BONE MARROW:

Bone marrow and adipocytes are found in the medullary canals of long bones and in the cavities of cancellous bones.

Types of bone marrow :

I-Red bone marrow, whose color is produced by an abundance of blood and hemopoietic cells.

A-Red bone marrow is composed of a **stroma hemopoietic cords** or **islands** of cells**,** and **sinusoidal capillaries.** The stroma is a meshwork of specialized fibroblastic cells called reticular or adventitial cells and a delicate web of reticular fibers supporting hemopoietic cells and macrophages.

B-Sinusoids are formed by a thin layer of endothelial cells. Differentiated blood cells from the hemopoietic cords enter the circulation by passing through openings in the endothelium .

C- Red bone marrow is also a site where macrophages phagocytose worn-out erythrocytes and store iron derived from hemoglobin breakdown.

II- Yellow bone marrow, which is filled with a dipocytes and essentially excludes hemopoietic cells.

A-In the newborn, all bone marrow is red and active in blood cell production, **but** as the child grows most of the marrow changes gradually to the yellow variety.

B-Under certain conditions, such as severe bleeding or hypoxia, yellow marrow reverts to red.

C-The matrix of bone marrow also contains collagen type I, proteoglycans, fibronectin, and laminin, the latter glycoproteins interacting with integrins to bind cells to the matrix.

MATURATION OF ERYTHROCYTES :

Changes in erythrocyte maturation:

1-Cell and nuclear volume decrease, and the nucleoli diminish in size and disappear.

2- The chromatin becomes increase denser until the nucleus presents a pyknotic appearance and is finally extruded from the cell.

3-There is a gradual decrease in the number of polyribosomes (basophilia decreases), with a simultaneous increase in the amount of hemoglobin (an acidophilic protein) within the cytoplasm.

4-Mitochondria and other organelles gradually disappear.

Steps of erythrocytes maturation:

1-The first recognizable cell in the erythroid series is the **proerythroblast,** a large cell with loose, lacy chromatin, nucleoli, and basophilic cytoplasm.

2-The next stage is represented by the **basophilic erythroblast**, with more strongly basophilic cytoplasm and a condensed nucleus with no visible nucleolus. The basophilia of these two cell types is caused by the large number of polyribosomes synthesizing hemoglobin.
3- During the next stage cell volume is reduced, polyribosomes decrease and some cytoplasmic areas begin to be filled with hemoglobin, producing regions of both basophilia and acidophilia in the cell, now called a **polychromatophilic erythroblast.**
4- In the next stage, the cell and nuclear volumes continue to condense and no basophilia is evident, resulting in a uniformly acidophilic cytoplasm—the **orthochromatophilic erythroblast**.
5- Late in this stage, this cell ejects its nucleus which is phagocytosed by macrophages. The cell still has a small number of polyribosomes that, when treated with the dye brilliant cresyl blue, form a faintly stained network and the cell is called the **reticulocyte**. Reticulocytes pass to the circulation, where they may constitute 1% of the red blood cells, lose the polyribosomes and quickly mature as erythrocytes.

MATURATION OF GRANULOCYTES:
Changes in granulocytes maturation:
1-Granulopoiesis involves cytoplasmic changes dominated by synthesis of proteins for the **azurophilic granules** and **specific granules.**
2-These proteins are produced in the rough endoplasmic reticulum and the prominent Golgi apparatus in two successive stages .
3-The azurophilic granules, which contain lysosomal hydrolases, stain with basic dyes, and are somewhat similar in all three types of granulocytes, are made first.
4-Golgi activity then changes to produce proteins for the specific granules, whose contents differ in each of the three types of granulocytes and endow each type with certain different properties.

Steps of granulocytes maturation:
1- The **myeloblast** is the most immature recognizable cell in the myeloid series .It has a finely dispersed chromatin, and faint nucleoli.
2-In the next stage,the **promyelocyte** is characterized by its basophilic cytoplasm and azurophilic granules containing lysosomal enzymes and myeloperoxidase. Different promyelocytes activate different sets of genes, resulting in lineages for the three types of granulocytes.
3-The first visible sign of differentiation appears in the **myelocytes**, in which specific granules gradually increase in number and eventually occupy most of the cytoplasm at the metamyelocyte stage.

4-These neutrophilic,basophilic, and eosinophilic metamyelocytes mature with further condensations of the nuclei. Before its complete maturation the neutrophilic granulocyte passes through an intermediate stage, the **stab** or **band cell**, in which its nucleus is elongated but not yet polymorphic.
5- The total time taken for a myeloblast to emerge as a mature, circulating neutrophil is about 11 days.

MATURATION OF AGRANULOCYTES:

Monocytes:

1-The **monoblast** is a progenitor cell that is identical to the myeloblast in its morphologic characteristics. Further differentiation leads to the **promonocyte,** a large cell with basophilic cytoplasm and a large, slightly indented nucleus. The chromatin is lacy and nucleoli are evident.
2-Promonocytes divide twice as they develop into **monocytes** . A large amount of rough ER is present, as is an extensive Golgi apparatus in which granule condensation occurs.
3-These granules are primary lysosomes, which are observed as fine azurophilic granules in blood monocytes.
4-Mature monocytes enter the blood stream, circulate for about eight hours, and then enter tissues where they mature as **macrophages** and function for several months.

Lymphocytes:

1-The first identifiable progenitor of lymphoid cells is the **lymphoblast,** a large cell capable of dividing two or three times to form **prolymphocytes.**
2-Prolymphocytes are smaller and have relatively more condensed chromatin but none of the cell-surface antigens that mark T or B lymphocytes.
3-In the bone marrow and in the thymus, these cells synthesize cell-surface receptors characteristic of the B or T lymphocyte lineages.

ORIGIN OF PLATELETS:

In adults, the membrane-enclosed cell fragments called platelets originate in the red bone marrow by dissociating from mature **megakaryocytes**, which in turn differentiate from **megakaryoblasts** in a process driven by **thrombopoietin.**

Megakaryocytes:

Megakaryocytes are giant cells, with irregularly lobulated polyploid nuclei, coarse chromatin, and no visible nucleoli. Their cytoplasm contains numerous

mitochondria, a well-developed rough ER, and an extensive Golgi apparatus from which arise the conspicuous specific granules of platelets, or thrombocytes.

Steps of platelets maturation:

1-To form platelets, megakaryocytes extend several long branching processes called **proplatelets**. These extending proplatelets penetrate the sinusoidal endothelium and appear as long processes disposed lengthwise with the blood flow in these vessels .

2-The proplatelet framework consists of actin filaments and a loose bundle of mixed polarity microtubules along which organelles, membrane vesicles, and specific granules are transported.

3- A loop of microtubules forms a teardrop-shaped enlargement at the distal end of the proplatelet and cytoplasm within these loops is pinched off to form platelets with their characteristic marginal bundles of microtubules, vesicles and granules.

4- Proplatelet elongation and Mature megakaryocytes have numerous invaginations of plasma membrane ramifying throughout the cytoplasm, called **demarcation membranes .**Each megakaryocyte produces a few thousand platelets.