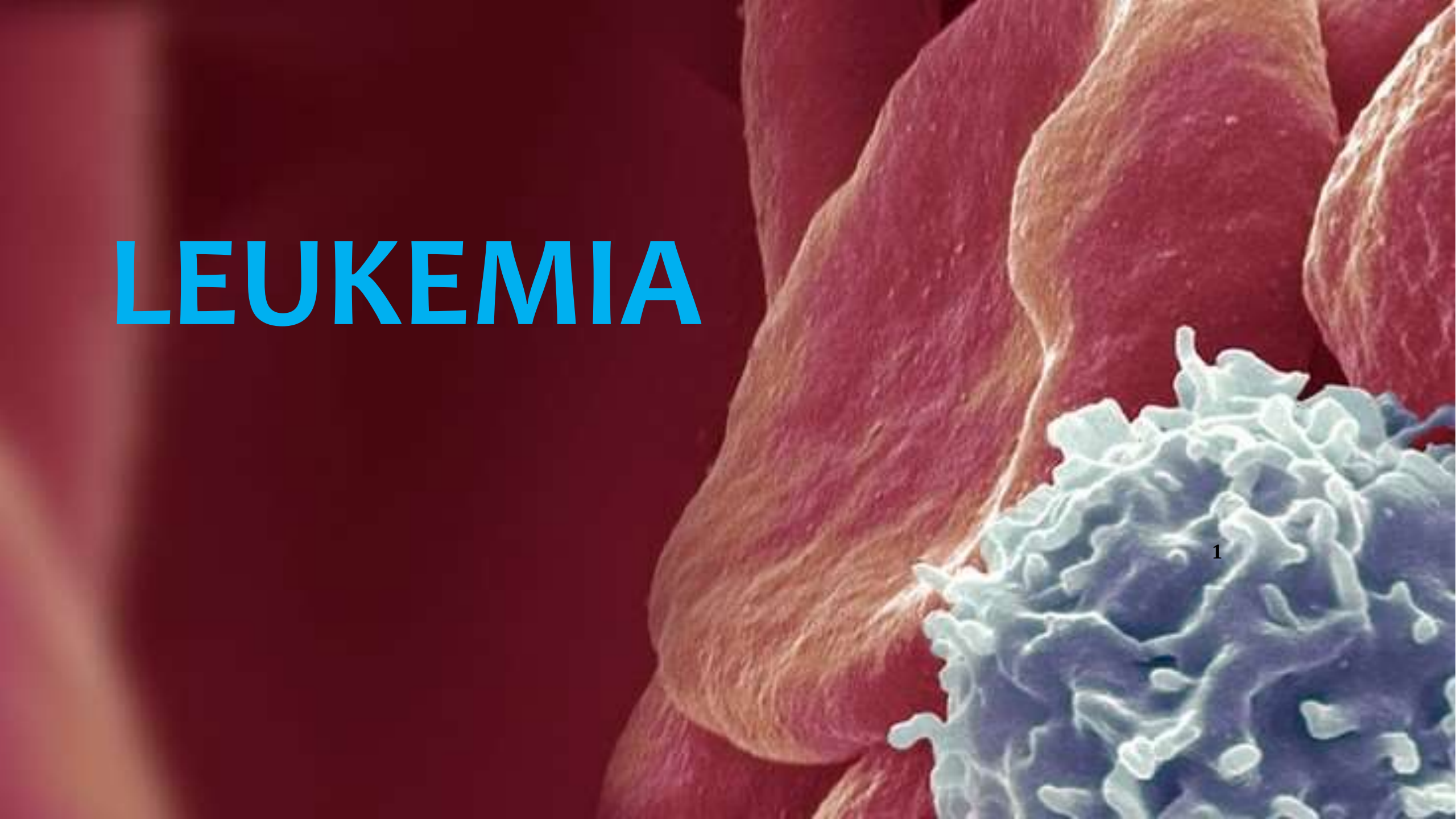
LEUKEMIA

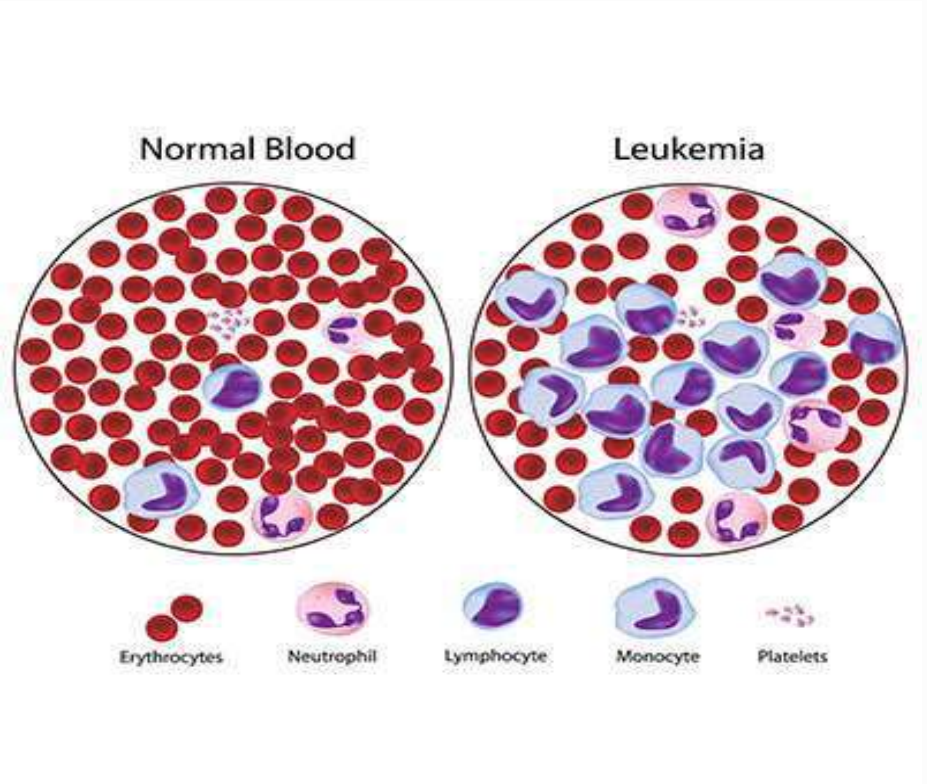


LEUKEMIA

What is Leukemia?

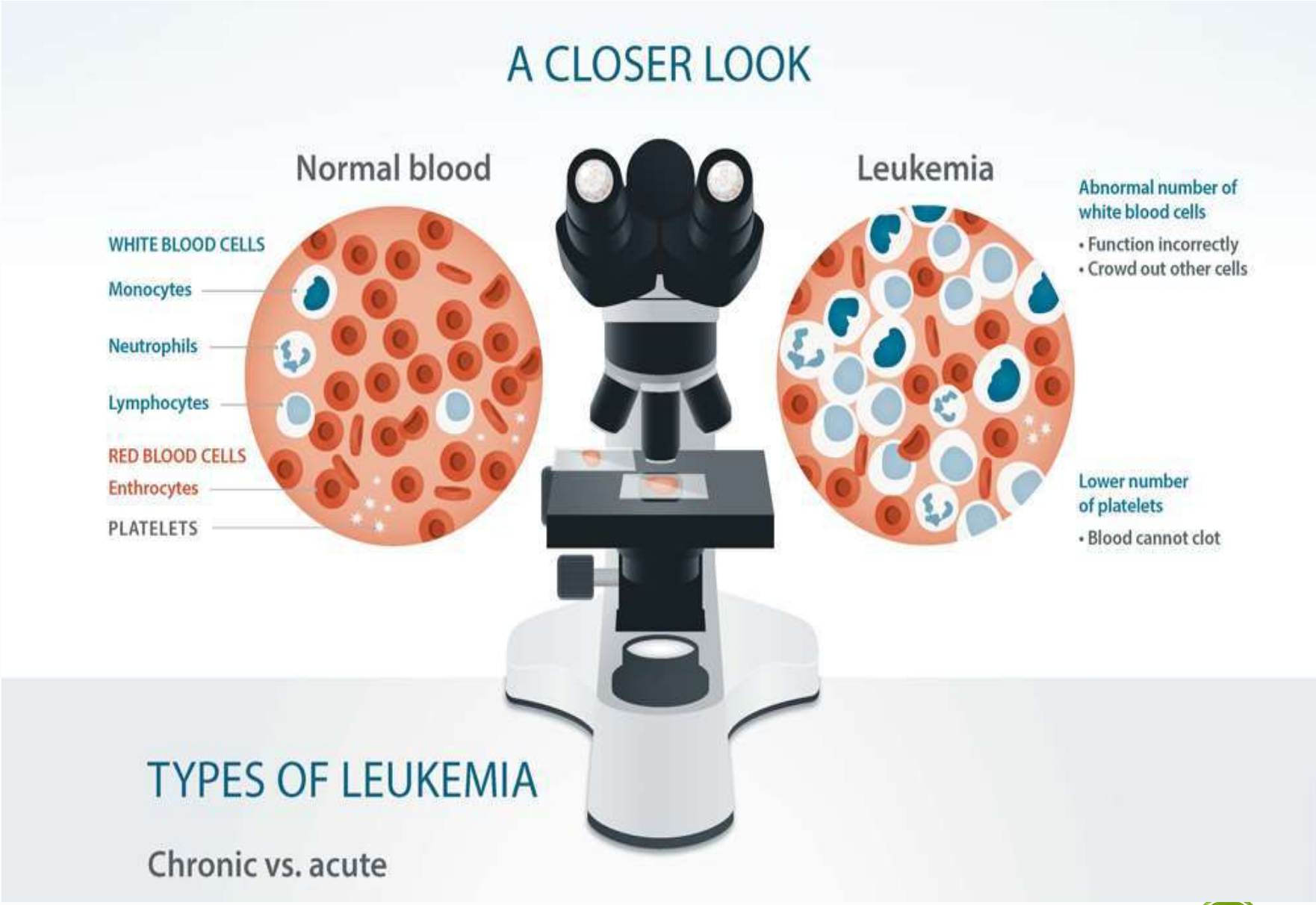
Leukaemia represents a group of diseases characterised by unregulated proliferation and incomplete maturation of the precursors to white cells and lymphocytes

- Occurs in all age groups
- Results in an accumulation of dysfunctional cells because of a loss of regulation in cell division, leading to a weakened immune system, anemia, and bleeding disorders.



LEUKEMIA

- *Leukemia is one of the most common cancers in children and adults.*
- *Early detection and advances in treatment have improved survival rates.*



ETIOLOGY AND PATHOPHYSIOLOGY

- No single causative agent
- Most from a combination of factors

Genetic Factors:

- Chromosomal abnormalities (e.g., Philadelphia chromosome in CML).
- Family history of leukemia.

Environmental Factors:

- Exposure to radiation or chemicals (e.g., benzene).
- Previous chemotherapy or radiation therapy.

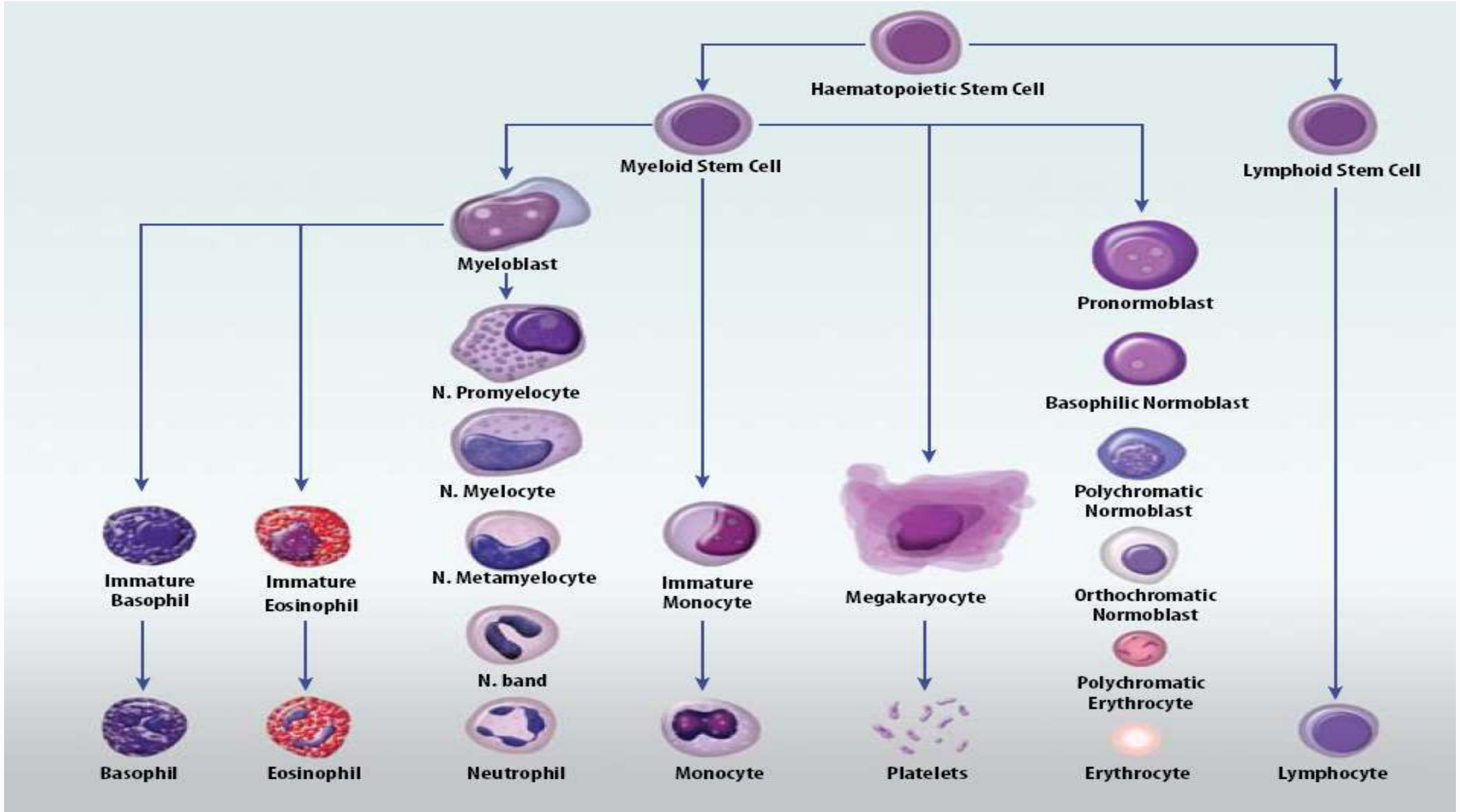
Lifestyle Factors:

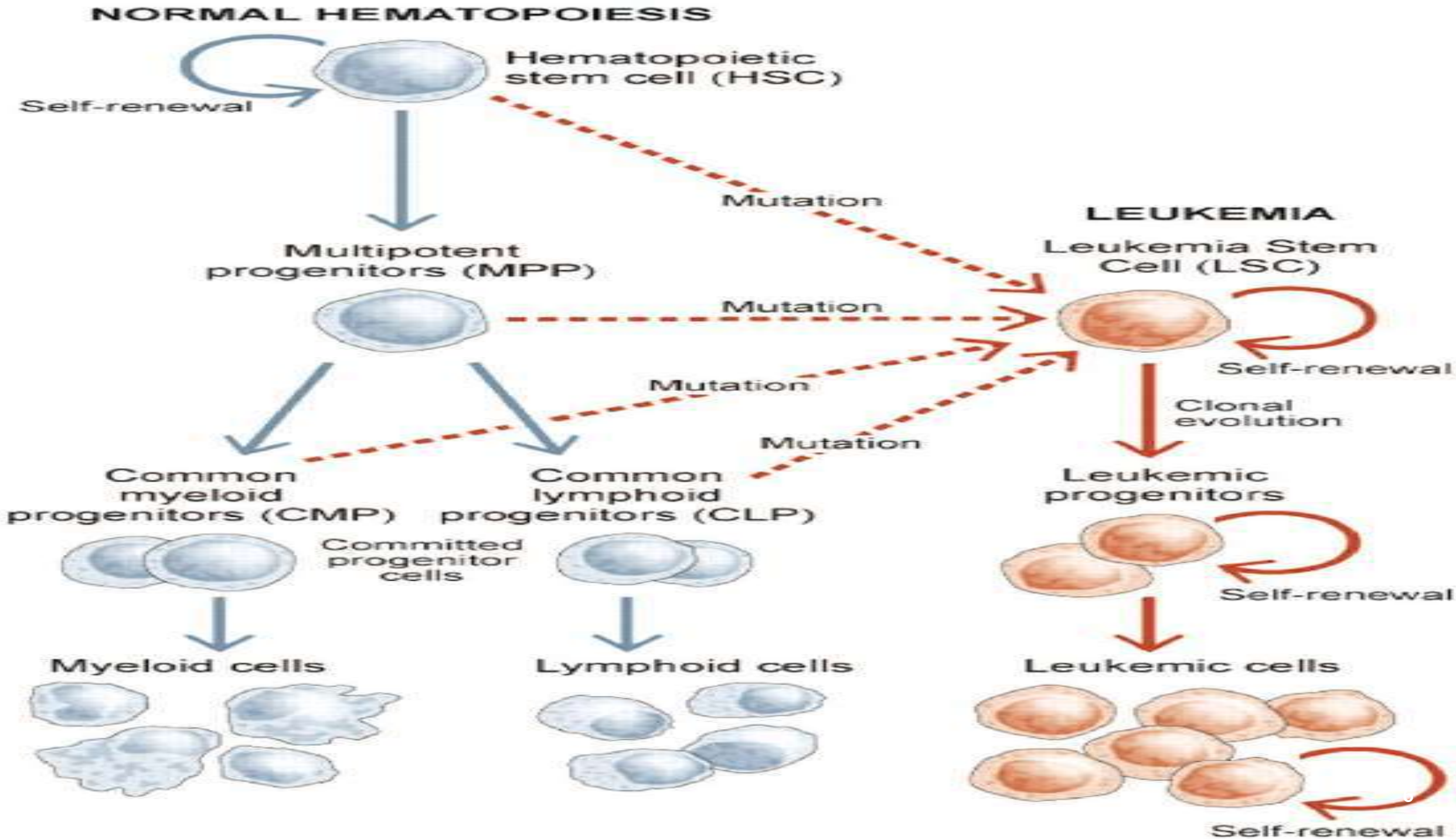
- Smoking.
- Obesity (linked to higher risk of AML).

Infections:

- Viruses like HTLV-1 (linked to adult T-cell leukemia).

Hematopoiesis




NORMAL HEMATOPOIESIS
Hematopoietic stem cell (HSC)
Self-renewal
Mutation
LEUKEMIA
Multipotent progenitors (MPP)
Leukemia Stem Cell (LSC)
Mutation
Self-renewal
Mutation
Clonal evolution
Mutation
Common myeloid progenitors (CMP)
Common lymphoid progenitors (CLP)
Leukemic progenitors
Committed progenitor cells
Self-renewal
Myeloid cells
Lymphoid cells
Leukemic cells
Self-renewal

CLASSIFICATION OF LEUKEMIA'S

Classification Based on Cell Type:

1. Acute leukemia

   Acute lymphoblastic leukemia (ALL)

   Acute myelogenous leukemia (AML)

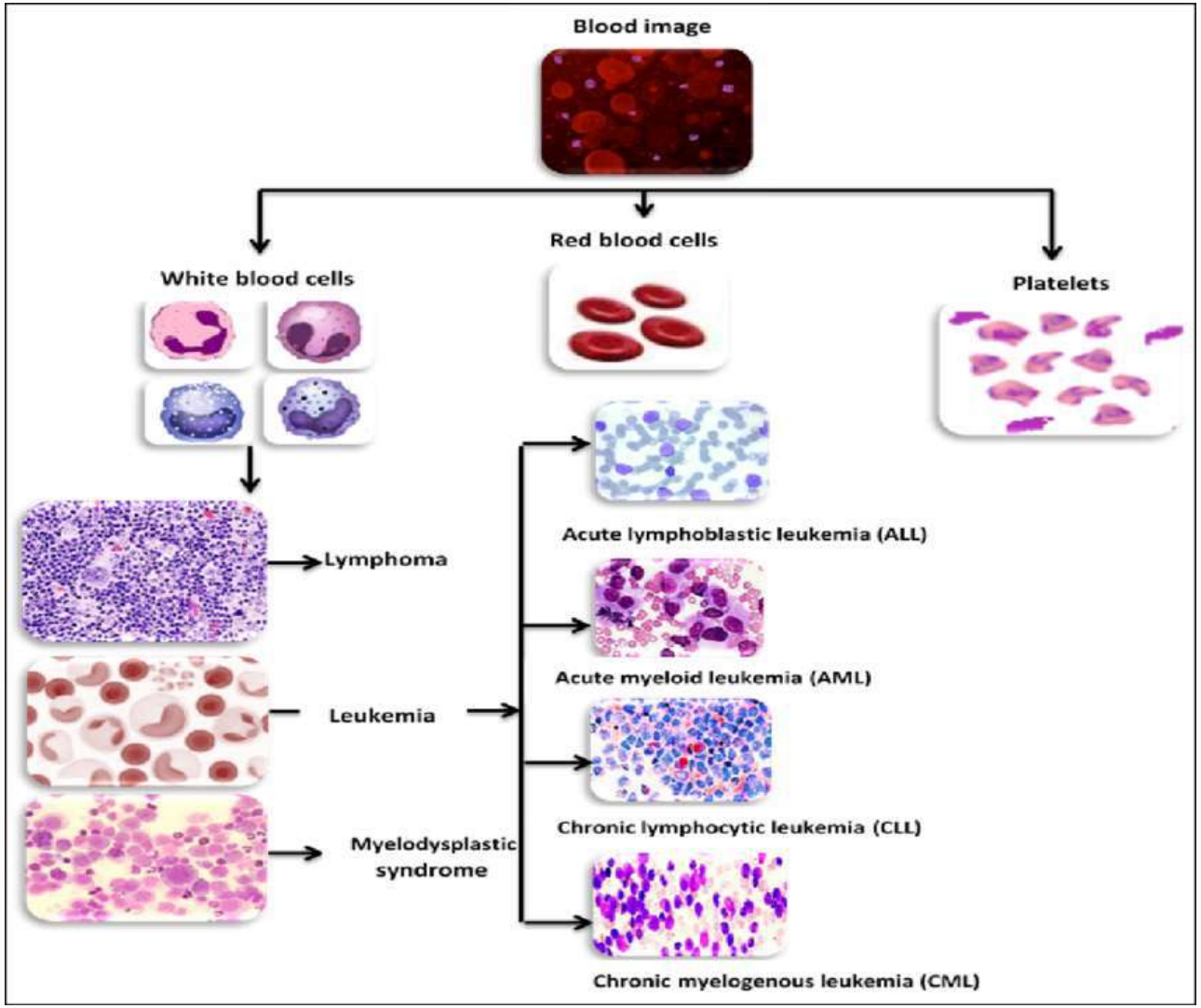
   (also "myeloid" or "nonlymphocytic")

2. Chronic leukemia

   Chronic lymphocytic leukemia (CLL)

   Chronic myeloid leukemia (CML)

(Within these main categories, there are typically several subcategories)

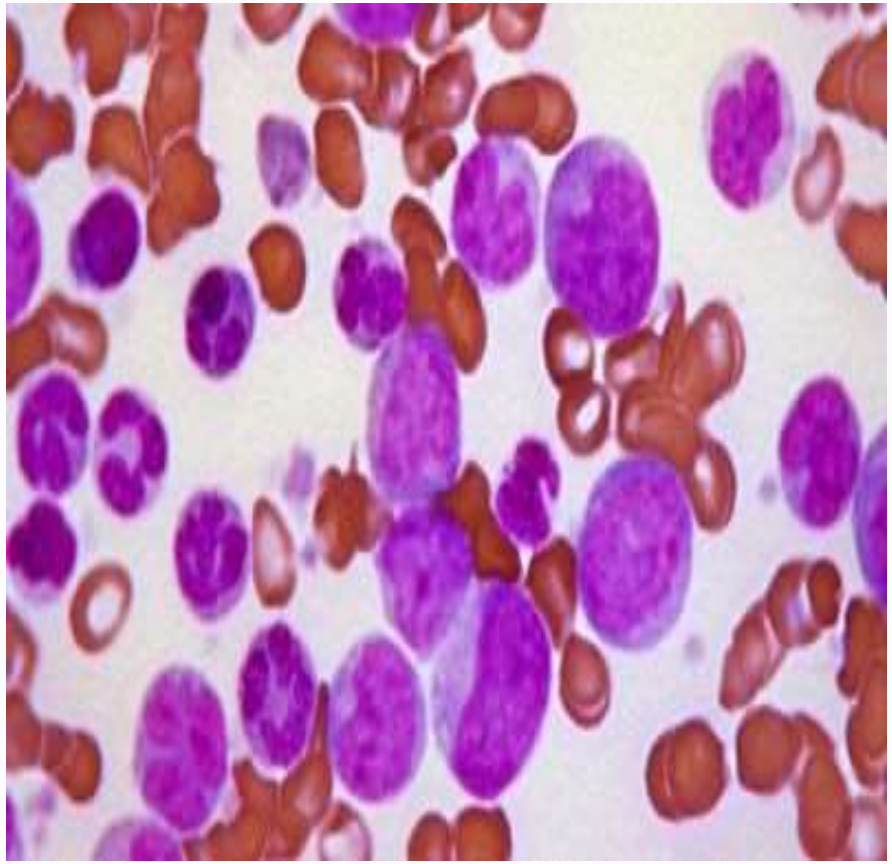


LEUKEMIA *CLASSIFICATION*

- Classification Based on Progression:
- Acute versus chronic
  - Cell maturity
    - Acute: clonal proliferation of immature hematopoietic cells (the formation of blood or blood cells)
    - Chronic: mature forms of WBC; onset is more gradual
- Nature of disease onset
    - Acute conditions are severe and sudden in onset. This could describe anything from a broken bone to an asthma attack. A chronic condition, by contrast is a long-developing syndrome, such as osteoporosis or asthma

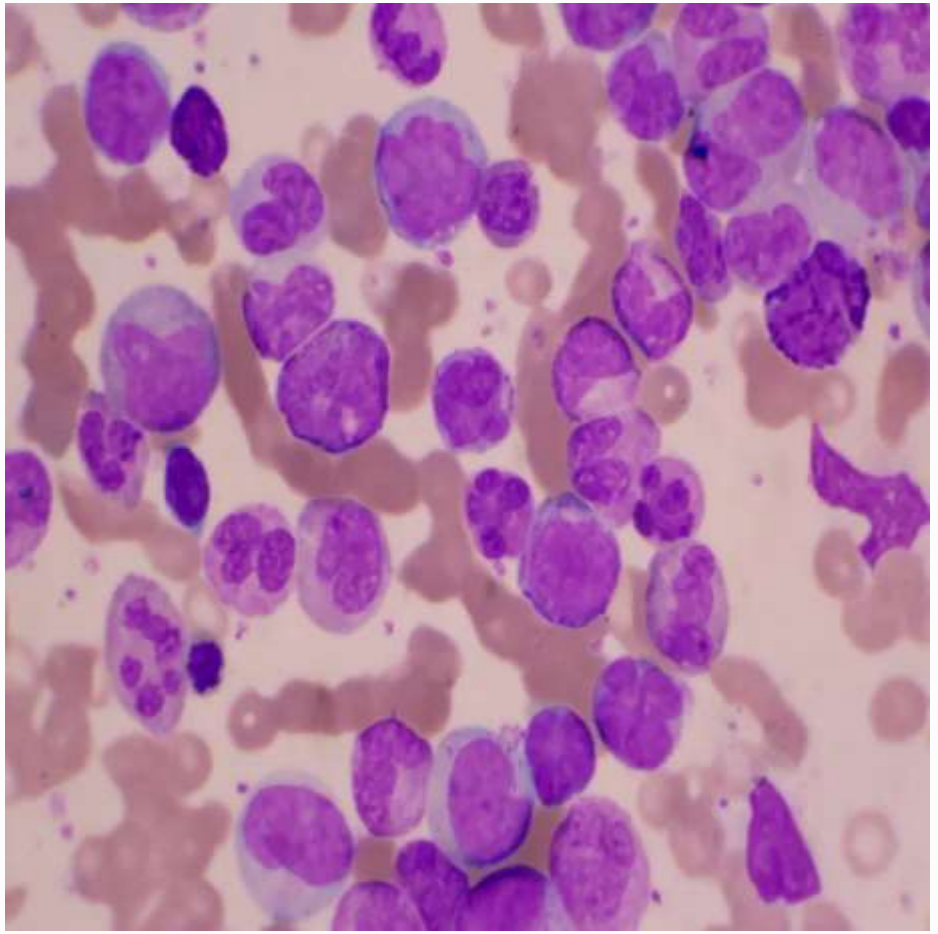
MYELOGENOUS LEUKAEMIA

- Proliferation of myeloid tissue (as of the bone marrow and spleen)
- Abnormal increase in the number of granulocytes, myelocytes, and myeloblasts in the circulating blood.
- Myeloid tissue has ability to perform haematopoiesis. It is mainly found as the red bone marrow in bones, and is often synonymous with this. However, myeloid can also be present in the liver and spleen .
- A myelocyte is a young cell of the granulocytic series, occurring normally in bone marrow, but not in circulating blood (except when caused by certain diseases).



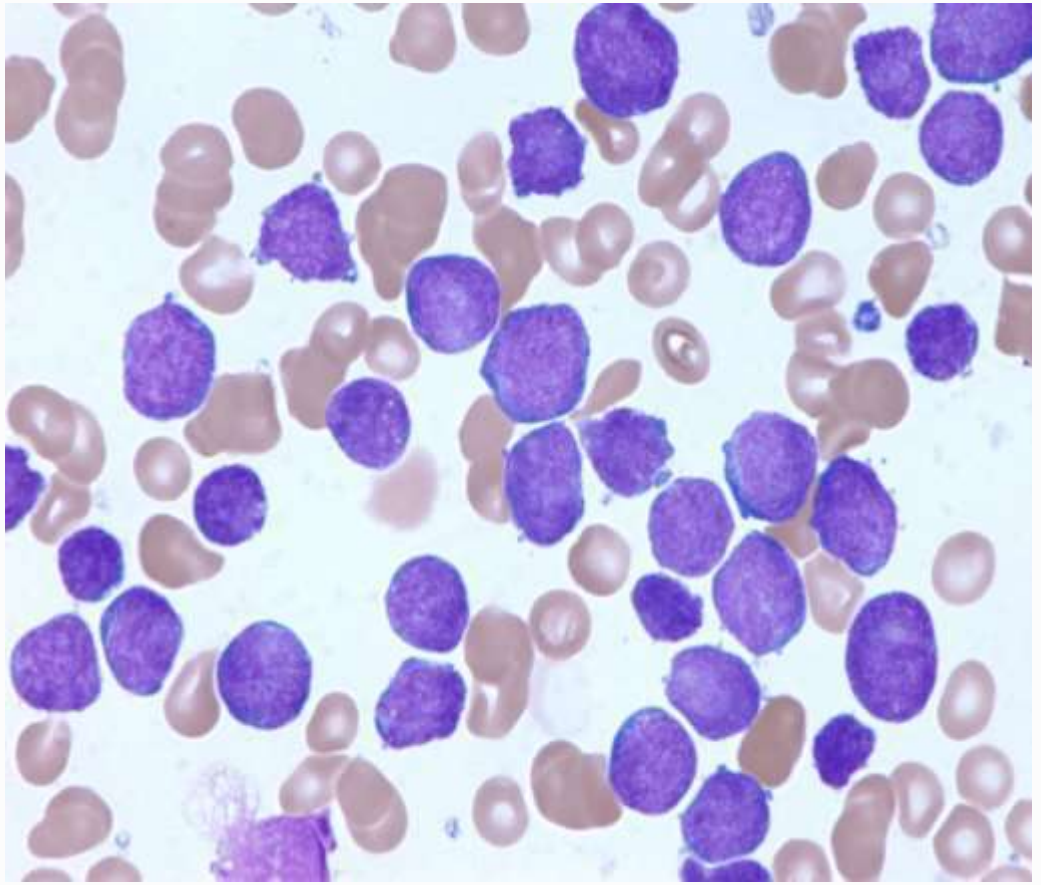
ACUTE MYELOGENOUS LEUKEMIA (AML)

- proliferation of myeloid tissue (as of the bone marrow and spleen)
- Abnormal increase in the number of granulocytes, myelocytes, and myeloblasts.
- One fourth of all leukemias
  - 85% of the acute leukemias in adults
- Abrupt, dramatic onset
- Serious infections, abnormal bleeding
- Hyperplasia of bone marrow and spleen



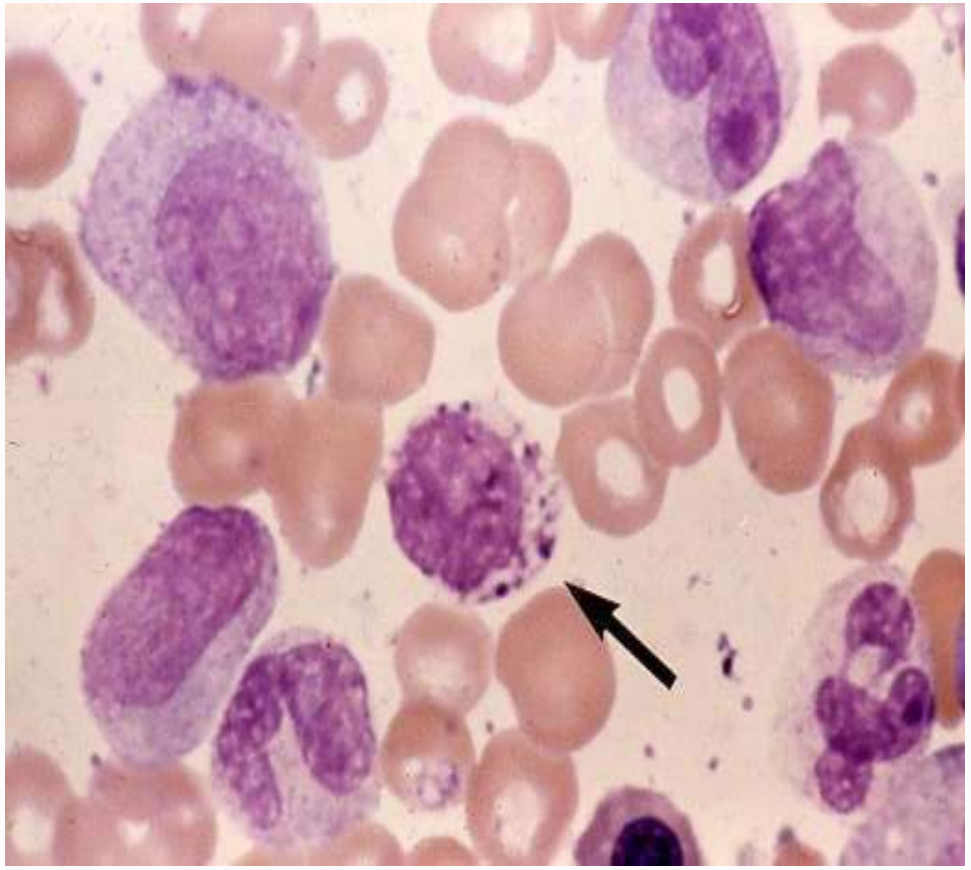
ACUTE LYMPHOCYTIC LEUKEMIA (ALL)

- Most common type of leukemia in children
- 15% of acute leukemia in adults
- Immature lymphocytes proliferate in the bone marrow
- Signs and symptoms may appear abruptly
  - Fever, bleeding
- Insidious with progressive
  - Weakness, fatigue
- Central nervous system manifestations

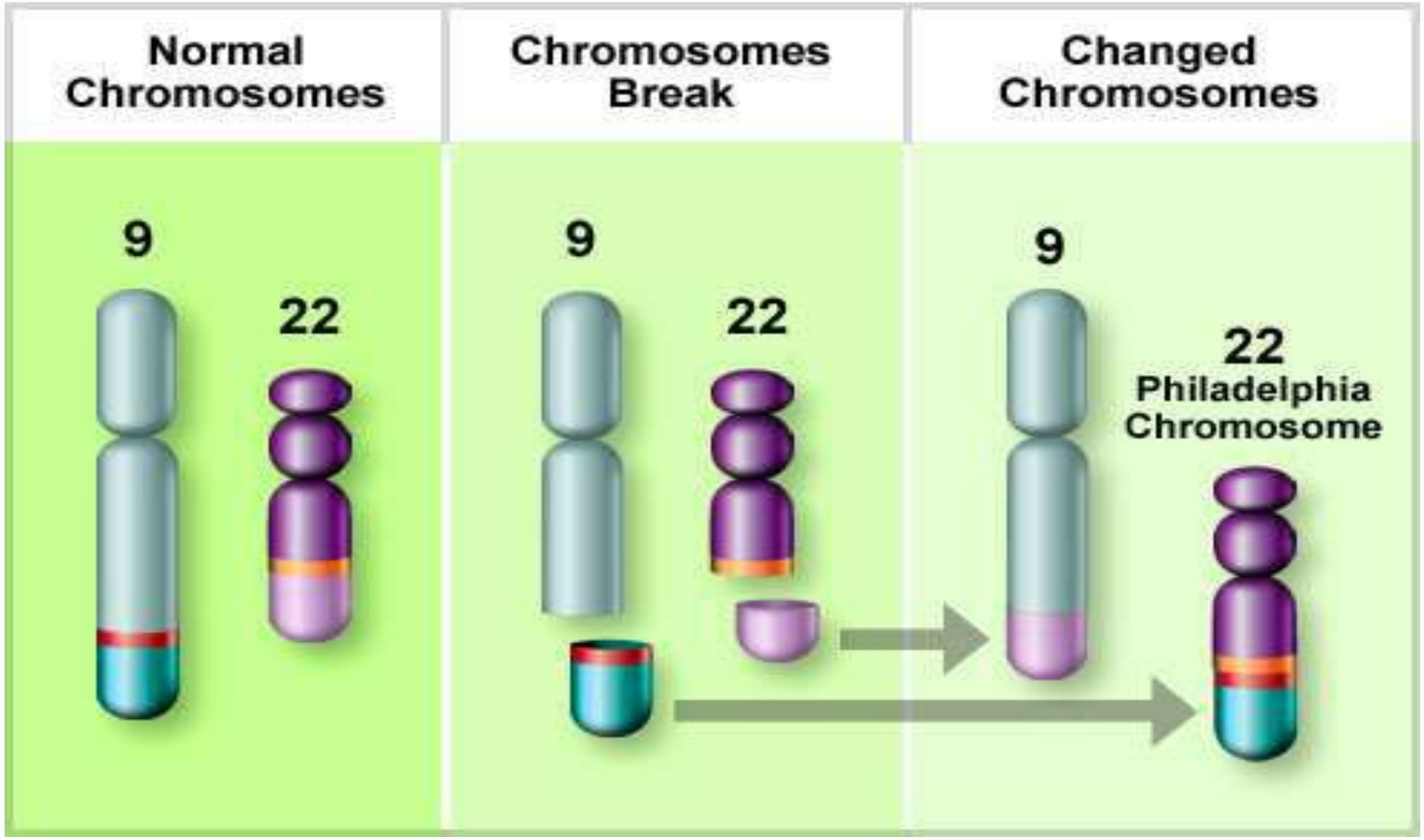


CHRONIC MYELOGENOUS LEUKEMIA (CML)

- Excessive development of mature neoplastic granulocytes in the bone marrow
  - Move into the peripheral blood in massive numbers
  - Ultimately infiltrate the liver and spleen
- *Philadelphia chromosome*
  - The chromosome abnormality that causes chronic myeloid leukaemia (CML) (9 &22)
  - Genetic marker
- Chronic, stable phase followed by acute, aggressive (blastic) phase

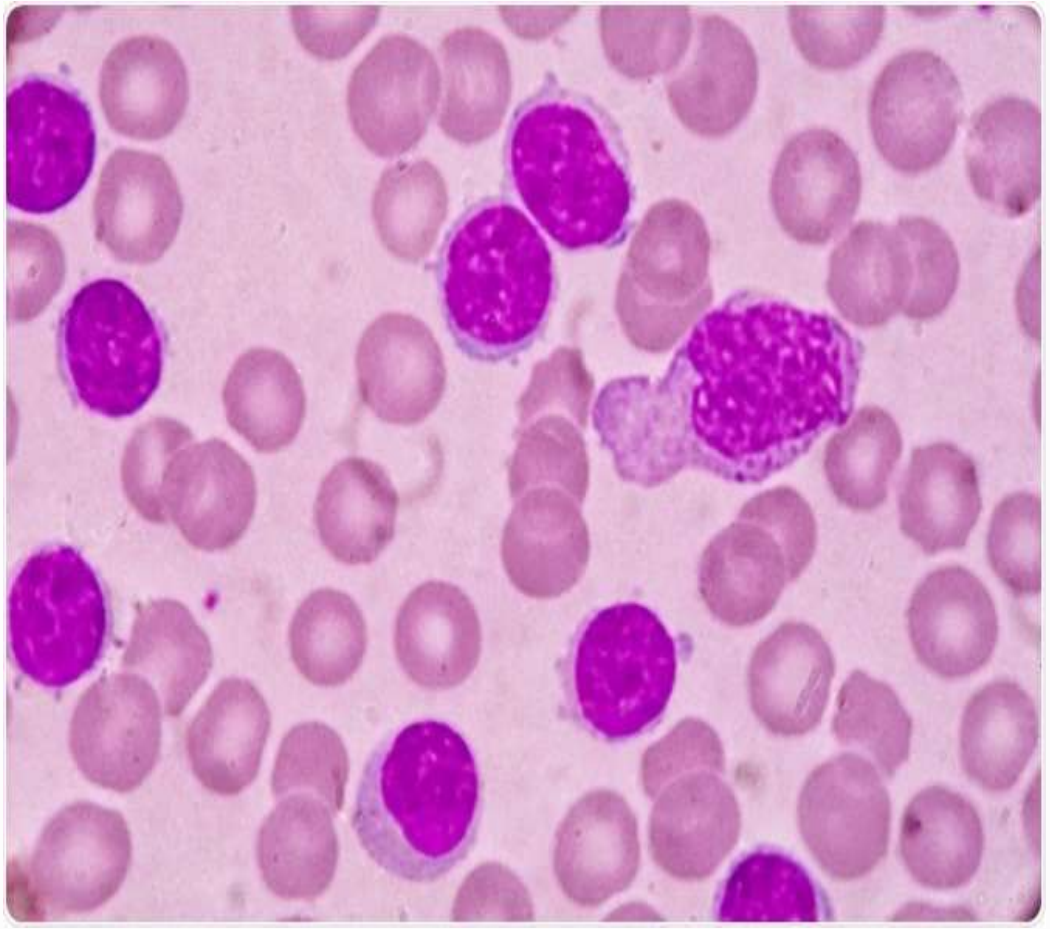


Philadelphia (Ph) chromosome,



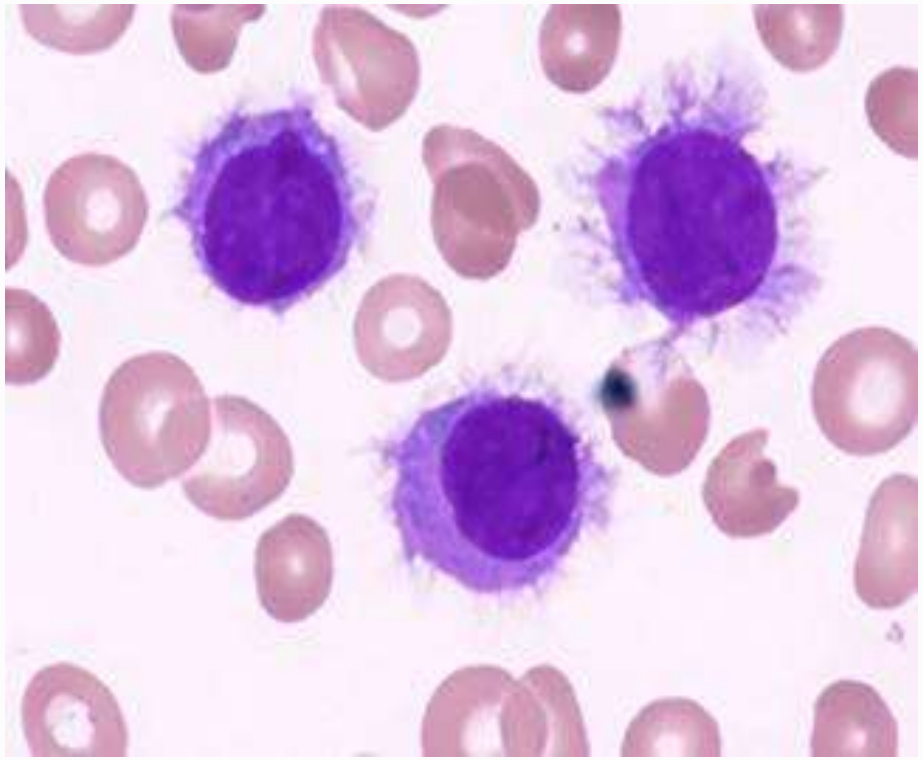
CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

- Abnormal proliferation lymphocytes that accumulate over time, leading to a weakened immune response.
- Primarily affects adults.
- **Key Points About CLL:**
- **Cell Type Involved**: CLL primarily affects B lymphocytes, which normally produce antibodies to fight infections.
- **Slow Progression**: CLL typically progresses slowly, and many patients may not experience symptoms for years.



HAIRY CELL LEUKEMIA

- Relatively rare chronic B-cell malignancy that involves the bone marrow, spleen, and peripheral blood.
- The complete blood count may reveal pancytopenia including monocytopenia
- 2% of all adult leukemias
- Usually in males > 40 years old
- Chronic disease of lymphoproliferation
  - B lymphocytes that infiltrate the bone marrow and liver
- Cells have a "hairy" appearance
- **Symptoms from**
  - Splenomegaly, pancytopenia, infection, vasculitis
- **Treatment**
  - alpha-interferon, pentostatin, cladribine



UNCLASSIFIED LEUKEMIA'S

- A rare acute leukemia of ambiguous lineage characterized by clonal proliferation of primitive hematopoietic cells.
- Unclassified leukemia refers to a form of leukemia that does not fit neatly into established categories like lymphoblastic or myeloid leukemia's.
- Subtype cannot be identified
- Malignant leukemic cells may have
  - Lymphoid, myeloid, or mixed characteristics
- Frequently these patients do not respond well to treatment
  - Poor prognosis

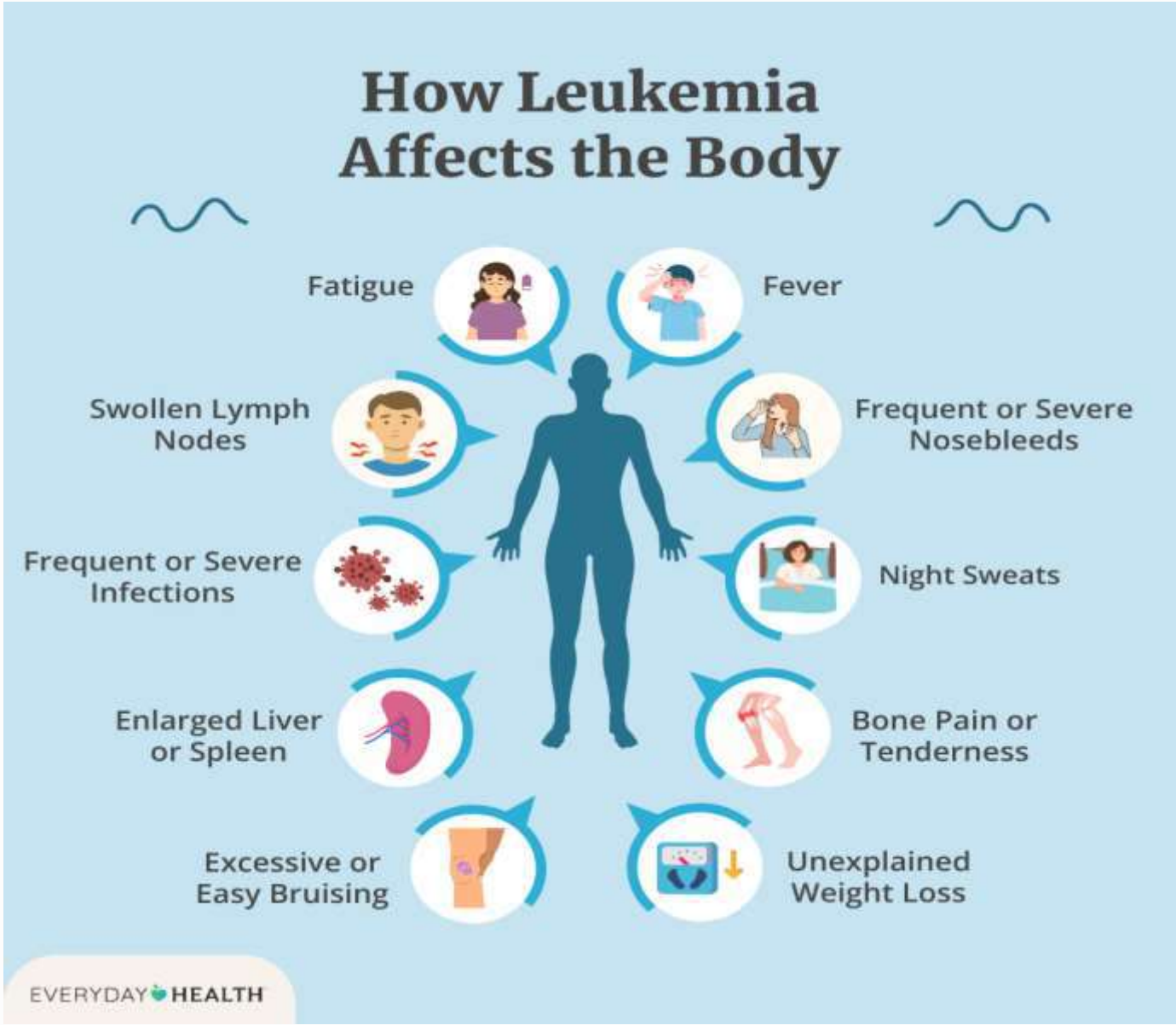
LEUKEMIA

CLINICAL MANIFESTATIONS

- Relate to problems caused by
  - Bone marrow failure
    - Overcrowding by abnormal cells
    - Inadequate production of normal marrow elements
    - Anemia, thrombocytopenia, ↓ number and function of WBCs
- Relate to problems caused by
  - Leukemic cells infiltrate patient's organs
    - Splenomegaly
    - Hepatomegaly
    - Lymphadenopathy
    - Bone pain, meningeal irritation, oral lesions (chloromas)

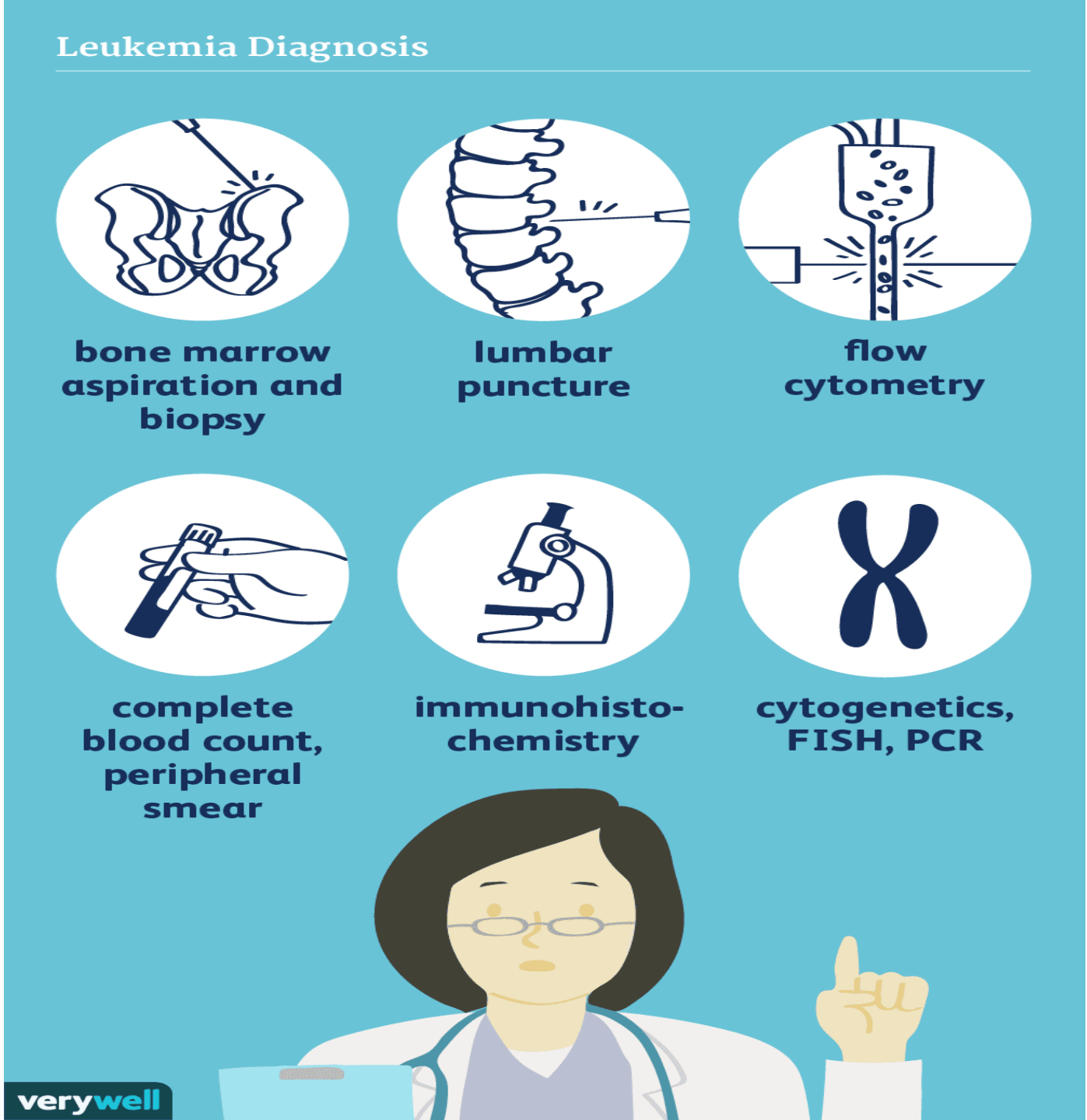
SYMPTOMS AND DIAGNOSIS

- **Common Symptoms:**
- Fatigue, weakness, and pale skin (anemia).
- Frequent infections (low white blood cells).
- Easy bruising or bleeding (low platelets).
- Swollen lymph nodes, fever, and weight loss.



Diagnostic Studies

- To diagnose and classify
  - Peripheral blood evaluation (CBC and blood smear)
  - Bone marrow evaluation
- To identify cell subtype and stage
  - Morphologic, histochemical, immunologic, and cytogenic methods
- Bone marrow biopsy.
- Imaging (CT, MRI, or X-rays).



LEUKEMIA
COLLABORATIVE CARE

- Goal is to attain remission (when there is no longer evidence of cancer cells in the body)
- Chemotherapeutic treatment
  - Induction therapy
    - Attempt to induce or bring remission
    - Seeks to destroy leukemic cells in the tissues, peripheral blood, bone marrow
    - Patient may become critically ill
      - Provide psychological support as well

LEUKEMIA

COLLABORATIVE CARE

- Chemotherapeutic treatment (cont.)
  - Intensification therapy
    - High-dose therapy
    - May be given after induction therapy
    - Same drugs at higher doses and/or other drugs
  - Consolidation therapy
    - Started after remission is achieved
    - Purpose is to eliminate remaining leukemic cells that may not be evident
  - Maintenance therapy
    - Lower doses of the same drug

LEUKEMIA
CHEMOTHERAPY REGIMENS

- Combination chemotherapy
  - Mainstay of treatment for most types of leukemia.
  - Can be administered orally or intravenously.
  - 3 purposes
    - ↓ drug resistance
    - ↓ drug toxicity to the patient by using multiple drugs with varying toxicities
    - Interrupt cell growth at multiple points in the cell cycle

LEUKEMIA –
BONE MARROW AND STEM CELL TRANSPLANTATION

- Goal
  - Totally eliminate leukemic cells from the body using combinations of chemotherapy with or without total body irradiation
- Eradicates patient's hematopoietic stem cells
- Replaced with those of an HLA-matched (Human Leukocyte Antigen)
  - Sibling (is a brother or a sister; that is, any person who shares at least one of the same parents)
  - Volunteer
  - Identical twin
  - Patient's own stem cells removed before

TREATMENT

Targeted Therapy:

- Drugs like Imatinib (Gleevec) for CML.
- FLT3 inhibitors for AML.

Immunotherapy:

- CAR-T cell therapy for ALL.
- Monoclonal antibodies (e.g., Rituximab for CLL).

Radiation Therapy:

- Used in specific cases, such as CNS involvement.

Stem Cell Transplant:

- Replaces diseased bone marrow with healthy stem cells.
- Can be autologous or allogeneic.

Supportive Care:

- Blood transfusions, antibiotics, and growth factors.

ADVANCES IN LEUKEMIA RESEARCH

- **Precision Medicine:**
  - Genetic profiling to tailor treatments.
- **Novel Therapies:**
  - Bispecific T-cell engagers (e.g., Blinatumomab)
  - Newer CAR-T cell therapies.
- **Clinical Trials:**
  - Importance of participating in trials for access to cutting-edge treatments.
- **Survival Rates:**
  - Improved outcomes due to early detection and advanced therapies.

- **Key Takeaways:**
  - Leukemia is a complex disease with various types and treatment options.
  - Advances in research have significantly improved outcomes.
- **Call to Action:**
  - Encourage regular check-ups and awareness of symptoms.
  - Support leukemia research and patient organizations.

RECOMMENDED BOOKS

- Essential Hematology (A. V. Hoffbrand, P. A. H. Moss)
- Uptodate
- Oxford Handbook of clinical hematology.