Hematology

HISTOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number: **1**

Subject: **Histology of blood**

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Price:

Histology of blood and lymphatic tissue

Definition of the blood:-

The blood is special type of connective tissue containing a variety of cells suspended in the plasma.

Main function of the blood:-

Vehicle for transport of cells, nutrients, gases (CO_2 and O_2), metabolic waste products and hormones.

Plasma is aqueous solution, always there is exchange with ECF (Extracellular fluid); Plasma will give nutrients and O_2 to the tissue and turn back CO_2 and waste products.

An important component of the plasma is the plasma proteins:

- The main bulk of the plasma proteins is **albumin**
- **Globulin**
- **Fibrinogen**

Collectively these three types of plasma proteins synthesized mainly by the liver and they are responsible for ***colloid osmotic pressure,*** which is necessary for exchange between plasma and ECF.

Albumin :

- Constitutes the bulk of plasma proteins.
- Can act as a carrier/ transporter:

Certain substances in the blood are insoluble in the plasma like the fatty acids (FAs), so FAs combine with albumin and albumin transports these FAs in the blood.

Globulins:

Immunoglobulins (antibodies) produced by plasma cells which are derived from B- lymphocytes.

Antibodies are responsible for immune reaction called **humoral immune reaction / antibody mediated immune reaction.**

Fibrinogen:

This plasma protein can polymerize and form fibrin; fibrin is a network forming the base of blood clot.

The difference between the blood clot and thrombus:

The **blood clot** is fibrin with some RBCs, when we add to (the fibrin and RBCs) platelets, WBCs → then we call it **thrombus**.

Fibrin + RBCs = clot
Fibrin + RBCs + WBCs/platelets = thrombus

There are three types of blood cells:

- RBCs - erythrocytes
- WBCs- leukocytes
- Platelets – thrombocytes

Thrombocytopenia- disorder in which there is decrease in the number of platelets, this will result in increasing tendency of bleeding.

Leukopenia – decrease the number of WBCs.

Leukocytosis- increase the number of WBCs because of acute inflammation for example.

Erythrocytes (RBCs) :

Their main function is transport of gases CO_2 and O_2.

RBCs react exclusively ***within the blood***; they do not work outside the blood. Unlike WBCs, which make use of the blood as vehicle and they function mainly ***within the tissues***, WBCs whenever they are needed in case of bacterial infection for example, in this case we need neutrophils so WBCs migrate from the blood vessels to the tissue.

WBCs are important part of defense of immune system.

Platelets (thrombocytes):

They play a vital role in the control of bleeding (hemostasis or haemostasis) by:

A) plugging the defects in blood vessels.
B) activating the blood clotting cascade.

Keep in mind that there is difference between **HO**meostasis and **HE**mostasis (**hae**mostasis) ; homeostasis is the tendency towards a relatively stable equilibrium between interdependent elements, especially as maintained by physiological processes while hemostasis is the stopping of a flow of blood.

Suppose we have a tear in small blood vessel (capillary for example), if the tear is ***small***, platelets will accumulate and stop bleeding. But suppose that the tear was ***considerable,*** the blood will come out and in

this case we cannot wait the platelets to perform their function, we have to ***compress*** to stop the bleeding and we have to find the source of bleeding and to promote a ***proper healing*** **sutures** is performed to *stop bleeding.*

"Platelets can stop minimal bleeding", minimal bleeding is very dangerous in the brain.

Methods used to study blood:

→ We make blood smear on a glass slide, a drop of blood/bone marrow, we spread it, and we use a stain. The stain that we use for blood is ***polychromatic stain.***

Examples of polychromatic stains:

1. Wright.
2. Giemsa.
3. Leishman.

Four distinctive staining characteristics (according to the affinity of various cellular organelles to the different stains employed):

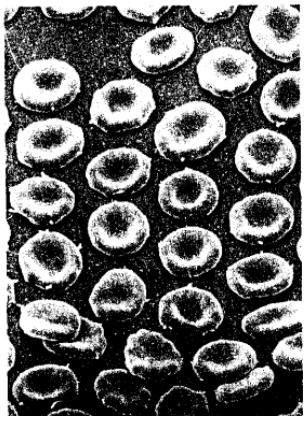
1. **Basophila (deep blue):** affinity for the basic dye methylene blue/ hematoxylin (basic stain interacts with acidic component of the cell; characteristic of DNA in nucleus , RNA in cytoplasm e.g. ribosomes).
2. **Eosophilia (pink):** affinity for acidic dye eosin , particulate feature for hemoglobin within erythrocytes (acidic stain interacts with basic component of the cell).

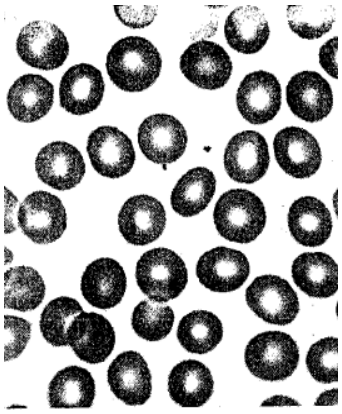
So why RBCs appear red? Because **they contain hemoglobin.**

3. **Azurophilia (purple):** affinity for **azure** dyes, typically of lysosomes (azurophilic granules in leukocytes) and the lysosomes contain hydrolytic enzymes.
4. **Neutrophilia:** stain specific granules in neutrophils (neutrophilia doesn't mean neutral stain but cells stained by specific stains).

***Erythrocytes**:*

This is the appearance of RBCs under scanning electron microscope and light microscope respectively.





- RBCs are **biconcave discs**, they are not sphere. Their central part is very thin, this means that it contains minimal amount of hemoglobin so it appears pale in color.
- Their shape (biconcave disc) increases the surface area by 20%-30% enhancing the ability to carry gases.
- The diameter of RBCs 7-8 µm.

We can estimate the diameter of other cells depending on RBCs, WBCs are 1.5 times the diameter of RBCs (10-12µm).

RBCs are 7-8 µm in diameter and the smallest blood vessels (capillaries) are 3-4 µm in diameter, so how RBCs can run through small blood vessels?

This is due to two factors:

1- Biconcave shape.
2- Fluidity (flexibility) of cell membrane.

All blood cells are formed in bone marrow. There are two different types red and yellow bone marrow; **only *Red bone marrow*** is able to form blood cells by a process called **hematopoiesis.**

In hematopoiesis at the last steps, RBCs **e*xtrude* their *nucleus*** and they become **enucleated.**

Mature RBCs consist of cell membrane surrounding hemoglobin there is no nucleus and limited amount of enzymes, which are necessary for maintenance of cell membrane.

RBCs are enucleated, this is responsible for the short life span of RBCs. (maximum 120 days)

	amount of hemoglobin	Number of RBCs
In males	13-16 gm/dL	4.5-6 million/ mm^3
In females	12-13 gm/dL	3.8-5 million/ mm^3

Males have higher RBCs count than females because androgens in males act as a stimulus for formation RBCs in the bone marrow.

Factors required for RBCs synthesis:-

- ***Erythropoietin:*** hormone released from the kidney.
- ***iron :*** supplied by food.

- ***Folic acid***
- ***Vitamin B_{12}***
- ***Proteins***

Reticulocytes :

- They are the ***immature*** form in which RBCs are released into the circulation.
- Reticulocytes contain 80% of hemoglobin,80% of hemoglobin have been synthesized. They contain sufficient amount of mitochondria, ribosomes and Golgi apparatus to complete the remaining 20% of hemoglobin synthesis.

How we identify reticulocytes?

- Reticulocytes contain a network of granules. This network represents remnants of ribosomes (RNA).
- In routinely stained blood smear, reticulocytes cannot be easily distinguished from mature erythrocytes.

When fresh blood is incubated with basic dye→**brilliant cresyl blue**_ a blue stained reticulin precipitate in the reticulocytes due to the interaction of the die with ribosomal RNA remnants.

Reticulocytes are normal cells, when reticulocytes increase in percentage this condition is abnormal. Normal blood contains 1% reticulocytes ; an elevation in the number of reticulocytes is called ***reticulocytosis***, commonly seen in anemia or acute blood loss.

Abnormalities in erythrocytes:

A change from the normal size, shape or staining properties of erythrocytes are important indicator of disease. However, some of these abnormalities may be found in healthy individuals.

1. Anisocytosis-abnormal variation in the ***size*** of RBCs.

Which may be:

A. Macrocytes (Large cells):

When it is large so there is ***folic acid deficiency or vitamin B_{12} deficiency***, larger red cells are always associated with insufficient numbers of cells and often also insufficient hemoglobin content per cell causing anemia ; **Megaloblastic Macrocytic Anemia.**

B. ***microcytes (smaller cells):***

RBCs are smaller than normal but total number of RBCs does not change thus hemoglobin will decrease resulting in anemia; **Microcytic hypochromic anemia and this condition is due to iron deficiency.**

Note: Folic acid and iron supplementation is recommended as part of the antenatal care to reduce the risk of the previous two types of anemia.

2. Poikclocytosis- abnormal variation in ***shape*** of RBCs.

A***. crenation*** : if normal cells are placed in hypertonic solution water will abstracted from the cells leaving it shrunken and bearing numerous projections.

B. One of the most severe changes in shape occurs during sickling of RBCs in ***sickle cell anemia.***

3. Hypochromia- decrease in the intensity of staining indicates a decreased amount of hemoglobin.

- Frequently accompanies microcytosis → hypochromic microcytic anemia.

Howel jolly bodies- nucleus fragments left over from the nucleated precursors of the red cells / remnants of nucleus seen in some diseases (usually healthy cells doesn't contain them).

White blood cells (leukocytes):

- WBCs are produced in the bone marrow.

WBCs are classified according to the ***shape of nucleus and the type of granules within the cytoplasm***. Therefore, there are two types of WBCs:

1- Granulocytes:

They are further subdivided into three types of cells depending on the type of granules they contain:

1) ***Neutrophils (polymorph/ microphage)***:

❖ Most common ***(40-75%)*** of circulating WBCs.

> ***Polymorph*** indicates that:
>
> the multilobed nucleus may assume many morphological shapes.

❖ Neutrophilia is an increase in the number of neutrophils in the blood because of **acute** inflammation.

- ❖ Shape of nucleus in ***mature neutrophil*** is ***5 lobes*** connected by chromatin ***(3-4 lobes in immature neutrophil)***, notice the different nuclear morphological shapes (polymorph).
- ❖ In neutrophils of female, there is condensed quiescent X chromosome or ***Barr body*** exists in the form of small drumstick shape appendages of the nuclear lobes→ visible in about 3% of neutrophils.

How to determine the sex of a baby in case the *external genitalia* do *not* look *clearly (*ambiguous genitalia)?

By searching about Barr body in neutrophils.

- In case the baby have a Barr body so he have two X chromosomes **commonly**, this is a female.
- No Barr body → absence of Barr body means single X chromosome which means **commonly** XY → male, and may be XO→ atypical female since there is one X chromosome in this genotype (XO).

- Two Barr bodies → super female (XXX).

❖ **Contain two types of granules:**

1. ***Specific granules:***
    - hardly seen.
    - Small, most numerous.
    - contain phagocytin and lysozyme which both are ***bactericidal*** enzymes (destroy cell wall).

2.***Azurophilic granules:***

- red-purple granules.
- Less numerous.
- Larger.
- Easily seen.
- they ***are modified lysosomes*** and contain the usual lysosomal hydrolases and a number of bactericidal agents including ***myeloperoxidase*** this can be demonstrated by the peroxidase stain and is used as a marker for the primary azurophilic granules and for identification of leukemia arising in neutrophil precursors.
- Both ***neutrophils and eosinophils*** contain myeloperoxidase.

❖ Function of neutrophils:
Acute inflammatory response, neutrophil is the first cell travel to the site of inflammation.

❖ First cell to travel to the site of an infection.

❖ Neutrophils help fight infection by ingesting microorganisms .

❖ They don't function in the blood.

2. Eosinophils (1-6%)

3. Basophils (less than 1%)

Note: Granulocytes contain ***single multilobed nucleus***, prominent type specific granules connected by chromatin.

2- Mononuclear leukocytes:

- Non lobulated nuclei.

Previously these cells were named Agranulocytes (without granules) but recently they discovered that they are not devoid of cytoplasmic granules so they were named as mononuclear leukocytes instead of agranulocytes.

- Two types of mononuclear leukocytes:

1) Monocytes:

- Monocytes circulate in the blood migrate from the blood to the tissue forming **macro**phage.

2) Lymphocytes:

- Play a key role in all immune responses. In contrast to the other leukocytes their activity is always directed against **specific foreign agents.**
- Monocytes and neutrophils are highly phagocytic; engulf microorganisms in **a non-specific manner.**

- There are two types of lymphocytes:

1. B-lymphocytes 2. T-lymphocytes

- B- Lymphocytes and T- Lymphocytes cannot be distinguished by their shape (histologically) , but functionally lymphocytes react with specific antigen.
- B-lymphocytes function in the ***humoral immunity by secreting antibodies***.
- T- lymphocytes are responsible for ***cell-mediated immunity***; they should reach the site of foreign cell.

ما أجملها من ابتسامة ترتسم على شفاه مريض

اقرأ بشغف اليوم لتكن سببا في رسمها غدا.... في ابتسامتهم حياة

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