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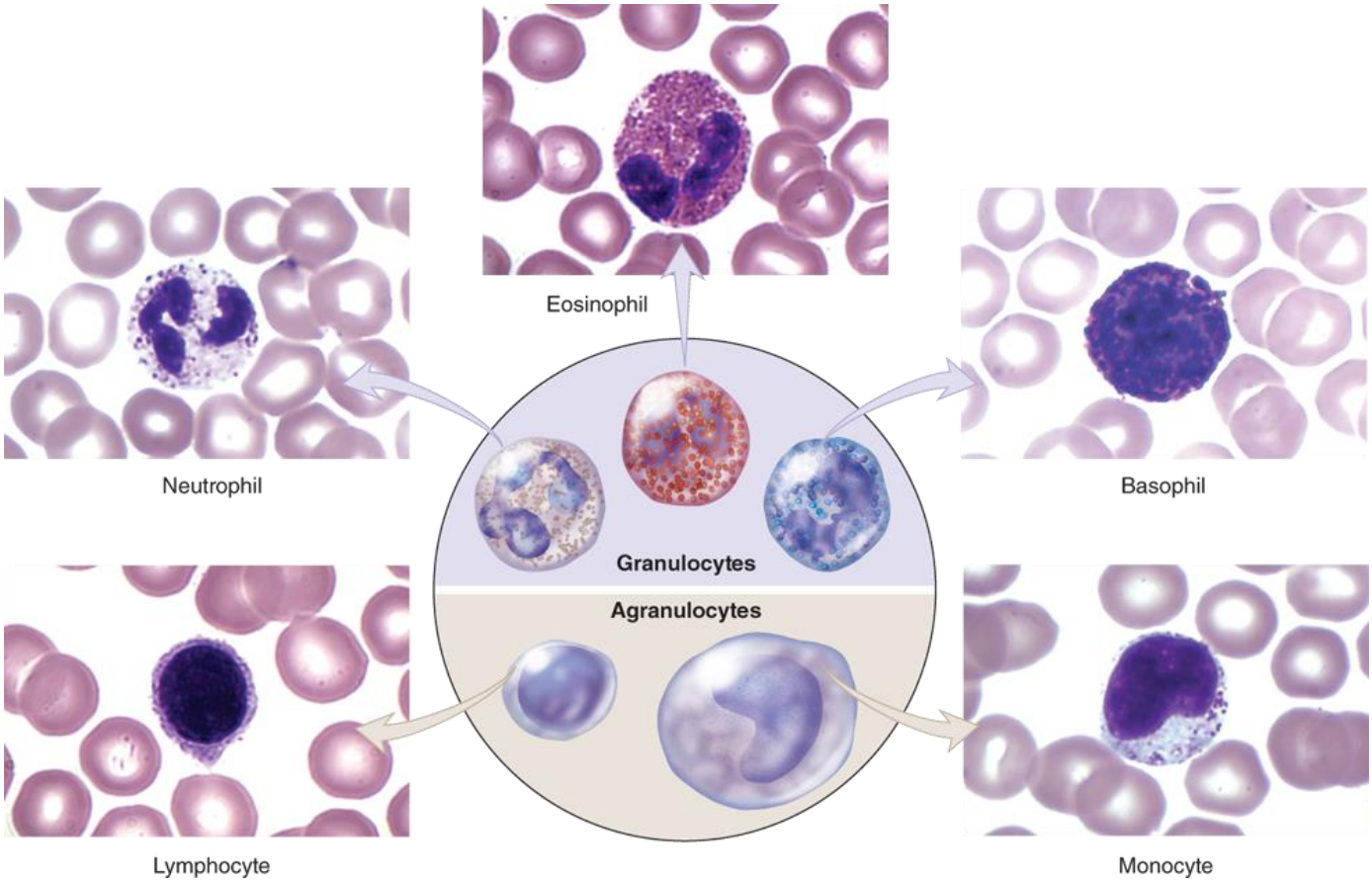

SUB-SYSTEM: PHYSIOLOGY

LECTURE: AGRANULOCYES – SHEET 4

DOCTOR: MOHAMMAD JAFAR

DATE: 5-3-2019

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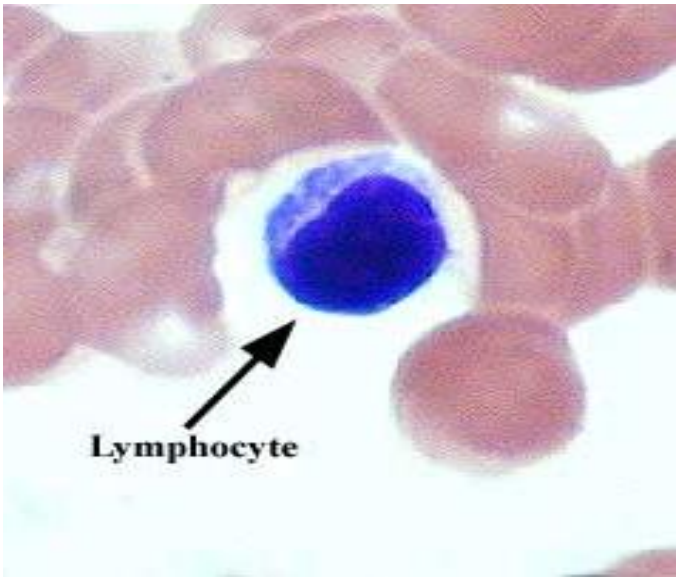
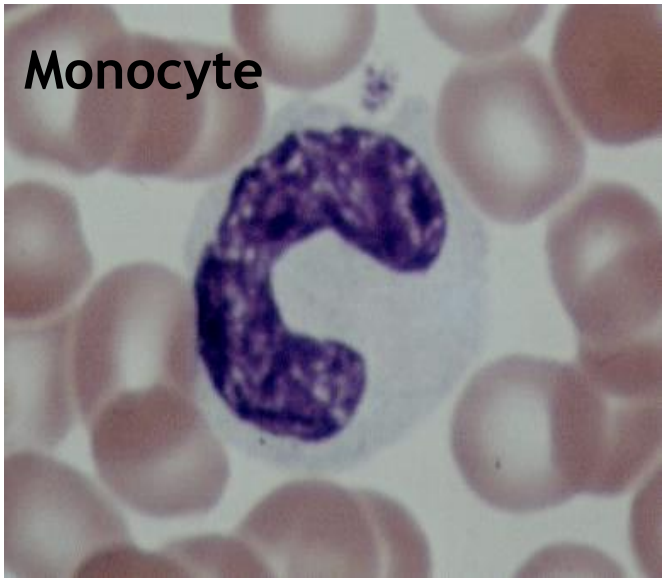
- In the previous lecture, we've talked about granulocytes, their types and functions
- In this lecture we will discuss Agranulocytes
- Agranulocytes are simply white blood cells that lack **visible granules**

Agranulocytes

- Lack visible cytoplasmic granules
- Include two types: lymphocytes and monocytes
- Lymphocytes are the main cells involved in immunity
- Immunity is defined as anybody's mechanism that protects it from any invasive foreign body:

1. Microorganisms, such as bacteria and viruses
2. Tissues, such as organs transplantation and blood transfusion



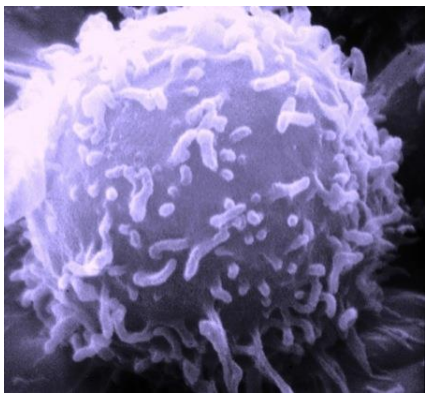


B lymphocytes

- Attack bacteria, viruses and toxins
- B lymphocytes originate and mature in bone marrow.
- NOTE: In birds, B cells mature in the bursa of Fabricius, a lymphoid organ. (The "B" from B cells comes from the name of this organ, where it was first discovered and not from bone marrow as commonly believed.
- Can be converted into :
  - Plasma cells: that is a type of immune cells that makes large amounts of a specific antibody. They develop in the bone marrow from B cells that have been activated. They are transported by plasma and lymphatic system, and they increase in number only in case of infections
  - Memory cells: Those keep a “record” of the pathogen’s antigens, so that when this pathogen attacks our body again, these cells remember the antigen and attack it rapidly to reduce the possibility of tissue damage by the pathogen “A very powerful mechanism that works like a computer.

T lymphocytes

- T cells originate in bone marrow and mature in the Thymus , in which the " T " referred to.
- T cells act directly against virus-infected cells and tumor cells

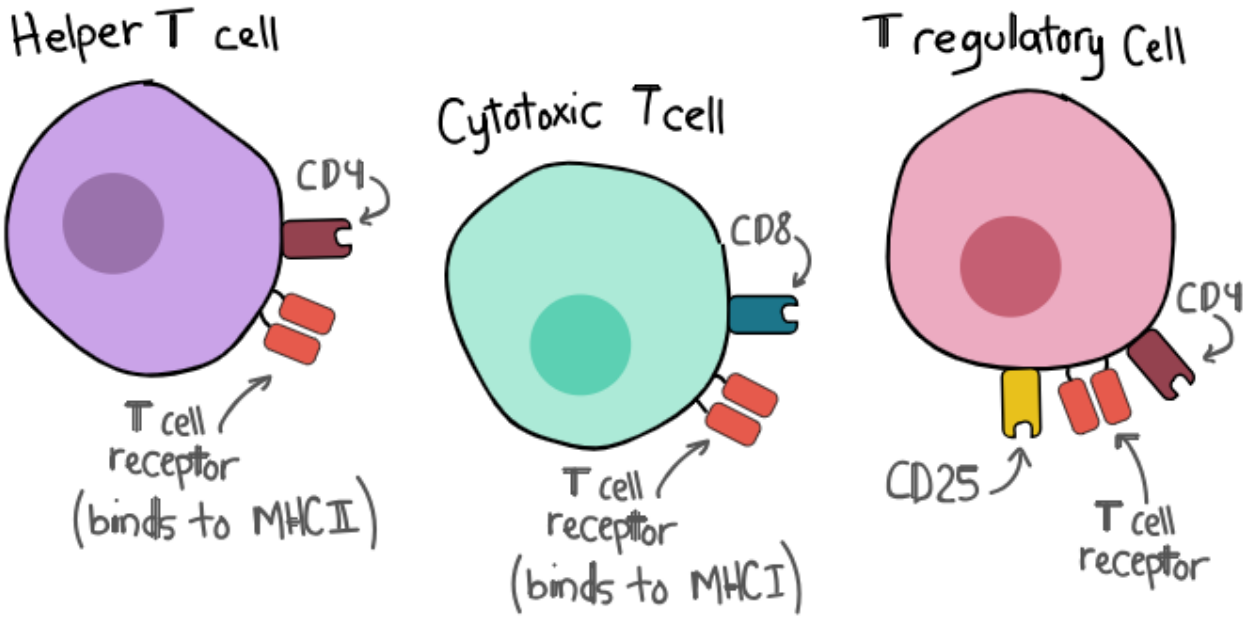


1. CD 4
   T helper cells
2. CD 8
   T cytotoxic cells
3. suppressor T cells

1. T Helper cells: the most numerous type of T cells. They help in the function of immune system , forming protein mediators called **lymphokinase** which cause:
   a. Stimulation of growth and proliferation of cytotoxic and suppressor T cells
   b. Stimulation of B cells growth and form plasma cells and antibodies.
   c. Activation of macrophage system.
   d. Feedback stimulatory effect on the T helper cells (positive feedback effect

- EXTRA NOTE: The doctor mentioned AIDS "Acquired immune deficiency syndrome" referring to the HIV that infects T-helper cells by attaching itself to them, fuses and takes control of its DNA. So it can replicate and release more HIV into the blood.

2. Cytotoxic cells : Killer cells, direct attack
3. Suppressor cells: Limiting the ability of immune system to attack a person's own body tissues (Immune tolerance)
   so without these cells, our defense mechanisms can attack the body's own cells, and 'Antigen-antibody' complexes can form, without the presence of any foreign invasive pathogen, and these diseases are called "autoimmune diseases"



Plasma cells

- A type of immune cell that makes large amounts of a specific antibody. They are developing in the bone marrow from B cells that have been activated. They are transported by plasma and lymphatic system

Mast cells

- Another type of cells that's important in immune reactions, is the 'Mast cells '
- Actually these cells aren't derived from T lymphocytes or B lymphocytes. Instead, they are a dependent class of cells that originate from the bone marrow .
- They contain granules, and are very similar to basophils
- Found widely in the body, particularly in connective tissues.
- They produce **histamine, Heparin, serotonin,** dopamine and also involved in the immunological, allergic and inflammatory conditions "but mostly they work in allergic reactions"

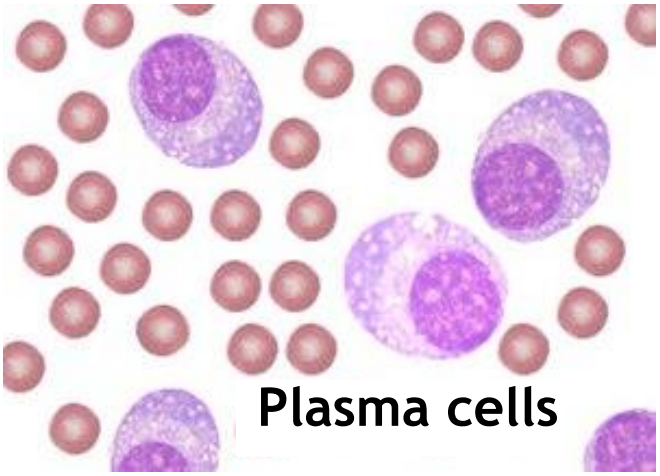
- NOTE : normally, both plasma cells and mast cells aren't found in blood " only a very few count", and they increase in specific conditions :

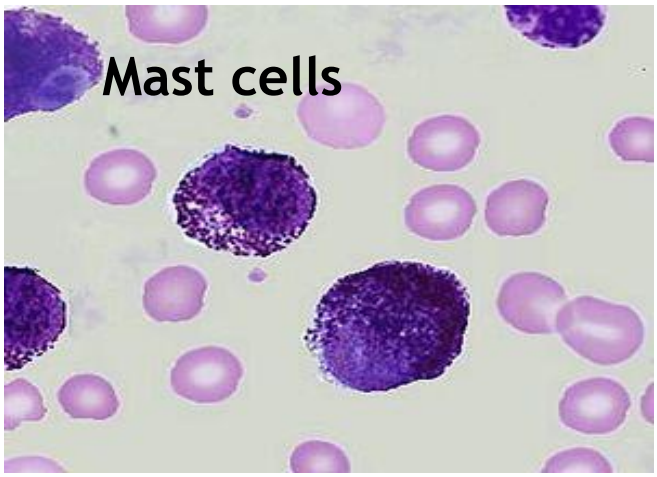
1. In inflammatory reactions, plasma cells number increases in blood, and mast cells number may increase a little
2. In allergic reactions, mast cells number increases.

- So, someone may ask: **"how do we develop diseases and symptoms if we have these immune mechanisms" ?**

✓We actually develop diseases only when the immunity isn't enough to control the effects of the foreign bodies, and with most of these diseases, the immune system is able to destroy the foreign bodies in few days, even if we don't take any drug.

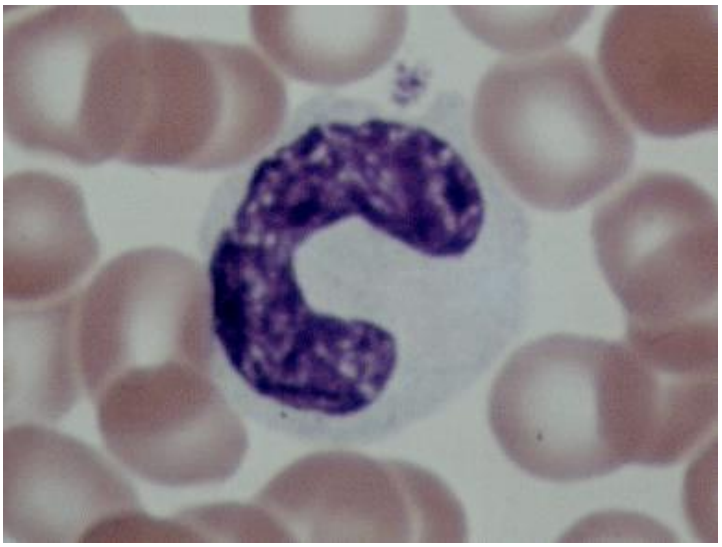
- An example of that is the **common cold**.





Monocytes

- They have abundant pale-blue cytoplasm and a darkly staining purple nucleus, which is distinctively U or kidney shaped
- Migrate from blood into tissues where they enlarge and become macrophages (which are phagocytic).
- Most powerful phagocyte
- They can phagocytize whole RBC, malarial parasites and dead neutrophils
- They are very important in starting immune responses
- They can be called different names when they stay in different tissues.
    1. Skin…..histiocytes
    2. Lungs...alveolar macrophage
    3. Liver….Kupffer cells



Leukocytosis & Leukopenia

- **Leukocytosis:** An increase in number of WBCs in circulation.

- Specific WBC type:
  Lymphocytosis, granulocytosis, neutrophilia.

- **Leukopenia:** A decrease in number of circulating WBCs. And may be caused by :
  - Irradiation, X-ray or gamma rays.
- So people who work in the radiology field must have a patch that shows how much radiation they have absorbed, and they always must be below the normal limits.
- Another example is cancer patients, because their treatment may include radiation therapy. In these cases, patients mostly die due to infections, because their WBCs count is very low to protect the body (only 500)
- Drugs, chloramphenicol, thiouracil, borbiturate hypnotics .
- **To compare :**
  - Abnormal hemoglobin is called : **Anemia**
  - High RBCs count is called : **Polycythemia**
  - High WBCs count is called : **Leukocytosis**
  - Low WBCs count is called : **Leukopenia**

Leukemia

- **Leukemia:** type of cancer that occurs in the bone marrow which causes uncontrolled production in WBCs.
  - Two types:

    1. Lymphocytic leukemia (the problem is in the Lymph nodes)
    2. Myelogenous leukemia (the problem is in the Bone marrow)
- Effects of leukemia:
  - Infection, Severe anemia, Bleeding tendency, Excessive use of metabolic substrate by cancerous cells cause debilitate of other tissues.

Role of macrophage and neutrophils in inflammation

- When bacteria get access to certain tissue, the first line of defense is macrophages which are already in that tissue.
- Within hour or so, the number of neutrophils starts to increase in the area.

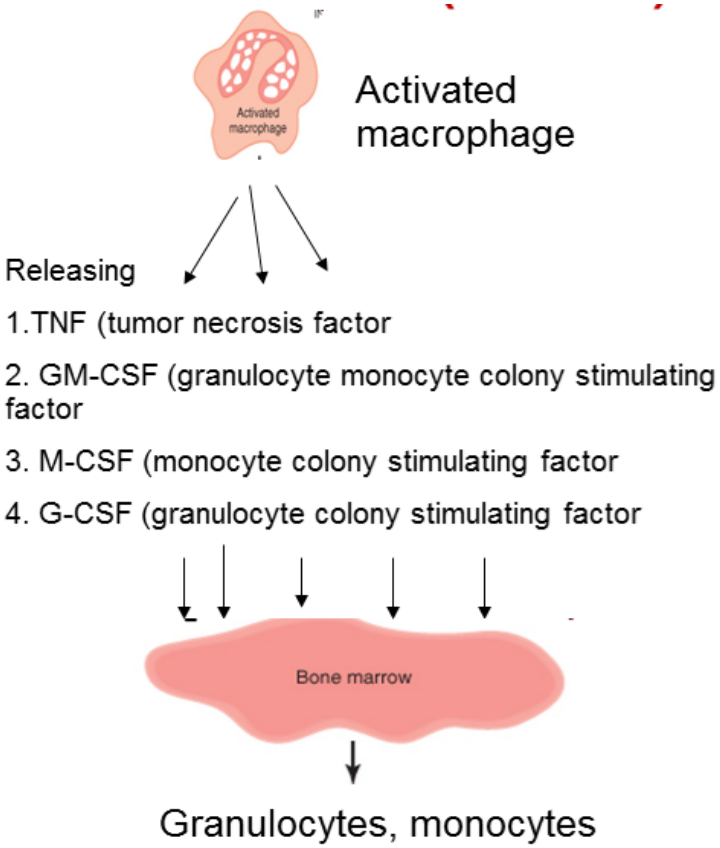
- Neutrophils form the second line of defense... These neutrophils come from blood due to liberation of chemotactic substances.
- In severe infection the number of neutrophils (neutrophilia) in the blood increases dramatically 3rd. Products of inflammation stimulate bone marrow to release the stored neutrophils there in bone marrow 4th.(Remember that bone marrow stores of WBCs are more than number of WBCs in the blood, so in this case, the infection stimulates the bone marrow to release its stored WBCs to the blood to attack the invader).
- Monocytes from blood enter the site of inflammation and become active macrophages in few days.
- Factors (Substances) released from activated macrophages stimulate bone marrow to produce new monocytes and neutrophils.
- **So in conclusion,**
- Infection ⟶ stimulates monocytes ⟶ macrophages are activated ⟶ substances released ⟶ stimulate the bone marrow ⟶ more monocytes and neutrophils are released to blood.

Characters of inflammation

- Vasodilators released by the inflamed tissue increase the permeability of the vessels supplying that tissue, so more interstitial fluid will accumulate in that area, and more inflammatory cells “granulocyte and monocyte" will be able to reach that tissue, thus swelling and redness of the tissue occur .
- **Inflamed tissue products:** Histamine, bradykinin, serotonin, and prostaglandin.
- **Walling off:** is a special mechanism done by the body, in which a wall is made around the inflamed area, to keep the inflammation as local as possible, trying to reduce the effects of inflammatory mediators on normal cells.

Feedback control of neutrophils and macrophages

- TNF, Interleukin 1(IL-1), GM-CSF, M-CSF, G-CSF
- These factors are formed by activated macrophages in the inflamed tissues.



Formation of pus

- Neutrophils and Macrophages engulf bacteria and necrotic tissues, then Neutrophils and macrophages die, so a cavity is formed in the inflamed tissue.
- This cavity contains necrotic tissue, dead Neutrophils, dead Macrophages and tissue fluid, this mixture is known as **pus**.

- So in this way, we've mentioned briefly the main types of WBCs and their basic functions, other details will be discussed in the immunity course.