Foundation Block

Physiology team 441

9,10- (4- White Blood Cells [WBC])

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MED441
KING SAUD UNIVERSITY

physiology
441

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Editing File

Color index

- Main Text
- Important
- Dr's notes
- Female
- Male
- Extra

Objectives

Part 1:

- Describe different Types of WBC
- Recognize the general functions of WBC
- Describe genesis and site of formation of WBC.
- Describe stages of neutrophil formation
- Describe the role of neutrophils in defending the body against infection
- Describe the process of phagocytosis

Part 2:

- Describe Eosinophils formation and functions.
- Describe Basophils formation and functions.
- Describe Monocytes and macrophage formation and functions.
- Describe Reticuloendothelial components and functions.
- Describe lymphocytes formation and maturation.
- Describe the functions of the different types of lymphocytes and Recognise leukocytosis and leukopenia

★ White blood cells

Formed in	Bone Marrow - Lymph tissues
Protect against infection by	Phagocytosis Secretion of antibodies
Range of WBC	Range of WBC in our body: 4000-1100/µl

★ Genesis of WBC

2 major lineages of WBC are formed:

Lymphocytic stem cells → lymphocytes
Myelocytic stem cells → granulocytes +monocytes

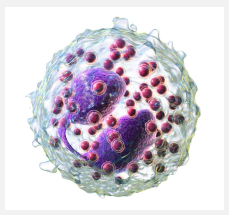
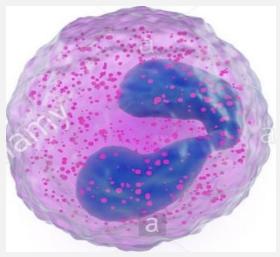
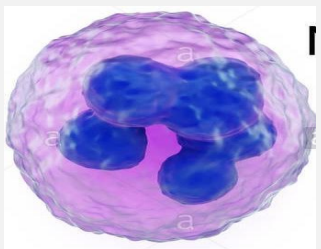
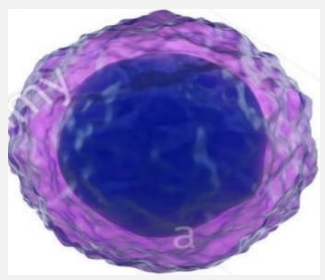
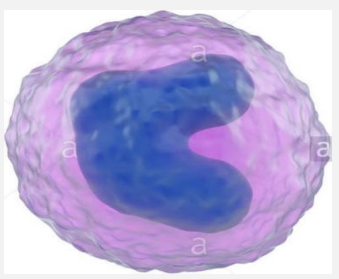
Name	Nucleus	Granules	No. & (%)	Life span	**Sites of formation**	Size
Neutrophil	Lobulated (2-5 lobes)	Purple cytoplasmic	3000-6000 (62%)	**Blood:** 4-8 hours **Tissue**: 4-5 days in tissues **Infection:** few hours. (die after ingesting bacteria)	Bone marrow	10-16µm
Eosinophil	Bilobed (2 lobes)	Coarse red	150-300 (2.3%)			12-18µm
Basophil	Rarely segmented	Large round bluish granules (hides the nucleus)	0-100 (0.4%)			10-14µm
Monocyte	Kidney shaped	Agranular	300-600 (5.3%)	Blood: 10-20 hours Tissue(macrophage): months		15-20µm
Lymphocyte	Large round	Agranular	1500-3000 (30%)	Blood(B lymphocyte): 2-7 days Tissue(T lymphocyte): 100-300 days	Bone marrow + thymus gland+lymph oid tissues	Large (9-15µm) Small (5-8µm)

★ Sites of WBC Formation & Life span of WBCs

	Granulocytes - neutrophil -basophil -eosinophil	**Monocytes** (the largest WBCs)	**Lymphocytes** - T lymphocyte - B lymphocyte - Natural killer cells (NKCs)
Site of formation	in bone marrow		-Bone marrow -Thymus -Lymphoid tissues
Life span of WBCs	-**In blood** ➜ 4-8 hours -**In tissues** ➜ 4-5 days where they ar needed. -During infection lifespan only few hours. because they die after ingesting bacteria.	- In blood➜ 10-20 hours. -Then they leave to tissues transform into macrophage, its life span goes up to months.	-Weeks to months according to its **type**

WBCs

- Granulocytes
  - Basophils
  - Eosinophils
  - Neutrophils
- Agranulocytes
  - Lymphocytes
  - Monocytes

★ Steps of phagocytosis

01 Chemotaxis

attraction of neutrophils to inflamed area due to chemotactic substance release, such as:

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

02 Margination

WBC stick and roll on the wall of capillaries.

03 Diapedesis

WBC squeezes through endothelial holes and leaves blood capillaries.

03 Amoeboid

WBC move by amoeboid motion toward inflammation

05 Phagocytosis

engulfing of foreign substances which are recognized by:

- Rough surface
- No protective protein coat
(protein coat prevents phagocytosis)
- Opsonization: marking by certain substance (e.g. complement proteins, antibodies).

★ Phagocytosis

Neutrophils → encircle bacteria with pseudopodia → engulf it inside vacuole (phagosome → takes 3-20 bacteria

★ After Phagocytosis:

1. Phagosome fusion with lysosome
2. Lysosome releases
   - proteolytic enzymes (e.g.myeloperoxidase, catalase) and/or
   - bactericidal (e.g. superoxide hydrogen peroxide)
3. These kill and digest the engulfed bacteria

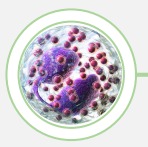
★ Types of immunity

01 Innate
- 2nd line of defense
- Present at birth
- Persists throughout life
- Quick
- Attacks all antigens equally

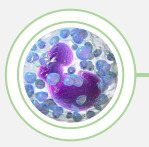
02 Adaptive
- 3rd line of defense
- Antigen specific
- Responds with proliferation of cells and generation of antibodies
- Slow (activated after 4 days)
- Immunologic memory

★ Granulocyte

Neutrophils



Eosinophils

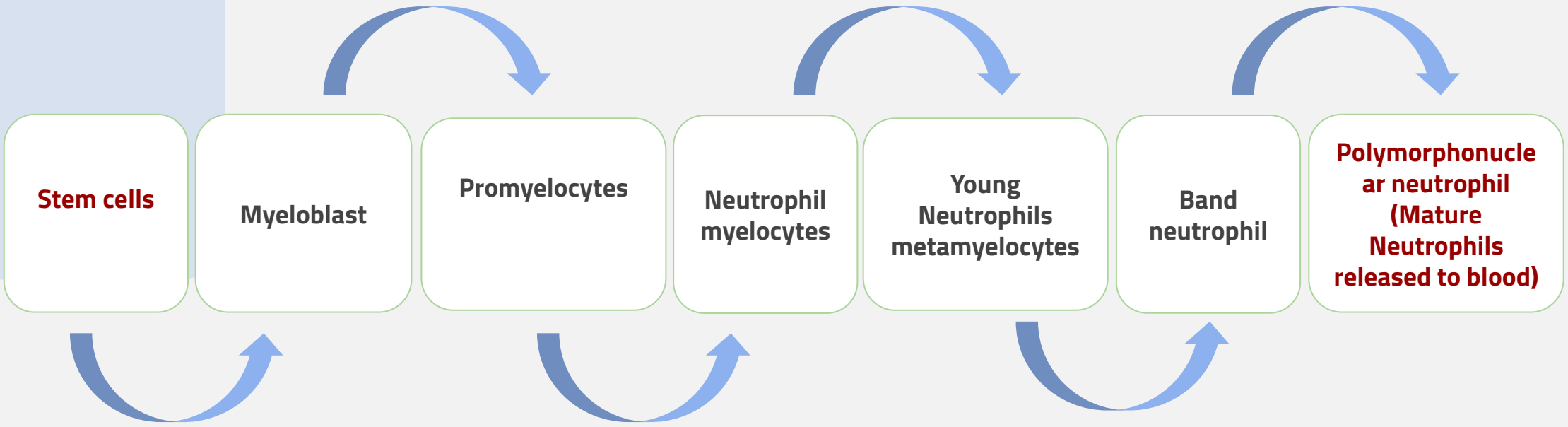


Basophils

1. They constitute 60-75% of WBCs
2. They have cytoplasmic granules
3. They contain small granules of both acidic and basic natures.
4. Very important at “clearing” bacterial infections
5. Polymorphonuclear
6. They are phagocytic cells (Phagocytosis); Microphages.
7. They constitute the first line of defence against bacterial infection

Dr's note:
المطلوب نعرف من وين تبدأ -النقطة الأولى و الناتج الاخير -النقطة .الاخيرة- فقط و الباقي غير مهم

★ Formation and Maturation of Neutrophils



★ Defensive Properties of Neutrophils

Chemotaxis	- The **attraction of the neutrophils to inflamed area** following chemotactic substance release from infected site - Many different **chemical substances in the tissues cause neutrophils and monocytes to move toward the source of the chemical.** This phenomenon is known as chemotaxis.. The chemotactic agents include a component of the complement system (C5a); leukotrienes; and polypeptides from lymphocytes, mast cells, and basophils.
Margination	- The **Neutrophils and monocytes aggregate** and stick along the walls of blood capillary.
Diapedesis	- **Neutrophils and monocytes** can **squeeze through the pores of the blood capillaries** by diapedesis. To enter the tissue spaces
Ameboid movement:	- Both **neutrophils and macrophages** can **move through the tissues** by ameboid motion.
Phagocytosis	- The most important function of the neutrophils and macrophages is phagocytosis, which means **cellular ingestion of the offending agent.**
Opsonization	- Some plasma factors act on the bacteria to make them "tasty" to the phagocytes (opsonization). The principal **opsonins coat the bacteria** for phagocytosis are immunoglobulins of a particular class **(IgG)** and complement proteins **(C3b & C4b)**.

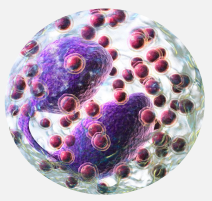
★ Types of CD (Cluster of differentiation)

	CD4 cells	**CD8 cells**
Number	Most numerous	Less numerous
Called	T helper cells (HIV hits this type of cells)	Cytotoxic cells
Function	1. Stimulate other cells in the immune system. 2. Major regulator of all immune functions	1. Directly attack cells. 2. Defense against malignant and virus infected cells. 3. Tissue transplant rejection.
Secretes	Interleukins, Interferon	Perforins

★ Formation and Maturation of Eosinophil

female slides only

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



- Has a nucleus
- with to lobes (bilobed)
- Red granules
- It accounts for 2-4% of white blood cells

★ Eosinophil Function

Phagocytosis

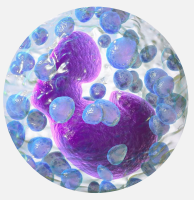
1. Parasitic **(hookworm, ascaris, bilharzia)**
2. Allergic **(asthma, rhinitis, drug reaction)**

Eosinophil attach themselves to parasites

Releases substances (hydrolytic enzymes, superoxide) to kill microbes/pathogens.

★ Formation and Maturation of Basophils

Stem cells → **Myeloblast** → **Promyelocytes** → **Basophil myelocytes** → **polymorphnuclear Basophil (Mature Basophil released to blood)**



- It accounts for 0-1 % of white blood cells
- Blue granules

★ Basophils

Similar to mast cells both secrete:

Heparin

to prevent clotting

Histamine,bradykinin&serotinin

for inflammation response

The release of those substances cause

Local and vascular reactions characteristic of allergic manifestation

★ Monocytes and macrophages

Monocyte is a young macrophage in the blood

Formed in Bone Marrow Stem

Stem cell → monoblast → promonocyte → mature

monocytes released into blood

Stay for 10-20 hours in circulation

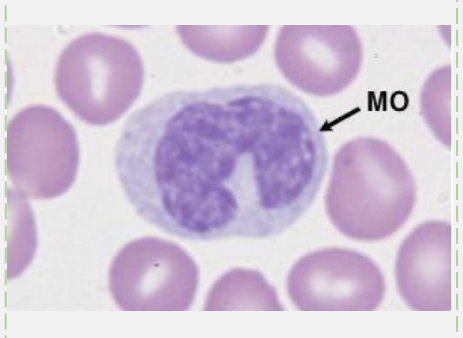
Then leave blood to tissues transforming into larger cells macrophage

Monocytes contain agranular cytoplasm but when they enter the tissues and converted into macrophages, they swell and their cytoplasm become filled by large number of lysosomes and then they are called macrophages.

Macrophage lifespan is longer upto few months

The monocytes are big phagocytes :

- 15-20 µm.
- active cells 60-80 um.
- They have longer lifespan than neutrophils.



It counts for 6-8% of white - blood cells

The largest type of WBCs

★ Functions of Monocytes and Macrophages

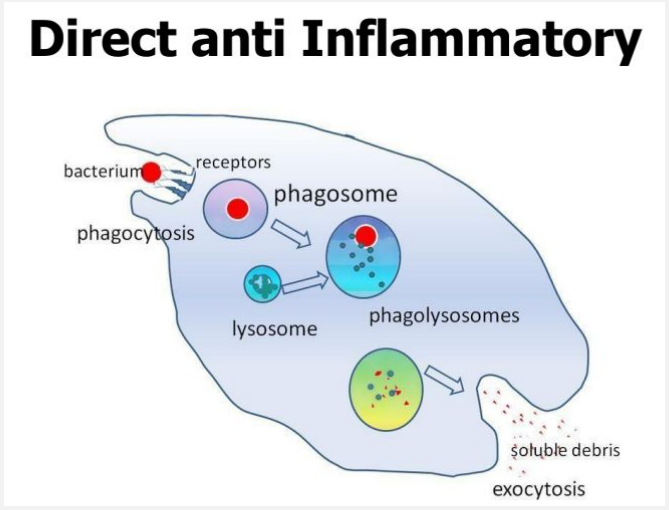
(In blood) (In tissues)

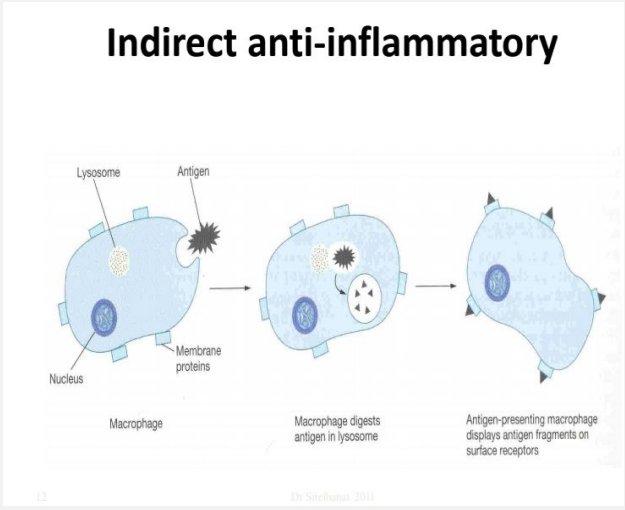
Macrophages are powerful phagocytic cells; first line defence

1. They ingest up to 100 bacteria
2. They ingest large particles as old RBCs
3. They get rid of waste and survive (scavengers)

Functions as an anti-inflammatory:

- **Directly: phagocytosis** of bacteria and dead cells.
- **Indirectly:** cooperating with **lymphocytes** by recognizing foreign body (take in foreign body process it and present it to lymphocytes)





★ Monocytes (macrophages)

Functions of monocytes/macrophages:
– Phagocytosis and killing of microorganisms. They are more Efficient than Neutrophils (100 bacteria vs 3-20 by Neutrophil, larger particles like old RBCs & malarial parasites).

❑ There are tissue-specific macrophages; fixed macrophages (monocyte-macrophage system; Reticuloendothelial system)

- Alveolar macrophage
- Peritoneal macrophage
- Kupffer cells in liver sinuses
- Osteoclasts in bone
- Microglial cells in brain
- Histiocytes in skin and subcutaneous tissue
- Mesangial cells in the kidneys
- Few specialized endothelial cells in the bone marrow, spleen And lymph nodes.

★ Macrophage and Neutrophil Responses During Inflammation

01

1st line of defense

Tissue macrophages, barriers and complement system (circulating molecules).

02

2nd line of defense

Neutrophil invasion of the inflamed area.

03

3rd line of defense

Monocyte-macrophage invasion of inflamed area.

04

4th line of defense

Increased production of granulocytes **and** monocytes by the bone marrow.

★ Reticuloendothelial system

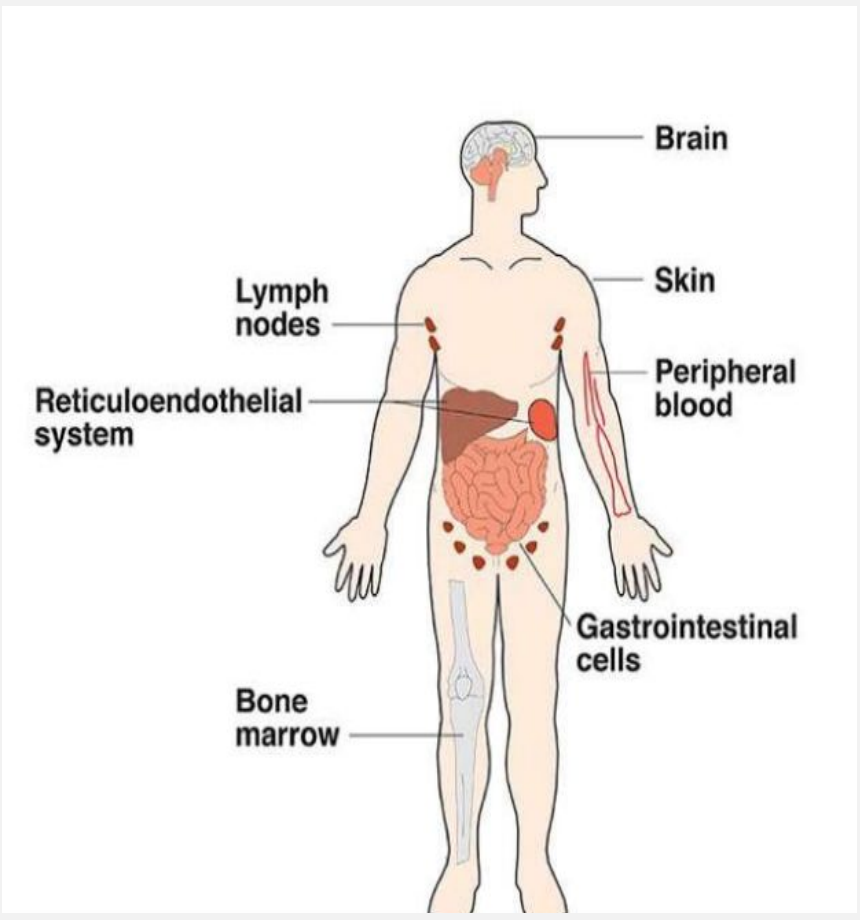
Phagocytic cells distributed all over the body.

They consist of:
-monocytes
-macrophages
-endothelial cells

Located in all tissues especially:
-skin (Histiocytes)
-liver (kupffer)
-spleen
-Bone marrow
-lymph nodes
-lung

Functions of Reticuloendothelial system:

1. Phagocytosis of bacteria, dead cells and foreign particles.
2. Breakdown of Hemoglobin
3. Immune function: Processing antigen and antibodies production (indirect)
4. **Storage** of iron



★ Lymphocytes

Site of formation	Formed in bone marrow, thymus, lymphoid tissues.
Maturation	Stem cell (thymus, lymphoid tissue & bone marrow) → lymphoblast → intermediate pyroninophilic blast cell → lymphocytes
Life span	Range from weeks to months **according to its type.**
Types	Types: 1.Thymus **dependent** (T-lymphocytes) 2.Thymus **independen**t (B-lymphocytes)
Function	**T-lymphocytes**: 1-cellular (cell-mediated) immunity (graft rejection,delayed hypersensitivity) 2-Antibody secretion . **B-lymphocytes:** 1-Humoral immunity 2-Antibodies secretion(plasma cell) **Natural killer cell NK**: Also called Non B Non T lymphocyte. Is a part of the non- specific immune system.

★ Lymphocytes-T&B cells

❑ Make up 20–40% of circulating leukocytes.

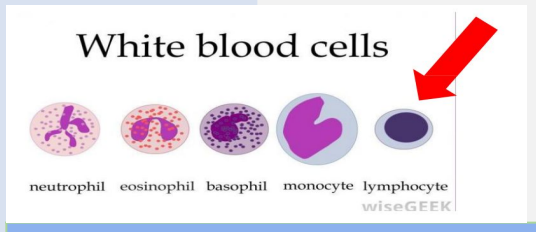
❑ Both types of lymphocytes are derived in the embryo from pluripotent hematopoietic stem cells that form common
lymphoid progenitor cells.

❑ A**ll of the lymphocytes** formed **end up in the lymphoid tissue**, but before doing so, they are further differentiated or “preprocessed”:

❑ The lymphoid progenitor cells that are destined to eventually form activated **T lymphocytes first migrate to and are preprocessed** in the **thymus gland**, and thus they are called **“T”** lymphocytes. They are responsible for cellular or **cell-mediated immunity**

❑ The **B lymphocytes** are preprocessed **in the liver during mid–fetal** life and in the **bone marrow in late fetal life and after birth**. They are changed to plasma cells and are responsible for **humoral immunity** or antibody-mediated immunity.

Only in male slides



	Humoral Cellular immune response	Immune response
Cells	B cells	T cells
Processing	Bone Marrow & liver	Thymus gland
Site of action	Blood	Tissues
Antigen	Bacteria	TB (tuberculosis), viruses & fungi Tumor Tissue rejection Delayed allergy
Types	Memory and Plasma	Memory, helper, cytotoxic

★ Lymphocytes

1

T-Lymphocytes (Thymus dependent)

Formed in: bone marrow, migrate to thymus for maturation.
Life spans 100-300 days
Circulate between blood, tissues, lymph.

Types of T-lymphocytes:

1. T-cytotoxic (Tc) or killer cell (Tk).
2. T-helper (Th)
3. Memory T cells subtypes.
4. Suppressor T cells subtypes.

Functions:
- Cellular immunity (graft rejection - delayed)
*مثل عند زراعة الأعضاء، يرفضه العضو لذلك تؤخذ أدوية خفض المناعه
- hypersensitivity Role in antibody secretion.

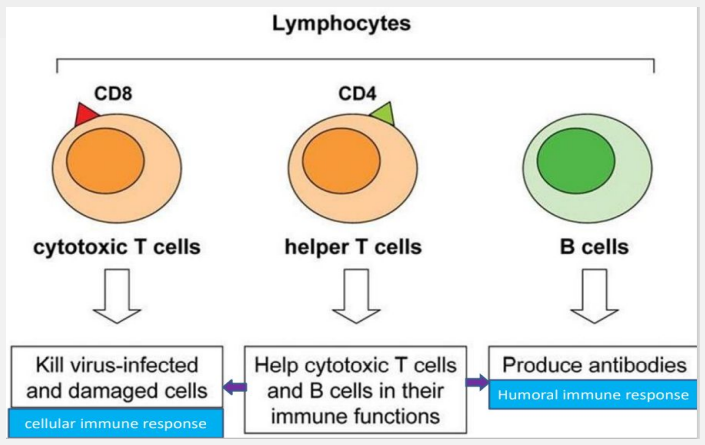
2

B- Lymphocytes (thymus independents)

Formed in: Bone marrow, germinal layer of lymph node, red pulp of spleen.
Life span 2-7 days.
Stimulated by antigen.
It transforms into large plasma cell (produce antibody).
Function:
- Humoral immunity.
- Role in antibody secretion.
Stimulated by antigen transforming.

Natural killer cell (NK cell) Also called Non-B Non-T lymphocyte. Is a part of the nonspecific immune system.

Functions of lymphocytes >>



★ Leukocytosis

Pathological Leukocytosis		
Condition	Definition	Causes
Neutrophilia	An increase in the number of neutrophils	❑ Infections: of all types as acute or chronic, bacterial, viral or fungal. ❑ Inflammation as rheumatic fever ❑ Tissue damage as trauma, burn ❑ Malignant tumors ❑ Smoking
Eosinophilia	An increase in the number of eosinophils	❑ Allergic conditions as asthma, hay fever, skin allergy ❑ Parasitic infection ❑ Leukemia
Basophilia	An increase in the number of basophils	❑ Allergic conditions as asthma, hay fever, skin allergy ❑ Leukemia
Monocytosis	An increase in the number of monocytes	❑ Chronic infection as in tuberculosis ❑ Leukemia
Lymphocytosis	An increase in the lymphocytes	❑ Chronic bacterial and viral infections ❑ Leukemia

- Increased WBC:
- **Physiological:**

–Diurnal decreased in morning increased in evening (Doctor's slides)

– After physical exercise

–Stress or Adrenaline injection

- **Diseases** :

-Bacterial infection (tonsillitis,Appendicitis)

-Worm infection.

★ Leukaemia

Leukemia is a malignant disease of bone marrow causing marked increase in WBCs may reach 500.000/µL.
-WBC more than 50.000
-Leukemia is associated with anemia and bleeding tendency (due to decrease in bone marrow area responsible for RBCs and platelet synthesis respectively).
-Cancer of white cells due to chromosomal abnormality caused by chemicals, radiation and viruses.

Types of leukaemia:
– Myeloblast leukaemia> myeloid cells
– Lymphoblast leukaemia> lymphocytic cells
1-Acute or chronic onset.
2-Accompanied with anaemia, bleeding.

★ Leukopenia

Leukopenia is Deficiency of the white blood cells.
-Leukopenia (leucopenia) means a decrease in the total leucocyte count below 4.000/mm3.
-In this condition the body is not protected against infections and death may occur.

It is caused by:
1-Bone marrow depression by radiation, drugs, and cancer chemotherapy.
2-Some bacterial infections as typhoid fever, brucellosis.
3-Some viral infectious as AIDS, influenza and hepatitis.
4.Malnutrition
5.B12 & folic acid decrease

Test yourself

★ MCQs

Q1: Which of the following is a Function Basophils			
A- secretes heparin	B-Break down Hb	C- storage of iron	D-Phagocytosis
Q2: Type of WBC released into blood			
A-Basophils	B-monocytes	C- eosinophil	D-lymphocytes
Q3: Humoral immunity is the function of:			
A-T-lymphocyte	B-B-lymphocyte	C- Basophil	D- eosinophil
Q4: Deficiency of white blood cells caused:			
A-Allergic condition	B-Leukemia	C-Truma	D-Leukopenia

1-A 2-B 3-B 4-D

MED441
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physiology 441

Foundation Block

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