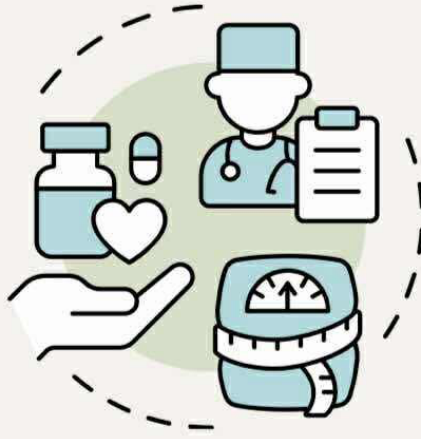


تفريغ كلىنكال



المحاضرة: Hematology

الصيدلاني/ة: ياسمين خليل



لجان الرفعات

اللهم علمنا ما ينفعنا وانفعنا بما علمتنا و زدنا علما

Hematology

علم دراسة الدم وكيفية تكوّنه ومكوناته ووظائفه وأمرضه

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? → نسيج سائل
منه خلايا معالمة نرى susp خلية كل اوعية جسم الانسان

❑ Blood is a fluid tissue containing many suspended cells and is found in the circulatory system transporting substances.
و يحمل على نقل مكونات
للجسم والاعضاء

❑ 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 عناصر ومواد عن تغذية الخلية

❑ Blood also serves to protect the body against pathogens.
WBCs

Blood Composition

Plasma

RBCs

White Blood Cells

(immune system)

Blood Platelets to prevent blood loss



البداية
*
Sample of whole blood

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

تعتبر هذه المايعة اناسها كبريتيد الهيدروجين قادر على التخلص منها

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

PLASMA PROTEINS

Albumins

(60%)
جميع كبريتات يعلق على الامحولة وتقل المحاد والمهرمونات

Globulins

(35%)

Fibrinogen

(4%)
يتحول الى فibrin وسد من الجدران

Regulatory proteins

(<1%)

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

عدول (هنا) بروتينات

PLASMA COMPOSITION

Plasma proteins (7%)

Other solutes 1%

Water 92%

① Transports organic and inorganic molecules, ② formed elements, and heat ③

FORMED ELEMENTS

Platelets 0.1%

White blood cells (WBCs) immune system

Red blood cells 99.9%

O_2 , CO_2 transporter (RBCs)

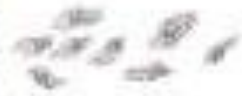
Fibrinogen converts to Fibrin
يرتبط بـ Fibrin
مع بعضه البعض

Plasma (46-63%)

Formed elements (37-54%)

عدول من الخلايا العالقة suspended cells

PLATELETS



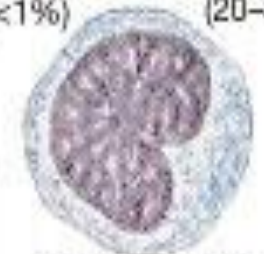
WHITE BLOOD CELLS

Neutrophils (50-70%)
مع نسيهم

Eosinophils (2-4%)

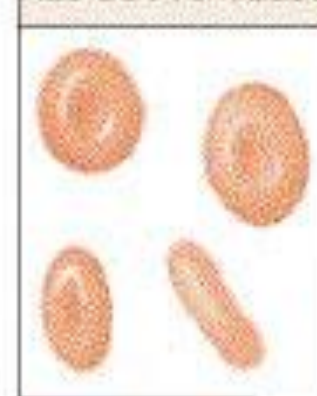
Basophils (<1%)

Lymphocytes (20-30%)



Monocytes (2-8%)

RED BLOOD CELLS



μm 0 5 10 15

Blood components

معلومات أساسية
على ضوءه بين بشكل
نقاط

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

❑ Its contents are :

❑ Water 90.0%

❑ Protein 8.0%

❑ Inorganic Ions ^{electrolytes = صانعي كاربون} 0.9%: Sodium, potassium, calcium, chloride, hydrogen, carbonate and phosphate

❑ Organic Substances ^{فيهم كاربون} 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. <sup>بسمتها صافي
الوظيفة الرئيسية</sup>

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

اللهم صلّ وسلم وبارك

على محمد

Blood components

plasma Protein Functions Include:

- ❑ Transportation of insoluble substances around the body by allowing them to bind to protein molecules
تتغلغل المواد غير الذائبة في الدم (الماء) عشاء تقدر تتشي في الدم وتروح للكلية الي بهما اياها

- ❑ Blood clotting

- ❑ Responses in accordance to disease (inflammatory response)
عن طريق يوسع الأوعية الدموية وتروح عشاء تتعالج الالتهاب

- ❑ 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
أحماض الكربون $\text{COOH}/\text{NH}_3/\text{NH}_2$ فعنده قدرة يضي H^+ لو عنده كثير OH^- وكمان الدم قاعري
amino acids
buffering system: كانه يضي ~ من عاده

Organic 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.
يخزن في مكانه
ويشتغل في مكانه
أثر في الجسم

- ❑ Medicine and drugs also circulate within the plasma.

Blood components

لما ننسب عينة دم من الدموع نرى 99% RBCs و 1% = مقسمة على platelet, WBCs

① Red Blood Cells (RBC) (Erythrocytes)

❑ Red blood cells are the most common cells found in blood.

في لو نقيسه لشفط عنده أكثر من 3-4 لتر دم نرى يكون رقم جدا كبير

❑ There are about 5 million RBC in each cubic millimeter of blood

❑ This number varies with individuals in accordance to heredity, gender ^{♂ males > females} and state of health.

❑ 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.

هناي مرحلة انحصار

السرا لن اقصي
HbA_{1c}

لما ابلو كوز يكون مرتفع
hemoglobin in

نوع من انواع WBCs وينتج عنه iron + in macrophages
تنتج من الحديد

❑ 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

صلبة والمركز فيها مقعر لله افلا

❑ 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.

صغيرة مع WBC، خلايا الـ RBC حانية فواء ولان منها انزل

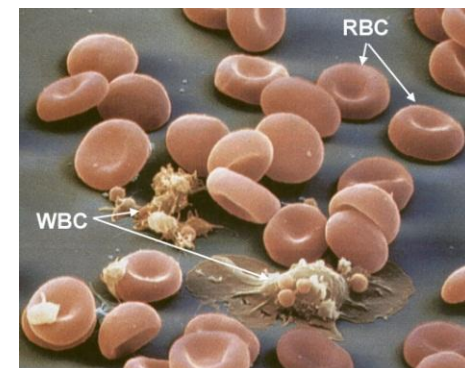
❑ Haemoglobin gives RBC its red color and Haemoglobin that contains iron, can easily transport gases such as O_2 and CO_2 .

عشانه تقدر تعب من الخلايا والعمرات الضيقة

❑ 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)

- ❑ White blood cells (WBCs) are responsible for the defense system in the body. مجهز دفاعی
- ❑ There are approximately 6,000 white blood cells per millimeter of blood کانت RBCs = 5-10 لاکھ در حجم 1mm³ WBCs
- ❑ 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 کانت تنج منہ (bone marrow) نفسہ (WBCs) تنج منہ
- ❑ 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. بحرما افسوس غر RBCs by macrophages

Structure of White Blood Cells

- ❑ WBCs are colorless, because they contain no haemoglobin. لاکھانہا هیو غلوبین
- ❑ It contains a nucleus and has an irregular shape. شکلها زی صفا سی یغل تفریزدی بتعمشی
- ❑ 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. برقو elastic زی RBCs

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.

يملأون الدم كأي جسم غريب محبب يمكنه فعل عددى أو جرح وهو أول ما يشي به الدفاع عن الجسم وضد أي شيء

❑ 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.**

الصد يد أو إلى يملأ من الجرح من سائل يكون تحوى neutrophils
عشان ذلك غريب يدخل من الجرح هاد

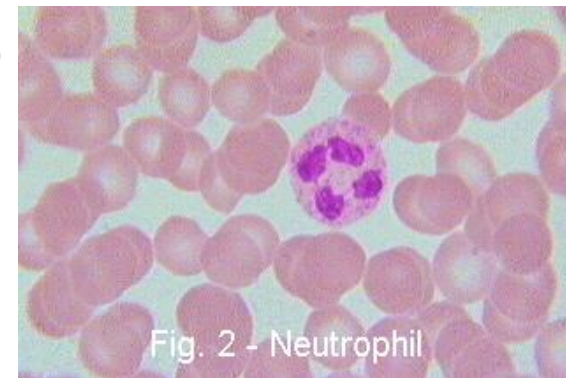
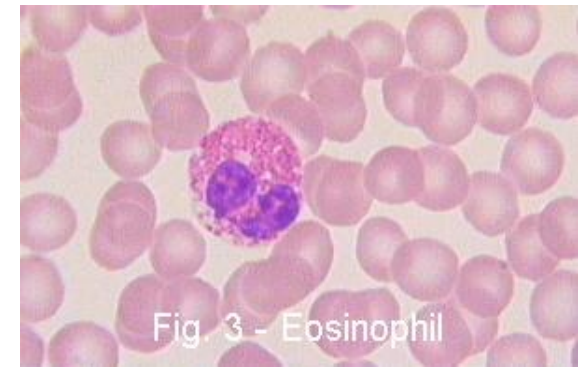


Fig. 2 - Neutrophil

White Blood Cells (Leucocytes)

Eosinophils

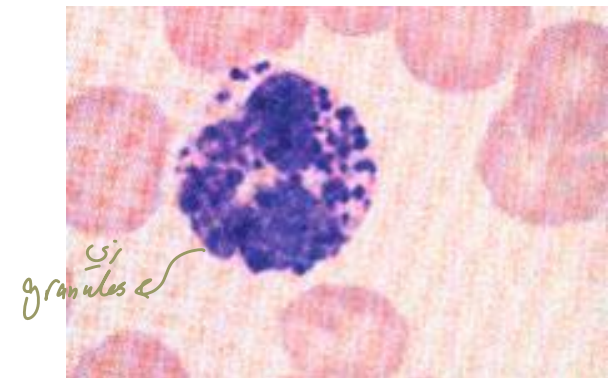
- ✓ Eosinophils make up 2%-5% of the total blood count and mainly attacks parasites and an antigen complexes.
 دافعيل ← ديار بوجام الجسم الغريب ← مهاجمة ←
- ✓ These cells are also responsible for allergic response within the blood.
 غير مسؤول كلياً بين هو ← مساهم في الاستجابة التحسسية ←



Basophiles

هائي مسؤول عن الاستجابة التحسسية أكثر من Eosinophils

- ✓ 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.
 الاستجابة من خلال :
① vaso dilation
② increase vessels' permeability
في تدمير المنطقة مجاور و حرارتها عالية



White Blood Cells (Leucocytes)

Monocytes

أكبر نوع حبيبات من أنو لي 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.

مكتنا أولا اشي يكافئ الجسم الغريب هو neutrophils و متدايمًا ينجم بابه
يصنعهم جنادة فول ف تاني اشي يلاقي الجسم الغريب هو monocytes

شيتل نبي مكانه اجبرج اما mono في الدم

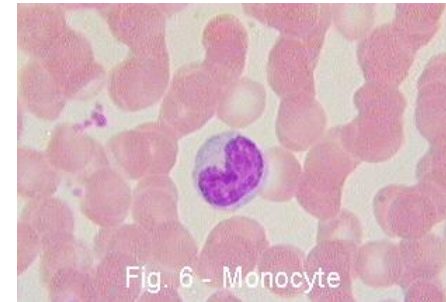


Fig. 6 - Monocyte

Lymphocytes

أهم دودة هي

بدرتها مبهار: المناعة صاير يتولى بانه عندي جسم غريب داخل الجسم

- ❑ 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.

عشاء هيك البتانه على هنا من فايردس او جيترا طلعوا جدير
لحد صاير يتوب جبهها المناعة بانها عندي بيدها بالتعاقب

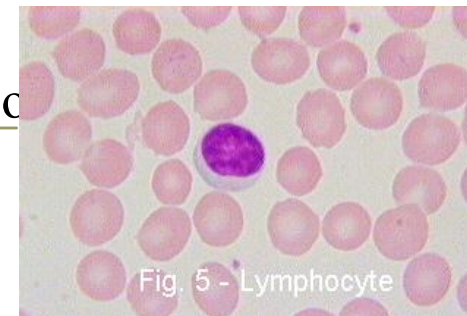


Fig. 5 - Lymphocyte

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.

الجزء الخارج هو النخيل

وزن دافني لـ صغرى وكمية منها المواد التي تسمى platelets تتجمع مع بعضها ليكو ١ plate

Functions of Blood Platelets

هو الصغالي يفرسي كجميع الـ serotonin
وتتداخل داخل granules التي جدرانها في الحايي جرح وبنانخل plate في serotonin يفرز الاوعية عند نزوح سكرهم ونسج الجرح

- ❑ 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.

MoA



Laboratory evaluation

- ❑ CBC, including RBC indices, a ^{for immature RBCs} reticulocyte index, examination of a ^{by using microscope} peripheral blood smear

أهم وأمر كانه يصدر لكل خلايا الدم قدوة عددها؟ قدوة حجمها؟ وكيف شكلها؟

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) ^①, red blood cell (RBC) ^②, and platelet ^③ populations present.
- ❑ This information includes the number, type, size, shape, and some of the physical characteristics of the cells. Any abnormalities found are noted.

كذلك أنواع WBCs البنية و RBCs الناعمة منها و immature (reticulocyte)

المتخض إلى عنده نقص و RBCs مع anemia في الجسم يحاول هو هذا النقص بإنه يضيف خلايا immature reticulocyte يعني نا منهج حجمها أكبر من RBCs mature

② Hemoglobin (Hgb):

صغيا من القدرة الحرة لربط الأكسجين
إنه يتنفس كونه يحمل O_2

- ❑ 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.

الذكور أعلى من الإناث لأنه هؤلاء العظام عندهم المملوء من البنية في bone marrow أكبر من البنية hemoglobin أكثر في قدرة على حمل O_2 أعلى

③ Hematocrit (Hct): = 3 * hemoglobin concentration

Pack cell volume

- ❑ 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

في عنده $Hgb = 15$

متخض عنده $Hct = 45$

لو عنده RBCs قليل
عن طريق الطرد المركزي
في قدوة حجمهم من السائل إلى هم متخض (الدماء) و يقسمهم على نصف

total volume

(edema) عاصبا (أكبر من الطبيعي) لدماء

حجم

③ حجم

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

③

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

③

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

③

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

③

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

③

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

③

حجمها صغير و عدد ما قليل

②

حجمها صغير و عدد ما قليل

Laboratory evaluation

④ RBC count: Same as Hct

بين الزمر هو أنه يشوف العدد ضمن 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 deficiencies, iron deficiency, and with a variety of other conditions.

macrocyte anemia (حجم RBC كبير وعتال)

also macrocytes anemia

microcytic anemia (حجم RBC صغير) hypochromic anemia (عريات لونهم أفتح من المعتاد)

يعني الحالات التي تقل anemia بهم أي بملو انقرا بعداد RBCs دخلوا بهل فرق anemia مختلفة

⑤ RBC indices:

تو من الحجم و مقدار الهيم في عريات الدم الحراء

❑ Wintrobe indices describe the size and Hgb content of the RBCs and are calculated from Hgb, Hct and RBC count

❑ MCV, MCH and MCHC

❑ Mean corpuscular volume (MCV) → متوسط حجم الخلية الحراء

❑ Hct/RBC count $\frac{Hct}{RBC \text{ count}} = \text{حجمه بكونه أنسب}$ قديم حجم الخلية الواحدة

Mean ❑ The average volume of RBCs

❑ Micro-, normo- and macrocytic

❑ Reticulocytosis → MCV مرتفع

❑ Mean corpuscular hemoglobin (MCH) →

❑ Hgb/RBC count $\frac{Hgb}{RBC \text{ count}} = \text{الكمية المتوسطة للهيم}$ الكمية المتوسطة للهيم

❑ The percent volume of Hgb in an RBC

❑ Microcytosis or hypochromia can reduce the MCH → iron deficiency

❑ Elevated MCH is macrocytosis

مشرقة الحكة لأنه واحد من أنواع الهيم هو HbA_1 و نوع HbA_2 و HbF و غيرهم و مكنة كما تكون $HbA_1 < 90$ يعني مشرقة الحكة

Laboratory evaluation

* يمكننا لحاظه MCH حالة عندي ضاربت ① حجم مفرد طبيعي
② حجم قليل غير طبيعي

صحيح كيف بهي أمده إذا المشكلة هي الأولى أو الثانية؟

Mean corpuscular hemoglobin concentration (MCHC)

صحيح لا يعتمد على الحجم (volume) ، نحسب بلون ماكريات الدم الحمراء ونقيض فيه hemو هو كبريات كبيرة مفردة من حجم

☐ Hgb/Hct في نغمة (MCHC) عندي تقمان حجم ، بل إنه ماني بالحاجة الرامة تحية معطائية

☐ The weight of Hgb per volume of cells

بلون ثقبنا الحجم فهو هو عيشة كبريات مفردة أو كبرية ما ماضي

☐ It is independent of cell size

☐ It can differentiate between microcytosis and hypochromia

صحيح فكلها مبرضا المشكلة في الأولى أو الثانية.

☐ A low MCHC always indicates hypochromia

هو استفدنا؟ إنه لحاظه MCH نازلة مبرمدي ضاربت في سالي ، فني بروج أقيس MCHC د! إذا له بره

نازل صغرها المشكلة hypochromic و فلهما الخا لو كان طبيعي في المشكلة microcytosis

اللهم ارحم والدينا

Total reticulocyte count:

☐ Indicates new RBC production

☐ Normal is 1%

أصا لو كثر من ١٪

بني ينتج RBCs immature
أو reticulocyte

Laboratory evaluation

❑ RBC distribution width (RDW)

لما يكون narrow والاشاي = 14.8 يكون ممتاز

❑ $RDW = (\text{Standard deviation of red cell volume} \div \text{mean cell volume}) \times 100$

❑ The higher the RDW, the more variable the size of RBCs

ماد صغرى اشاي صبيح

❑ Helpful in the diagnosis of mixed anemia

iron deficiency + folate deficiency
or

iron deficiency + B₁₂ deficiency

or iron + B₁₂ + folate deficiency

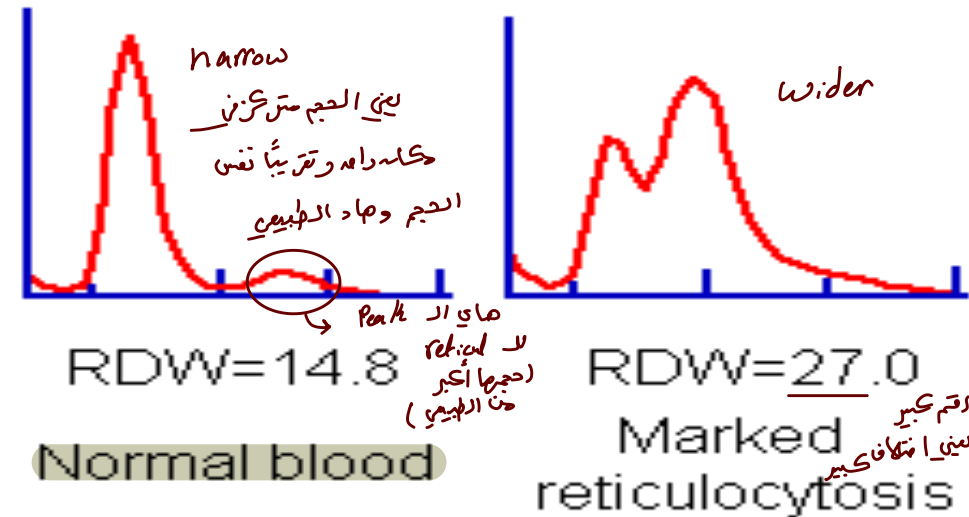
نحسها ممكن للنفوحوات اسانبة

❑ Peripheral smear:

عنا ملو به امل عينة ادم على سلايد وتحت المايكرو سكوب

❑ Complements other clinical data

❑ It provide information on the variation in cell size and shape



myoglobin
تخزن في العضلات
iron

مكون أساسي في بروتينات

مثل الهيموغلوبين

في كازم نتيجه لحفزه الحديد



في جسم الشاب (الرجل)

4g صه 2/3 هيموغلوبين

0.1/4 مخازنه صه

له البقي: free, labile

❑ 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.

❑ Most of the reminder 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.

ينتقل من مكانه
بشكل آخر

❑ The mean daily intake of iron is about 20 mg but less than 10% of this is absorbed.

كمية استهلاك الحديد في اليوم الواحد (صه) من حديد، إذ اننا نأخذ كمية قليلة من حديد كثير

❑ 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).

تعملية كريات الدم الحمراء في يزداد استهلاك الحديد

كمية حديد المخازن كافية، الجسم يحيد حديد من مخازنه

❑ 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+} .

الحديد في بروتين اللحم

الحديد في الطعام موجود على شكل Ferric (Fe^{3+}) في تأخذ حديد في كونه مشكل المتالي حديد

كمية حديد أنه يحول Ferric إلى Ferrous ويغيره بروتين HCl يخل نفس الاثر (الحضيات بطلا عام نفس المعد)

في اللحوم والمحتجانات الحيوانية يكون الحديد بشكل Fe^{2+} (ferrous) أما الخضروات ودورمات فيها Ferric (Fe^{3+})

إلى يخذل أدوية المعدة والقوة وتقال مونة المعدة بنكيلهم ينتبهوا على صيدهم ومساواة

Iron

Ferric $\xrightarrow{\text{Ascorbic acid}}$ Ferrous

يزيد امتصاص الحديد
+ انماضات معدنية

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.

قل تحسن
تغير

يحد من يقدوا امتصاص الحديد لكونه يقدوا
مع الحديد لامتصاصه insoluble complex

❑ Once absorbed into the intestinal mucosal cells, iron is either transported directly into the blood stream, or else combines with apoferritin, 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 apoferritin content of mucosal cells decreases and a greater proportion of absorbed iron reaches the blood stream.

①

②

يحتفظ
الحديد في الدم

لحماء صير تاكل في حاي الطبقة وتنتج لتقولونه
والامعاء والدماء من الجسم حاد يقدوي الى نقصه مخزونه الحديد يكونه فيها حازمه الحديد في تاكله والدماء فيها
تحتفظ حاي عند نقصه في الحديد ، يستجيب الجسم لذلك عند مخزونه انه يقلل apoferritin كانه في مساره للعديد في الدم مباشرة
في سببانه الله الجسم يغير المسار في الدم والتاني يهمل
شيء سيء ولازم فعله

apoferritin

❑ 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**

1/3 مشبع حديد و 2/3 حاي يربط مع حديد

بين تسمية بصفة من الحديد المر حاي تكونه سامة

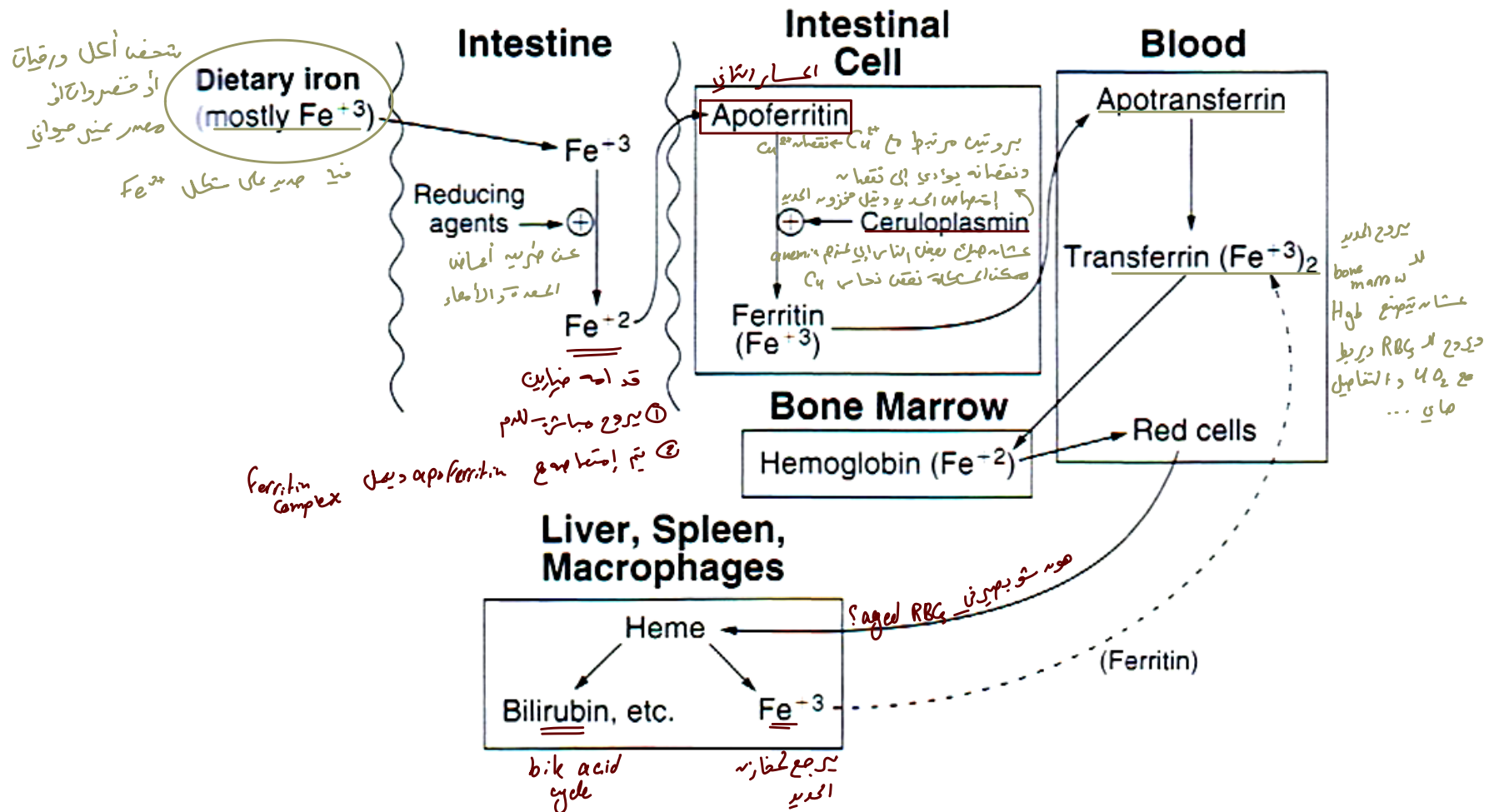
الحديد يرتبط مع ferritin في الانسجة ومع transferrin في الدم

❑ 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.

شاي عندك انما خذ حديد

وتوقف تحسنت لشهر اذا تحسنت روح اخذها الحديد ، لو تحسنت فكل الشهر يكون عندك نقص حديد ، اما لو مات تحسنت بتكونه اشياء تاني : $\downarrow B_{12}$ ، $\downarrow folic$ ، ...

Transport of iron



مخازن حديد

Plasma ferritin

less than 20 $\mu\text{g/L}$ \rightarrow iron depletion
and empty stores if it's less than 12 $\mu\text{g/L}$

قياس أهم من plasma iron لأنه أدق بكثير

- ❑ 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 $\mu\text{g/L}$ indicate depletion, and below 12 $\mu\text{g/L}$ suggests a complete absence of stored iron.

صافي fluctuation

- ❑ 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.

← يزيد ادخلى حالات الـ inflammation
← يختلف المقدار تبعه حسب النوع الـ هيمو للشخص

مريض عنده التهاب حاد

دفعه plasma ferritin
ممكن طبيعي بس هي مغلقة عليه وحسن طبيعي بس عنده التهاب بارتفاع الـ ferritin

يتحول داخل الجسم إلى حمض فوليك ويستخدم في نقل الكربون واحد فقط منه مكانه الآخر في جزيء حمض الفوليك metabolism كاشي معين

دا يحتاج نقل كربون واحد فقط منه مكانه الآخر في جزيء حمض الفوليك
 موجود في الخضراوات
 نقصه نادرًا ما يحصل
 Co-enzyme

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
 يعني DNA في RBCs immature (مطبوخة ربيعية)
 DNA
- ❑ Folate is absorbed from dietary sources such as green leafy vegetable.
- ❑ 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.
 مخزون حمض الفوليك = 5 mg وفي اليوم نستخدم 50 µg يعني لو 3 أشهر ما أخذنا حمض الفوليك من طعام وبنفسه عشان بكرة نقصه (نادرًا ما يحصل)

$$\frac{5000 \mu g}{50 \mu g} = 100 \text{ days} \approx 3 \text{ months}$$
- ❑ Folic acid deficiency is relatively common; its manifestation is as a macrocytic anaemia:
 بتكون حجم إيري يات macro أكبر
 من الطبيعي .
- ❑ Inadequate intake, decreased absorption, hyperutilization (during pregnancy, malignancy), and inadequate utilization
 في ما هي الاماكن يتم استهلاك حمض الفوليك كثير
 اسرطانات سرطانة
 ①
- ❑ It is destroyed by cooking or processing.

يفسد حمض الفوليك لما نطبخه أو الأكل المعبأ فيه حمض الفوليك خاسر acid

Vitamin B₁₂

حاجتنا منه هي 0.5 μg
 ذبيرة B₁₂ فيها
 500 000 μg
 يعني تقريبا حاجتنا أكثر من ألف مرة
 (1000 μg / 0.5 μg)
 يعني حاجة 2000 يوم

❑ Vitamin B₁₂ refers to a group of physiologically active substances chemically classified as cobalamins. Same as vit 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. ما هي المصادر كافية تقريبا
 حاجة الإنسان اليومية

❑ 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.**

water soluble vitamin
 عناصر حليج
 عناصر فقيرة
 عناصر أكثر
 أخذوا لو يتكبر عندي
 نقص

نحتاج 5 سنوات متتالية امتحانها عناصر بين تقريبا B₁₂ كل يوم يتغير

بعد ما يخلو complex ويوصل B₁₂ لحازنه في ileum يفتكو اعني يفتن ويرجع IF للمعدة يصبى مكانه B₁₂

❑ 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.

نقص IF يؤدي إلى نقص B₁₂ وفي نوع انيميا يكون في نقص IF ، يتحسن إنتاجه عند الأكل ، تناول فيتامينات و مضبوط من طريقه vagal blockade / stress

Vitamin B₁₂ ^{Huge RBCs size}

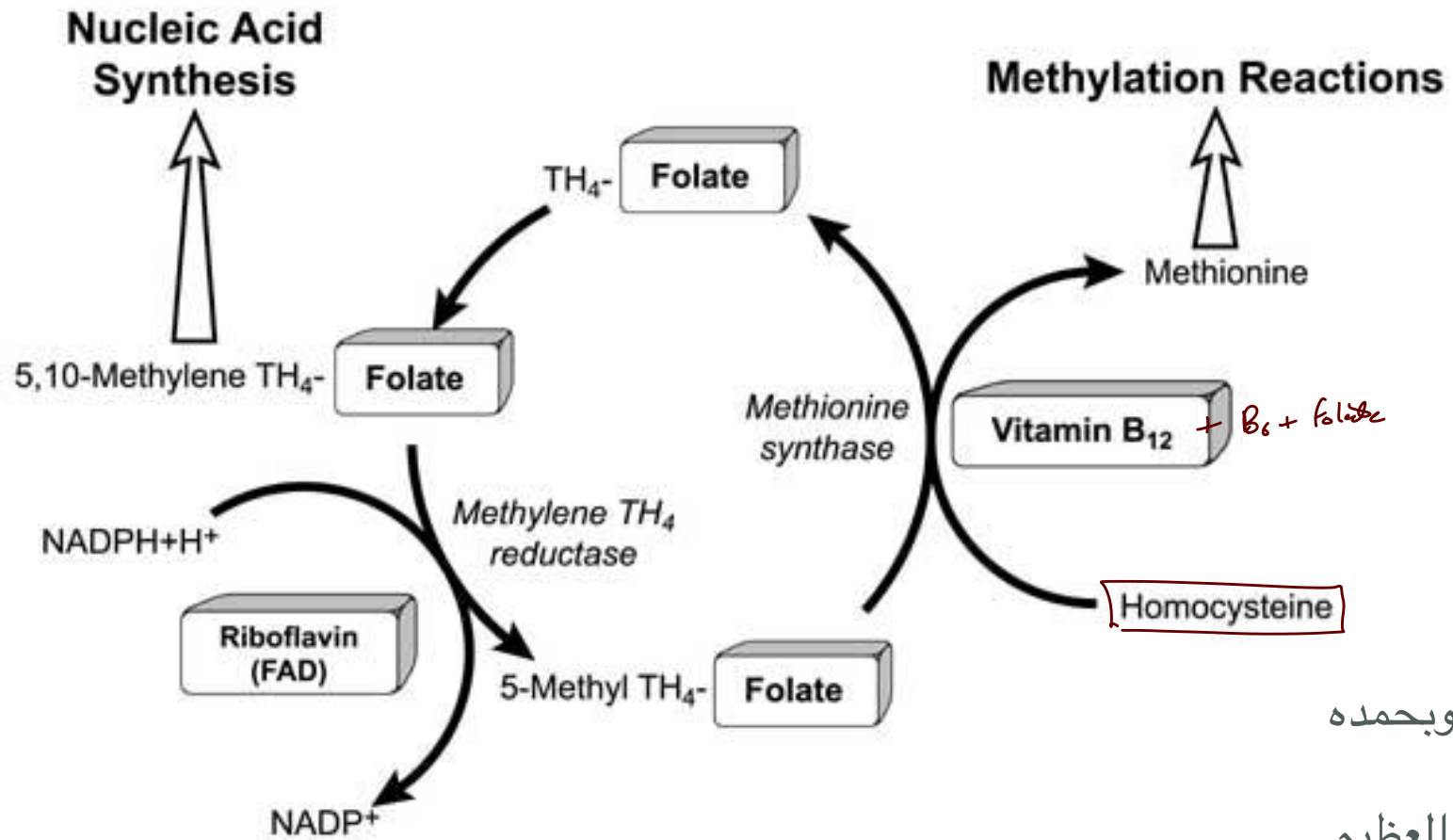
عند اننا كى اننا نسير بيوه عزم نقف

- ❑ The deficiency of vitamin B₁₂ in humans is associated with **megaloblastic anaemia**.
نقص كريات الدم الحمراء وحجم الكريات يكون أكبر من الطبيعي (macro)

- ❑ **Pernicious anaemia**: ^{↓ IF} 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.
يقتد الشهور بالحرارة العالية
جهد، داء باردة
جهد، الداء هو أن
نقص الحواس
عدم إدراك وقتاً أو زمن
خرف

Tests for vitamin B₁₂

1. Vitamin B₁₂: **serum values are maintained at the expense of vitamin B₁₂ tissue stores**.
إعتر (B₆) / B₁₂
Produced by amino acids metabolism then converted to methionine
2. **Homocysteine**: vitamin B₁₂ and folate are required for conversion of homocysteine to methionine. **It can be also elevated in B₆ deficiency**.
3. **Methylmalonic acid (MMA)**: a vitamin B₁₂ coenzyme is needed to convert methylmalonyl coA to succinyl coA. **Increased urinary excretion of MMA is a more specific marker of vitamin B₁₂ deficiency**
يؤدي نقصه إلى عرق وزهايم



سبحان الله وبحمده

سبحان الله العظيم

Amino acids metabolism

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

Propionyl CoA

Biotin B_7

Methylmalonyl CoA

← ترشحہ فراموشی
دلیل کی نقص B_{12}
کو نہ ہو سکتا ہے اس لیے
Succinyl CoA

Vitamin B12

Succinyl CoA

TCA Cycle

Ferritin deficit means low level of Fe but the last deficit will indicate that the patient has anemia is serum iron علاوة على fluctuation في مستوياتها

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

منه متأكدة
بين على الأغلب من صفو

صفو مهم

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

CONDITION	SERUM IRON	TRANSFERRIN	FERRITIN	PERCENT SATURATION	TIBS
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
Hematochromatosis	Increased	Slightly decreased	Increased	Increased	Slightly decreased
Malnutrition	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/increase
Chronic anemia	Decreased	Normal/decreased	Normal/ increased	Decreased	Normal/decreased
Sideroblastic anemia	Increased	Normal/decreased	Increased	Increased	Normal/decreased

كلشي ناقص

كله عالي

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

TIBC من حيثها لزيادة
Saturability في نسبة serum و iron

تزداد دقة الفحص لما يعطى نتائج
عنايته كل type من أنواع WBCs الخاصة

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.
 normal range is : 4000 - 10000 → less than 4000 : weak immunity
 → more than 10000 : infection → higher than 50000 - 60000 : leukemia, or deep infection within organs
- ❑ Low white blood cell count will make the individual susceptible and vulnerable to diseases and foreign invasive organism.
 صناعته منخفضة جداً سهل يمرض
 كائنات ضارة

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^①/cancer^②/physical stress^③.
 ارتفاعهم مع بعض معنى عدوى بكتيرية
- ❑ High monocyte and eosinophil count usually points at bacterial infection.
 زيادة : مرضية
- ❑ With allergies, there may be an increased number of eosinophils
 فحسب داء حساسية و WBCs ترفع جداً عند باقي الأنواع
- ❑ 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.
 النسيج المرتفع من ناكته منه أشياء والتمثيل غير ناضجة وغير مبرجة.

Platelet Count

عدد الصفائح في حجم دم معين

هر تبليو
مع انشاي
اللاصة في حياه
زنا
سليمه

Thrombocyte count:

- ❑ Platelets are essential in the coagulation
- ❑ If there are insufficient platelets → hemophilia
نزيف لا يتوقف
لو نقصت ما عنده صفائح كافيه نقل الدم سق بهير؟
- ❑ Hence platelet counts are usually done before an operation.
في قبل اجراء أي عملية جراحية تتطلب تكبير جرح بعد الإبرتها، لازم أدخل هاد الفحص
- ❑ 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

- ❑ 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
كمه أكثر من 9 دقائق وما ستر يعني hemophilia
- ❑ Quantitative and qualitative platelets



Formation of a blood clot

خطوات تكبير 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 bleedings starts.

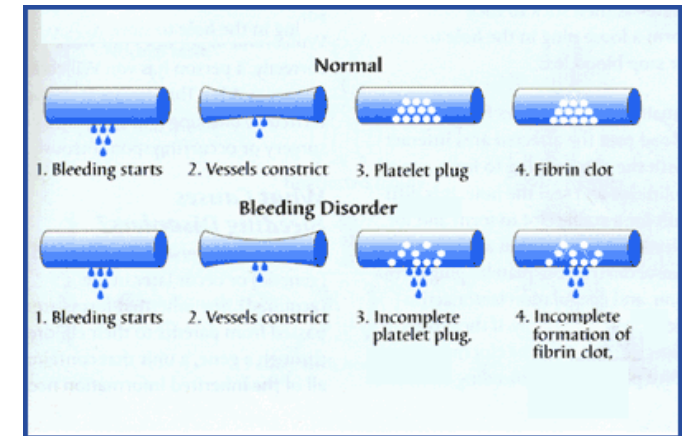
تبدل الأوعية الدموية إلى أنبوب يضيق Contracture ثم تقل الواسطة للجرح

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

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 VIII and IX circulating in the blood are activated on the surface of the platelets to form a mesh-like fibrin clot

يصلوا إلى شبكة



وتقزم الوعاء صغرى ثم يقلل الوعاء العريضة إلى أنبوب يضيق الجرح

بعض الصفائح تلتصق على جدار الوعاء الدموي

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

تحتفظ كما يحويه الضرر_الدوية_الموتية
وصائي ضرر على الأنجة

The Clotting Cascades

Extrinsic pathway

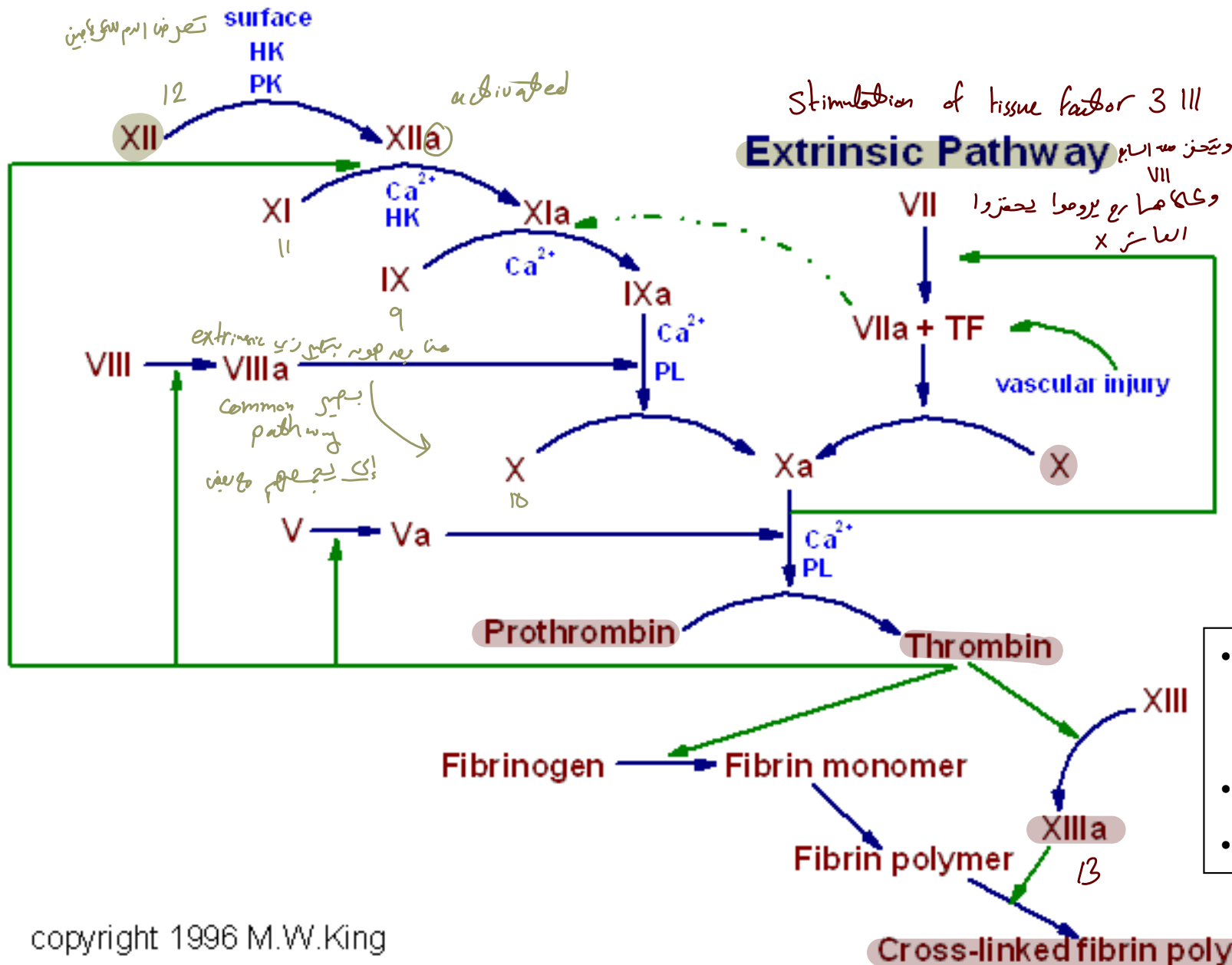
كما تضرر الأنجة بهوه الاوتية

- ❑ 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 ^{both extri + intrinsic} common pathway that leads to clot formation.
- ❑ The formation of a ^{clot inside the vessels} 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**.
- ❑ 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.

اللهم استر على المسلمين والمسلمات

The Clotting Cascades

Intrinsic Pathway



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

The clotting cascades

يبدأ إلى الخلية العازلة بعدد لدها من لدا
تتعرضها للدم ويصير عليها دم فالجسم يتوجب إنه يفرج ماز
(عندئذ ينزرو مرج ف يبه ا ماز ال pathway)

- The intrinsic cascade is initiated when contact is made between blood and exposed endothelial cell surfaces.
عين يبدأ بها 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.
يبدأ TF + III لما ينكشف الجسم يتوجب إنه ماز غشوي ماز

- 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
عنده يلتقي 2 pathways
هادا الكلام
شرح الرسمة فوهم (صفر فكل factor شو شغل)

- 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 13 (XIIIa)

هو الذي يربط كوكابين مع الصفائح عن طريق glycoprotein معين

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 يتواجد في

تأني أبسط من
bleeding time بعد

prolong
prothrombin
time ← no clotting factors are synthesis
vit K deficiency
لي معلومات تشاير liver

Prothrombin time (PT)

- ❑ It assess the function of ^① **extrinsic** and the common pathways ^②
- ❑ It measures the activity of vitamin K dependent proteins (factors II, VII, IX, and X and proteins C and S)

نحتاج في تصنيع vit K في نقص vit K على نيل نقص في عوامل الـ factors

- ❑ It reflects the time required for fibrin strands to appear after the addition of tissue thromboplastin to a patient's plasma

- ❑ Plasma obtained from blood to which a calcium-binding anticoagulant (citrate or oxalate) has been added, will clot in a few seconds when recalcified in the presence of tissue factor (obtained from animals)

العينة إلى تُعاشر مع Plasma و يضاف إليها citrate أو oxalate عشان ما يغير تخثر

- ❑ 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**

مع فحصي عنه في INR تحت
(دواء وقائي مناصداً جلية
ثانية بعد الثانية)

العينة من كلاً ما تُصحبها كانه بهي افحصها ← نعتبر Ca binding coagulants: بر تبطو ليع ٩، ويصبروا كل اسكال يوم في العينة عشان ما يغير تخثر خارج تحتوي كايدي افحصها يميني

عاليوم و TF من

مفسر فارسي (معلومات)

وتقيس الرقبة او الهمية

لماذا تتكون الشرة

اللهم ردنا إليك رداً

جميلاً

Prothrombin time (PT), INR

أدومنا PT

عنا نزيل الفرد قاتني الأمهرة و
التي مختلفة

- ❑ 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:
$$INR = (PT_{pat}/PT_{cont})^{ISI}$$

أفزيج PT لعشرين شخصاً / المعادى ← لتقيس تأثير warfarin
- ❑ Where PT_{pat} is the prothrombin time of the patient and PT_{cont} is the mean of 20 normal patient prothrombin times

هل في fibronogen في الجلبه؟ نو

⑥

- یہ یو فر طرح خوشن
د سیتل شغل
کو کا بین

ما دقله من (as) هو بي اقيس آخر خطوة:
تحويل Fibrin الى Fibrinogen

8. نہ ہر فی سبب از صفوہ۔

الادوية الوصية الى الطبيب + هي أدوية 1/2 vit

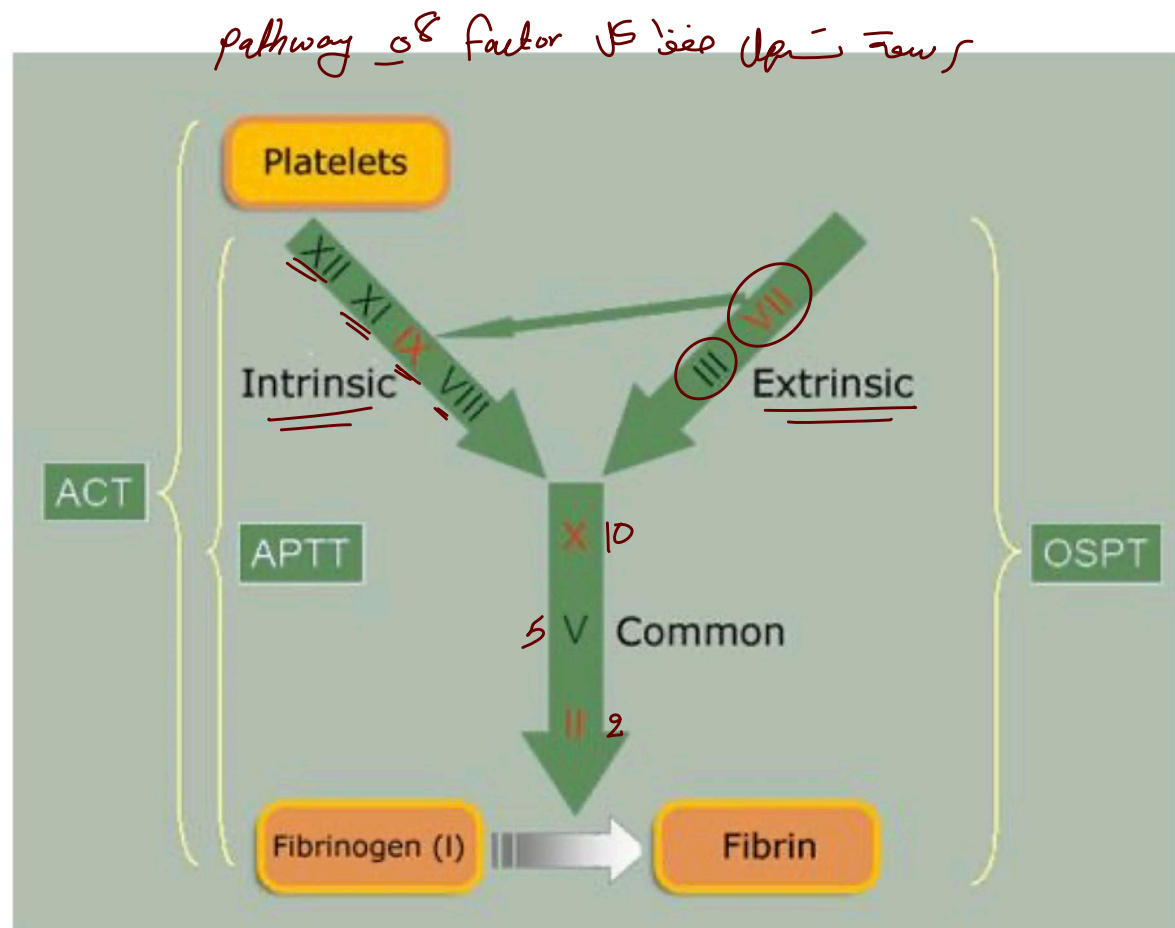


Figure 2. Schematic diagram of the intrinsic, extrinsic, and common pathways of coagulation. The vitamin K-dependent clotting factors (II, VII, IX, and X) are shown in red. Factor IX is in the intrinsic pathway, factor VII is in the extrinsic pathway, and factors X and II are in the common pathway. These 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])