله العظيم

Amino acids metabolism

Valine, Isoleucine, Methionine, Threonine and Odd chain fatty acids



Ferritin defic: means low level of Fe but the last defic will indicate that the patient has anemia is serum iron (which is fluctuation)

TABLE 17-3 REFERENCE INTERVALS FOR PARAMETERS USED TO ASSESS IRON STATUS^{47,84}

PATIENT POPULATION	SERUM IRON (mg/dL)	TRANSFERRIN (mg/dL)	FERRITIN (mg/dL)	PERCENT SATURATION	TIBC (μg/dL)
Newborn	100–250	130–275	25–200	12–50	100–400
Infant	40–100	200–360	200–600	12–50	100–400
Child	50–120	200–360	7–140	12–50	100–400
Male, adult	50–160	200–380	20–250	20–55	250–425
Female, 16–40 years	45–150	200–380	10–120	15–50	250–425
Female, >40 years					10–250

↑ تصلب جسم
↓ تصلب عصبية
↑ تصلب عصبية

↑ تصلب جسم

TABLE 17-4 LABORATORY MARKERS OF IRON STATUS IN SEVERAL DISEASE STATES

CONDITION	SERUM IRON	TRANSFERRIN	FERRITIN	PERCENT SATURATION	TIBC
Normal intervals	50–160 μg/dL	200–400 mg/dL	20–250 μg/L	20%–50%	250–350 μg/dL
Iron deficiency	Decreased	Increased	Decreased	Decreased	Increased
Iron overdose	Increased	Decreased	Increased	Increased	Decreased
Hemochromatosis	Increased	Slightly decreased	Increased	Increased	Slightly decreased
<u>Malnutrition</u>	Decreased	Decreased	Decreased	Variable	Decreased
Malignancy	Decreased	Decreased	Increased	Decreased	Decreased
Chronic infection	Decreased	Decreased	Increased	Decreased	Decreased
Viral hepatitis	Increased	Increased	Increased	Normal/increased	Increased
Acute liver disease	Increased	Variable/increased	Increased	Increased	Variable/increased
Chronic anemia	Decreased	Normal/decreased	Normal/increased	Decreased	Normal/decreased
Sideroblastic anemia	Increased	Normal/decreased	Increased	Increased	Normal/decreased

Source: Adapted with permission from Jacobs DS, ed. Laboratory test handbook. Boca Raton, Fla.: Lexi-Comp Inc, 1996.

↑ Transferrin binds to TIBC

↓ Saturation & ↑ free serum iron

↑ تردد دقة المنهج لـ نتائج معملي
↑ معاشرة كل من أنواع WBCs

White Blood Cell Count

- It is a count of the actual number of white blood cells per volume of blood.
- An unusually high white blood cell count can lead to leukemia and infection within the organs.
 - more than 10000: infection
 - normal range is: 4000 - 10000 → less than 4000: weak immunity
 - higher than 50 000 - 60 000: leukemia, or deep infection within organs
- Low white blood cell count will make the individual susceptible and vulnerable to diseases and foreign invasive organism.
 - جهاز المناعة ضعيف
 - جهاز المناعة ضعيف

Differential Blood Count of WBCs

- The differential blood count is done to calculate the percentage of each type of WBCs
- It also gives a clearer picture in a diagnosis for the cause of a disease. These may temporarily shift higher or lower depending on what is going on in the body.
- A high neutrophil count would suggest infection/^①cancer/^②physical stress.
 - ارتفاع نسبته مع دخول مرض
- High monocyte and eosinophil count usually points at bacterial infection.
- With allergies, there may be an increased number of eosinophils
 - نوع دايموند WBCs مترافق مع اعراض الحساسية
 - allergy: ارتفاع نسبته
- With leukemia, there may be a much higher percentage of a single type of cell, such as a lymphocyte. In this case, the cell may be present in large numbers, in a mature form and in a variety of immature forms.
 - النوع المترافق ناتج من انتشار واحتكاك عزبة وعزمية.

عدد الأغمات في جم دم مillin

Platelet Count

نریف کا یتوفن
لو سخن مانند اغمات کا فنہ تھل کے ٹو بیوں
نریف کا یتوفن
جراحتی تھل کی تکمیر جرح پر اپنٹھاں ڈنم اپنی ٹھاں
Heparin

Thrombocyte count:

- Platelets are essential in the coagulation
نزف کا یتوفن
لو سخن مانند اغمات کا فنہ تھل کے ٹو بیوں
- If there are insufficient platelets → hemophilia
نریف اپنے ایسی ٹھلیتی جراحتی تھل کی تکمیر جرح پر اپنٹھاں ڈنم اپنی ٹھاں
- Hence platelet counts are usually done before an operation.
- The platelet count is the number of platelets in a given volume of blood.

Simple laboratory tests

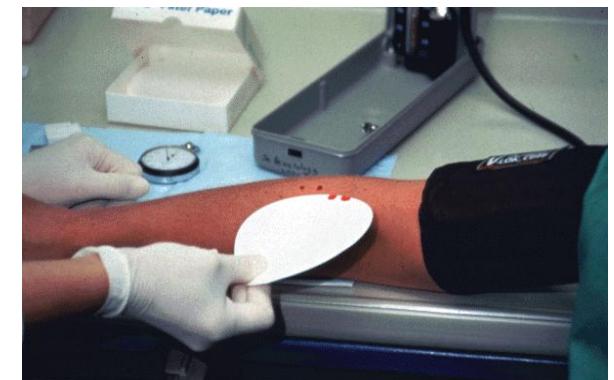
- Bleeding time, prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (TT), D-dimer, mixing test, antiphospholipid antibodies

Bleeding time

فتح جرح دنستون فردا
بیوں عتیانہ سیکر

صوبی ٹھوکو اغمات
لکھاں الجرح

- It assess platelet and capillary function
- It reflects the time to cessation of bleeding following a standardized skin cut
- Normal Values: the bleeding stops within 1 to 9 minutes
کم اکثر من 9 دقائیں دے سکر سیکر
hemophilia
- Quantitative and qualitative platelets



Formation of a blood clot

خثوات تكير الجرح :

When a blood vessel is damaged, there are **four** stages in the normal formation of a clot

Stage 1: The blood vessels is damaged and the bleeding starts. تبدأ النزف و تختفي بسرعة بداعي تم تكير الجرح

Stage 2: The blood vessels constrict to slow the flow of blood to the injured area.

و تقدر زمرة ملحوظة تدخل العروق المترتبة إزها تتجه لخارج الجرح

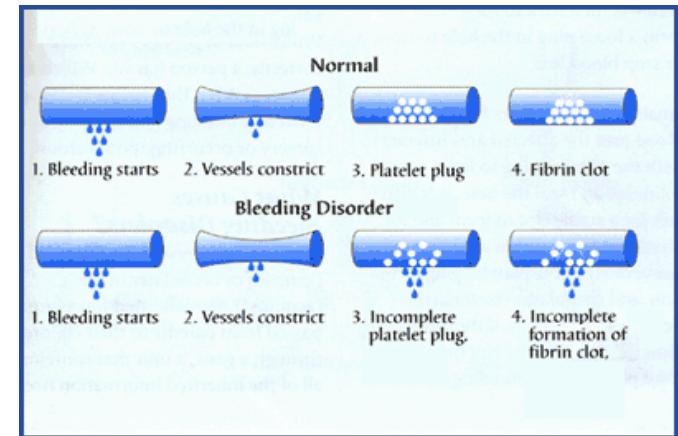
Stage 3: Platelets stick to, and spread on, the walls of damaged blood vessels. This is called platelet adhesion. These spreading platelets release substances that activate other nearby platelets which clump at the site of injury to form a platelet plug. This called platelet aggregation

Stage 4: The surface of these activated platelets then provides a site for blood clotting to occur. Clotting proteins like Factor VIII⁸ and IX⁹ circulating in the blood are activated on the surface of the platelets to form a mesh-like fibrin clot

يعملوا على إزالة تجفيف

بخار الصمامات تاليفه على باب العيادة المدرسية

These proteins (Factors I, II, V, VII, VIII, IX, X, XI, XII AND XIII and Von Willebrand Factor) work like dominos, in a chain reaction. This is called the coagulation cascade.



Intrinsic pathway

تحفيز كاميكو المزمن للأذنحة المزمنة
وكانى مزمن على الأذنحة

Extrinsic pathway

كاميكور الأذنحة بجهة الأذنحة

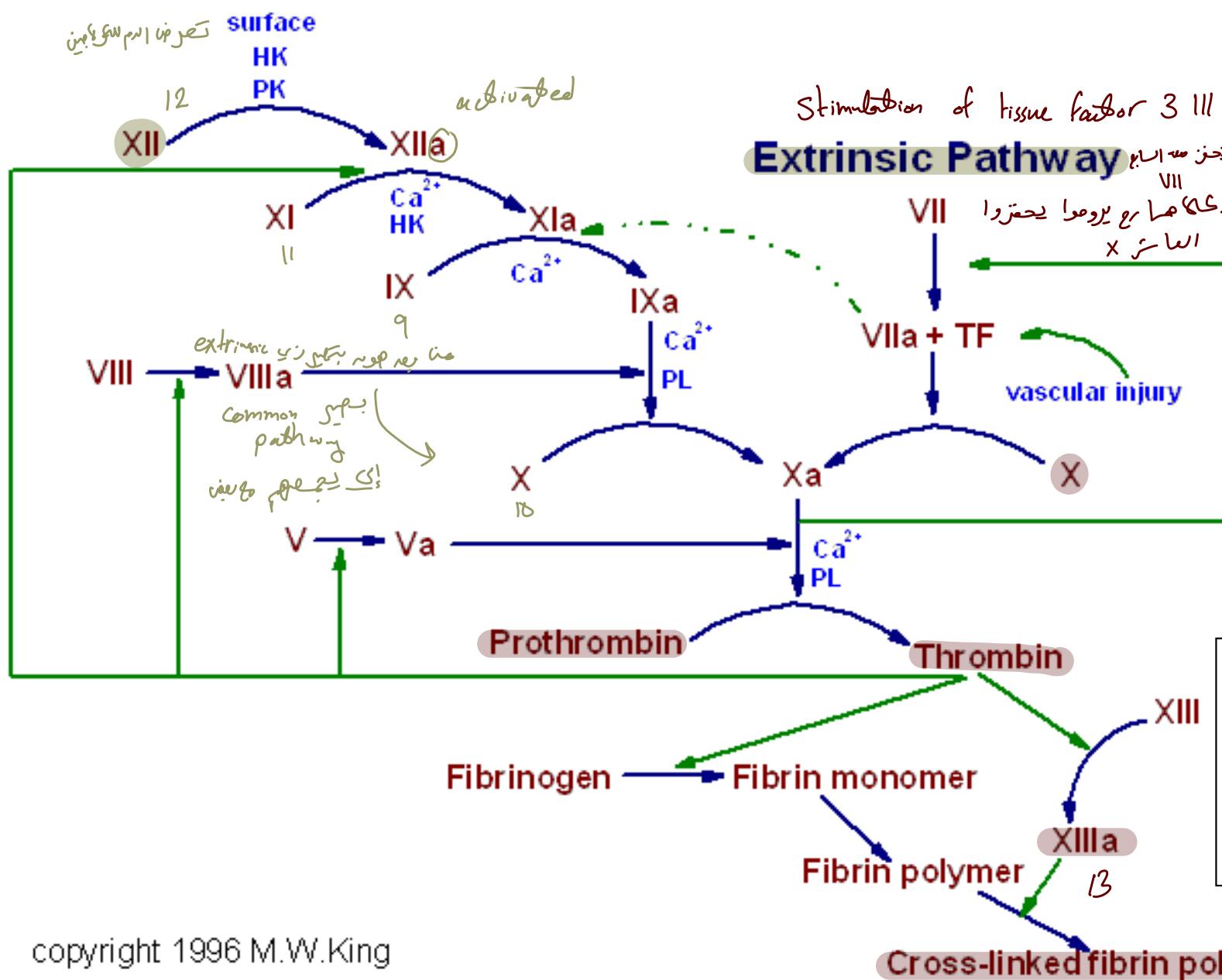
The Clotting Cascades

- Two pathways lead to the formation of a fibrin clot: the intrinsic and extrinsic pathway. Although they are initiated by distinct mechanisms, the two converge on a **common pathway** that leads to clot formation.
- The formation of a red thrombus or a clot in response to an abnormal vessel wall in the absence of tissue injury is the result of the **intrinsic pathway**.
Clot inside the vessels
- Fibrin clot formation in response to tissue injury is the result of the **extrinsic pathway**.
- Both pathways are complex and involve numerous different proteins termed clotting factors.

الله استر على المسلمين والمسلمات

The Clotting Cascades

Intrinsic Pathway



- HK = high molecular weight kininogen.
- PK = prekallikrein.
- PL = phospholipid

The clotting cascades

يعد الماء بالدم وفتحت الأوعية الدموية في الجسم يتوجه إلى مسار
الartery blood vessel
الartery blood vessel
عند مسار جم فبيه مسار
pathway

- The intrinsic cascade is initiated when contact is made between blood and exposed endothelial cell surfaces.
عند مسار
factor VII
- The extrinsic pathway is initiated upon vascular injury which leads to exposure of **tissue factor (TF)** (also identified as **factor III**), a subendothelial cell-surface glycoprotein that binds phospholipid. *extrinsic*
- The dotted arrow represents a point of cross-over between the extrinsic and intrinsic pathways. The two pathways converge at the activation of factor **X** to Xa. Factor Xa has a role in the further activation of factor VII to VIIa as depicted by the arrow. Active factor Xa hydrolyzes and activates prothrombin to thrombin. Thrombin can then activate factors XI, VIII and V furthering the cascade.
Common pathway
2 pathways
عند مسار
عند مسار
عند مسار
عند مسار
- Ultimately the role of thrombin is to convert fibrinogen to fibrin and to activate factor XIII to XIIIa. Factor XIIIa cross links fibrin polymers solidifying the clot.
Factor XIII (XIIIa)

فؤادي يربط كوكايين و المعنائج
coca glycoprotein receptor

Platelet Activation and von Willebrand Factor (vWF)

- In order for hemostasis to occur, platelets must adhere to exposed collagen, release the contents of their granules, and aggregate. The adhesion of platelets to the collagen exposed on endothelial cell surfaces is mediated by **von Willebrand factor (vWF)**.
- The function of vWF is to act as a bridge between a specific **glycoprotein** on the surface of platelets and collagen fibrils. In addition to it binds to and **stabilizes coagulation factor VIII**. Binding of factor VIII by vWF is required for normal survival of factor VIII in the circulation.
endothelial cells *في الإي*

ناقص أبسط مفعول
 bleeding time

Prolong Prothrombin time no clotting factors are synthesized
 ناقص فعالة ناقص مفعول
 vit K deficiency liver

Prothrombin time (PT)

- ① لقياس خواص
 It assess the function of **extrinsic** and the common pathways
- ② نحتاج في ترسيب البروترومبين مع نصف الدورة مع فيتامين K
 It measures the activity of vitamin K dependent proteins (factors II, VII, IX, and X and proteins C and S)
- It reflects the time required for fibrin strands to appear after the addition of tissue thromboplastin to a patient's plasma
- الصيغة التي تُقاس هو بدمshot كثافة ملحوظة تختبر plasma
 المعيار من 17-21 ثانية كثافة بروترومبين تختبر في المعيار oxalate أو citrate
 تعتبر كل المعايير Ca^{2+} binding coagulants: Ca^{2+} binding coagulants
- The elapsed time between the addition of calcium-tissue factor mixture and the presence of a detectable clot is the prothrombin time
- PT yield evidence about: current synthetic capacity of the liver, vitamin K absorption, the inhibition of clotting factor synthesis by **warfarin**
- Reference Range: 10-12 seconds

درجة ذهاب عن المعيار
 (دواء وعائي مناصب دوائية)
 (أدوية بعد الـ 12 ساعة)

اللهم رددنا إلينك ردًا

جميلًا

Prothrombin time (PT), INR

أو دم من PT

الخطابة reagents عادة نعمل الفرقان في الأدوية

- PT is expressed as an International Normalized Ratio (INR) to normalize the values due to the wide variation among reagent and instrument systems
- The sensitivity of a reagent used with an instrument is compared to an international standard
- Each manufacturer gives an ISI (International Sensitivity Index) for any tissue factor they make. The ISI value indicates how the particular batch of tissue factor compares to an internationally standardized sample.
- The INR is the ratio of a patient's prothrombin time to a normal (control) sample, raised to the power of the ISI value for the control sample used.
- The INR of the patient can then be calculated by the formula:
$$\text{INR} = (\text{PTpat}/\text{PTcont})^{\text{ISI}}$$
- Where PTpat is the prothrombin time of the patient and PTcont is the mean of 20 normal patient prothrombin times

Activated Partial thromboplastin time (aPTT) and thrombin time (TT)

Activated Partial thromboplastin time (aPTT)

نحو اجلعه بـ Fibrinogen

⑥

- It measures the activity of the **intrinsic** and common pathways
- It reflects the time required for a fibrin clot to form after a **partial thromboplastin, calcium and an activating agent** are added to the patient's plasma (extrinsic tissue factor) صور صادر تـ F
- The PTT is measured by using a citrated sample, in order to activate the intrinsic pathway, phospholipid and another activator are mixed into the plasma sample (such as silica or kaolin), and calcium, the time is measured until a clot forms
- The test is termed "partial" due to the absence of tissue factor from the reaction mixture
- **Reference Range: 25-35 seconds**
- aPTT is widely used for monitoring **heparin therapy** → aPTT for warfarin → INR (international normalized ratio) PT

Thrombin time (TT, TCT)

ماضي اخراج صور بـ اقتين آخر خطوة
Fibrin تـ F:brinogen

بـ هـ

- It measures the conversion of fibrinogen to fibrin
- It is affected by quantitative and qualitative **abnormalities of fibrinogen**
- It measures the time required for the formation and the appearance of the fibrin clot after thrombin is added to plasma
- **Reference Range: 18-22 seconds**
- It is **unaffected** by **Vitamin K antagonist therapy** (V.K. antagonist test) cascading via
- TT is **unaffected** by most **drugs** that alter platelet function

pathway of factor \int lies up to now

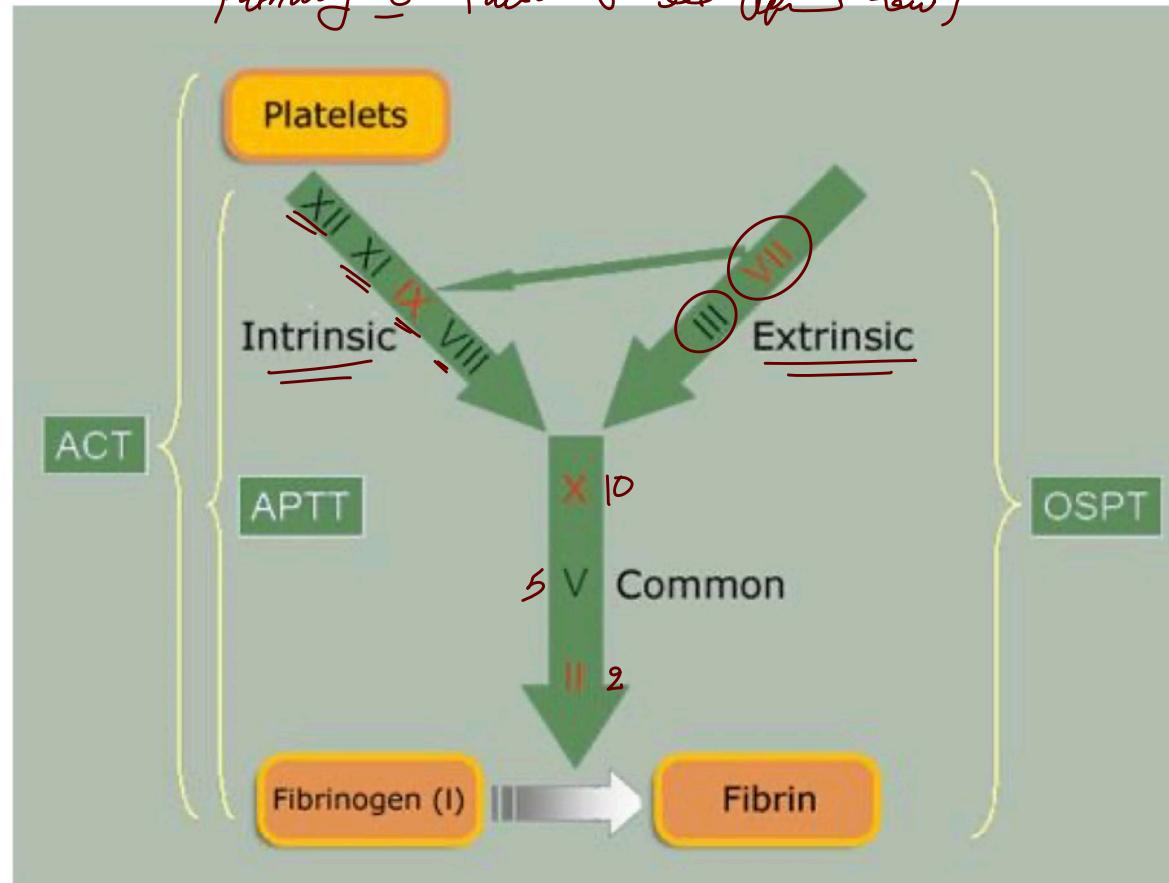


Figure 2. Schematic diagram of the intrinsic, extrinsic, and common pathways of coagulation. The vitamin K-dependent clotting factors (II, VII, IX, and X) are shown in red. Factor IX is in the intrinsic pathway, factor VII is in the extrinsic pathway, and factors X and II are in the common pathway. These four clotting factors are not activated if the function of vitamin K₁ is inhibited.

(One-stage prothrombin time [OSPT or PT], activated partial thromboplastin time [APTT or PTT], thrombin time [TT], and activated clotting time [ACT])