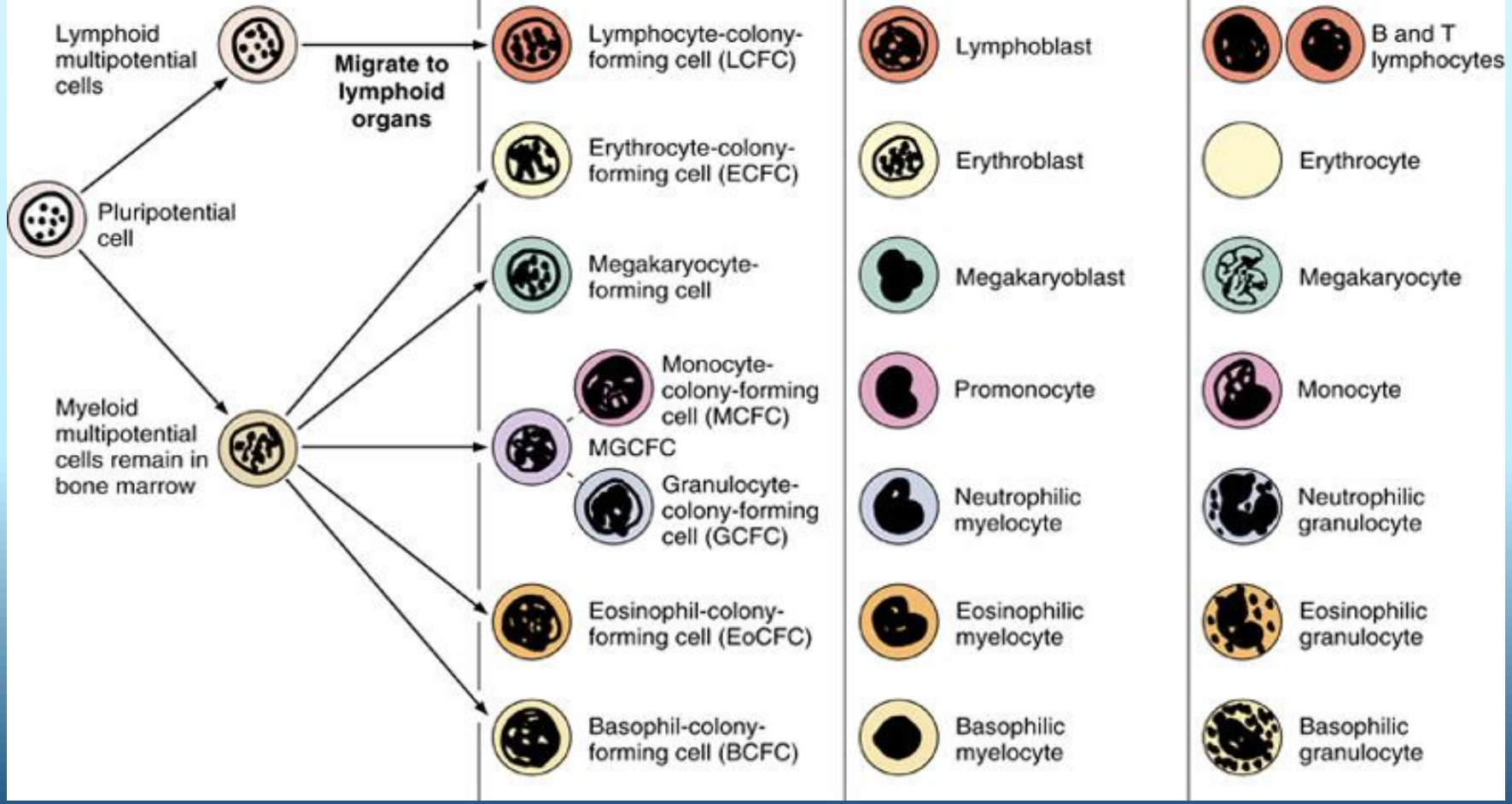
Disorders of White Blood Cells and Lymphoid Tissues

Phase	Stem Cells	Progenitor Cells	Precursor Cells (Blasts)	Mature Cells
Early morphologic	Not morphologically distinguishable; have the general aspect of lymphocytes		Beginning of morphologic differentiation	Clear morphologic differentiation
Mitotic activity	Low mitotic activity; self-renewing; scarce in bone marrow	High mitotic activity; self-renewing; common in marrow and lymphoid organs; mono- or bipotential	High mitotic activity; not self-renewing; common in marrow and lymphoid organs; monopotential	No mitotic activity; abundant in blood and hematopoietic organs



The number of WBC in the peripheral circulation normally ranges from 5000-10000 cell/ µl. of blood.

- About 50-70% of WBC is granulocytes (neutrophils, eosinphils, and basophils)
- about 20-30% are lymphocytes
- about 2%- 8% are monocytes.

Lymphopenias

- less common;

  they are associated with congenital immunodeficiency diseases, or are acquired in association with specific clinical status, such as treatment with corticosteroids.

Neutropenia= Granulocytopenia

- A reduction in the number of granulocytes in blood is known as neutropenia. Sever reduction in the number of granulocytes in the blood is known agranulocytes.
- Total WBC count reduces to 1000 cell/ µl. In some cases the total WBC count reduce to 200-300 cell/ µl.
- Reduction in the WBC number that leads to increase the susceptible to infections which may be sever enough to cause death.

Etiology and pathogenesis

The mechanisms that cause neutropenia can be broadly divided into two categories:

- 1). Defect in neutrophils production.
- 2). Acceleration of neutrophils remove from circulation

1). **Defect in neutrophils production due to:**

- Exposure to radiation
- Cytotoxic drugs admistration
- Bone marrow cancer.

2). **Removal of neutrophils from circulation is acceleration due to:**

- Inflammation - Idiopathic
- Infection -Immune destruction
- Splenomegaly (increase destruction neutrophils in spleen).

Clinical Symptoms:

- The initial symptoms are malaise, chills, and fever.
- followed by marked weakness and fatigue.
- Ulceration and necrotic infection of the buccal cavity, gum, throat and other sites are the major problem.

Treatment

- Removal the causative agent like drug, infection.
- Current treatment administration of recombinant haemopoitic growth factors such as granulocyte colony stimulating factor (G-CSF) these factors stimulate neutrophils production by the bone marrow.

Neoplastic Disorders of Haemopoitic System and Lymphoid Tissues

The Neoplastic disorders include:

- Leukemias
- Lymphomas
- Multiple Myeloma

Leukemias

- Leukemias are malignant tumors of the haemopoitic stem cells characterized by diffuse replacement of bone marrow by neoplastic cells.

- The leukemic cells proliferate mainly in bone marrow, circulate in the blood and infiltrate in the spleen, lymph nodes, and other organs.

Classification:

Leukemias are classified according to the:

1). Type of malignant cells i.e. the precursor of the malignant cells are either lymphogenic or myelogenic.

2). Their incidence i.e. either acute or chronic. In acute cases are characterized by replacement of the bone marrow with immature cells and rapidly fetal.

- So there are four types or class of leukemia these are:

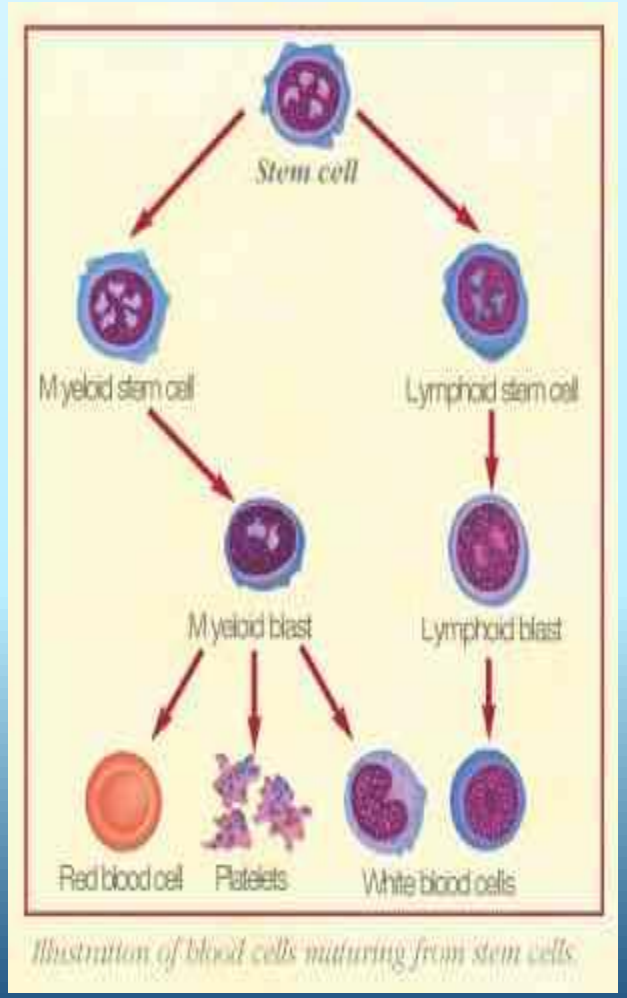


Illustration of blood cells maturing from stem cells.

1). Acute Lymphocytic Leukemia (ALL):

This type of leukemia characterized by:

- Accumulation of lymphoblasts.
- It occurs mostly in childhood with peak incidence between 2-7 years.
- Etiology of ALL is unknown, but cytogenetic studies reveal some abnormality of chromosome number and structure may lead to produce ALL.

The pathogenesis of clinical disease in all relates to the progressive accumulation in the bone marrow of lymphoblasts.

2). Chronic Lymphocytic Leukemia (CLL):

- It is the most indolent of all leukemia, most often seen in old people "older than 50 years". The leukemic cells are B cells in 95% of cases, but in rare cases 5% the leukemic cells are T cells. The T cell leukemias are much more aggressive than the B cell CLL.

- The leukemic B cells fail to respond to antigenic stimulation i.e. unfunctional B lymphocytes.
- -About 50% of patients have chromosomal abnormality.

Clinical Features:

- CLL is often asymptomatic. When symptoms are present, they are nonspecific and include;

  easy fatigability, weight loss, and anorexia, increase susceptibility to bacterial infection. Total leukocyte count may be increased only slightly or may reach 200000 per microliter. Many patients live more than 10 years after diagnosis.

3). Acute Myeloid Leukemia (AML):

- The leukemic cell is myeloid multipotential haemopoitic stem cell.
- AML primarily affect adult. Its incidence increases steadily with age, with the median age being 50 years.
- The etiology of AML is not known.
- The risk factors include the following: toxic agents, radiation, genetic abnormalities, and hematologic disorders. Exposure to benzene for a long period is a known risk factor. This carcinogen is a solvent used in industries that create drugs, rubber, dyes, plastics and other things. People working in these industries have a higher risk of developing AML

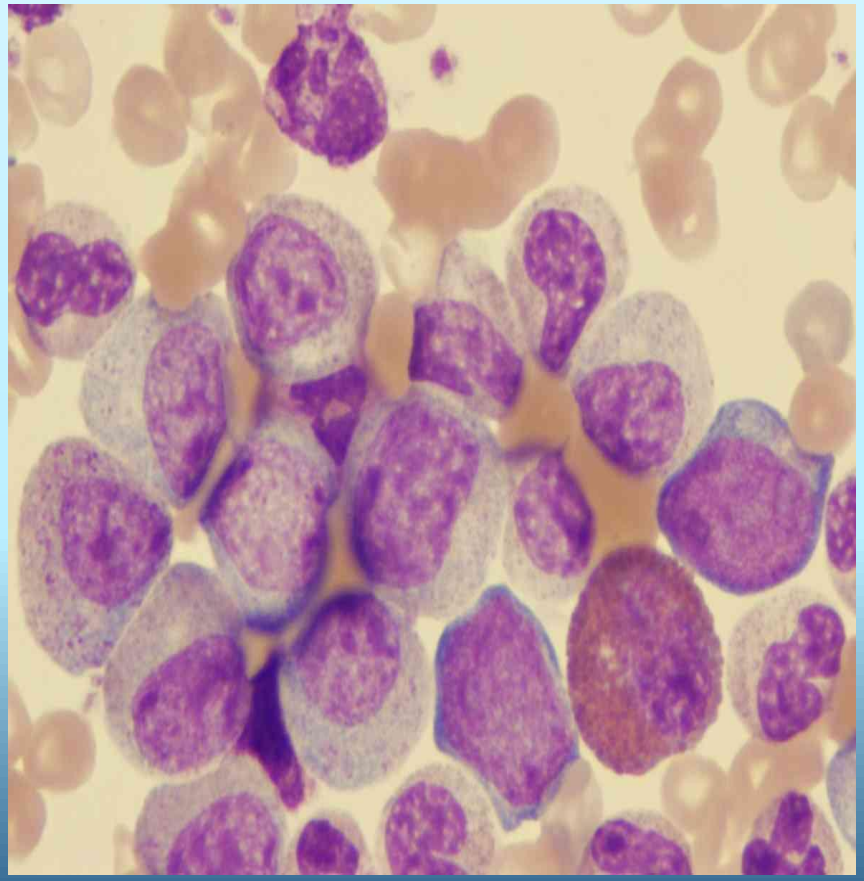
4). Chronic Myeloid Leukemia (CML):

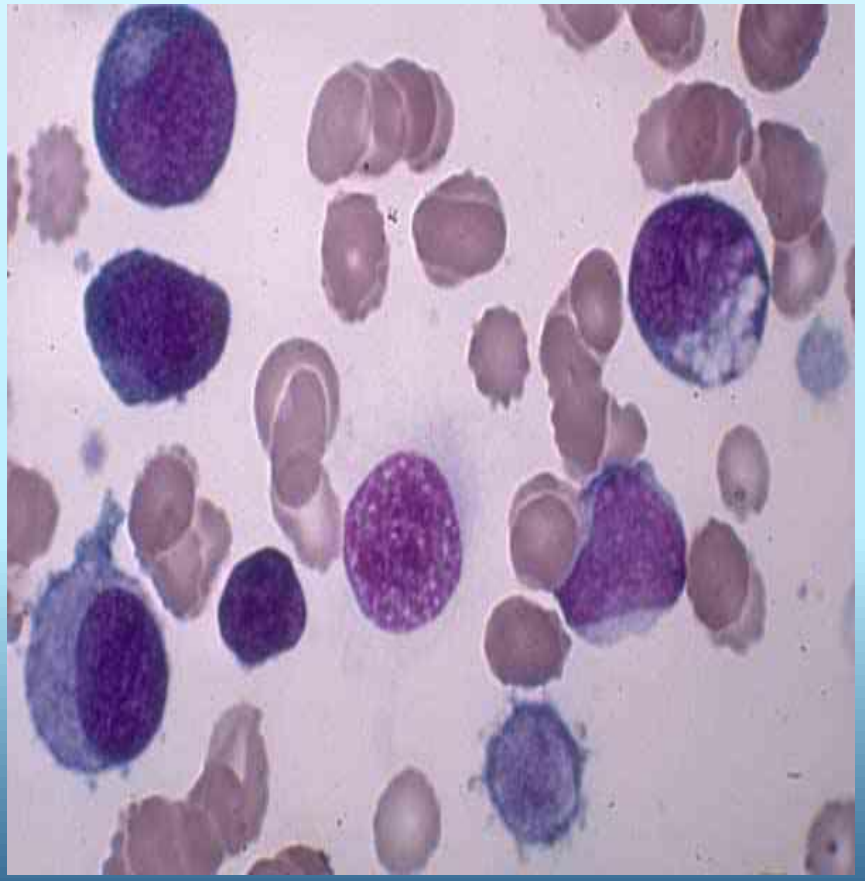
- CML affects adults between 25-60 years of age and accounts for 15% to 20% of all cases of leukemia.

- **Clinical features:**

- Splenomegaly , the laboratory finding, there is marked elevation of the leukocyte count commonly exceeding 100000 cell per microliter, the circulating cells are predominantly neutrophils and myelocytes, but basophils and eosinophils are prominent, about 50% of patients have thrombocytosis. The course of CML is one of slow progression. Median survival is 3 years.

Chronic Myeloid Leukemia





Lymphomas

- **Types of Lymphomas**
- **Hodgkin's Lymphomas = Hodgkin's Disease**
- **Non Hodgkin's Lymphomas (NHL)**
- **Burkitt's Lymphoma**

Hodgkin's Lymphomas = Hodgkin's Disease

- It is a malignant neoplasm of lymphatic structures characterized by painless and progressive enlargement of single lymph node or group of lymph nodes. More often localized to a single axial group of nodes (cervical, mediastinal, para-aortic).

- Hodgkin's disease is somewhat more common in men than in women and in the white than in blacks. The peak incidence in the late 20 years of age , a decrease in frequency during the 4^{th} and 5^{th} decades, and a gradually increasing incidence after age of 50 years.
- -Early and increased exposure to an unidentified agent of low oncogenic potential may be important in its development.
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- Young adults who have experienced Epstein-Bar virus infection (infectious mononucleosis) have a threefold increased risk of developing Hodgkin's lymphoma.

- -Genetic factors may play a role in developing.

- There is an increased incidence of HD in patients with immunodeficiency and autoimmune diseases such as rheumatoid arthritis

- -Hodgkin's lymphoma originate within one area of the lymphatic system and if unchecked will spread throughout the lymphatic network (disseminate).
- -Hodgkin's lymphoma is characterized by the presence of distinctive neoplastic giant cells called Reed- Sternberg (SR) cells admixed with a variable inflammatory infiltrate.
- The Reed- Sternberg (RS) cell has abundant, slightly eosinophillic cytoplasm. Particularly characteristic are two mirror image nuclei, each containing a large (inclusion-like) acidophilic nucleolus surrounded by a distinctive clear zone: together they impart an owl-eyed appearance.

Signs and Symptoms:

- In early stages there is no systemic complication but the advanced stages there is systemic complication like:

  fever, night sweat, loss weight, fatigue, pruritis, and anemia. In the advanced stages the liver, lungs, GIT, and CNS may be affected.

Diagnosis:

- -Biopsy for histopathologic examination.
- -CT scan.
- -Radiologic visualization of abdominal and pelvic lymph nodes.

- -Treatment: Radiation and chemotherapy are used in treating the disease.

Non Hodgkin's Lymphomas (NHL)

- NHLs are malignant tumors originated in lymphoid tissue usually in the lymph nodes (65%of cases) or in the lymphoid tissue of parenchymal organs (35%). It characterized by multicentric in origin and spread early to various tissues throughout the body specially the liver, spleen and bone marrow.
- NHLs are tumors of immune cells so it may origin in T, B cells or histiocytes (macrophages of lymphoid tissues). Most NHLs (80-85) % are of B cell origin; the remainders are in large T cell tumor. Tumors of histiocytes are quite uncommon.

- The neoplastic cells of B cell origin may either aggregate as nodule or spread diffusely in lymphoid tissue. Aggregation as nodule is called nodular lymphoma, while diffusely spread called diffuse lymphoma

- All T cell lymphomas are diffuse.

- Nodular lymphomas are indolent tumors with long survival but not curable.

- Diffuse lymphomas are aggressive tumors that are rapidly fatal unless treated, but with appropriate therapy, many can be cured.

Burkitt's Lymphoma

- This is a high grad tumor of B lymphocytes, clinically aggressive. In fact this tumor is the most rapidly proliferative of all human tumors. Mostly affect children.

- Currently Burkitt's lymphoma can be occurs as endemic, the sporadic and the immunodeficiency which are associated HIV and AIDS.
- The children with impaired immunity can infected with Epstein-Barr virus (the causative agent of Burkitt's disease), the disease involves the jaw or other facial bone, distal ileum, cecum, overies, kidney or the breast.