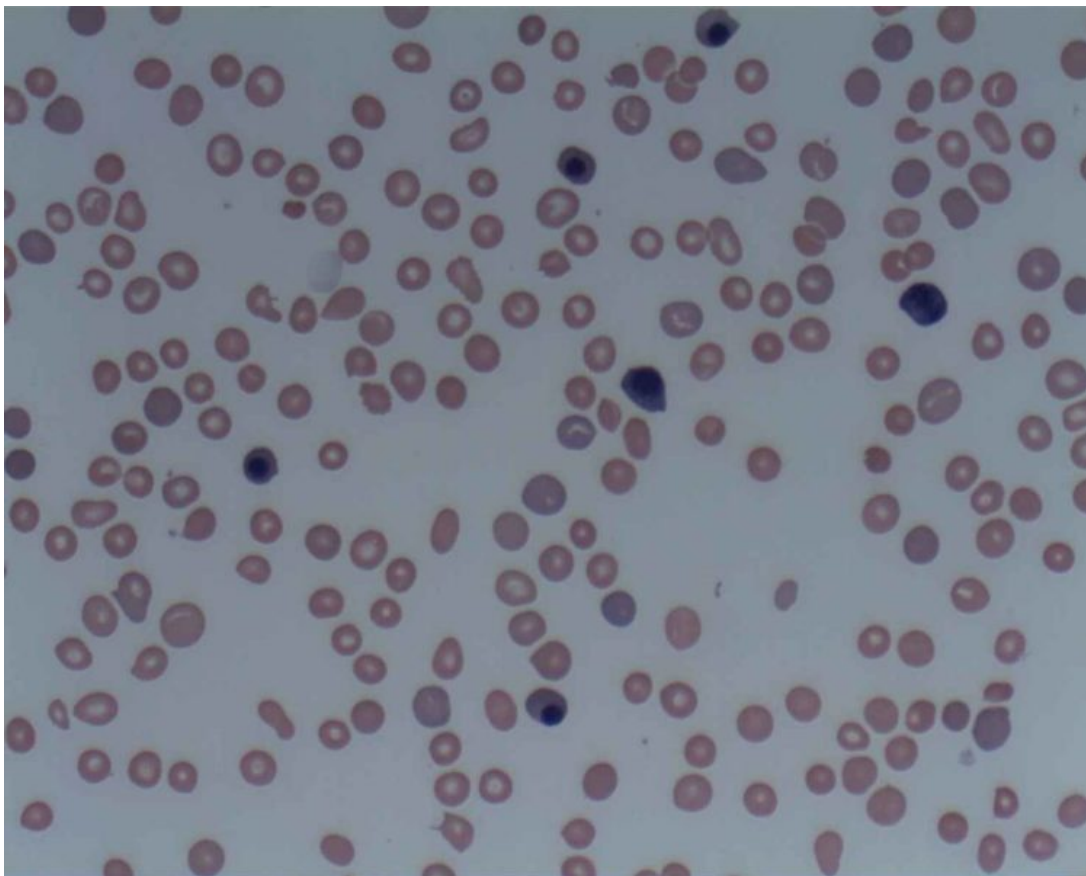


Connective Tissue: Bone Marrow and Hematopoiesis

[See online here](#)

Bone marrow is the type of tissue in the marrow cavities of bones where blood cells are formed and later released into the circulation. The process of production of blood cells is called hematopoiesis. This includes erythropoiesis (the production of red blood cells), leucopoiesis (the production of white blood cells) and thrombopoiesis (the production of platelets).



Hematopoiesis

Hematopoiesis is the production of all the blood cells including RBCs, WBCs, and platelets. **Bone marrow** is the major site of hematopoiesis. As the RBCs and platelets have a limited life span, they need to be replaced continuously. The **pluripotent stem cell**, also called the **hematopoietic stem cell**, is the main type of cell that differentiates into all the blood cell lines.

Hematopoietic stem cells (HSCs) are located in the **medulla of the bone marrow**. They have the ability to differentiate into all of the mature blood cell types and tissues.

Along with **differentiation**, these cells also **renew themselves**.

As they proliferate, one of the daughter cells remains as HSC, which is a process referred to as **asymmetric division**. Other daughter cells include **myeloid** and **lymphoid progenitor cells** which follow the other differentiation pathways but cannot renew themselves. This is one of the main processes in the body.

Sites of Hematopoiesis

Initially, blood formation occurs in clusters that are aggregated in the **yolk sac**, called the **blood islands**. In later stages, this process moves to the **spleen**, **liver** and **lymph nodes**. With the growth and development of bone marrow, the whole process is shifted to the marrow.

Still, the maturation, activation and some proliferation of the lymphoid cells occur in the spleen, thymus and lymph nodes later in life. In children, this process occurs in the long bones, such as the femur and tibia, while in adults it occurs in the pelvis, cranium, vertebrae, and sternum. In some cases, the extra-medullary sites also start the process of hematopoiesis at a later point in life. This process is called **extra-medullary hematopoiesis**.

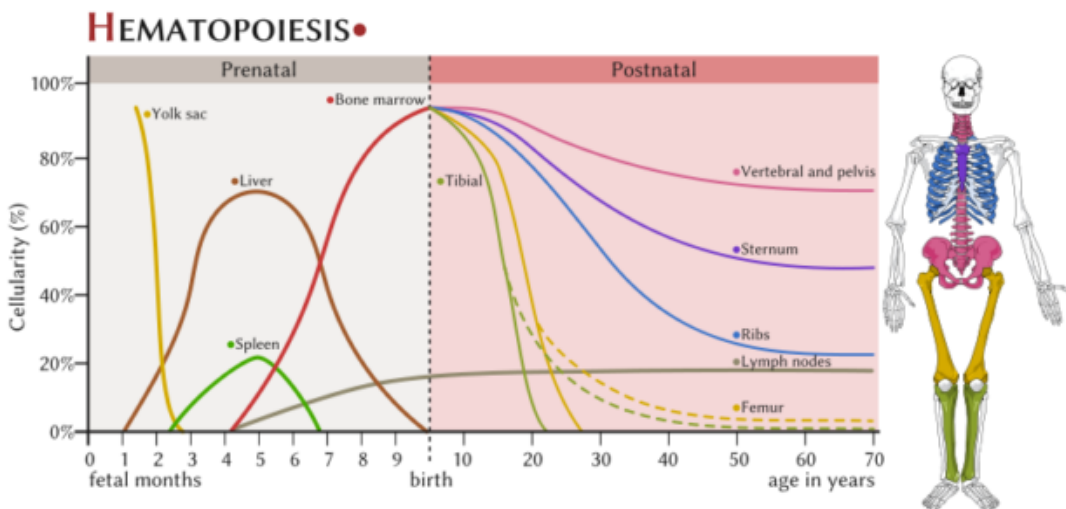


Image: "Sites of hematopoiesis," by Michał Komorniczak (Poland). License: [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

Various blood cell lines are:

Erythroid cells: These include red blood cells that carry oxygen. Premature RBCs (reticulocytes) and mature RBCs (erythrocytes) are released into the blood. The reticulocyte count is used clinically to estimate the rate of **erythropoiesis** in the body.

Lymphocytes: These are the major constituents of the body's immune system. They have common lymphoid progenitors. The lymphoid lineage includes T-cells, B-cells and NK cells (natural killer cells), and their production is called **lymphopoiesis**.

Myelocytes: The myeloid progenitor cells differentiate further under the influence of cytokines and growth factors like CSF (colony-stimulating factors). These consist of **granulocytes**, **megakaryocytes**, and **macrophages**. They are derived from a common myeloid progenitor and play a major role in the process of **innate immunity**, adaptive immunity, and blood clotting. Production of these cells is called **myelopoiesis**.

Granulopoiesis (or granulocytopoiesis) is the differentiation or production of granulocytes.

Megakaryocytopoiesis is the production of megakaryocytes.

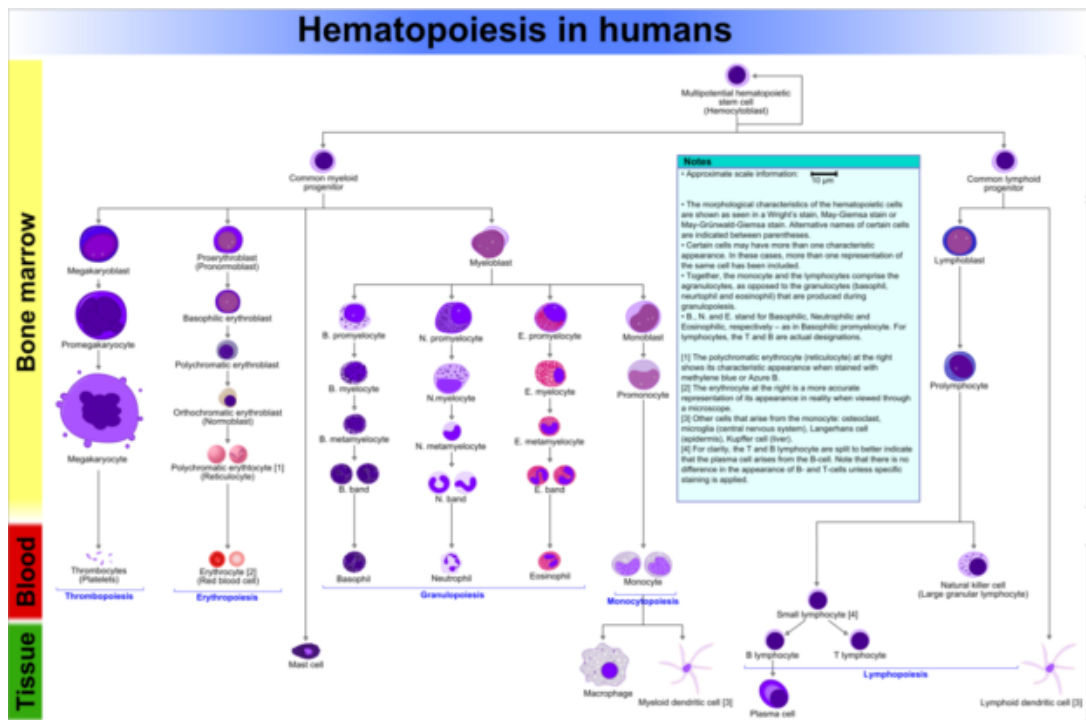


Image: "This diagram shows the hematopoiesis as it occurs in humans," by A. Rad - Own work. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Erythropoiesis

Erythropoiesis is the production of RBCs. Decreased oxygen in the blood stimulates the production of erythropoietin in the [kidneys](#), which promotes the process of erythropoiesis in the bone marrow. In newborns this process occurs in the [liver](#); later, with the maturation of bone marrow until the seventh month of life, erythropoiesis starts in the bone marrow.

Erythrocyte differentiation

The following stages of development occur within the bone marrow:

Initially, the **hemocytoblast**, which is the multipotent hematopoietic stem cell, becomes a **unipotent stem cell**. It later differentiates into a **pronormoblast**, also called proerythroblast. These precursor erythrocytes further differentiate into a basophilic cell named **early normoblast** (also called erythroblast), then into an **intermediate normoblast**, and later into **late normoblast**.

At this stage, the nucleus is expelled before the cell becomes a **reticulocyte**. These new precursor cells are released into the [circulation](#) and make about 1% of the total RBC count. After 1-2 days, reticulocytes are converted into **erythrocytes**.

Proerythroblasts have mild basophilia and are of size 12-20 µm in diameter.

Basophilic erythroblasts have strong basophilia and are of 10-15 µm in diameter.

Polychromatophilic erythroblasts are smaller, 12-20 µm in diameter.

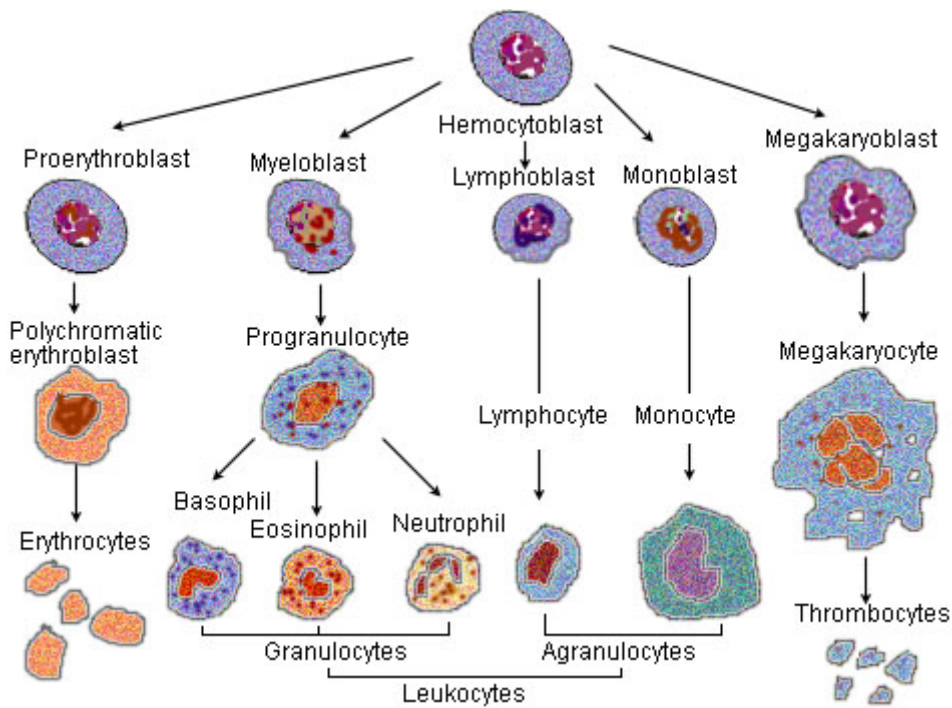


Image: "Erythropoiesis." License: Public Domain

Thrombopoiesis

The process of thrombocyte production is called thrombopoiesis. Platelets are fragmentations of special cells called **megakaryocytes**. A single megakaryocyte can give rise to thousands of thrombocytes. Like erythropoietin, **thrombopoietin** stimulates megakaryopoiesis.

Megakaryopoiesis refers to megakaryocyte maturation and differentiation. Intracellular signaling on the stimulation of thrombopoietin promotes megakaryocyte growth and maturation. It also enhances membrane stability and promotes platelet granule formation. The cytoplasm of the megakaryocytes defines regions that fragment into mature platelets. This last step of a pro-platelet process and platelet formation is independent of thrombopoietin.

Granulopoiesis

The main output of this process is a **neutrophil**. It starts with a **myeloblast** which differentiates into a **neutrophilic promyelocyte**. These promyelocytes are relatively larger cells with purple-staining azurophilic granules (this is why they are called granulocytes).

Promyelocytes differentiate into **myelocytes**. The presence of small specific or secondary granules is specific for myelocytes. The number of specific granules per cell is increased during this stage while the number of azurophilic granules per cell decreases. As a result, cytoplasmic basophilia is gradually lost. The production of granules stops by the end of the myelocyte stage.

In the later stages, a reduction in cell size and a change in nuclear shape occur. When the nucleus becomes flattened and the chromatin is condensed, the cell is called a **metamyelocyte**. When the nucleus becomes horseshoe-shaped, it is called a **band cell**.

The cell is considered a **mature neutrophil** when the nucleus becomes segmented into lobes.

Applied Conditions

Bone marrow can get affected by various conditions, for example, malignancies, infections such as tuberculosis, exposure to harmful rays such as X-rays, and strong chemicals. These factors derange blood cell production in bone marrow. Many underlying causes need to be diagnosed accurately using a **bone marrow biopsy**.

Bone marrow biopsy is done by **bone marrow aspiration under local or general anesthesia**. Common sites for aspiration are iliac crest or sternum, in case of children it can be done from the upper part of the tibia.

References

[Hematopoiesis](#) via cshlp.org

[Hematopoiesis](#) via nih.gov

[Thrombopoiesis](#) via nih.gov

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