



Hematology



PHYSIOLOGY

☒ Sheet

☐ Slide

☐ Handout

Number: 6

Subject: **Leukocytes (White Blood Cells)**

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Date: 00/9/2016

Price:

Test yourself!!!

(reviewing the previous lectures).

A patient came to your clinic with general fatigue, weakness and shortness of breath. Blood tests for this patient showed that MCHC = 0.3, each red blood cell contains –on average- 20×10^{-12} g of hemoglobin, plasma volume represents about 69% of total blood volume, WBCs and platelets together represent 1% of total blood volume and platelets represent 37% of buffy coat. (Assume that differential count of WBCs remained in the normal range).

Depending on this case, answer all the following questions:

1. which of the following possibilities is (are) true:

- a. folic acid deficiency.
- b. lead poisoning.
- c. pernicious anemia.
- d. more than one of the above.
- e. extra piece of information must be provided.

2. hemoglobin concentration in the patient's blood is:

- a. 9g/dL b. 4.5g/dL c. 15g/dL d. 1.5g/dL

3. the percentage of neutrophils volume **of total blood volume** is:

- a. 63% b. 1% c. 0.38% d. 0.62% e. none of the above

Answers: 1. B 2. A 3. C

Leukocytes (white Blood cells):

General view:

The normal range of WBCs is **4000- 11000 cells/ micro-liter (mm^3)** so if the number exceeds 11000, this means *leukocytosis* while if the number is lower than 4000, this means *leukocytopenia*.

Unlike the RBCs, there is no difference between males and females in the number of leukocytes , but even in the same individual the WBCs count changes from time to time ; reaching its maximum in the evening and its minimum in the morning.

WBCs count increases after having a meal, doing exercise and in pregnancy. *Remember that doing exercise increases the number of neutrophils apparently shifting the equilibrium towards the circulating neutrophils on the expense of the marginating neutrophils (taken from histology lectures).*

Based on **the old classification**, WBCs are divided into :

1. **Granulocytes**: neutrophils ,eosinophils and basophils.
2. **Agranulocytes**: lymphocytes and monocytes.

Remember that the new classification of WBCs divides them into Granulocytes and mononuclear leukocytes instead of Agranulocytes because lymphocytes and monocytes contain azurophilic granules (taken from Histology lectures).

Granulocytes contain single multilobed nucleus and specific granules.

Life span of WBCs differs depending on the type of the cell ranging from 1-4 days in neutrophils, hours to years in monocytes (*According to Junqueira's basic Histology*), also the duration of action is different from one cell to another.

Half-life of WBCs differs depending on the type of the cell ranging from hours in neutrophils (if they are intravascular) to days-months and sometimes about a year in monocytes (According to Dr.saleem).

All WBCs are produced from the bone marrow except for a type of lymphocytes which have another site of origin which is the lymphoid tissue. *I think that Dr.saleem was talking about B and T – memory cells since when resting B and T lymphocytes are produced from bone marrow and get immunocompetent either in bone marrow or in thymus gland respectively they travel to secondary lymphoid organs (spleen , lymph nodes and diffuse lymphatic tissue) where an antigen recognition occurs producing activated lymphocytes (plasma cells, T-helper and T-cytotoxic cells) and **memory cells** so lymphoid organs are considered as another source for the production of lymphocytes in addition to bone marrow. (taken from histology lectures).*

The bone marrow is actually one of the largest organs in the body, approaching the size and weight of the liver. It is also one of the most active. Normally 75% of cells in bone marrow belong to the white blood cell-producing myeloid series and only 25% are maturing red cells, even though there are over 500 times as many red cells in the circulation as there are white cells. This difference in the marrow reflects the fact that **the average life span of WBCs** is short whereas that of red cells is long.

The measured count of WBC is 50% of the actual number of WBCs because the other 50% of WBCs are adhering to inner walls of blood vessels and this adhered part is called **Marginal pool**, these cells are released in some conditions such as in hemorrhage and hemolysis. Usually neutrophils have higher count than the others,

but in rare cases lymphocytes might have a count equal to that of neutrophils or even higher.

Concentrations of the different WBCs in the blood (Differential leukocyte count) and the main characteristic feature of each them:

1. **Neutrophils:** *60% of leukocytes* and characterized by presence of 3-5 lobes of nucleus.
2. **Eosinophils:** *4% of leukocytes* and characterized by presence of red to orange granules.
3. **Basophils:** *less than 1% of leukocytes* and their nucleus is covered by the large granules.
4. **Lymphocytes:** *30% of leukocytes* and their large nucleus occupies most of the cytoplasm and if there is a small apparent part of the cytoplasm, it appears blue.
5. **Monocytes:** *5% of leukocytes* and characterized by pale blue-grey cytoplasm.

Significance of high white blood cells count:

1. **Neutrophils:** increase mainly in *bacterial* infections.
2. **Lymphocytes:** increase mainly in *viral* infections.
3. **Monocytes** : increase mainly in *viral or fungal* infections.
4. **Eosinophils:** increase during *allergy*, so if a patient come to you and you suspect that he has allergy , the first test you will ask is eosinophils count, also in *parasitic* infections.
5. **Basophils:** also increase in allergic reactions but less than eosinophils do increase.

General characteristics of leukocytes:

1. They are able to pass through the walls of the capillaries to enter the tissues , this process is called **Diapedesis**.
- 2.They move between the blood vessels (from one to another) in the circulation and also in the tissues, this is called **Amoeboid motion**.
3. They are attracted to the site of infection by certain chemicals, this is Known as **Chemotaxis**.
- 4.They have the ability to engulf and digest bacteria and dead cells (**phagocytosis**).

Remember that macrophages (derived from monocytes) and neutrophils (microphages or polymorph) are capable of phagocytosis (taken from histology lectures).

Leukopoiesis (the production of WBCs):

- Leukopoiesis is a very complicated process because of the following points :
1. The stem cell is affected by many factors (IL-1 , IL-6, then IL-3, GM-CSF, Granulocyte-CSF and stem cell factor) , if any of these is deleted or become not functioning , the production of WBCs will be affected.
NOTE: CSFs (colony stimulating factors) are so called because in vitro, if we use any of them on one cell in a culture, this cell will produce a **colony of cells**.
 2. Each one of these factors is produced by many cells or tissues.
 3. Of course , there are many steps in leukopoiesis and in each step , there are many factors affect each step and the production of the cells .

4. Sometimes one factor affects many steps, and there is overlap between ILs and CSF.

- The duration of leukopoiesis is similar to the duration of erythropoiesis which is about 6 days , but WBCs remain in the bone marrow for another 6 days , so they remain in the bone marrow about 12 days.
- During the production of WBCs , other cells (RBCs and platelet) are also affected , and remember that in pernicious anemia even neutrophils are affected, so,there is a relation between the production of WBCs and RBCs.
- When leukocytosis occurs, if the cause is eliminated, the number of WBCs will return back to normal . But if there is a great uncontrolled increase in the number of WBCs, this is called leukemia.

Leukemia:

- It is the malignant proliferation of WBCs precursor cells, or partially and completely differentiated cells and this happens at the expense of the production of RBCs and platelets, so anemia and thrombocytopenia occur.

- **Causes of leukemia :**

1. **Genetic causes** : some families have high incidence of leukemia.
2. **Environmental factors:** the incidence of leukemia is high in certain areas.
3. **Radiation:** such as what happened in Nagasaki in Japan.
4. **Chronic exposure to some chemicals and some viruses.**

- Usually , leukemia affects all types of WBCs , but sometimes it doesn't affect the 5 types , so it might be neutrophilic leukemia , eosinophilic leukemia , basophilic leukemia , monocytic leukemia or lymphatic leukemia and no body knows why and how this happens.

- There are 2 types of leukemia :

1. **Acute leukemia** : appears mostly in children , the onset is **stormy** (suddenly, the patient experience flu-like symptoms: (feeling sick, having fevers, chills, feeling fatigued), bone pain, the patient suffers from anemia , tendency to bleeding and frequent infections).

Remember that in acute leukemia , the malignant cells are immature granulocyte precursors mainly myeloblasts and very few mature neutrophils are being formed making the cells ineffective in immune response and this explains the frequent infections (taken from histology lectures).

2. **Chronic leukemia** : appears mostly in old ages (above 45 yrs) , develops slowly , the symptoms are less severe.

- In general , leukemias are divided into 2 types according to the origin :

1- **Lymphocytic leukemias**

2. **Myelocytic leukemias**

- The leukemia cells are bizarre (unusual in appearance) and undifferentiated and not identical with any of the normal white blood cells, Usually the more undifferentiated the cells, the more acute the leukemia is .Leukemic cells especially the very undifferentiated are nonfunctional , and because of that , the patient suffers from frequent

infections. And with some of the more differentiated cells , the process will be quite chronic.

Effects of leukemia on the body :

1. Metastatic growth of leukemic cells in abnormal areas of the body. Because of that , if the disease is discovered early , it can be cured ,but if it is discovered in late stages there will be no hope of curing.

2.The leukemia cells of the bone marrow invade the surrounding bone, almost all leukemia spread to the spleen, the lymph nodes, the liver and vascular regions.

3. 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.

4.Frequent infections , severe anemia and bleeding tendency caused by thrombocytopenia.

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

6.Tremendous demands are made on the body for food stuffs, especially the amino acids and vitamins. Consequently, the energy of the patient is greatly depleted, rapid deterioration of the normal protein tissues of the body.

And as Einstein says :'' Imagination is more important than knowledge''.

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