

Asst. lecturer Sajad A alghazali

M.Sc. Pathology

Leukocyte Disorders

Non-malignant leukocyte disorders:

1- Disorders of neutrophils

The quantitative neutrophil disorders are manifest as an increased number of circulating neutrophils (neutrophilia) and those where the neutrophil count is lower than normal (neutropenia).

Normal variations in neutrophil count:

It is normal for the neutrophil count to rise during:

- **Pregnancy**
- **Immediate post-delivery neutrophil counts are frequently significantly raised.**
- **People of African descent have slightly lower neutrophil and monocyte counts and higher eosinophil counts.**
- **Normal diurnal variation in neutrophil count, with highest levels in the afternoon.**
- **Strenuous exercise is associated with a significant leukocytosis.**

Neutrophilia

Neutrophilia is the body's normal response to bacterial infection. In extreme cases this numerical increase and appearance of immaturity may mimic

leukemia, the so-called "leukemoid reaction", in which very early forms are released from marrow.

Other causes of neutrophilia besides bacterial infections include inflammatory conditions (Crohn's disease, collagen disease, rheumatoid arthritis, etc.), tissue destruction (trauma and surgery, tissue necrosis and infarction, neoplasia), hemorrhage and hemolysis, metabolic abnormalities (e.g. metabolic ketosis, uremia, gout, etc.) and certain drugs (e.g. steroids).

Neutropenia

Neutropenia is defined as a reduction in number of neutrophils in the peripheral circulation below that which is normal for age, gender, ethnicity and taking account of various physiological conditions, including pregnancy and exercise.

Neutropenia may be classified into **mild** (absolute neutrophil count (ANC) 1.0-1.5 x 10⁹/L), **moderate** (0.5-1.0 x 10⁹/L) and **severe** (< 0.5 x 10⁹/L). These categories correspond well to the clinical risk of severe bacterial and fungal infection.

Acquired neutropenia

Bone marrow failure includes both inherited and acquired conditions and is characterized by damage or defect of hematopoietic stem cells or the bone marrow microenvironment. There are many causes of acquired neutropenia, **including:**

1- Infection

Many types of infection are associated with neutropenia, including viral infections (e.g. human immunodeficiency virus {HIV}), severe bacterial infections (e.g. tuberculosis), fungal infections (histoplasmosis), parasitic infections (malaria). The mechanisms vary from direct attack on the hemopoietic mechanisms to increased utilization and destruction.

2- Drug or chemical reactions

Drug-induced neutropenia is more common in patients over the age of 60 years, and women are more commonly affected than men.

3- Latrogenic causes

Neutropenia is consequence of cytotoxic chemotherapy for malignant disease. Also, radiotherapy can have similar effects.

4- Micronutrient deficiencies

Vitamin deficiency such as vitamin B12 and folic acid or copper are frequently associated with neutropenia.

5- Immune mechanisms

Primary autoimmune neutropenia (AIN) is caused by the development of antibodies directed against neutrophil surface antigens, resulting in splenic sequestration and destruction. In adults, AIN usually occurs in patients with other autoimmune conditions such as rheumatoid arthritis and systemic lupus erythematosus.

6- Hematological malignancy

Solid tumors that have metastasized to the bone marrow can be associated with neutropenia due to occupation of the marrow space by malignant cells.

7- Splenomegaly

This disease is often accompanied by a degree of neutropenia due to splenic sequestration crisis (SSC).

Qualitative neutrophil disorders:

1- **Pelger-Huet anomaly**: anomaly inherited in an autosomal dominant and occurring in about 1 in 5000 individuals. **The neutrophil nucleus does not segment** beyond the two-lobed and may also appear round with no segmentation. The presence of excessive coarse **clumping of chromatin** in the **nucleus aids** in the differentiation of abnormal cells.

2- Hypersegmentation

Larger-than-normal neutrophils with six or more nuclear segments (hypersegmented neutrophils) found in megaloblastic anemia. These cells are found together with **pancytopenia** and **macroovalocytes** that typically accompany deficiencies of **folate** or **vitamin B12**.

3- Pyknotic Nucleus

Pyknotic, or degenerating, nuclei are found in neutrophils in blood or body fluid preparations. The nuclear chromatin condenses and the segments disappear, becoming smooth.

4- Dohle bodies

Dohle bodies are light gray-blue oval inclusions in the cytoplasm of neutrophils and eosinophils. Dohle bodies are composed of **aggregates of rough endoplasmic reticulum**. They are often present in conjunction with

toxic granulation. They may be seen in **severe infections, burns and cancer**, and as a result of **toxic drugs**.

5- Toxic granules

The toxic granules are large, deep, black primary granules in the cytoplasm of neutrophils and sometimes in bands. Toxic granulation is found in granulocytes, particularly neutrophils, in patients with inflammatory conditions.

6- Cytoplasmic vacuoles

Cytoplasmic vacuoles appear as clear, unstained areas. Vacuoles probably represent the end of phagocytosis. **They are usually seen in same conditions as toxic granulation and Dohle bodies.**

7- Intracellular organisms

Such as Ehrlichiosis is a tick-borne bacterial infection caused by bacteria of the genera Ehrlichia and Anaplasma. The leukocyte eventually ruptures and releases the organisms that then infect other leukocytes.

Hematological malignancies

Classification of the hematological malignancies

Neoplasm

Neoplasm (tumor) literally means "new growth". Neoplasm arises as a consequence of dysregulated proliferation of a single transformed cell. Genetic mutations in the transformed cell reduce or eliminate the cell's dependence on external growth factors to regulate proliferation.

Neoplasms are either **malignant** or **benign**. **Benign neoplasms** are formed from highly organized, differentiated cells and do not spread or invade surrounding tissue. A **malignant neoplasm** is a clone of abnormal, anaplastic, proliferating cells, which often have the potential metastasis.

Neoplasms of hematopoietic cells in the bone marrow are phenotypically grouped as **lymphoid** or **myeloid**. The lymphoid and myeloid malignant bone marrow neoplasms are collectively known as **leukemia**.

Leukemia

The term leukemia "which means 'white blood'" is used when abnormal cells are seen in both the bone marrow and peripheral circulation. Leukemia is a progressive malignant disease of hematopoietic stem cells characterized by an inability of these cells to mature into functional peripheral blood cells.

Failure of normal hematopoiesis is the most serious consequence of malignant neoplasms. As the neoplastic cell population increases, the concentration of normal cells decreases.

Leukemia can be classified as following:

1. Acute leukemia

Acute leukemia is characterized by a rapid increase in the number of immature blood cells. Which the bone marrow unable to produce healthy blood cells. Acute forms of leukemia are the most common forms of leukemia in children.

2. Chronic leukemia

Chronic leukemia: abnormal white blood cells. The cells are produced at a much higher rate than normal, resulting in many abnormal white blood cells. Chronic leukemia mostly occurs in older people.

Signs and symptoms

Lack of blood platelets, which are important in the blood clotting process

Patient's immune system to be unable to fight off a simple infection or to start attacking other body cells.

infected tonsils, sores in the mouth, or diarrhea to life-threatening pneumonia or opportunistic infections.

Risk factors

The different leukemias likely have different causes. The following factors are widely regarded:

- 1- Ionizing radiation.**
- 2- Therapeutic drugs such as fertility drugs.**
- 3- Chemicals, notably benzene.**
- 4- Viruses such as human T-lymphotropic virus.**
- 5- Familial and genetic factors.**

Diagnosis

Diagnosis is usually based on the following tests:

- 1- Complete blood count.**

2- Bone marrow examination.

3- Lymph node biopsy.

4- Blood chemistry tests.

5- X-ray.

6- MRI.

7- Ultrasound.

8- CT scans.

Treatment

Theoretically, ideal treatment for malignancy requires the selective and total removal or destruction of malignant cells in the absence of significant toxicity to normal cells, although this ideal is seldom attainable in practice. The most widely employed modes of treatment in hematological malignancy are:-

1- Cytotoxic chemotherapy.

2- Hemopoietic stem cell transplantation.

3- Radiotherapy (less commonly).

4- Pharmaceutical medication,

5- Blood transfusion.

6- Supportive care.

Lymphoma

Abnormal proliferation of lymphoid cells sometimes occurs within the lymphatic tissue or lymph nodes. These solid tumors are referred to as **lymphoma**. Only cancers that start in the lymph tissue are considered **lymphomas**. If the lymphoma affects the bone marrow and the lymphoma cells are found in the peripheral circulation, the leukemic phase of lymphoma is present.

Lymphoma

Hodgkin's lymphoma or disease (HD) and non-Hodgkin's lymphoma (NHL) are the two major types of lymphoma. The most common symptom of HD is swelling of the lymph nodes. The main difference between Hodgkin's lymphoma and NHL is the presence of a type of abnormal cell called the Reed-Sternberg cell (owl eye appearance). This type of abnormal cell is only present in Hodgkin's lymphoma. Hodgkin's lymphom