HEMATOLOGY
&LYMPH SYSTEM

physiology | sheet

Number	6
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Leukocytes (White Blood Cells)

As we , leukocytes (white blood cells) are of two types :

1- *Granulocytes :*have granules in the cytoplasm and include neutrophils , eosinophils and basophils .

2- *Agranulocytes:* don't have granules in the cytoplasm and include monocytes and lymphocytes .

White blood cells count

**The normal range of WBCs is 4000- 11000 cells/ micro-liter (mm3)

1- High white blood cell count

White blood cell count increases in ALL infections ; bacterial , viral or parasitic infections .

However , there is a specification for each of these cells . How so??

- **Neutrophils** increase in all infections : bacterial or viral , acute or chronic .

- **Lymphocytes** also increase in infections but mainly in viral infections . In other words , if there was an increase in lymphocytes' number , a viral infection has taken place .

- **Monocytes** increase in infections as well but mainly in parasitic infections .

- **Eosinophils** increase mainly in allergic reactions . So if you have a high eosinophil count after doing the eosinophil test , it means you have allergy .

- **Basophils** don't usually have specifications ; they generally increase in infections but not too much .

** It is NOT important to know the count for each type of white blood cells , just know that a high white blood cell count means there is an infection, and focus on the specifications above .

2- Low white blood cell count

In contrast with high white blood cell count , there are some cases in which specific kinds of leukocytes decrease in number leading to a low white blood cell count .

- Neutrophils decrease in number in :

a- prolonged exposure to radiations
b- Drug toxicity
c- Vitamin B12 defficiency

- Lymphocytes decrease in prolonged immunosuppressive illnesses

- Monocytes decrease in :

a- Bone marrow failure
b- Cortisol treatment

- Eosinophils decrease in :

a- Drug toxicity
b- **Prolonged** stress

- Basophils decrease in :

a- Pregnancy
b- Hyperthyroidism

**Black people (in Africa , America …) have low white blood cell count , this is familial (genetic)

We need to differentiate between two terms : Leukocytosis and Leukemia

- **Leukocytosis :** is an increase in the number of leukocytes tepmorarily , and whenever the cause is eliminated , the count returns to its normal level .

- **Leukemia :**is an **uncontrolled** production of the white blood cells in which the count **does NOT** return to its normal level .

Let's talk more about **leukemia**

- In leukemia , the number of white blood cells is greatly increased so that it might reach hundreds of thousands , that's why we don't use the hemocytometer of the white blood cells to count them , in fact we use the hemocytometer of the red blood cells because of the high count.

- Leukemia is a tumor condition in which the cause is unknown yet in most cases . Anyways , the cause of leukemia was known in some cases such as the prolonged exposure to radiations (like what happened in Japan) as well as certain chemicals (petrol and its derivatives). In addition to that , viral infections for long time might cause leukemia . Genetic factors may also play a role in leukemia.

- Leukemia occurs in two forms :

  a- Acute form: More common in children . It occurs suddenly accompanied with symptoms similar to the 'Cold زكام' symptoms including bone pain, paleness, tendency to bleed and frequent infections .

  b- Chronic form: More common in adults after 40-50 years old. It occurs slowly and without warning , many cases were actually discovered during protein check . Sometimes several years may pass before significant symptoms appear in the blood . The symptoms of chronic leukemia is similar to those in acute leukemia .

- Leukemia has two types depending on the site of appearance of the disease:

1- ***Lymphocytic Leukemia***: in the lymphoid tissue
2- ***Myelocytic Leukemia :*** in the bone marrow

Remember : White blood cells are produced in the bone marrow,as for lymphocytes they are produced , in addition to bone marrow , in the lymphoid tissue (like the lymphoid tissue in the spleen).

- Leukemia cells are bizarre (غريبة) , undifferentiated (can not be distinguished) and **NOT** identical to any of the normal white blood cells .

- Usually the more undifferenntiated the cell is , the more acute the leukemia is . In contrast , the more differentiated the leukemia cell is , the closer it is to a chronic form leukemia , where it might take 15-20 years to totally develop .

- Leukemia cells especially the undifferentiated cells are ususally nonfunctional.

- **<u>The effects of leukemia on the body :</u>**

  1- The first effect of leukemia is metastatic growth of leukemic cells in abnormal areas of the body

  2- The leukemic cells of the bone marrow invade the surrounding bone .

  3- Almost all leukemias spread to the spleen ,the lymph nodes , the liver and vascular regions .

  4- In each of these areas , the rapidly growing cells invade the surrounding tissues , utilizing the metabolic elements of these tissues and consequently causing tissue destruction .

  5- Very common effects in leukemia are the development of infections, severe anemia &bleeding tendency caused by thrombocytopenia (lack of platelets). (thrombocytopenia is due to the high production of WBC at the expense of platelets)

  6- The most important effect of leukemia on the body is the excessive use of metabolic substrates by the growing cancerous cells.

  7- Tremendous demands are made on the body for foodstuffs, especially the amino acids &vitatnins. Consequently, the energy of the patient is greatly depleted, rapid deterioration of the normal protein tissues of the body.

8- Obviously, after metabolic starvation has continues long enough, this alone is sufficient to cause death.

As we said previously , leukocytes are of two types :

a- Granulocytes : include eosinophils, neutrophils and basophils
b- Agranulocyte : include monocytes and lymphocytes

○ Characteristics of Leukocytes

1- Granuocytes:

a- **Neutrophils:** the nucleus is segmented (sometimes 6 or 7 segments) , the cytoplasm is bluish pink in color and contains fine granules (حُبيبات دقيقة) which stain purplish . Usually the cell's outline is distinct (مميز-واضح)

b- **Eosinophils:** the nucleus is usually bilobed (consists of two lobes) but very rarely trilobed . The cytoplasm stains pink and contains the characteristic large spherical bright red (or orange) granules. Usually the cell's outline is not that distinct.

c- **Basophils:** the nucleus is not lobulated . The cytoplasm is plentiful (وافر) and stains pink and contains large coarse rounded or oval dark deeply staining granules which overlie the nucleus .Sometimes you can see the granules outside the cell because the cell's outline is not that distinct.

2- Agranulocytes:

a- **Lymphocytes:** they are round cells with NO lobulation . The nucleus usually occupies the whole cytoplasm .The cell's outline is distinct . A very important characteristic about lymphocytes is that the cytoplasm stains blue , from which we can diffrentiate between lymphocytes and monocytes .

b- **Monocytes:** the cytoplasm stains muddy grey or light grey . The cell's outline is not that distinct .

Platelets (thrombocytes)

Platelets are developed from the giant cells called "megakaryocytes" in the bone marrow

Platelet's count is 150-450 $\times \mathbf{10}^9$ /litre or 150-450 $\times \mathbf{10}^3$ /microlitre

Low platelet count → thrombocytopenia
High platelet count → thrombocytosis

Platelets do not contain nuclei .

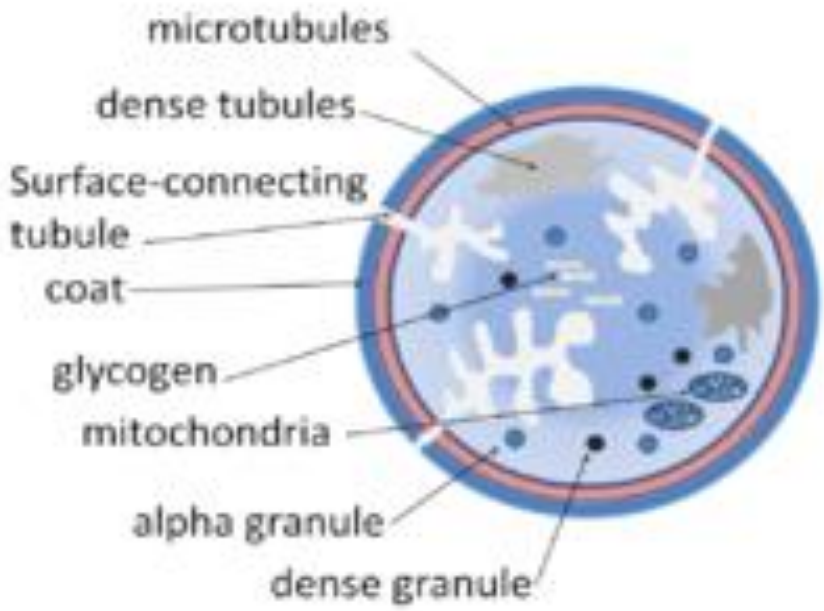
The differentiation time for platelets is 10 days , whereas in RBCs it is 6 days and in WBCs is also 6 days.

The production of platelets is regulated by a hormone called 'Thrombopoietin' which is produced by kidneys . The liver and the spleen produce a little of thrombopoietin as well.

Half life of platelets is about 10 days .

Platelets contain many substances which are important in hemostasis (hemostasis is a process which causes the bleeding to stop) .

Diagram of the platelet



We can see above the diagram of the platelet . It does not contain nucleus .
In fact , platelets contain mitochondria and two types of granules:

a- **Electron dense granules**which contain nucleotides(ADP, ATP…), calcium , catecholamines, and serotonin
b- **Specific alpha (α) granules**which contain acid hydrolyses, growth factors, fibrinogen, factor V (factor 5) ,Factor VIII (factor 8) , Von Willebrand factor, fibronectin, thromboglobulin, heparin antagonist.

We can also find other substances in the platelet like potassium, magnisium, histamine, adrenaline,albumin , antiplasmin,lipoproteins ,prostaglandins and thromboxanes .

All these substances are very important in hemostasis.

Humanbeings may develop thrombocytpenia more quickly than erythrocytopenia or granulocytopenia, because the bone marrow only contains one day reserve .

Platelets produce substances which maintain the capillaries integrate. In severe defficiency or absence of the platelets, RBCs migrate from capillaries into tissues.

Hemostasis

Hemostasis is stopping the bleeding through injured blood vessels and it occurs in the three following steps :

1- ***Vasoconstriction***
2- ***Platelet clot formation***
3- ***Fibrin threads formation***

First: Vasoconstriction of the blood vessels

Vasoconstriction happens to reduce the blood flow during bleeding .

Factors that are involved in vasoconstriction are :

- **Myogenic contraction**: refers to a contraction intiated by the myocyte cells after the physical injury (the blood vessel vasoconstricts) .
- **Endothelin 1:** a potent vasoconstrictor which is released from the injured cells
- **Serotonin:** a vasoconstrictor released from platelets
- **Thromboxane A2 :** a potent vasoconstrictor produced by platelets during the formation of platelet clot
- **Adrenaline :** also a vasoconstrictor

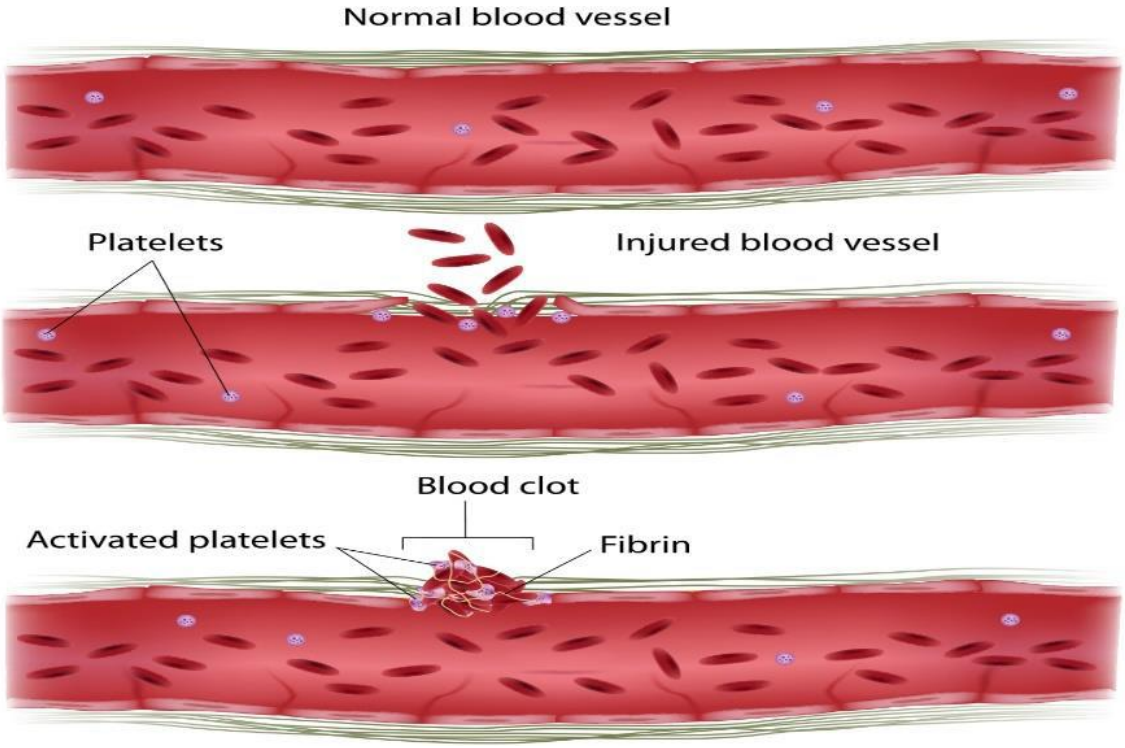
Second : Platelet clot formation

We will discuss now the steps of platelet clot formation in order to stop the bleeding . We have an injured blood vessel , so how is the blood clot going to be formed ?

- **Collagen** is released from the injured surfaces of the blood vessel
- **Collagen** attracts the platelets
- Platelets adhere to the injured surfaces , and this is the **first step** of platelet clot formation which we call **Platelet Adhesion**
- When platelets adhere to the injured surfaces , they are stimulated , and they rupture (disintegrate)
- As a result of the **platelets' disintegration , they release the substances inside them(release reaction)** , which is the **second step** of clot formation

- The substances released from platelets lead to the accumulation of the platelets above each other , we call this step **platelet aggregation** and it's **the third step**

- **Finally,** the medium is prepared for the clotting and is called platelet procoagulant activity . So platelets in this stage fuse the injury and stop the bleeding .



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