Biology

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Bone Marrow:

Is one of the largest organs in the body, it is the main site for hematopoiesis, it is found in the medullary region of long bones & in cavities of cancellous bones. We have two types of bone marrow:

1. red bone marrow: whose color is due to the presence of blood & blood forming cells.
2. yellow bone marrow: whose color is due to the presence of large number of adipose tissue and excludes hemopoietic cells.

In newborns, all bone marrow is red & active, but as the child grows most of the marrow changes to yellow type, but with severe bleeding or hypoxia, yellow marrow reverts to red marrow.

Red bone marrow:

Also called hematopoietic bone marrow, is formed of stroma which is a meshwork of reticular fibers containing the hematopoietic cords & macrophages. Between the hematopoietic cords are very large number of sinusoidal capillaries. The main function of red bone marrow is the production of blood cells & storage of iron derived from breakdown of Hemoglobin.

Hematopoiesis

Mature blood cells have a short life span & they must be continuously replaced by proliferation of stem cells that are found in the hemopoietic organs. In the earliest stages of development, blood cells arise from the yolk sac mesoderm. In the second trimester, the liver and spleen will act as a temporary hematopoietic organs. From the third trimester, the bone marrow will become an increasingly important hematopoietic tissue. At birth the bone marrow will be the main site of hematopoiesis.

Stem cells:

All blood cells arise from a single type of cells found in the bone marrow called stem cells and because these cells are able to produce all blood cell types they are called pluripotential stem cells. These cells will divide continuously to maintain their number within the bone marrow & some of the daughter cells will differentiate and mature into various types of blood cells.

Stem cells will proliferate and differentiate in two ways:

1. where the cells will eventually become lymphocytes (lymphoid cells)
2. where the stem cells will form the myeloid cells that will develop in the bone marrow leading eventually to the formation of erythrocytes, granulocytes, monocytes & megakaryocytes.

- Progenitor cells (colony-forming units(CFUs)):

Stem cells will proliferate to produce the progenitor cells, however the progenitor cells are still so similar to stem cells so they cannot be distinguished morphologically & both are similar to lymphocytes in shape. The progenitor cells will be named after the cell which will be formed eventually. So we have:

- Lymphoid lineage of CFU-lymphocytes of all types (CFU-L).
- Erythroid lineage of CFU-erythrocytes (CFU-E).
- Thrombocytic lineage of CFU-megakaryocytes (CFU-Meg).
- Granulocyte-monocyte lineage of CFU-granulocytes-monocytes (CFU-GM).

The progenitor cells will divide continuously to form more progenitor cells & to form precursor cells. Hematopoietic growth factors called colony-stimulating factors (CSF) are proteins with complex functions:

1. Stimulating proliferation (mitogenic activity) of immature progenitor & precursor cells.
2. Supporting differentiation of maturating cells.
3. Enhancing the functions of mature cells.

e.g. granulocyte (G-CSF), Erythropoietin (EPO), thrombopoietin (TPO) which are important clinically to increase marrow cellularity and blood cell counts in immunodeficient diseased conditions, BM transplant and malignancies.

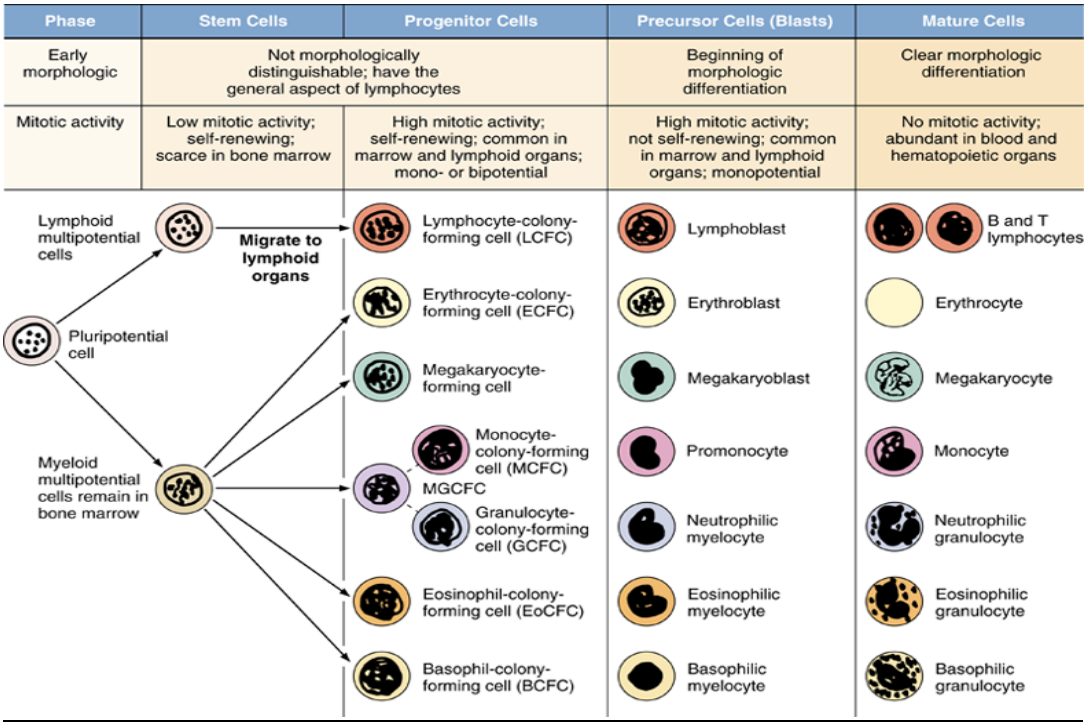
- Precursor cells: (blast cells)

In these cells the morphologic characteristics will differentiate for the first time suggesting the cell types they will become.

Additional information:

Are stem cells only present in embryos?

Actually, this is a common misconception brought on by a media focus on embryonic stem (ES) cells. In reality, any actively dividing tissue requires a form of stem cell to act as the original source of cells. The difference is that many ES cells are totipotent—meaning that they retain the ability to form almost any type of cell—though most adult stem cells are pluripotent. Pluripotent cells have undergone an additional stage of specialization and, therefore, can only produce a limited variety of new cell types.

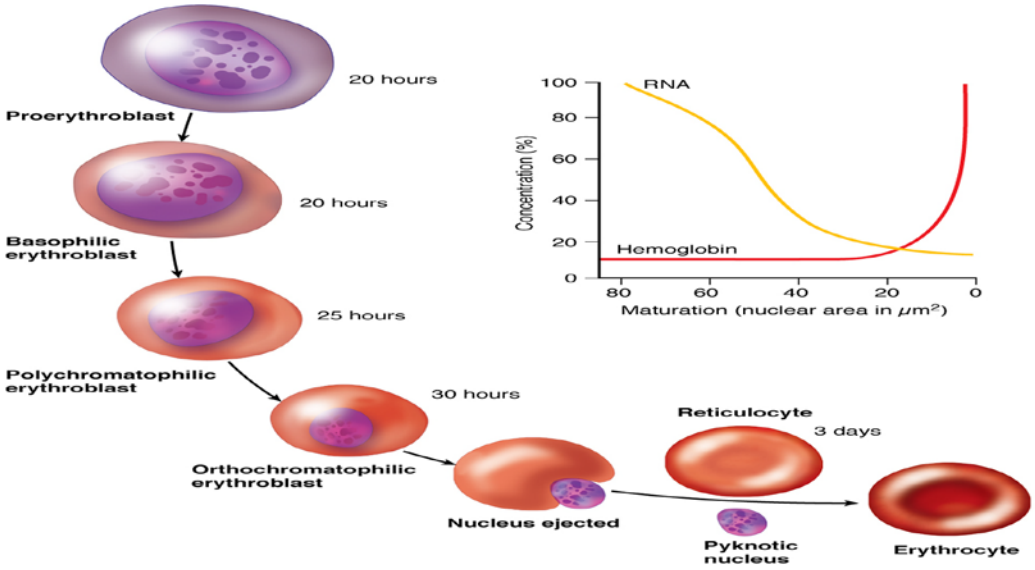


Erythropoiesis:

During formation of erythrocytes several changes will occur in the precursor cells so the cell volume will decrease nucleolus will decrease in size until it is invisible, nucleus also decrease in size and finally extruded from the cell, at the same time there will be increase in the amount of hemoglobin within the cytoplasm. So the formation of erythrocyte involve the formation of:

- proerythroblast: large cell, large round or oval nucleus occupies most of the cell with prominant nucleoli, with thin rim of basophilic cytoplasm.
- basophilic erythroblast: smaller in size, smaller round nucleus, more strong basophilia due to abundance of polyribosomes synthesizing hemoglobin.
- polychromatophilic erythroblast: contain both regions of basophilia and acidophilia.
- normoblast (orthochromatophilic erythroblasts): small size, small round nucleus, acidophilic cytoplasm, this cell eject its nucleus which phagocytosed by macrophages. The cell still has a small no. of polyribosomes that stained blue.
- Reticulocytes: contain polyribosomes network, pass to the circulation and constitute 1% of RBC and then loss the polyribosomes and quickly mature to erythrocytes.

the process of development of RBC from the proerythroblasts into the release of reticulocytes into the circulation takes about 7 days & it is under control of the hormone erythropoietine.



Clinical correlation:

Increasing reticulocyte count (reticulocytosis) in the circulation (i.e. > 1%) indicating an underlining condition of acute blood loss (hemolytic anemia or hemorrhage) in which high production of red blood cells is needed to replace the loss resulting in increasing immature red blood cells in the circulation because of active bone marrow.