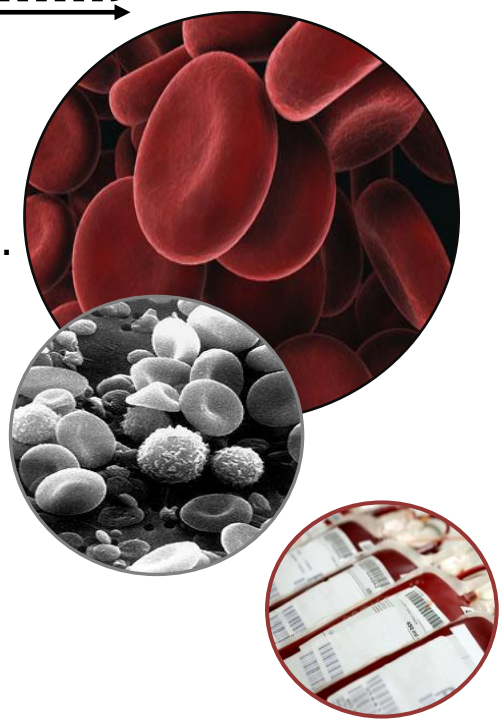
431

Foundation Block

Physiology Team Notes 3



For ALL Blood Lectures:

- ✓ Composition and Blood Function(RBC).
- ✓ Essential Elements and Anemias.
- ✓ WBC1.
- ✓ WBC 2.
- ✓ Blood Groups.
- ✓ Coagulation .

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تمت مراجعتها من قبل د.ست البنات

Lecture 1

Composition and Blood Function

Blood Composition:

1. **Cellular components:**
   - Red Blood Cells (Erythrocytes)
   - White Blood Cells (Leucocytes)
   - Platelets (Thrombocytes)

Erytho= red Cytes=cell
Leuco=white
Thromo = clot

2. **Plasma:**
   - 98% water, ions, plasma proteins (Albumin, globulin, Fibrinogen)
   - Same ionic composition as interstitial fluid

Function Of Blood :

- **Transport:**
  1. O2, CO2, nutrient, hormones, waste product.
- **Homoeostasis:** = keeping internal environment constant.

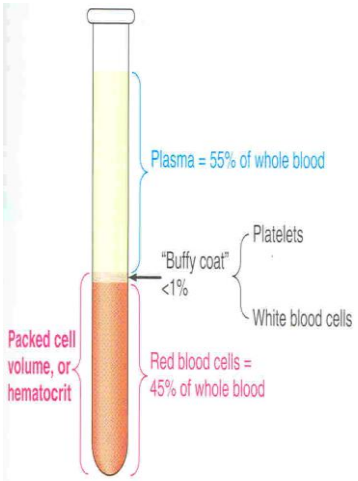
  Regulation of body temperature, ECF pH

  Keep body temperature at(37c) and ph for extracellular fluid at(7.4)
  - **Protecting against infections:**
    White Blood Cells, Antibodies.
- **Blood clotting prevent blood loss.**

Blood Volume:

5 liter in adult:

- **45%** is packed cells volume (PCV)
- **55%** is plasma volume



Blood Cells Formation: (Opoiesis = Formation)

- **Erythropoiesis:** Formation of RBC (erythrocytes)
- **Leucopoiesis:** Formation of WBC (leucocytes)
- **Thrombopoiesis:** Formation of platelets (thrombocytes)

Function of RBC:

- O_2 transport
- CO_2 transport
- Buffer

Buffering agent (hemoglobin in case of blood) is a weak acid or base used to maintain the acidity (pH) of a solution at a chosen value (7.4 in blood) The **function of a buffer** is to prevent a rapid change in pH when acids or bases are added)

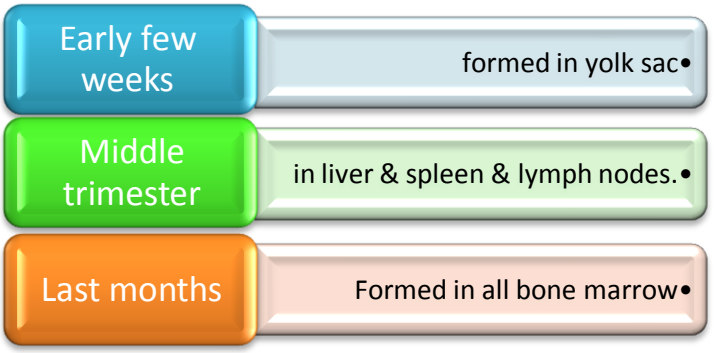
Shape & size

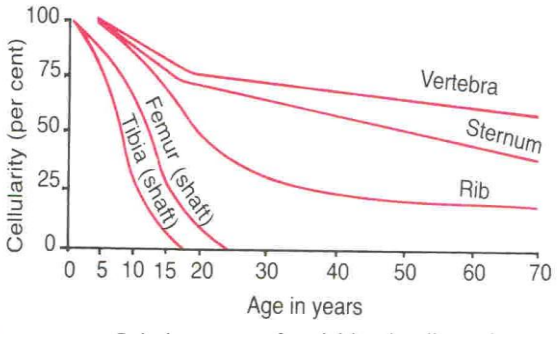
- Flat Biconcave Disc
- Non-nucleated Diamter 7-8 mm x 2.5 mm , 1 mm
- Average volume 90-95 mm^3
- Flexible
- Number =4.7-5 $x10^6$
- Hb =34g/dl **of cells**
- Hb= 14-16 g/dl **in the blood**

Production Of RBC:

- Early few weeks of embryo nucleated RBCs are formed in **yolk sac**.
- Middle trimester mainly in **liver & spleen & lymph nodes**.
- Last months RBCs are formed in bone marrow of **all** bones
- Bone marrow of **flat bone** continue to produce RBC into adult life.
- Shaft of long bone stop to produce RBC at puberty while **epiphysis** continued.

To Remind you:
Diaphysis: shaft of long bone.
Epiphysis: rounded end of a long bone.





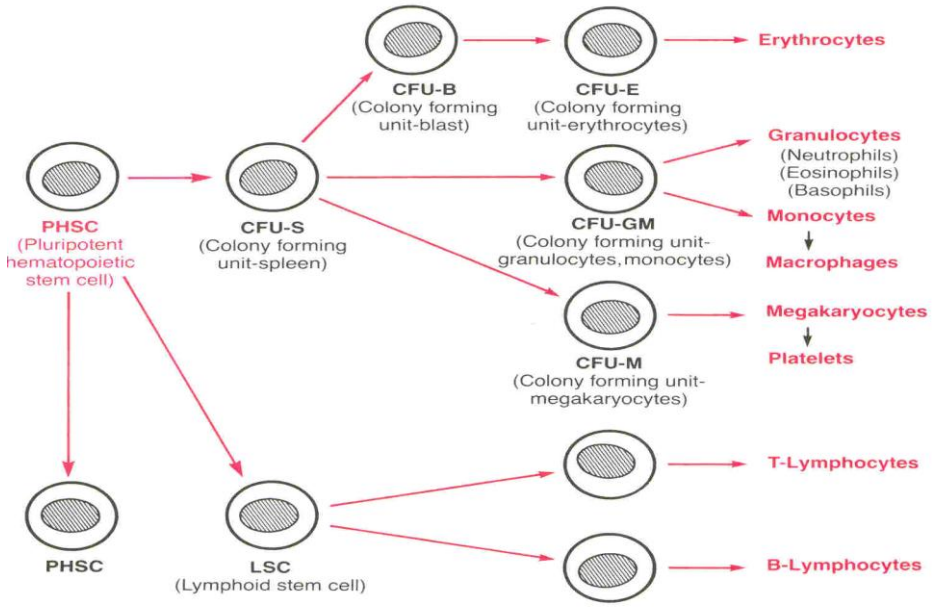
RBC genesis:

All blood cell are formed from **Pluripotential hematopoietic** stem cells ⇒ committed cells:

- Committed stem cells for RBC
- Committed stem cells for WBC

كل خلايا الدم منشأها من :-
Pluripotential hematopoietic stem cells
وبعد ذلك من خلال:- Growth factor
تتحول إما خلايا دم حمراء او خلايا الدم البيضاء

Growth of different stems cells are controlled by different growth factors.



Stages of RBC development:

- Committed stem cell
  - Proerthroblast
  - basophil erythroblast
  - polychromatophil erythroblast
  - orthochromatic erythroblast
  - Reticulocytes
  - Mature erythrocytes
- Rapid RBC production $\rightarrow \uparrow$ reticlocytes in the circulation

Erythropoiesis:

❖ **RBC development is characterize by:** ذكرها الدكتور كثير في المحاضرتين

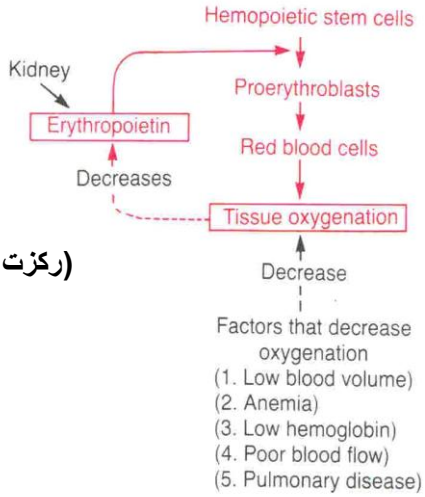
- decrease in cell size
- disappearance of nuclus
  (خلايا الدم الحمراء هي الخلايا الوحيدة في الجسم التي لا تحتوي على أنوية)
- appearance of haemoglobin

Regulation of RBC production:

- Erythropoiesis is stimulated by erythropoietin hormone produced by the kidney in response to hypoxia (low oxygen in the blood
- Hypoxia caused by:
  - Low RBC count (Anaemia)
  - Hemorrhage
  - High altitude (المناطق المرتفعة : كلما ارتفعنا لأعلي يقل الضغط ويقل الأكسجين)
  - Prolong heart failure
  - Lung disease

Tissue oxygenation and RBC formation:

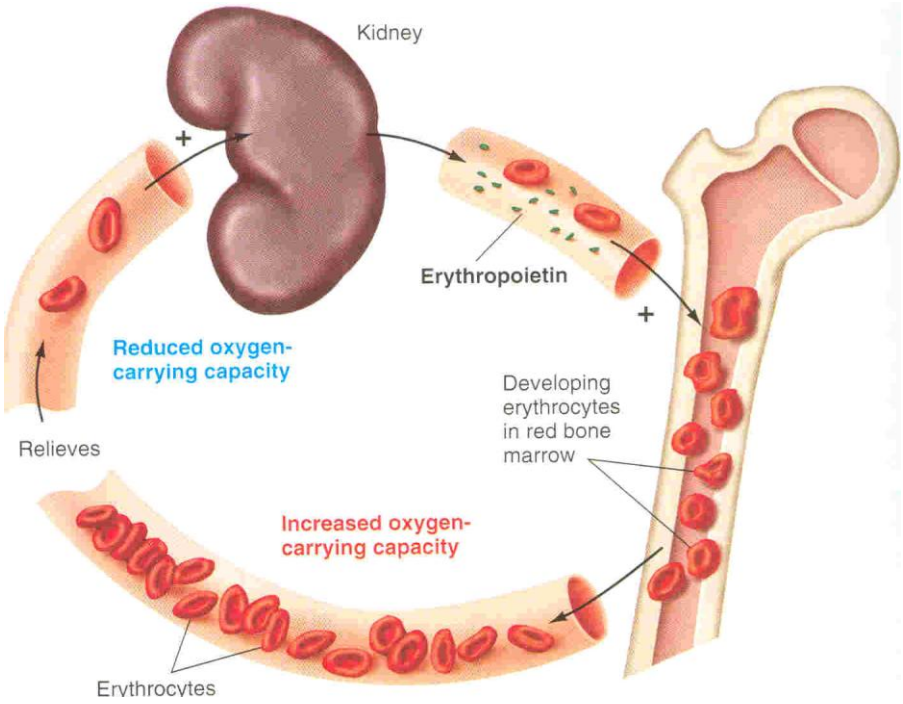
Erythropoietin:



- Glycoprotein
- 90% from renal cortex 10% liver
- Stimulate the growth of early stem cells
- **Does not affect maturation process (ركزت الدكتورة على هالنقطة)**
- Can be measured in plasma & urine
- High level of erythropoietin
  - anemia
  - High altitude
  - Heart failure

(الاشخاص الذين يعانون من امراض في الكلى يكونون اكثر عرضه للاصابه بالانيميا لقله افراز هرمون Erythropoietin)

Role of the kidneys in RBC formation:



Lecture 2

Essential Elements and Anemias

Certain elements are essential for RBC formation and maturation:

1) **Amino acid:**
   formation of globin in Hb, sever protein deficiency leads to anaemia.
2) **Iron:**
   formation of Hb, iron deficiency results in small cells (microcytic) anaemia.
3) **Vitamins**
   1- Vit B12 and Folic acid ركز عليها الدكتور
   •Synthesis of **nucleoprotein**
   •Deficiency of both causes anemia
   2- Vit B6, Riboflavin, nicotinic acid, biotin, Vit C, Vit E
4) **Essential elements**
   –Copper, Cobalt, zinc, manganese
5) **Hormones**
   –Androgens, Thyroid, cortisol & growth hormones
   –Deficiencies of any one results in anaemia

Nucleoprotein :- protein with nucleic acid

Vitamin B12 & Folic acid (very important in case of pregnancy)

•Important for DNA synthesis and final maturation of RBC

•Dietary source: meat, milk, liver, fat, green vegetables

•Deficiency of VIT B12 & folic acid leads to:

–Failure of nuclear maturation & division

–Abnormally large & oval shape RBC

–Short life span

–reduced RBC count & Hb content

–Macrocytic (megaloblastic) anemia (عبارة عن أنيميا ناتجة عن زيادة غير طبيعية في حجم الخلية)

Malabsorption of Vit. B12 - Pernicious Anemia

•VB12 absorption needs intrinsic factor secreted by parietal cells of stomach

•VB12 + intrinsic factor is absorbed in the terminal Ileum

(Ileum في يسهل امتصاصة بالأمعاء الدقيقة بالتحديد parietal cells في المعدة لكي من يفرز عامل داخلي إلى يحتاج B12فيتامين)

•Causes of deficiencies

–Inadequate intake

–Poor absorption due to Intestinal disease

•Give rise to megaloblastic anaemia

HAEMOGLOBIN

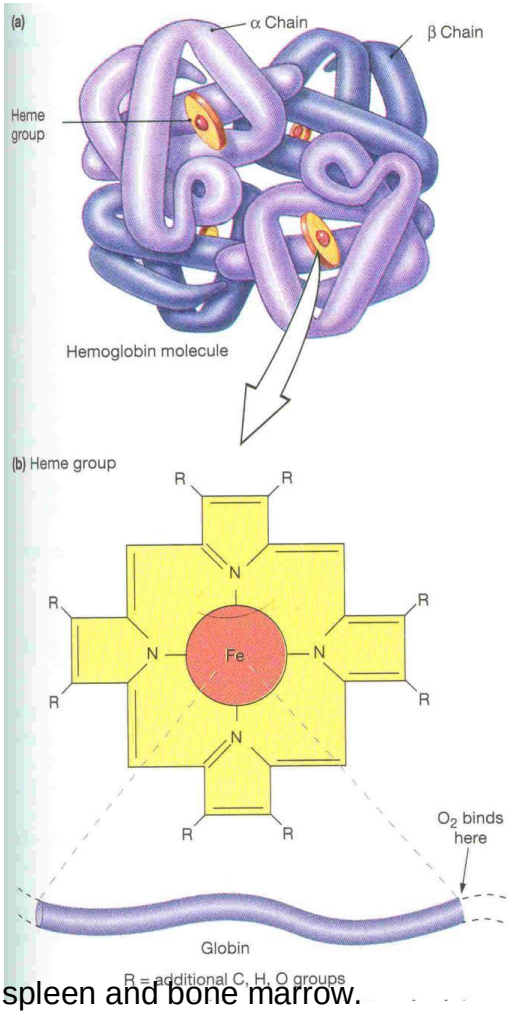
Heme: هي المادة التي تعطي اللون الاحمر للدم وتحتوي على الحديد

Globin: نوع من أنواع البروتينات

•Hb molecules consist 4 chains each formed of heme & polypeptide chain (globin)

•Heme consist of **protoporphyrin ring + iron**

•Abnormality in the polypeptide chain - abnormal Hb (hemoglobinopathies) e.g thalassemias, sickle cell (الثلاسيميا)



Functions of Hemoglobin

- **Carriage of O2**
  - –Hb reversibly bind O2 to form oxyhemoglobin, affect by pH, temperatre, H+
- **Carriage of CO2**
  - –Hb bind CO2 = carboxyhemaglobin
- **Buffer**

Iron metabolism

Iron is needed for the synthesis of Hb, myoglobin cytochrome oxsidase, peroxidase & catalase

•Total Iron in the body = 4-5g

- –65% Haemoglobin
- –5% other hems
- –1% bound to **transferrin** (betaglobulin) in blood
- –15-30% stored iron in the form of ferritin in the liver, spleen and bone marrow.

Transferrin is a glycoprotein that binds iron to transfer it through circulation.

Iron absorption

•Iron in food mostly in oxidized form (Ferric) F^{+3}

•Better absorbed in reduced form (Ferrious) F^{+2}

•Iron in stomach is reduced by gastric acid, Vit. C.

•Rate of iron absorption depend on the amount of iron stored

(اذا كانت كمية الحديد المخزنة في الجسم قليلة، سوف يتم امتصاص كميات كبيرة من الحديد الموجود بالغذاء ، والعكس صحيح)

Transport and storage of iron

•Iron is transport in plasma in the form of Transferrin (apotransferrin+iron)

•Iron is stored in two forms

–**Ferritin** (apoferritin+iron)

–Haemosiderin (insoluble complex molecule)

Ferritin: is a protein found inside cells that stores iron so your body can use it later.

•Daily loss of iron is 0.6 mgm in male & 1.3mgm/day in females

Destruction of RBC

•RBC life span in circulation = 120 days

•Metabolic active cells

•Old cell has a fragile cell membrane, cell will rupture as it pass in narrow capillaries (spleen)

•Released Hb is taken up by macrophages in liver, spleen & bone marrow

•**Hb is broken into its component:**

–Polypeptide broken to aminoacids to storage.

–Iron degraded to ferrtin and stored.

–Porphyrin ring transfer to bilirubin, secreted by the liver into bile.

ANAEMIAS

–**Definiation**

•Decrease number of RBC

•Decrease Hb

–**Symptoms:** Tired, Fatigue, short of breath, heart failure

<u>Causes of anaemia</u>:

- **Blood Loss**

–**acute:** accident (RBC return to normal 3-6w)

–**Chronic** : microcytic hypochromic anaemi (ulcer, worms)

- **Decrease RBC production**

معلومة إضافية ذكرها الدكتور داخل المحاضرة:
Iron deficiency anemia is the most common type of anemia in the world and it is more common in women

–**Nutritional causes**

•Iron : microcytic anaemia

•VB12 & Folic acid : megaloblastic anaemia

–**Bone marrow destruction**

by cancer, radiation, drugs Aplastic anaemia.

Note:
Hemolytic is the result of fragile RBCs that rupture as they pass through the capillaries.

- **Haemolytic :excessive destrction** (تكسر غير طبيعي لخلايا الدم الحمراء)

–Abnormal cells or Hb

•Spherocytosis

Spherocytosis: production of (RBCs), that are sphere-shaped,rather than bi- concave disk shaped

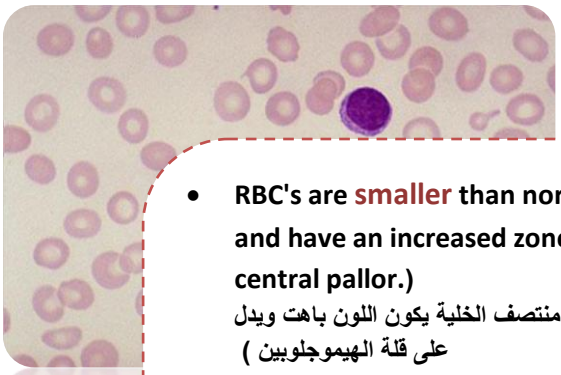
•sickle cells

–Incompatible blood transfusion

–Erythroblastosis fetalis

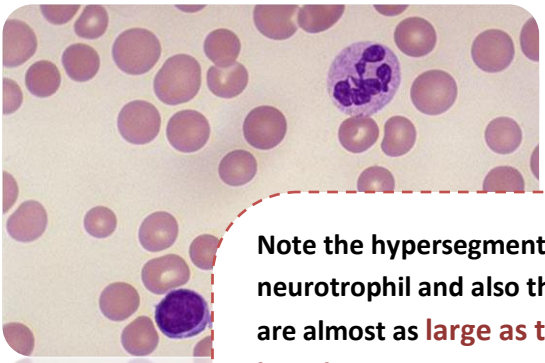
Erythroblastosis fetalis: life-threatening blood disorder in a fetus or newborn infant as a result of ABO incompatibility or Rh incompatibility. Mother's blood will produce antibodies that destroy red blood cell of the fetus. (تم شرحه بتوسع في المحاضرة الخامسة)

Types of Anemia's:



- **RBC's are smaller than normal and have an increased zone of central pallor.)**
  (في منتصف الخلية يكون اللون باهت ويدل على قلة الهيموجلوبين)
- **This is indicative of a hypochromic (less hemoglobin in each RBC) microcytic (smaller size of each RBC) anemia.**
- **There is also increased anisocytosis (variation in size) and poikilocytosis (variation in shape).**

Microcytic anemia



Note the hypersegmented neurotrophil and also that the RBC are almost as large as the lymphocyte.

(حجم الخلايا الحمراء كبير ويقارب حجم الخلايا البيضاء في هذه الحالة)

Finally, note that there are fewer RBCs.

Macrocytic anemia

Polycythemia → Poly =many, Cyto= cells

Increased number of RBC.

Types:

Rubra= red, Vera= PCV

Note: Polycythemia greatly increases the viscosity of the blood; as a result, blood flow through the vessels is often sluggish. (بطيء و خامل)

1.Primary (polycythemia rubra vera): uncontrolled RBC production

2.Secondary to hypoxia: high altitude (physiological), chronic respiratory or cardiac disease

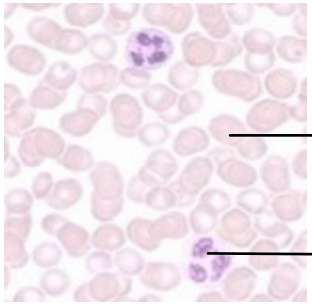
توضيح

High Altitude → hypoxia → Erythropoietin → More RBCs → Secondary Polycythemia

مناطق مرتفعة → نقص الأكسجين → Erythropoietin إفراز هرمون → إنتاج كريات دم حمراء

Lecture 3

White Blood Cell (WBCs) 1



red blood cells(5-6-million /ml)

white blood cells (5000/ml)

White Blood Cells (Leucocytes):

WBC is transparent cell (شفافة). Actually, WBC is not white .but we need to put the white pigment to see it.

- Formed in bone marrow, lymph tissue
- Protection against infection by:
  - **–Phagocytosis**
  - **–Secretion of antibodies**
- WBC count = 4000—11000/ml

Types of WBC :

1.Granular (polymorphnuclear PMN):

Granular = containing cytoplasmic granules

- **Neutrophil 62%.**

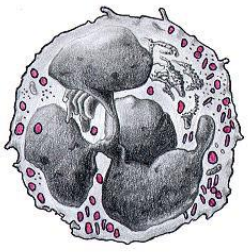
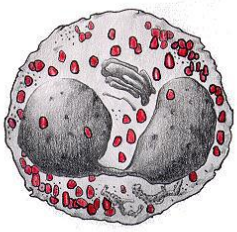
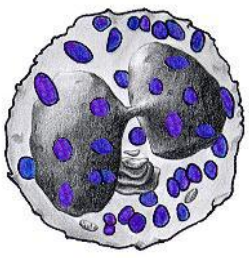
–10-16um, lobulated nucleus 2-5, purple cytoplasmic granules

- **Eosinophil 2.3%.(It is acidophilic (red))**

–12-18um, 2 lobe nucleus, coarse red granules

- **Basophil .4%. (It is Basophilic (Blue))**

–10-14um, rarely segmented nucleus, nucleus hidden by large round bluish granules

type	Neutrophil	Eosinophil	Basophil
size	10-16um	12-18um	10-14
Shape	lobulated nucleus 2-5 lobes, **purple** cytoplasmic granules. 	2 lobe nucleus**, coarse red** granules in cytoplasm. 	rarely segmented nucleus, nucleus hidden by large round **bluish** cytoplasmic granules. . 
Percentage of total WBC	62%	2.3%	4%

2. Agranular

Agranular= does NOT contain cytoplasmic granules

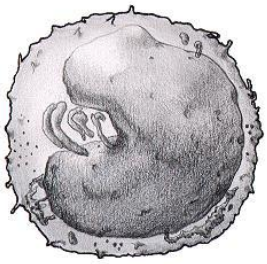
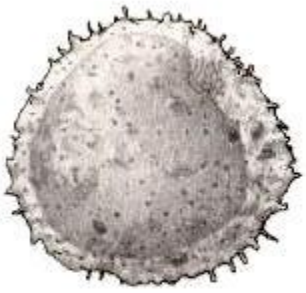
- **Monocytes 5.3%**

15-20um, kidney shape nucleus

- **Lymphocyte 30%**

round nucleus

–small (5-8um) –large (9-15um)

Type	Monocytes	Lymphocyte
Size	15-20um	– small size(5-8um); – large size(9-15um)
Shape	kidney shape nucleus. 	round nucleus. 
Percentage of tatal WBC	5.3%	30%

Genesis of WBC

Two major lineage of WBC are formed:

1.Myelocytic: granular,monocytes

2.Lymphocytic: lymphocytes

Sites of WBC Formation

•**Granulocytes**: (neutrophil, basophil, eosinophil) in bone marrow

•**Monocytes:** bone marrow

•**lymphocytes:** bone marrow, thymus, lymphoid tissues

Life span of WBCs

•Granulocytes=
*4 to 8 hrs (transit time) in blood circulation .
4-5 days in tissues, **During infection life span only few hours** because they die after ingesting bacteria.

•Monocytes =
10-20- hours then they leave blood to tissues transform into macrophage, its life span goes up to **months**.
•Lymphocytes = weeks to months according to its type

NEUTROPHILLS

Formation and Maturation of Neutrohils :Formed in Bone Marrow

1.Stem cells

2.Myeloblast

3.Promyelocytes

4.Neutrophil myelocytes

5.Young neutrophil metamyelocytes

6.Band neutrophil

7.Polymorphnuclear neutrophil (Mature Neutrphils released to blood)

Neutrophil Function

Defense against infection:

Neutrophil has the ability of engulfing bacteria or organism by a process of phyagocytosis.

Steps of Phygocytosis

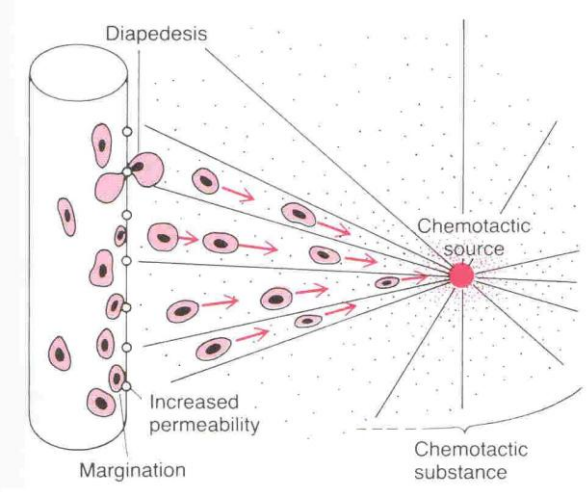
1.Chemotaxis

2.Margination

3.Diapedesis

4.Ameoboid movement

5.Engulfing and killing of a microbe.(phagocytosis).

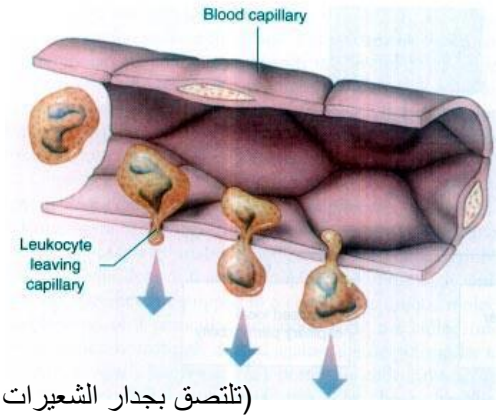


Chemotaxis

•The attraction of the neutrophils to inflamed area following chemotactic substances release from infected site:

Chemotactic substances: (مواد تؤدي إلى انجذاب الخلايا البيضاء)

- Bacterial toxin
- Degenerative products of inflamed tissue
- Complement system
- Reaction product of plasma clotting



Margination & Diapedesis

•WBC marginate along the wall of blood capillaries. (تلتصق بجدار الشعيرات الدموية)

•WBC squeezes itself through endothelial holes leaving blood capillaries (diapedesis)

(diapedesis عملية خروج الخلايا البيضاء من الشعيرات الدموية من خلال المسافات بين خلايا الأنسجة الطلائية تسمى)

•WBC move by amoeboid motion towards inflammation area following chemotactic substance released from site of infection

•Upon reaching the site of infection neutrophils start to engulf infecting organism.

Phagocytosis: Selective process.

Foreign substance recognize by:

1.Rough surface .

2.No protective protein coat: which prevents phagocytosis

3.Marked by certain substance: e.g Complement 3 or antibodies making them ready for killing a process known as **opsonization**

process by which a pathogen is marked for ingestion. After Opsonization, phagocytes are attracted to the pathogen (phathogen is ready to be eaten now by WBCs)

Neutrophils encircled the bacteria with pseudopodia and engulf it inside into a vacuole (phagosome), takes 3-20 bacteria.

HOW the WBCs can recognize the bacteria and kill it without killing other normal body cells?

Because bacteria have special type of proteins that found on it surface such as (C3B) which is responsible for the attraction of WBCs to the bacteria , where as the normal body cells do not have these proteins, so they are not attacked by WBCs.

Microbial killing

•Digestion of organism **inside** the phagosom.

•Fusion of intracellular lysosomes with phagosome vacuole

•Lysosomes discharge its proteolytic enzymes such as myeloperoxidase, catalase into the vacuole, killing and digesting the engulfed bacteria.

And/ or **(**outside**)**

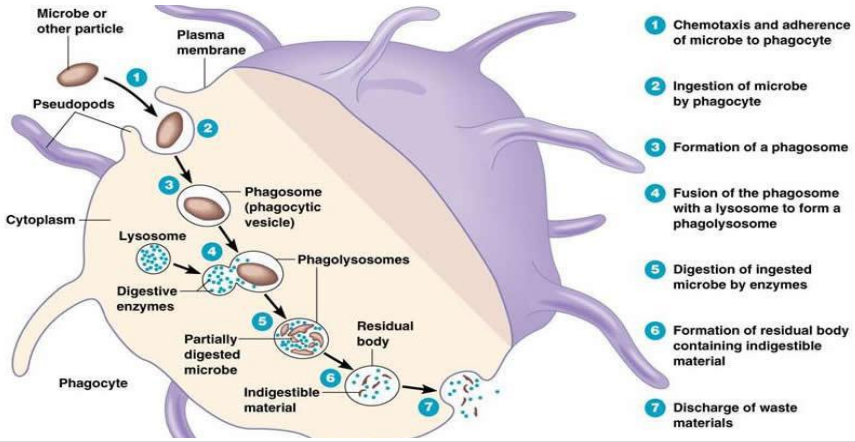
•Release of bactericidal such as superoxide, hydrogen peroxide to kill the bacteria

(**فيه منه نوعين** : نوع يتم داخل الخلية بعد ما تمم عملية Phagocytosis وتحصل في Phagocytic cells

ونوع آخر خارج الخلية عن طريق إفراز الأنزيمات القاتلة مثل الـ Eosinophil)

Neutrophils attach to bacteria & encircled it with pseudopodia and take it into a vacuole (phagosome).

- One Neutrophil can engulf 3 to 20 bacteria
- One Macrophage can engulf up to 100 bacteria



Lecture 4

White Blood Cells (WBCs) 2

EOSINOPHILLS

Formed in: Bone Marrow

Maturation : Stem cells →Myeloblast→Promyelocytes→
Eosinophil myelocytes→
Eosinophil metamyelocytes →
polymorphnuclear eosinophil (Mature Eosinophil released to blood).

Eosinophil Function

•Phagocytosis : is same as neutrophil, **but less efficient.**

Chemotaxis : attracted By **eosinophil chemotactic factor.**

•High eosinophil count:

–**Parasitic** (hook worm, ascaris, bilharzia)

–**Allergic** (asthma, **(** rhinitis=حساسية في الأنف**)**, drug reaction)

•Eosinophil attach themselves to parasites and releases substances (hydrolytic anzymes, superoxide) to kill it.

Formation and Maturation of Basophils

Formed in Bone Marrow

Maturation :Stem cells→ Myeloblast→ Promyelocytes→
Basophil myelocytes→
Polymorphnuclear Basophil (Mature Basophils released to blood)

Basophils

Similar to mast cells both secrets:

•Heparin to prevent clotting,

•Histamine, bradykinin & serotinin contribute to inflammation response

•The release of those substances cause local and vascular reactions characteristic of allergic manifestation

(إفراز هذه المواد يؤدي إلى أعراض حساسية موضعية مثلا : احمرار ، انتفاخ وغيرها من أعراض الحساسية)

Monocytes and Macrophages

Formed in : Bone Marrow

Maturation: Stem cell → monoblast → promonocyte→ mature monocytes released into blood.

Stay for :10-20 hours in circulation .Then leave blood to tissues transforming into larger cells macrophage .**Macrophage** life span is longer up to few months.

Function of Monocytes and Macrophages

Monocyte &macrophage come from the same cell , if it is in blood circulation It's called monocyte , but if it migrates to the tissue It's called macrophage

•Macrophages are **a powerful** phagocytic cells;

first line of defense

–Ingest up to 100 bacteria,

–Ingest larger particles as old RBC

–Get rid of waste and **survive**

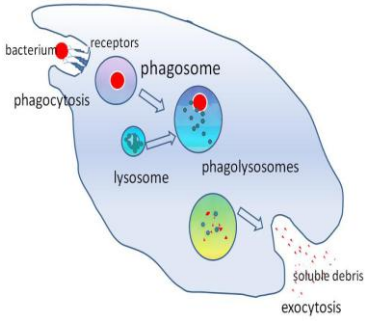
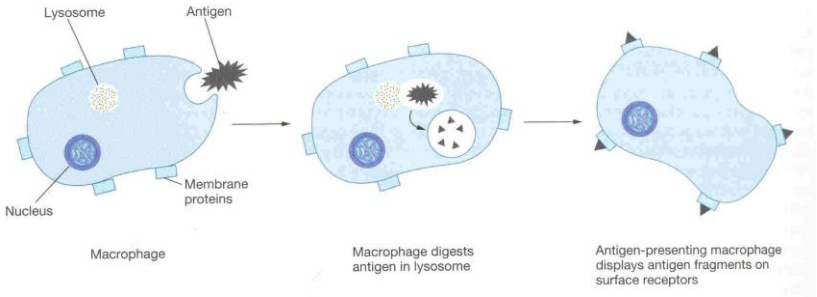
(المايكروفيج تتميز بأنها خلايا قوية وتستطيع أبتلاع عدد كبير من البكتيريا وتظل حية لفترة معينة بعد الإبتلاع أما النيوتروفيل مثلا فإنها تموت بعد ابتلاع عدد قليل من البيكتريا)

•Functions: anti-inflammatory

when it is get activated after transforming to macrophage

–**Directly:** phygocytosis of bacteria, dead cells

–**Indirectly:** cooperating with lymphocytes by recognizing foreign body (take in foreign body process it and present it to lymphocytes)

Direct anti Inflammatory	Indirect anti Inflammatory
	
phygocytosis of bacteria, dead cells تبتلع المايكروفيج البكتيريا أو الخلايا الميتة وتتخلص منها **مباشرة**	cooperating with lymphocytes by recognizing foreign body (take in foreign body process it and present it to lymphocytes) تقوم بالمايكروفيج بابتلاعة وأخذ أجزاء منه ووضعها على السطح لكي يتم العرف عليه وإنتاج أجسام مضادة من قبل الخلايا اللمفاوية .

Reticuloendothelial system

is system of cells in human body that have ability to phagocyte foreign substances

Consist of:

- –Monocytes
- –Macrophage
- –Endothelial cells (bone marrow, spleen, lymph node)

Located in all tissues especially; skin (histocytes), liver (kupffer), spleen, bone marrow,lymph nodes, lung

When the macrophage is found in the liver, it is called **kupffer.**

Functions of Reticuloendothelial system

1.Phagocytosis: Bacterial, dead cells, foreign particles

2.Breakdown of Hb

3.Immune function: processing antigen and antibodies production (indirect)

4.Storage of iron

LYMPHOCYTES

Lymphocytes Formation and Maturation:

Lymphopoiesis: is production of lymphocyte

Formed in: bone marrow, thymus, lymphoid tissues

Maturation : Stem cell (thymus, lymphoid tissue & bone marrow) →lymphoblast→ intermediate pyronophilic blast cell → lymphocytes

Life Span Of Lymphocytes range from weeks to months **according to its type**.

LYMPHOCYTES :

- **Function:** Immunity
- **Types:**
  1. Thymus dependent (T-lymphocytes)
  2. Thymus independent (B-lymphocytes)

T-Lymphocytes (Thymus dependent)

- **Formed in:** bone marrow or lymphoid tissue migrate to thymus for maturation
- **Life spans:** 100-130 days.
- Circulate between blood, tissues, lymph.

- **Types of T-lymphocytes :**
  - –T-helper
  - –T-cytotoxic
  - –Natural killer

Graft rejection : is an immune response by the body to destroy foreign cells in transplanted tissue. These rejections occur because the transplanted tissue or organ has antigens on its cells that do not match the person's own cell antigens.

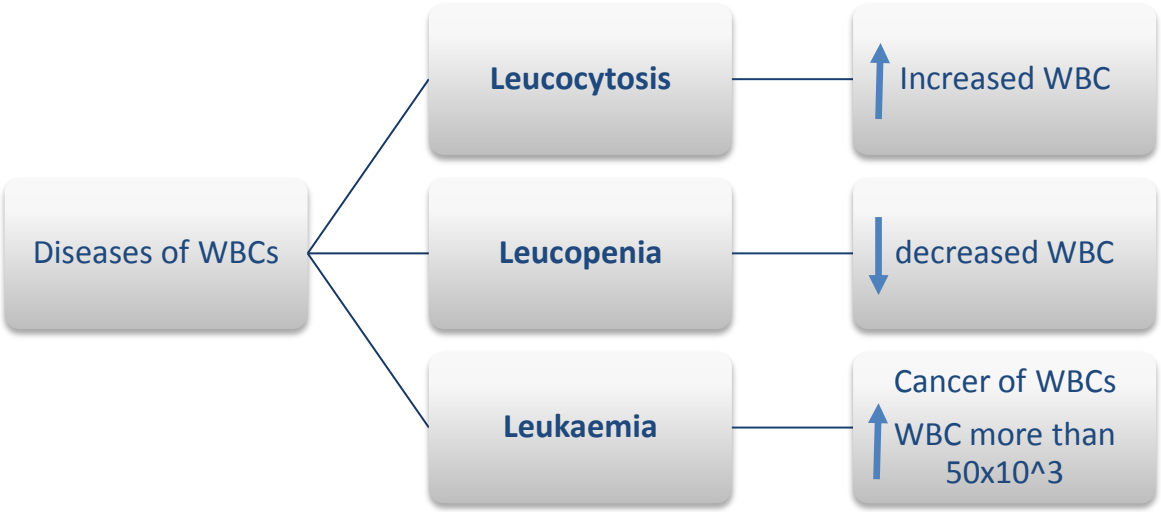
- **Functions :**

–Cellular immunity (**graft rejection** delyed hypersensitivity)

–Role in antibody secretion.

B- Lymphocytes (thymus-independents)

- **First discovered:** in Bird Bursa
- **Formed in**: Bone marrow, germinal layer of lymph node, red pulp of spleen
- **Life span** 2-7 days
- **Stimulated by:** antigen transforming it into large plasma cell (produce antibody)
- **Function:** Humoral immunity.



Leucocytosis

Increased WBC

•Physiological

–Diurnal↓morning ↑evening

During the day, the number of WBCs can modify, with more white blood cells in the evening, and less in the morning, **without any apparent reasons(سببه غير معروف)**

–After physical exercise

–Stress or Adrenaline injection

•Disease

–Bacterial infection (tonsillitis, appendicitis)

–Worm infection

Leucopenia →

Lueco = White
Penia = deficiency (نقص)

↓ WBC : caused by:

–Malnutrition

-Typhoid fever

–Depressed bone marrow

(نخاع العظم مسؤوول عن إنتاج خلايا الدم ومنها البيضاء وعند تعرضة لأمراض يقل عدد الخلايا التي ينتجها)

–Deficient Vit B12 or folic acid

Leukaemia

It is uncontrolled division of white blood cells in bone marrow (سرطان الدم)

Cancer of white cells due to chromosomal abnormality caused by chemicals, radiation, and viruses .

•WBC more than 50x10^3

Types of leukaemia

–Myeloblast leukaemia→myeloid cells → (is a type of leukemia affecting **myeloid cell**)

–Lymphoblast leukaemia → lymphocytic cells→ (is a type of leukemia affecting **Lymphocytic cell**)

•Acute (حاد)or chronic (مزمن)onset

•Accompanied with anaemia, bleeding

Lecture 5

Blood Groups and Transfusion

Let's Start with this Question For A better Understanding of Blood Group

How Blood groups are classified?

and Why are they classified into these groups?

A Blood group is a classification of blood based on the **presence or absence of inherited antigenic substances (Antigens)** (الأنتيجينات الموروثة)on the surface of red blood cells (RBCs). These antigens (usually **glycoproteins**)

Depending on that :

if RBC carries one protein **(A)** ⟶ we call it group **A**

if RBC carries one protein **(B)** ⟶ we call it group **B**

if RBC carries two protein **(A)** and **(B)** ⟶ we call it group **AB**

if RBC carries **No** protein ⟶ we call it group **O**

Also , you must know that every red blood cell may have or may not have a protein that we call it **(D)**

If this protein is **present** , we call it positive. **(Rh+)**

If This protein in **absent** , we call it negative.**(Rh-)**

BLOOD GROUPS

•The chief blood groups are:

1. **A-B-O**
2. **Rh (Rhesus)**

•Blood groups are **antigen (glycoprotein)** on the surface of RBC.

•The ABO system: Depends on whether the RBC contain one, both or neither of the two blood antigens A & B.

Group	Agglutinogen (Antigen)	Agglutinin (Antibody)	%
A	A	Anti-B	41%
B	B	Anti-A	9%
AB	A & B	No antibodies	3%
O	-	Anti-A & anti-B	47%

Notice that:

Agglutinogen=Antigen

But

Agglutination= interaction between Atigen and Antibody.

•**The Four main ABO groups:** A, B, AB, O

Agglutinins A, B antibodies

•Anti-A & Anti-B are **naturally occurring antibodies**.

•Not present at birth, appear 2-8 weeks after delivery may be due to antigens in food .

Genetic determination of the agglutinogens

•Two genes are inherited from each parent
•Blood group genotype:
A = AA, AO
B = BB, BO
O = OO
AB = AB
•Use of genotype of child in paternal dispute(. يستخدم النمط الجيني لدم الطفل لحل خلافات الأبوة)
•Frequency of ABO has ethenic variation.(اختلاف مجموعات الدم يتأثر باختلاف الأعراق)

Transfusion reaction

•If a person with blood group A transfused with blood of group B
•The anti-B in plasma of recipient blood group A will agglutinate the transfused cell (B)
•The clumped cells plug small blood vessels
•Sometimes causes immediate **hemolysis**
•Transfusion reaction

hemolysis : **hemo**=blood , **Lysis**=breaking
is the rupturing of RBCs as a result of Transfusion Of wrong blood type.

Blood group typing

RBC	Anti A	Anti-B
O	-	-
A	+	-
B	-	+
AB	+	+

+ there is agglutination
- No agglutination

•Before transfusion blood from donor and recipient should be typed to now its group
•A drop of blood is mixed with ant-A and ant-B & Rh then inspected for agglutination
•**Cross matching**, donor cells + recipients serum .

Cross-matching It is Blood test that is performed before blood transfusion, to make sure that donor's blood is compatible with the blood of the recipient,

Rh Blood types

•Presence of the Rhesus antigen (D) on the surface of RBC.
•**Rhesus antigens are: C, D,E, c, d, & e commonest D**
•Presence of antigen D (Rh+ve); absence of D (Rh–ve)
•Rh+ve are 85% in European, 100% in Africa

E , e , C , c , d
they are not clinically important in transfusion . Only D is Clinically most important in transfusion .

Rh Immune response

•When a Rh-ve person is transfused by Rh+ve blood he will develop Anti-D agglutinin in circulation (not naturally present).

•Anti D antibodies can be acquired by:
–Transfusion of Rh-ve individual with Rh+ve blood
–Rh-ve mothers having a Rh+ve baby due to blood mixing at delivery time.

(Erythroblastosis Fetalis)
Hemolytic disease of the newborn

- Rh-ve mother pregnant with her first Rh+ve baby, the mother will develop Anti-D at the time of delivary.**(because of blood mixing).** (First child escape)

- Second Rh+ve child, already formed anti D (IgG) cross the placenta and destroy baby's RBC leading to haemolytic disease of new born (haemolytic anaemia, erythroblastosis foetalis,)

- If the mother is transfused with Rh+ve blood before, first child will be affected. **(because the mother is having anti-D already)**
- This reaction could be prevented by giving the mother an **injection of Anti D** at delivery of first baby. **Why? (To destroy the Antigen D of the baby that pass to her ,To prevent her from making her own Anti-D)**
- Replace baby blood with Rh-ve several times.

For A better Understanding, It is important to know that:

- The mother's blood and the baby's blood do Not mix during pregnancy.
- But at delivery in the case of rupture of the placenta. Some of the baby's blood can mix with mother's blood
- This mixing will cause the mother to produce Anti-D
- First baby is Not affected because he left his mother's body,
- The second baby will be in danger if he Rh+ve because Anti-D have been preduced.
- If the mother have produced Anti-D already before her First pregnancy (for example if she has transfused with Rh+ve Blood) each baby with RH-ve will be affected even the first baby .

Suppose that the mother is Rh-ve and she gets pregnant with Rh+ve baby for the second time. Her system has produced Anti-D because of her First pregnancy with Rh+ve baby.

If she didn't take any medical help to fix this, What would happen to her second baby?

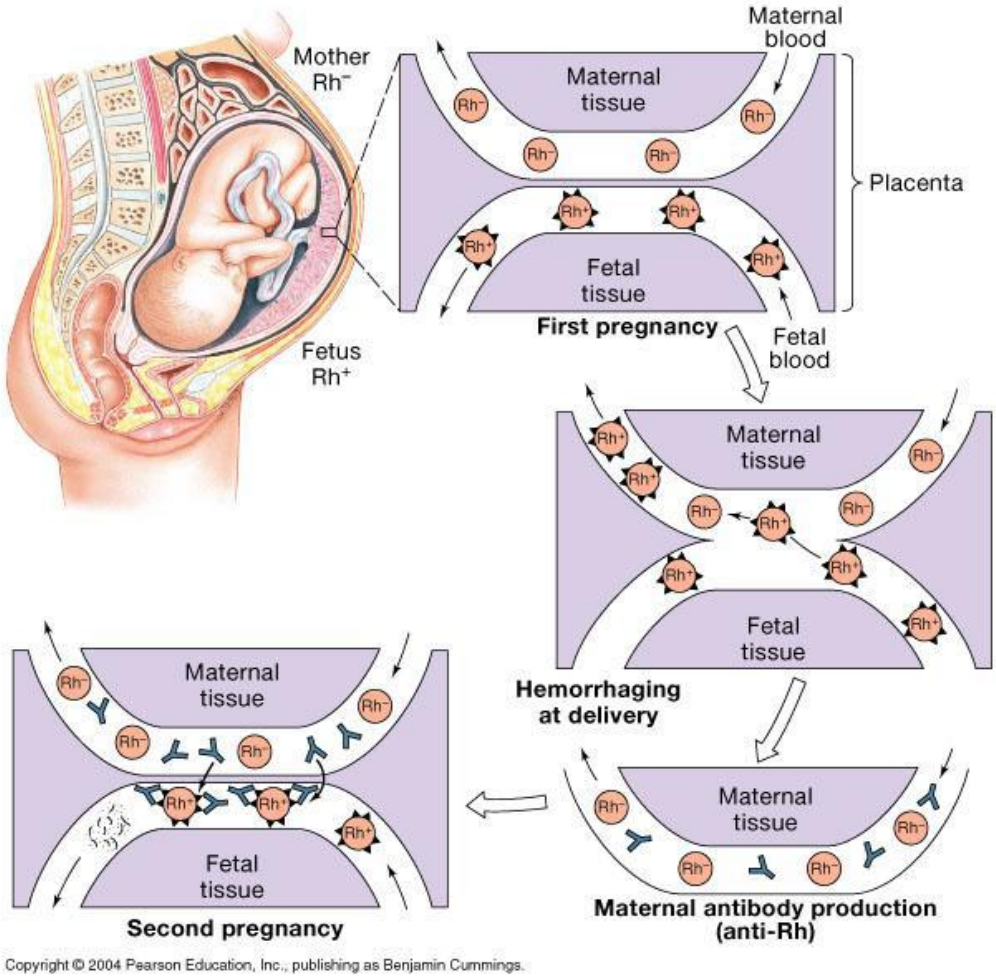
The Antibodies that was formed from her first pregnancy will pass through placenta and enter baby's blood , then it will destroy his RBCs because it consider it as foreign thing. Which will cause one of these diseases :

- **Death of the fetus**. →If the Amount of Anti-D produced is too much
- **Severe anemia**→ If the Amount is a lot but not that much.
- **Just anemia**→ If there is a little amount.

Wait , I have a Question !

You have said that the mother Blood and the baby's blood don't mix during pregnancy, then how can the Anti-D pass through to the baby's blood if there is no blood mixing?

You are right ! there is no blood mixing during pregnancy, **But** there is some fluids (not blood) that pass to the baby for **nutrition** which contain Anti-D .



Complication of blood transfusion

1.Immune reaction:

Incompatible blood transfusion leading to immediate or delayed reaction, fever, haemolysis(انحلال الدم), allergic reaction

2.Transmission of diseases; malaria, syphilis, viral hepatitis & Aids

3.Iron overload due to multi-transfusion in case of sickle cell anemia and thalassemia .

Lecture 6

Haemostasis and Blood Coagulation

Platelets & Megakaryocyte (Thrombocytes)

Megakaryocyte is a bone marrow cell responsible for the production of blood platelets(تتكسر وتعطي الصفائح الدموية)

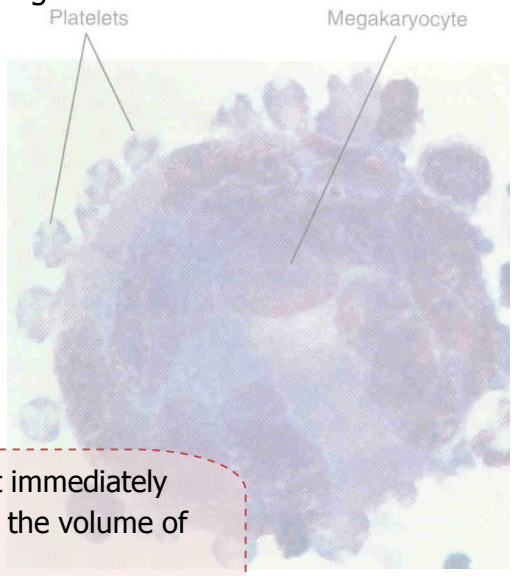
•Platelets:

–are round disc formed in bone marrow
–Stem cells → Promegakaryocyte → megakaryocyte → breaking pieces of cytoplasm (platelets)
–Platelet count = 150x103-300x103/ml,
–life span 8-12 days
–Active cells contain contractile protein,
–Contain high calcium storage & rich in ATP
–Coated by a **glycoprotein layer** (**why?**) to prevent its sticking to normal endothelial cells.

Contractile Protein:is protein that participate in contractile processes (عمليات التقلص)

•Platelets Functions:

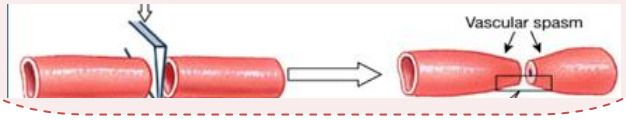
–Adhere to injured site of blood vessel to stop bleeding
–Secretes substances which are important for clot formation.



Haemostasis

Mechanisms that prevent blood loss
1.Vasoconstriction
2.Platelet plug
3.Blood clot formation

Blood vessel once it injured, it immediately contracts,(**why?**) to decrease the volume of blood losing.



Vasoconstriction

Immediately After injury a localize constriction of blood vessels occurs due to:

1.Hurmoral factors: local release of thromboxane A2 by platelets, systemic release of adrenaline

2.Nervous factors

3.Myogenic contraction

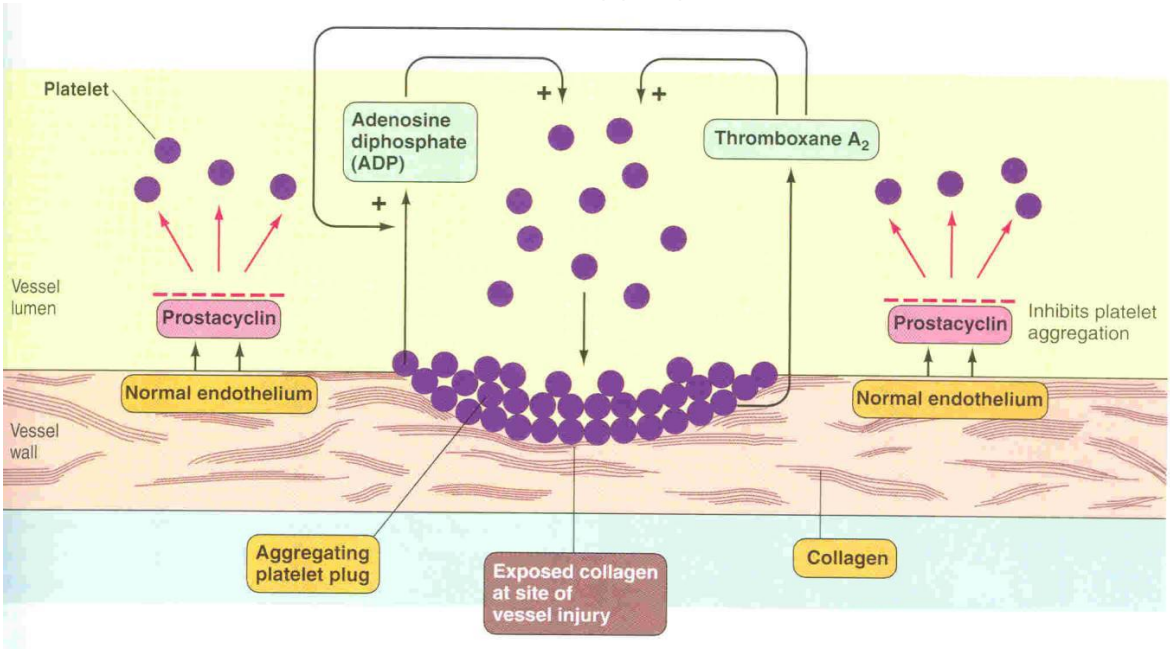
Myogenic Contraction of the blood vessel = contraction done by the myocyte cell of blood cell itself instead of an outside stimulus such as nerve innervation. (حركة انقباضية تقوم بها الخلية نفسها بدون تحفيز من أي مؤثر خارجي-مؤثر خارجي مثل الإشارات العصبية من الأعصاب مثلا-)

Platelet Plug

•Platelets in contact with exposed collagen from injured endothelial, platelets swells and contract to release several substances such as 5HT, ADP, thromboxane A2
•The released substances increases the stickiness of platelets leading to platelets aggregation and plugging of the cut vessel
•These substances are also **vasoconstrictor**

vasoconstrictor is any substance that causes the layer of smooth muscle in the blood vessels to contract,

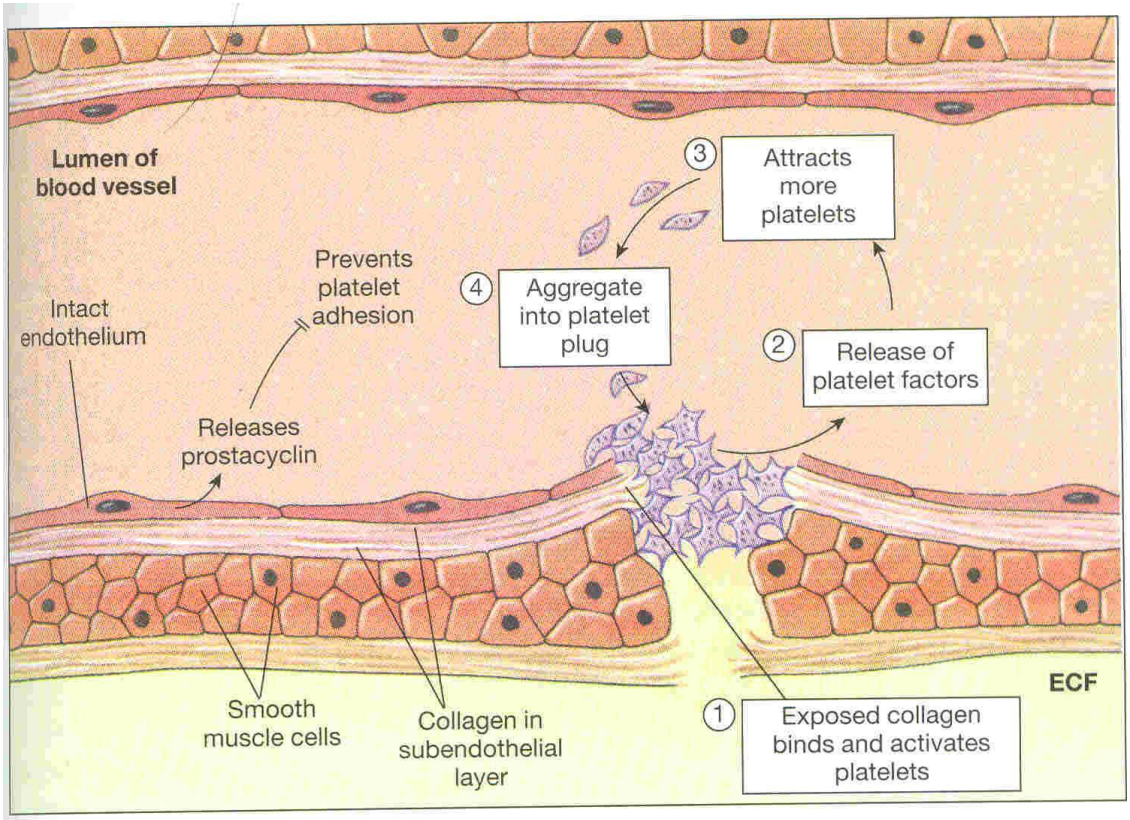
Platelets aggregation



Activated platelet

Secrets:

1. **5HT** → vasoconstriction
2. **ADP** → aggregator
3. **Platlet phospholipid** (PF3) needed for clot formation
4. **Thromboxane A2** (TXA2) is a prostaglandin formed from arachidonic acid causes vasoconstriction and aggregator. Inhibited by **aspirin .**



Blood coagulation (clot formation)

•A series of biochemical reaction leads to the formation of blood clot within few second after injury.

•This reaction leads to the activation of thrombin enzyme from inactive form prothrombin

•Thrombin will change fibrinogen (plasma protein) to fibrin (insoluble protein)

•Prothrombin (inactive thrombin) is activated by a long intrinsic or short extrinsic pathways

•Activation cascade reaction involve 12 clotting factors, circulating in inactive precursor forms

Clotting Factors Names	Factors
Fibrinogen	I =1
Prothrombin	II =2
Thromboplastin	III =3
Calcium	IV =4
Labile factor	V =5
Stable factor	VII =7
Antihemophilic factor	VIII =8
Antihemophilic factor B	IX =9
Stuart-Power factor	X =10
Plasma thromboplastin antecedent (PTA)	XI =11
Hagman factor	XII =12
Fibrin stablizing factors	XIII =13

Blood clot

Intrinsic pathway

•The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass.

•Activate factor (XII**a**) will activate XI

•XI**a** will activate IX

a= activated

•IX**a** + VIII + platelet phospholipid + Ca activate X

•Following this step the pathway is common for both

Extrinsic pathway

•Triggered by material released from damaged tissues (tissue thrombopl

• tissue thromboplastin + VII + Ca → activate X

Common pathway

•Xa + V +PF3 + Ca (prothrombin activator) it is a proteolytic enzyme activate prothrombin ⋅ thrombin

•Thrombin act on fibrinogen → insoluble thread like fibrin

•Factor XIII + Ca → strong fibrin (strong clot)

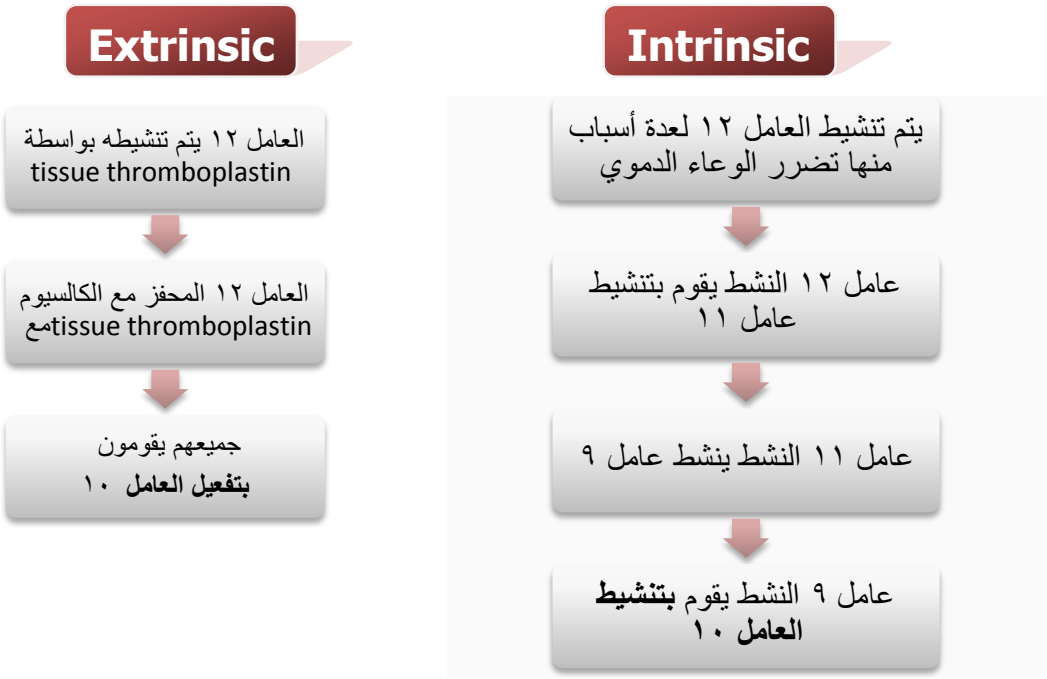
المسارات هذه مشروحة بالأسفل ، الأفضل يتم الإطلاع علي الشرح أولا قبل قراءة هذه المعلومات

شرح مسارات تخثر الدم :

- الجلطة حتى تتكون لا بد أن البروثرومبين(برو=غير نشط) يتحول لثرومبين (نشط) (لماذا ؟) لأن الثرومبين يحول الفبرينوجين (أيضا جين=غير نشط) إلى فيبرين ، والفيبرين وظيفته تكوين خيوط الفيبرين التي تدعم الصفائح الدموية وتقويها لمنع النزيف.
- وحتى تتهم هالعملية وتتكون الجلطة لابد من تحفيز العامل **12**.
- وتحفيز العامل **12** له طريقتين :
  - أما من خلال عامل خارجي وهو tissue thromboplastin ونسمي هذه الطريقة أو المسار مسار خارجي لأن يتطلب وجود عامل من خارج الدم .**Extrinsic Pathway**
  - أو من خلال عامل داخلي موجود في الدم ونسمي هذه الطريقة أو هذا المسار مسار داخلي . **Intrinsic Pathway**

بعد ذلك : كل مسار له خطواته المميزة له ،ولكن وفي النهاية نلاحظ أن المسارين يتشابهان في الخطوات الأخيرة، ولأنها مشتركة فنسميه المسار المشترك Common Pathway وهو يعتبر جزء من المسارين السابقين وليس مسار مستقل .

الأن نشرح عمل كل مسار مثل ما قلنا البداية تكون من تحفيز العامل **12** :



الآن جميعهم يهدفون لتحفيز **10** ، **لماذا ؟**

لأن عامل **10** المحفز يدخل في تركيب الأنزيم الذي سيقوم بتحويل البروثرومبين إلى ثرومبين وبالتالي الفيبرنوجين إلى فيبرين (تكون الجلطة).

وهذا الأنزيم يسمىprothrombin activator وهو يتكون من عامل **10** النشط+ الكالسيوم +عامل **5** (غير نشط) + **PF3**

وخطوة تكوين هذا الأنزيم هي خطوة مشتركة فيCommon Pathway

Intrinsic Pathway	Exterinsic pathway
Contact activation ↓ XII →XIIa ↓ XI →XIa ↓ IX → IXa ↓VIII, Ca,P X → Xa	Tissue factor ↓ ↓ VII,Ca ↓ ↓ Xa ← X
Xa ↓ ↓ V, Ca, P Prothrombin (II) → Thrombin (IIa) ↓ Fibrinogen (I) → Fibrin (soluble) ↓ XIII, Ca insoluble fibrin	

Coagulation

•Both pathway are needed for normal haemostasis.
•Both pathways are activated when blood come in contact with tissues outside blood vessel
•Thrombin is important factor in both
•Extrinsic pathway is faster (15 sec) while intrinsic may take up to 1-6 min

Thrombin

•Thrombin change fibrinogen (inactive) to fibrin (active) .
•Thrombin is essential in platelet morphological changes to form primary plug
•Thrombin stimulate platelet to release ADP & thromboxaneA2 **both** stimulate further platelets aggregation
•Activate factor V

Fibrinolysis is the breakdown of fibrin to remove blood clots while **Coagulation** is the forming of blood clut . These two process work to maintain proper blood flow.

Fibrinolysis

•Formed blood clot can either become **fibrous** or **dissolve**
•Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therfore prevent intravascular blocking

•There is balance between clotting and fibrinolysis
–Excess clotting→blocking of Blood Vessels
–Excess fibrinolysis→ tendency for bleeding

Plasmin

•Plasmin is present in the blood in inactive form plasminogen
•Plasmin is activated by tissue plasminogen activators (t-PA) in blood.
•Plasmin digest intra & extra vascular deposit of Fibrin → fibrin degradation products (FDP)
•Unwanted effect of plasmin is the digestion of clotting factors

Plasmin:

•Plasmin is controlled by:

–Tissue Plasminogen Activator Inhibitor (TPAI)

–Antiplasmin from the liver

•Uses:

–Tissue Plasminogen Activator (TPA) used to activate plasminogen to dissolve coronary clots (يستخدم لتذويب جلطات الشريان التاجي)

Coagulation balance