# Anatomy



Sheet: #2

- Lecture title: blood cells and hemopoiesis
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# Leukocytes

### Leukocytes

- Originate in the bone marrow and released continuously into the blood
- Travel in bloodstream but function mainly **OUTSIDE blood vessels (in loose CT)**
- Leukocytes form a mobile army that helps protect the body from damage by bacteria, viruses, parasites, toxins and tumor cells
- <u>5 types organized into 2 groups depending</u> on nuclear shape and cytoplasmic granules

### -Granulocytes (single, multi-lobed nucleus)

- I. Neutrophils
- II. Eosinophils
- III. Basophils

### -Agranulocytes (mononuclear leukocyte)

- I. Lymphocytes
- II. Monocytes



- Red bone marrow  $\rightarrow$  main function is production of blood .
- Yellow bone marrow is filled with adipose tissue and it doesn't produce blood.
- Function of leukocytes is outside the circulation, they function in the connective tissue

- تصنيف خلايا الدم البيضاء حسب ال granules فكرو انه ال monocytes +lymphocytes فيهم، بس طلع فيهم

- Both types have granules but the granulocytes have special(specific ) granules.
- The agranulocytes have only lysosomes(primary granules)
- Multi-lobed nucleus (but single) is associated  $\rightarrow$  granulocytes
- Mononuclear is associated  $\rightarrow$  agranulocytes

Leukocytes, or WBCs, are nucleated and subdivided into granulocytes and agranulocytes, depending on the presence or absence of specific granules in their cytoplasm



**<u>Lymphocyte</u>** play a key role in all immune responses, in contrast to the other leukocytes their activity is always directed against specific foreign agents

All the leukocytes perform their function in the tissues and merely use the blood as a vehicle for transit between sites of formation, storage, activity

Neutrophils and monocytes are highly phagocytic and engulf micoorganisms, cell debris in a non-specific manner.



### Granulocytes

- •<u>Cytoplasmic granules</u> (containing enzymes or chemicals)  $\rightarrow$  makes cytoplasm look grainy
- Single multi-lobed nucleus (segmented)
- •All are phagocytic; they engulf and consume foreign cells and material
- 3 main types:



The granules are hardly seen? Because it doesn't have specific affinity for dyes It needs high magnification to be seen.



neutrophil

Small granules, pale pink/salmon pink





eosinophil

### Large granules, Red





basophil

Large granules, blue

### Agranulocyte

Lysosomes All the same name for the same gran

### Neutrophil

- The most common leukocyte in blood
- constitute <u>40-75%</u> of circulating leukocytes
- Characterised by the shape of the nucleus which contains small lobed connected by thin filaments
- When mature there are usually 5 lobes connected by fine strands of nuclear material. In less mature neutrophils the nucleus is less lobulated
- 2-5 lobes in nucleus connected by "threads" of nuclear material (polymorphs) —— Same name for neutrophiles
- Light pink cytoplasm
- Called neutrophils because cytoplasm takes up red (acidic) and blue (basic) stains equally





The specific granules color is light pink The number of lobes of the neutrophiles differs from to other **according to AGING →** اول ما تنصنع (2 lobes) → at site of infection (5 lobes)

in clinical application

### nfection (5 lobes) site of infection اول خلايا توصل ال

- Specialized for responding to: lacksquare
- bacterial invasions 1.
- Acute infections 2.
- acute pyrogenic infections Pyrogenic = infections with (fever حسب ), (pus ), (pus ), (pus 3.
- Neutrophils are short-lived cells with a half-life of 6-8 hours in blood and a life span of ullet1-4 days in connective tissues before dying by apoptosis.

Half life in tissues  $\rightarrow$  Days(dies by apoptosis), Half life in circulation  $\rightarrow$  hours



Neutrophils are the first WBCs that leave the blood in large numbers to reach the site of inflammation

**Cells of acute infection** 

1-<u>The most abundant</u> 2-The most motile 3-Neutrophil chemotactic factors (chemotaxins) are the first released





	_How to know that this blood sample is from fe
t note	
	-Ans: Drumstick like appearance (structure), wl
	inactive X of the female (xx) sex chromosomes
	-Can there be a 2 Barr bodies?
	Ans: Yes, in super female case (xxx), because it

In females, the inactive X chromosome (Barr body) may appear as a drumstick-like appendage on one of the lobes of the nucleus (about 3% of neutrophils in peripheral blood)

's must be only one active (X)

### hich is due to Barr body (the



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### **Granules in neutrophils**



The ability of neutrophils to survive in an anaerobic environment is highly advantageous, because they can kill bacteria and help clean up debris in poorly oxygenated regions, for example, damaged or necrotic tissue lacking normal microvasculature

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### **Neutrophilia:**

- increase in the number of neutrophils in the circulation
- this does not necessarily imply an increase in neutrophil production  $\bullet$

Intense muscular activity and administration of epinephrine can produce APPARENT neutroplelia they causes neutrophils in the marginating compartment to move into the circulating compartment

**Glucocorticoids**:

increase the mitotic activity of neutrophil precursors in the marrow  $\rightarrow$  increase blood count of neutrophils

Neutrophilia that occurs during bacterial infections  $\rightarrow$  increase production of neutrophils for short duration of these cells in bone marrow

Neutropenia  $\rightarrow$  Decrease in number of neutrophiles.

<u>Neutrophilia</u> DOESN'T always indicate a pathologic condition. Because the neutrophiles are found at different pools outside the circulation in exercise and stress conditions, the neutrophiles travel to the circulation. and after the (stress, exercise) stops the neutrophiles return to the pools.



**Eosinophils** 

 Accounts for 1-6% of leukocytes in circulating blood

زي النظارة Like glasses

- Usually have <u>bi-lobed nuclei</u> connected by a short "thread" of nuclear material
- Large cytoplasmic granules, which stain red with the <u>acidic eosin dye</u>
- <u>Functions:</u>
- Eosinophils are <u>phagocytic cells</u> but less bacteriocidal than neutrophils
- Eosinophils have a particular phagocytic affinity for antigen-antibody complex
- Help <u>in ending allergic reactions</u> and in fighting <u>parasitic</u> infections
- All eosinophils have receptors for IgE (important in the destruction of <u>parasites</u>, this is <u>not</u> present on neutrophils







**Eosinophilia**: increase number of circulating eosinophils

are found in

- many types of *parasitic disease* (defense against parasites is one of their principle functions)
- in some *allergic disease* such as hay fever and asthma 2

يعنى اول ما يبلش تفاعل الحساسية يتم افرازه لانهاء تفاعل الحساسية وما يطول.



The eosinophils granules are **lysosomes** and contain the usual lysosomal enzymes, they show a higher content of peroxidase than do the azurophilic granules of neutrophils and lack lysozyme and phagocytin

طيب إذا عندها granules اكثر من ال neutrophiles تعتبر اقل bactericidal -اقل عدد (نسبتها 6%) -جوا ال neutrophiles انزيمات بتخليها اقوى في قتل البكتيريا. Lysozyme, Phagocytin



### **Crystalloid granule**

### **Basophils**

• Rarest leukocyte – might not see these under the microscopes (less than 1%)

Very large specific granules, blue in color, which covers the nucleus

- Usually have bi-lobed, <u>S-shaped</u> nuclei obscured by the large basophilic granules [ زي النظارة ] Eosinophils ( shaped)
- Has large granules that stain dark purple/ blue in basic dyes (basophil= basic loving)
- Granules contain histamine, heparin and
  eosinophilic chemotactic factor that mediate inflammation in allergic reactions and parasitic

infections

ECF-A

Initiate allergic reaction





Both basophils and mast cells have surface receptors for **immunoglobulin E (IgE)**, and secrete their granular components in response to certain antigens and allergens.



**Basophils account for up to 15% of infiltrating** cells in allergic dermatitis and skin allograft rejection

كيف تأكدو انه اله دور في تفاعل الحساسية؟ ?allergic reaction -in skin dermatitis  $\rightarrow$  basophiles increase from 1% to 15%



### To initiate immune reaction



### systemic response.

Basophils and mast cells may rapidly degranulate, pro vasodilation in many organs, a sudden drop in blood pres other effects comprising a *potentially lethal condition* Anaphylaxis or anaphylactic shock.

to allergen antigen

n, such a	S	
adverse	sys	اذا اثر على اكثر من tem in the body
ducing		Anaplylactic shock
ssure, an	d	
called		
		18

### Agranulocytes

• Single non-lobulated nucleus

• Granules in cytoplasm are too small to see (nonspecific granules, azurophilic granules, primary granules, lysosomes)

•2 types based on structure (not cell lineage):

-Lymphocytes -Monocytes



### Monocytes

- <u>Largest</u> leukocytes
- Constitute 2-10 % of leukocyte in peripheral blood
  شکل السیتولازم زي الزجاج المغشی نتيجة؟تواجد ال Iysosomes بکثرة
  Bluish cytoplasm (frosted glass appearance)& a large C-

shaped nucleus

• Highly motile and phagocytic

•Travel through bloodstream to reach connective tissues, where they transform into **macrophages (large phagocytic** 

cells) [

بس توصل النسيج بصير اسمها macrophage

### Chronic infections

Are precursor cells of macrophages, osteoclasts, microglia, and other cells of the **mononuclear phagocyte system in connective tissue** 

All monocyte-derived cells are antigen-presenting cells







### **MONONUCLEAR PHAGOCYTIC SYSTEM**

(all characterized by phagocytic activity)



first defensive system.

الوضع الطبيعي تطلع ال monocytes من الدم وتروح ل site of infection وبصير اسمها macrophage
 بس في اماكن محدةة بتكون دايما ال macrophageمتواجدة فيها resident ؛ليش؟لأنه هذه الأماكن بتكون من أكثر الأماكن
 المعرضة لل infections are very common in these places) infections)

### Lymphocytes

- Smallest leukocytes (slightly larger than erythrocytes) erythrocytes القريبا نفس حجم ال
- •The second most common leukocyte in circulating blood and make up 20-25% of differential white cell count
- Round nucleus occupies most of cell volume
- Cytoplasm is light clear blue

of cytoplasm (حافة او اطار) of cytoplasm

• Increased numbers are commonly seen in viral infections



### Lymphopoiesis: the process by which lymphocytes are formed In bone marrow\*



بس اذا راحت عالدم بتصير طوالي active

The amount of cytoplasm depends **upon state of activity** of the lymphocyte, in circulating blood there is:

When in it is inactive, slightly larger than erythrocyte (and small rim of cytoplasm with large nucleus)

- Predominance of small inactive lymphocytes (6-9  $\mu$ m in diameter) 1
- Large lymphocytes (9-15  $\mu$  m) make up about 3% of lymphocytes in peripheral blood

When it becomes active the cytoplasm becomes less dark-blue, and the amount of cytoplasm increased

represent activated lymphocytes en route to the tissues where they will become antibody-secreting plasma cells, they also include natural killer cells

In the large lymphocyte  $\rightarrow$  the cytoplasm is readily visible but in the small lymphocyte the cytoplasm is almost too sparse to be seen (contain few mitochondria, rudimentary golgi apparatus, minimal endoplasmic reticulum but large number of ribosomes $\rightarrow$ account for basophilia (blue cytoplasm)



Darkly stained cell

### ما تشوفها هيك طوالي: Active lymphocyte of natural killer cells

•Lymphocytes vary in life span according to their specific function, some live for a few days and some live for many years

Cell mediated immunity

•T cells

-Has different types, some directly kill foreign or infected cells; others activate

phagocytes to destroy microbes

Lymphocytes  $\rightarrow$  highly specific, adaptive immunity response for specif antigens

Humoral immunity

- B cells
- -Differentiate into plasma cells

-Secrete <u>antibodies</u> that bind to <u>specific antigens</u> and mark them for destruction by

phagocytic cells

Long term immunity

Do B lymphocytes go to site of infection? No, but send the antibodies to site of infection (naming reason (humoral immunity الاستجابة السائلة))

Unlike the macrophages and neutrophiles immunity which it's immunity name(innate immunity) (which do the phagocytosis to all antigen

Neutrophils and monocytes are highly phagocytic and engulf microorganisms and cell debris in a **NON-SPECIFIC manner (Innate immunity)** 

While the activity of lymphocytes is always directed against SPECIFIC foreign agents (Adaptive immunity)





Size relation to erythrocytes

The small lymphocyte has scanty cytoplasm (contain few organelles but large number of ribosomes) Account for basophilic

**Innate immunity:** We are born with innate immunity. It is non-specific, which means that the innate cells are not able to distinguish one type of pathogen from another.

**Adaptive (acquired) immunity:** is the body's ability to recognize and respond to specific foreign substances (antigens: microbes, parts of microbes, or non-microbial substances, such as pollen)

Cells of innate immunity: Neutrophils, Basophils, Eosinophils, Mast cells, Monocytes (macrophages and dentritic cells), natural killer cells

Cells of adaptive immunity: B and T lymphocytes



Kill virus infected, transplanted and neoplastic cells (innate immunity)

Any cell that doesn't present MHC-1 antigen, will recognize it as abnormal cell and destroy it \*\*\*I think MHC-1 is the self antigin مولد ضد ذاتى الى ما بخلى هاي الخلايا تهاجم خلايا الجسم

After the infection ends, those cells come and inactive T and B. If there is a problem in these cells there will be an immune disease.

Suppressor T cells switch off the immune response when the stimulus is removed Damage to suppressor cells can result in **autoimmune disease** 

Memory cells allow a more rapid response if the antigen appears again later which allows a very rapid response upon subsequent exposure to the same antigen. Basis of immunity/vaccination

Natural killer cells and T cells play a major role in graft rejection

Туре	Nucleus	Specific Granules <sup>a</sup>	Differential Count <sup>b</sup> (%)	Life Span	<b>Major Functions</b>
Granulocytes					
Neutrophils	3-5 lobes	Faint/light pink	50-70	1-4 d	Kill and phagocytose bacteria
Eosinophils	Bilobed	Red/dark pink	1-4	1-2 wk	Kill helminthic and other parasites; modulate local inflammation
Basophils	Bilobed or S-shaped	Dark blue/purple	0.5-1	Several months	Modulate inflammation, release histamine during allergy
Agranulocytes					
Lymphocytes	Rather spherical	(none)	20-40	Hours to many years	Effector and regulatory cells for adaptive immunity
Monocytes	Indented or C-shaped	(none)	2-8	Hours to years	Precursors of macrophages and other mononuclear phagocytic cells

# Never Let Monkeys Eat Bananas



Most common to least

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### **Thrombocytes (Platelets)**

- Small non-nucleated cytoplasmic fragments
- Formed by fragmentation of the cytoplasm of <u>megakaryocytes</u> in the bone marrow
- •Number: 200,000-400,000/mm3
- •Shape: biconvex discs
- •Cytoplasm: purple, granular
- •Diameter: 2-4 um
- •Lifespan about 10 days





In bone marrow  $\rightarrow$  sinusoidal capillaries  $\rightarrow$  there is processes of megakaryocyte which have cytoplasmic processes  $\rightarrow$  The blood flow causes the fragmentation of these cytoplasmic processes  $\rightarrow$  and this fragments are the platelets

-

•Control the bleeding by plugging the defects in blood vessels and activating blood clotting cascades

In stained blood smears, platelets often appear in

clumps

Platelete has 2 zones

1 <u>Outer pale basophilic (clear) perpheriral zone:</u>

Hyalomere (smooth, glassy like, likely hyaline)

2 Central dark granular zone: granulomere



often appear in clumps



# In stained blood smears, platelets

### **Hyalomere:**

### contains cytoskeleton and membranous channels

**Cytoskeletal elements** 

- Microtubule
- Actin filaments

Membrane channels

- Open canalicular system
- Dense tubular system

**Contains Ca+2 (calcium for blood clotting)** 

### Maintain shape and help contractions of platelets and squeezing

### **Granulomere:**

contains granules and organelles

Alpha granules: clotting factors, growth factors

<u>Dense (delta) granules: serotonin</u> (absorbed from plasma), ATP, ADP ما بتصنعها بتجيبها من برا

Invaginations from plasma membrane to granulomere

To increase surface area of exchange and make it easier

Lambda granules: lysosomes (aid in clot resorption)





Surface connected

Glycogen

Dense

Dense tubular

granule

α-Granules

microtubules

Their main function is to continually monitor the vascular system and detect any damage to the endothelial lining of the vessels.

If the endothelial lining breaks, the platelets adhere to the damaged site and initiate a highly complex chemical process that produces a blood clot  $\rightarrow$  Thus preventing blood loss



## اعطت هذا الشكل لانه سطحها سكرى ف لزقو ببعض

# Hemopoiesis

Dr. Silvia Boyajian



Formation of blood cells in bone marrow  $\rightarrow$  medullary hemopoiesis outside bone marrow  $\rightarrow$  extra medullary hemopoiesis.



### **Pluripotent hemopoietic stem cells**

It is believed that **ALL** blood cells arise from a single type of stem cell in the bone marrow called a pluripotent stem cell This cell can produce all blood cell types  $\boxed{}$ 



Early in their development, lymphoid cells migrate from the bone marrow to thymus or to the lymph nodes, spleen, and other lymphoid structures where they proliferate and differentiate



### all develop in bone marrow



### **Sheet Note 4**

When the stem cells duplicates it gives rise to another stem cell, to save and keep a reserve of it, the progenitor cell does the same. But the precursor cell only give rise to mature cell it never gives rise to precursor cell, because it's not a stem or progenitor cell. رح يتم ايضاحه باخر سلايدين\*\*

-

### **Progenitor and precursor cells:**

the pluripotent stem cells give rise to daughter cells with *restricted* potentials called:

Progenitor cells or colony-forming units  $\rightarrow$  CFUs (since they give rise to colonies of ONLY ONE cell type when cultured or injected into spleen)

### **Progenitor cells are 4 types:**

- A- Erythroid lineage of CFU-erythrocytes (CFU-E)
- B- Thrombocytic lineage of CFU- megakaryocytes (CFU-Meg)
- C- Granulocyte-monocyte lineage of CFU- granulocyte- monocytes (CFU-GM)
- D-Lymphoid lineage of CFU-lymphocytes of all types (CFU-L)

All four progenitor/ CFUs produce  $\rightarrow$  precursor cells or blasts

Where morphologic characteristics begin to differentiate suggesting the mature cell types they will become

Stem cells and Progenitor cells cannot be morphologically distinguished and resemble large lymphocyte



Rate of cell division : slow in stem cells rapid in progenitor and precursor cells

Progenitor cells: can divide and produce both progenitor cells and precursor cells

Precursor cells: produce only mature blood cells

Stem Cells	Progenitor Cells	Precursor Cells (Blasts)	
Potentiality			
		Mitotic activity	
		Typical n	m
Self-renewing capacity			
	Influence of g	rowth factors	

1-Potentiality is the potential to give rise to more than one type of cell

2-mitioc activity is the highest at precursor cells and mature cells don't divide

3-you can't differnitae between the blood cells until they reach the mature cell phase (even at precursor cell(blast phase) the cells almost the same E.g. T,B and natural killer cells are derived from lymphocytes.

انه ما بتكتسب الوظيفة الا تقريبا لما توصل لاخر مرحلة :differentiated functional activity القدرة انها تنقسم وتعطي خلية مماثلة الها 9-self renewing

Mature Cells

orphologic characteristics

Differentiated functional activity Stem cells are capable of asymmetric division and self-renewal

### Stem cells can maintain the original population



### Erythroblast



Every time the stem cell multiplies, it	All erythroblasts
will give two cells, one differentiate	differentiate into
into mature RBCs and the other cell	(erythrocytes) a
add to the original population	left in the end
تجربة بتوضلحك لو حطينا growth factors مع نوعين من الخلايا	
CTENAcell since the emotion and renew itealf by	ervthro
giving rise to another stem cell	to eryth

### Precursor cells produce only mature blood cells



### s multiply and o mature RBCs and no erythroblasts are

### erythroBLAST it will only give rise to erythrocytes it will not give erythonlast Or renew itself