Biology

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Granulopoiesis:

In sections of bone marrow, cords of granulopoietic cells can be distinguished by their granule-filled cytoplasm from erythropoietic cords.

Myeloblast: a large cell with finely dispersed chromatin & visible nucleoli.

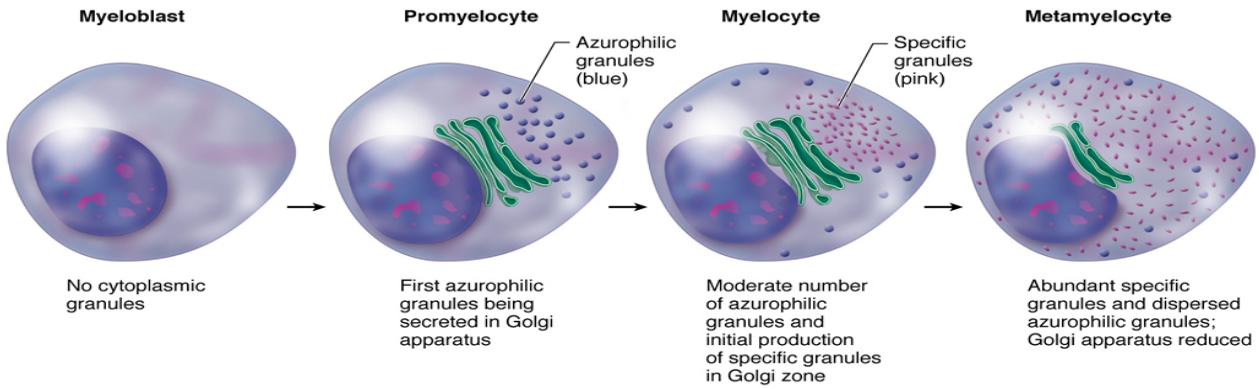
Promyelocyte: a cell with basophilic cytoplasm filled with azurophilic granules. This cell gives rise to 3 types of cells:

Myelocyte (neutrophilic, eosinophilic, basophilic): these cells have ↓ number of azurophilic granules & ↑ number of specific granules that stain according to the type of granulocyte. In more mature myelocytes, the nucleus is further condensed, the cytoplasm is filled with specific granules & has no azurophilic granules.

Metamyelocyte (neutrophilic, eosinophilic & basophilic): the nucleus is more condensed, has a restriction but not fully lobulated.

Band cell (only in neutrophilopoiesis): the nucleus resembles a curved rod.

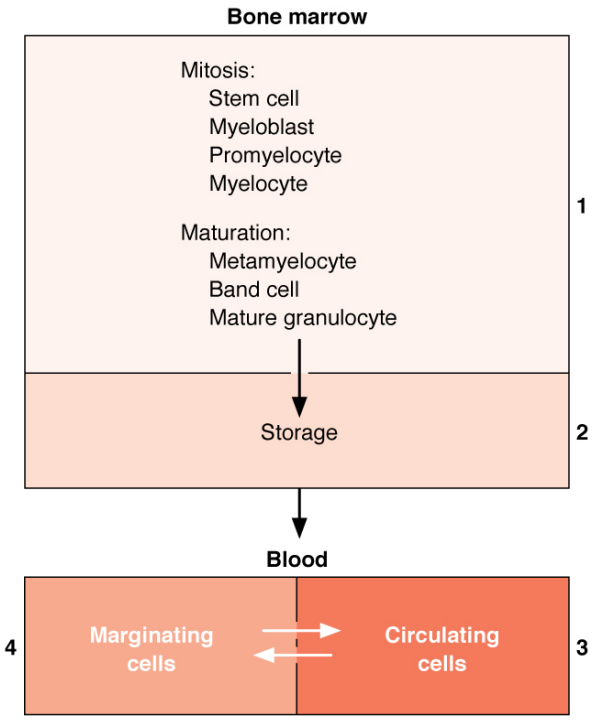
Mature granulocyte: the nuclei are lobulated (with fine chromatin threads joining lobules) or S-shaped. Specific granules fill the cytoplasm.



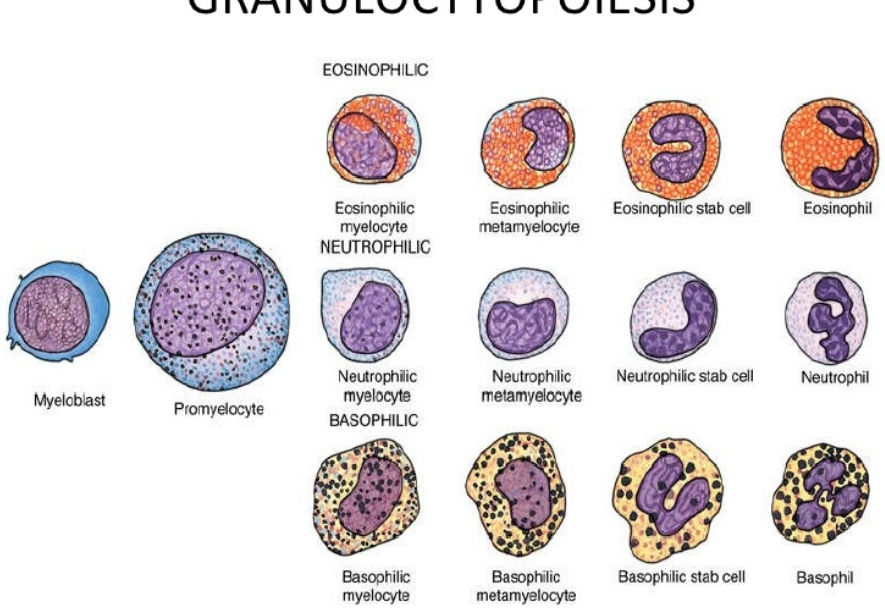
The vast majority of granulocytes are neutrophils. The total time taken for a myloblast to become mature is about 11 days.

The developing and mature neutrophils were exist in 5 functionally and anatomically defined compartments:-

1. Granulopoietic compartment in marrow.
2. Storage as mature cells in marrow until release.
3. The circulating population.
4. Marginating population of cells adhering to endothelial cells of post capillary venules and small veins.
5. Connective tissue by migrating through intercellular junction between endothelial cells of post capillary venules where they remain for few days and then die whether they perform their function or not.



The top row represents the eosinophilic cell line, the middle row represents the neutrophilic line, and the bottom row represents the basophilic line. Note the decrease in cell size, the decrease in cytoplasmic basophilia (meaning decrease in polyribosomes), the increase in cytoplasmic granules (these first become specific and distinguishable as eosinophilic or basophilic at the myelocyte stage), and an increase in lobulation of the nucleus.



Agranulopoiesis:

Monocytes:

- monoblast is the progenitor cell which is identical to myeloblast.

- further differentiation to promonocyte (large cell with basophilic cytoplasm and large nucleus with evident nuclei) which divide twice and develop monocytes.
- mature monocytes enter the blood stream, circulate for about 8 hours then enter tissues where they mature as macrophages.

Lymphocytes:

All lymphocyte progenitor cells originate in the bone marrow. Some of these migrate to the thymus where they become T lymphocyte. Other bone marrow lymphocyte differentiate in to B lymphocytes in the bone marrow and then migrate to peripheral lymphoid organs. The first identifiable progenitor of lymphoid cells is the lymphoblast (large cell) divided to form prolymphocytes (smaller and have more condensed chromatin). In the bone marrow and in the thymus, these cells synthesize cell surface receptors characteristic of B or T lymphocyte.

Clinical correlation:

1. Abnormal stem cells in bone marrow can produce diseases based on cells derived from that tissue. Leukemias are malignant clones of leukocyte precursors. They occur in lymphoid tissue (lymphocytic leukemias) and in bone marrow (myelogenous and monocytic leukemias). In these diseases, there is usually a release of large numbers of immature cells into the blood. Some symptoms of leukemias are a consequence of this shift in cell proliferation, with a lack of some cell types and excessive production of others. The patient is usually anemic and prone to infection.
2. Presence of band cells (immature neutrophils) in the peripheral blood (bandemia) is suggestive of bacterial infection requires moving all the mature & the immature neutrophils into the circulation to fight back the infection.

Megakariocytopoiesis:

Platelets originate from megakariocyte by numerous invaginations of plasma membrane that ramify throughout the cytoplasm, forming the demarcation membranes, which represent the lines of separation of cytoplasmic fragments that form platelets. Megakariocytes arise from the differentiation of megakarioblast (very large size, basophilic cytoplasm, very large rounded nucleus) in the bone marrow.

In certain forms of **thrombocytopenic purpura**, a disease in which the number of blood platelets is reduced, the platelets appear to be bound to the cytoplasm of the megakaryocytes, indicating a defect in the liberation mechanism of these corpuscles. The life span of platelets is approximately 10 days.

Bone Marrow Aspiration and Biopsy

- Bone marrow **aspiration** removes a small amount of bone marrow fluid and cells through a needle put into a bone. The bone marrow fluid and cells are checked for problems with any of the blood cells made in the bone marrow. Cells can be checked for chromosome problems. Cultures can also be done to look for infection.
- A bone marrow **biopsy** removes bone with the marrow inside to look at under a microscope. The aspiration (taking fluid) is usually done first, and then the biopsy. A bone marrow aspiration can also be done to collect bone marrow for medical procedures, such as stem cell transplant or chromosomal analysis.

Bone Marrow Cellularity

It is the most important indicator of bone marrow function. The assessment of bone marrow cellularity represents the ratio of hemopoietic cells to adipocytes obtained from the microscopic examination of a bone marrow biopsy that preserves the general organization of the marrow (bone marrow smear is less accurate than biopsy in assessing cellularity).

Marrow cellularity changes with age. Normal bone marrow cellularity for a specific age can be calculated as follows:

Bone marrow cellularity index (%)= 100 – age ± 10%

For example; a 30 year old individual's bone marrow contains 60-80% of active-producing cells; in contrast, a 70 year old individual's marrow got 20-40% active cells.

The number of hemopoietic cells decreases with age, so any deviation from age-specific normal index indicates pathologic (abnormal) change in bone marrow.

In hypocellular bone marrow, occurs in aplastic anemia or after chemotherapy, only small number of blood forming cells can be found in marrow biopsy (thus, a 50 yr old individual with this condition might have BM cellularity index of 10-20%).

Hypercellular bone marrow is characteristic of bone marrow affected by tumor from hemopoietic cells, such as a 50 yr old individual with a cellularity index of 80-90% is likely to have leukemia and the abnormal cells occupying most of the BM).