LEC.14

ORIGIN AND DEVELOPMENT OF GRANULOCYTES

Granulocytes develop in the bone marrow from undifferentiated stem cells. Maturation of the granulocytic series of cells is characterized by the development of granules. Granules are initially formed in the progranulocytes and are called **"primary or azurophil" granules**. The maturation sequence continues, the primary or azurophil granules lose their acid mucopolysaccharide and, therefore, will not stain with Wright's stain. However, the myelocyte stage is characterized by the appearance of "specific" or secondary granules that persist throughout the maturation process. Cells which have granules with an affinity for blue or basic dye are identified as basophils; cells that are stained reddish-orange with the acid dye eosin are called eosinophils; and the cells with granules which do not stain intensely with either dye are called neutrophils.

GRANULOCYTE MATURATION SEQUENCE :

Several different developmental stages of granulocytes can be recognized morphologically. The stages are:

1- Myeloblast .
2- Progranulocyte.
3- Myelocyte -- Basophil, eosinophil, neutrophil .
4- Metamyelocyte -- Basophil, eosinophil, neutrophil .
5- Band Cell -- Basophil, eosinophil, neutrophil .
6- Segmented Cell -- Basophil eosinophil, neutrophil .

1 - MYELOBLAST :

1- The first cell that can be recognized in the granulocytic series.
2 - It is the most immature granulocytic precursor.
3 - The cell possesses a relatively large round to oval nucleus, with one to several nucleoli.
4 - The chromatin material of the nucleus is finely stippled or has a light ground glass appearance.
5 - The cytoplasm is somewhat scanty, basophilic, and does not contain granules.

2 - PROGRANULOCYTE :

1- The nuclear chromatin material is coarser and slightly more clumped than that of a myeloblast.
2- Remnants of the nucleoli may still be present.
3- The cytoplasm is less basophilic than the myeloblast

and contains darkly stained non-specific granules called "**primary or azurophilic granules.**" These granules are peroxidase positive.

3 - MYELOCYTE :

1- The nucleus of the myelocyte remains somewhat round to oval and the chromatin material is more closely clumped.
2- This cell contains **"secondary"** or specific granules that are identified by their staining properties as neutrophils, eosinophils, and basophils. These granules are peroxidase negative.
3- The myelocyte and all subsequent cells of the granulocytic series should be characterized as neutrophils, eosinophils and basophils.
4- These granules vary greatly in shape, size and concentration in family species.
5- As maturation of the granulocytes continue, the **"specific granules"** will increase and the **"azurophilic granules"** will not take the Wright's stain.
6- The myelocyte stage is the last stage of cell division and the first cell capable of phagocytosis.

4 - METAMYELOCYTE :

1- This cell closely resembles the myelocyte.
2- The nucleus often resembles a kidney bean.
3- Nucleoli are not present and the nuclear chromatin material is coarser and clumped.
4- Cytoplasmic granules are also present.

5 - BAND CELL :

1- This cell has a horseshoe shaped nucleus.
2- The opposite sides of the nucleus are more or less parallel.
3- This cell may be differentiated from the metamyelocyte by the nuclear shape and the tendency for the nuclear sides to become parallel.
4- The nuclear chromatin material is markedly clumped.

6 - SEGMENTER CELL :

The nucleus may be mono-lobed with clumped chromatin material, or may consist of several lobes separated by constrictions or by filaments. The cytoplasm stains very faintly.

LEUKOCYTE LYSOSOMES :

The term lysosome is used to describe intracellular membranous sacs containing acid hydrolytic enzymes. When leukocytes phagocytize,

there is a release of lysosomal contents. Primary granules (**azurophil granules**) contain acid phosphatase, acid hydrolytic enzymes, basic protein and one-third of the lysozyme. Secondary granules (**specific granules)** contain alkaline phosphatase, lactoferrin and two-thirds of the lysozyme.

ORIGIN AND DEVELOPMENT OF AGRANULOCYTES

The agranulocytic series is comprised of leukocytes devoid of specific granulation. These cells generally originate in the lymphatic system, but like the granulocytic series, they may be produced in another place in the body. This series includes the lymphocytic and monocytic groups.

LYMPHOCYTIC MATURATION SEQUENCE :

The lymphocytic series refers to the development of the lymphocytes. The cells arise mainly from the reticular tissue of the lymph nodes and lymphoid tissue from which they derive their name. Lymphocytes are the most undifferentiated of all blood cells normally found in the peripheral blood. The nucleus does not become segmented and specific granules do not develop. Therefore, lymphocytes are **"peroxidase negative".** The lymphocyte cytoplasm does not develop past the blue stage.

The stages in lymphocytic development are:

1. Lymphoblast
2. Prolymphocyte
3. Lymphocyte

1 - LYMPHOBLAST :

1- Cell is similar to other blast cells. It is round or oval, very large, with a large round to oval reddish-purple nucleus.
2- The nuclear chromatin material is fine and well distributed but perhaps more coarse than in myeloblasts.
3- The nucleus contains one or two nucleoli.
4- The cytoplasm is bluish and nongranular and forms a thin rim around the nucleus.

2 - PROLYMPHOCYTE :

1- The nucleus is round or oval in shape but smaller than the lymphoblast.
2- The nuclear chromatin is coarse and slightly clumped.
3- Nucleoli or remnants of nucleoli may be present.
4- There is an rich amount of light blue cytoplasm around the nucleus. Also, there may be a few azurophilic granules in the cytoplasm.

3 - LYMPHOCYTE :

This is the mature cell of the lymphocytic series and the only cell form found in the peripheral blood in health.

Lymphocytes vary greatly in size and may be classified as small, medium or large. However, size does not determine age of these cells.

The cells are easily distorted and often appear in irregular shapes in stained preparations. The nuclear chromatin is condensed to form large, discrete almost solid clumps, with thickening of the nuclear membrane. Nucleoli are absent. Non specific granules may be observed in the cytoplasm of these cells.

MONOCYTIC MATURATION SEQUENCE

The monocytic series refer to the stages of development of the monocyte. These cells may be formed from RE cells. One of the most important sites of origin is the spleen.

The stages in the monocytic development are:

1. Monoblast
2. Promonocyte
3. Monocyte

1 - MONOBLAST :

The cell is large with a round or oval nucleus. A nucleolus is present. The nuclear chromatin material is fine and well-distributed. There is a thin rim of clear blue cytoplasm around the nucleus. There are no granules present in the cytoplasm.

2 - PROMONOCYTE :

The cell is somewhat smaller than the monoblast with the nucleus being irregularly-shaped.The nuclear chromatin material is fine and spongy. There may be a nucleolus or a remnant of the nucleolus present. The cytoplasm is grayish blue and may contain non-specific granules.

3 - MONOCYTE :

The cell is larger than a neutrophil in the thin portions of a smear. The shape of monocytes is variable.The nuclei are usually round or kidney-shaped, but may be deeply indented or have two or more lobes connected by narrow bands. Blunt pseudopods and digestive vacuoles may be present. Monocytes are most difficult to identify and to differentiate from other cells. They are frequently mistaken for immature neutrophils and large lymphocytes.The three most characteristic features of the monocytes and the most helpful in diagnosis are the dull grayish-blue color of the cytoplasm, blunt pseudopods and the brain-like convolution of the nucleus.

ORIGIN AND DEVELOPMENT OF Thrombocytes/platelets

Cells of the megakaryocytic system are peculiar in that the nucleus undergoes multiple mitotic divisions without cytoplasmic separation, thus producing giant polyploid cells. The multiple nuclei usually remain attached to each other and are often superimposed giving a lobular appearance. The cytoplasm undergoes maturation changes characterized by the development of granules and membranes, culminating in platelet differentiation and liberation.

The stages in thrombocyte development are:

1. Megakaryoblast
2. Promegakaryocyte
3. Megakaryocyte
4. Thrombocyte **(Platelet)**

1 - MEGAKARYOBLAST :

The cell is large, irregularly shaped with a single or several round or oval nuclei and with a blue, nongranular cytoplasm. Nucleoli are usually present.

2 - PROMEGAKARYOCYTE :

This cell differs from the megakaryoblast in that there are bluish granules in the cytoplasm adjacent to the nucleus. The nucleus in this second stage of maturation has usually divided one or more times and the cell has increased in size.

3 - MEGAKARYOCYTE :

The cell is very large with relatively large amounts of cytoplasm, and multiple nuclei. The cytoplasm contains numerous small, uniformly distributed granules that are reddish-blue in color.

4 - THROMBOCYTE/platelet :

Platelets are fragments of the cytoplasm of megakaryocytes. They vary in size and shape from a barely visible structure to masses larger than red cells or leukocytes. The cytoplasm stains a light blue and contains variable numbers of small blue granules (**azurophilic**).