

Blood

- Connective tissue
- PH : 7.4
- More oxygen → brighter the red
- Less oxygen → duller the red
- In adults : 5-6 Liters of blood move unidirectionally within the closed circulatory system.

* Non living (Matrix) 55%
"plasma (pale yellow fluid)" :-

- Mostly water
- Albumin : The most abundant plasma protein / is made in the liver / helps maintain osmotic pressure in capillaries / transport steroid hormones & fatty acids.
- Fibrinogen : The largest plasma protein / is made in the liver / important for clot formation.
- α & β globulins : are made by liver transport fat soluble vitamins, lipids & iron.
- γ -globulins (immunoglobulins) "antibodies" : secreted by plasma cells

The importance of proteins inside the plasma is to prevent fluid loss & to create osmotic pressure (to keep the blood inside the blood vessels).

* serum = everything in plasma minus the clotting factors.

* Hematocrit : ratio of the volume of RBCs to the volume of whole blood.

* Blood film / smear : a drop of blood is spread on a glass slide & left dry in air.

* Leishman's stain :

- 1-Eosin : acidic dye / pink to red
 - 2-Methylene blue : basic dye / blue to purple.
- both are dissolved in methyl alcohol (fixative)
- 3-Azure dye.

* Living 45% (formed elements):

1- Erythrocytes (RBCs):-

- Transport oxygen & CO₂
- Cytoplasm is full with hemoglobin molecules
- High content of hemoglobin
 - ↳ Eosinophilia / acidophilia
- Have no nuclei (not true cells) or organelles (No mitochondria → No ATP production).
- Survive for 100-120 days in the circulation
- Worn out RBCs are removed by macrophages of the spleen, bone marrow & liver.
- The submembranous meshwork of proteins (spectrin & Ankyrin) stabilizes the membrane, provides the cell elasticity & maintains the cell shape → small, biconcave discs → ↑ surface area, facilitating gas exchange
 - permits erythrocytes to bend & adapt to the small diameters & irregular turns of capillaries.
 - pale staining of the central region (Normochromic RBCs)
 - 1/3 the size of the RBCs
- Function exclusively within vascular system
- Non motile

- Erythrocytes can be used as a size reference for other cell types.

* Mutations in spectrin & Ankyrin
↳ hereditary spherocytosis

* Glycocalyx: glycoprotein & glycolipid.

* Rouleaux formation :-

- RBCs adhere to one another
- In slow (not in normal) circulation
- due to surface tension caused by their biconcave surface (reversible).

* Abnormalities of Erythrocytes :-

1- Abnormal sizes:

- a. Microcytes (< 6 μm "10⁻⁶")
- b. Macrocytes (> 9 μm)
- c. Anisocytosis (different sizes)

2. Abnormal staining:

↓ hemoglobin → ↓ intensity of staining → Hypochromia (accompanies microcytosis)

Hypochromic microcytic anemia

3. Abnormal shapes (Poikilocytes)

"Poikilocytosis": due to changes either in the cell membrane or Hb content

- a. spherocytes
- b. Ovalocytes (elliptocytes)
- c. Dacrocytes: teardrop shaped cells.

d. Sickle cells: crescent like cells

* ↓ Mass of RBCs/hemoglobin
↳ anemia

* ↑ Mass of RBCs → Polycythemia

* Hypoxemia → the kidneys
produce Erythropoietin →

↑ erythrocytes in the bone marrow

- RBC plasma membranes have
glycoprotein antigen on their
external surfaces.

- Glycophorin A (integral
membrane protein) → ABO blood
typing system

2- Buffy coat:-

a) Leukocytes (WBCs):

- Function mainly outside blood
vessels (in loose CT),

- Motile, true cells, spherical

1. Granulocytes:

- Single multi-lobed nucleus
(segmented), all are phagocytic

a. Neutrophil: The most common
leukocyte, 2-5 lobes in nucleus
(polymorphs), light/pale pink

cytoplasm, small granules, short-
lived cells with a half-life of 6-8
hours in blood & a life span of 1-4
days in CT, the most motile,

Neutrophil chemotactic factors
are the first released.

- Specialized for responding to
bacterial invasions, Acute infections,
Acute pyrogenic infections.

* Barr body: inactive X chromosome
appears as a drumstick-like appendage
"in females"

* Non specific granules (Azurophilic;
primary): defensins, acid hydrolase,
myeloperoxidase

* Specific granules (secondary):

- Lysozyme: action cell membrane

- Phagocytin: bactericidal

- Lactoferrin: bacteriostatic

- collagenase

* Pus: dead neutrophils, bacteria,
lysed ECM & tissue fluid

- Neutrophils survive in an
anaerobic environment

* Pyrogenic: bacterial infections
that make pus

* Pyrogenic: heat production

- Pus is pyrogenic.

- Neutrophils = polymorphs = pus cells
= cells of acute inflammation

= microphages = myelocytes

- Have the most phagocytic
activity

b. **Basophils**: Rarest leukocyte, have the least phagocytic activity, bi-lobed, S-shaped nuclei, large granules that stain dark purple/blue.

- Contain histamine, heparin & eosinophilic chemotactic factor that mediate inflammation in allergic reactions & parasitic infections

- Both basophils & mast cells have surface receptors for immunoglobulin E (IgE)

* **Immediate or type 1 hypersensitivity**

- **First exposure to an allergen**:
↳ production of specific IgE antibodies → bind to receptors

- **Second exposure**: the allergen combines with the receptor-bound IgE molecules →

degranulation of basophils & mast cells → inflammatory mediators → vasodilation

→ a sudden drop in blood pressure → Anaphylaxis / anaphylactic shock

c. **Eosinophils**: bi-lobed nuclei, large cytoplasmic granules which stain red.

- Help in ending allergic reactions & in fighting parasitic infections

- have a particular phagocytic affinity for antigen-antibody complex.

* **Specific granules (Crystalloid granules)**: oval in shape.

↳ **externum (pale)** → histaminase & sulfatase

↳ **internum (dark)** → basic

protein to kill parasites.

* **General features of granulocytes**:

- Spherical in blood stream, irregular in CT.

- Highly motile with different shapes due to their amoeboid movement.

- Leave blood stream by migrating between the endothelial cells (**diapedesis**).

2. Agranulocytes:

- Single non-lobulated nucleus
- Granules are too small to see (nonspecific/azurophilic/primary granules/lysosomes).

a. **Monocytes**: largest leukocytes, large C-shaped nucleus, bluish cytoplasm (frosted glass appearance), highly motile & phagocytic.

- All monocyte-derived cells are antigen-presenting cells.
- Are precursor cells of mononuclear phagocyte system (Kupffer cells "liver", microglia "CNS", dust cells "lung", dendritic cells "lymph node & spleen", langerhans cells "epidermis", macrophages "BM & CT", osteoclast "bone resorption").

b. **Lymphocytes**: smallest leukocytes, round nucleus occupies most of cell volume, cytoplasm is light clear blue, increased numbers are seen in viral infections.

- **Large lymphocytes**: active, more cytoplasm, lightly stained cell.
- **Small lymphocytes**: inactive, less cytoplasm, predominant in circulation blood, darkly stained cell, have scanty cytoplasm (few organelles but large number of ribosomes) → basophilic cytoplasm.

① **Natural killer cells**: null lymphocytes, large granular activated lymphocytes, play a major role in graft rejection, kill virus infected, transplanted & neoplastic cells (innate immunity).

② **T lymphocyte**: cell mediated immunity, from the thymus.

→ **Suppressor**: suppresses immune response of T & B lymphocyte/self Ag - If it is damaged → autoimmune disease.

→ **Cytotoxic**: adaptive immunity, kill virus-infected, transplanted & neoplastic cells, react only with antigen on MHC-I (on surface of all nucleated cells) & requires CD8 protein - Ag-MHCI complex binds to receptor on CD8 T cell → proliferation & activation → ↑ perforins (form pores in the cell membrane) & granzymes "proteases" (enter the cell membrane inducing apoptosis).

→ **Helper**: adaptive immunity, HIV affects these cells, react only with antigen on MHC-II (on surface of APCs, coupled to peptide product of Ag digestion) & requires CD4 protein. - Ag-MHCII complex binds to receptor on CD4 T cell → activation & proliferation

→ ↑ Lymphokines (cytokines) → stimulate cytotoxic T cells & B cells.

- Immunohistochemistry: direct method using Anti-CD4 labeled with fluorescent tag → green color

↳ T-helper lymphocyte

No green color → we can't determine it.

③ B lymphocytes: humoral immunity, from BM, their receptors are immunoglobulin that bind antigen directly (without CD)

- Ag-MHC-II complex, T-helper cells bind to it → proliferation & activation → plasma cells → antibodies
↳ memory cells
↳ life long immunity (vaccination)

* APC: macrophage, dendritic cell, B lymphocyte

* In normal cell → self-peptide/antigen bound to MHC-1

b) Thrombocytes (Platelets): small non nucleated cytoplasmic fragments, biconvex discs, formed by megakaryocytes in BM, diameter: 2-4 μm , cytoplasm is purple & granular, lifespan: 10 days, have a thick glycocalyx.

- have 2 zones:

① Outer pale basophilic (clear) peripheral zone (hyalomere): contains cytoskeleton (microtubule & actin filaments) to maintain shape & help contractions of platelets & squeezing, clot retraction & membranous channels (open canicular system & dense tubular system).

② Central dark granular zone (granulomere): contain alpha granules (clotting factors, growth factors) / dense "delta" granules (serotonin "absorbed from plasma", ATP, ADP) / lambda granules (lysosomes: aid in clot resorption).

Euchromatin: extended active chromatin (pale)

* DNA

↳ Heterochromatin: condensed inactive chromatin (dark)

* Nucleolus: spherical dark mass not surrounded by a membrane.

↳ ribosomal RNA (rRNA)
↳ protein

- The nucleus stains blue by H & E

↳ active: lightly basophilic

↳ inactive: deeply basophilic & small

- The cytoplasm stains pink/red by H&E.

- Dense irregular CT: bundles of collagen fibers are randomly interwoven.

↳ resistance to stress from all directions.

↳ dermis of skin, organ capsules, submucosa.

- Dense regular CT: parallel bundles of collagen fibers.

- Parenchyma of organ consists of that tissue (conducts specific function of the organ). **Stroma** is everything else.

- Continuous capillaries: endothelium forms solid lining, adjacent cells are held together with tight junctions.

- Fenestrated capillaries: endothelium contains pores, found wherever active capillary absorption or filtrate formation occurs, found in endocrine glands, small intestine & kidney.

- Sinusoidal capillaries: wide diameters with wide gaps between endothelial cells, basement membrane incomplete or absent, found in liver, spleen & BM, allow large molecules (proteins & blood cells) to pass between the blood & surrounding tissues.

Hematopoiesis

Early embryo: yolk sac mesoderm

Second trimester: liver & spleen

Third trimester & after birth: BM

- The red BM (consist of hematopoietic stem cells) is found in axial skeleton.

- long bones → yellow BM

- Under certain conditions (severe bleeding or hypoxia) yellow BM

reverts to red

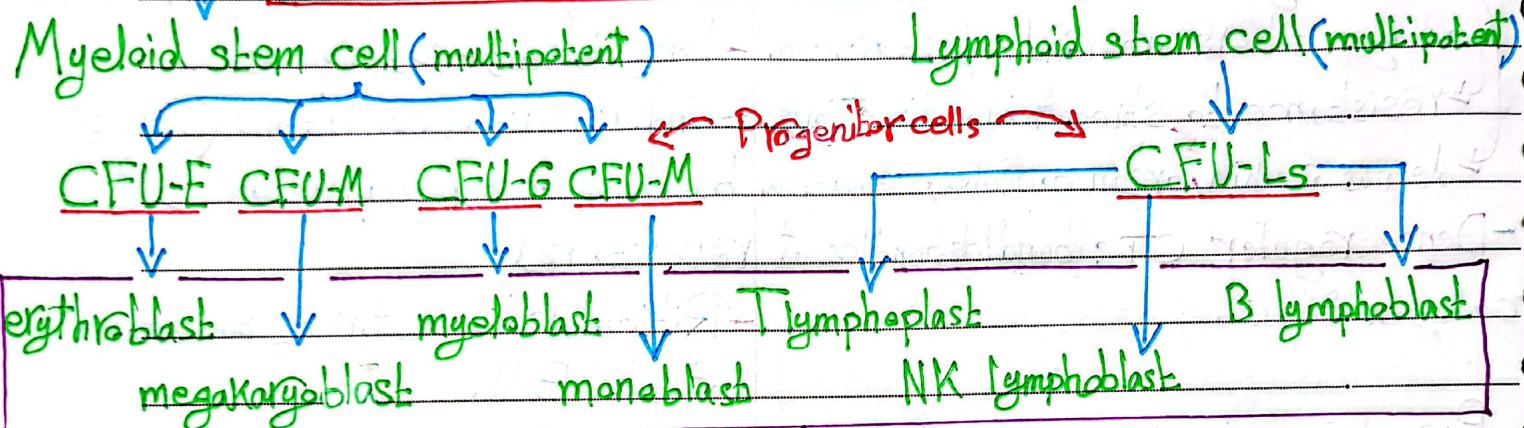
- Reticular tissue forming the stroma of the BM.

- Between the hematopoietic cells run the sinusoids.

- Defective erythrocytes undergo phagocytosis by macrophages in the red BM.

Hematopoietic stem cell (Pluripotent)

Stem cells are capable of asymmetric division & self renewal maintain original population
 stem cell → RBCs
 stem cell



progenitor cells & committed, unipotent stem cells.

"precursor cells"
 ↓ produce only :
 Mature blood cells

- Stem cells & progenitor cells cannot be morphologically distinguished & resemble large lymphocytes.

- Rate of division : in stem cells : slow
 in progenitor & precursor cells : rapid

Erythropoiesis (takes 1 week)

* decreasing cell size
 * progressive loss of organelles
 * progressive increase in Hb content (nucleus became darker)

- Proerythroblast : large pale nucleus, prominent nucleolus/pale basophilic cytoplasm.
- Basophilic erythroblast : deeply basophilic cytoplasm
- Polychromatophilic erythroblast : cytoplasm become violet
- Normoblast (acidophilic erythroblast) : cytoplasm is acidophilic
- Reticulocyte : immature RBC, No nucleus, can produce Hb, contains remnants of ribosomes forming reticulum, can be stained by supravital stains

(brilliant cresyl blue), 1% of all RBCs in the blood stream, circulate for 1-2 days then
 - Erythrocyte ←