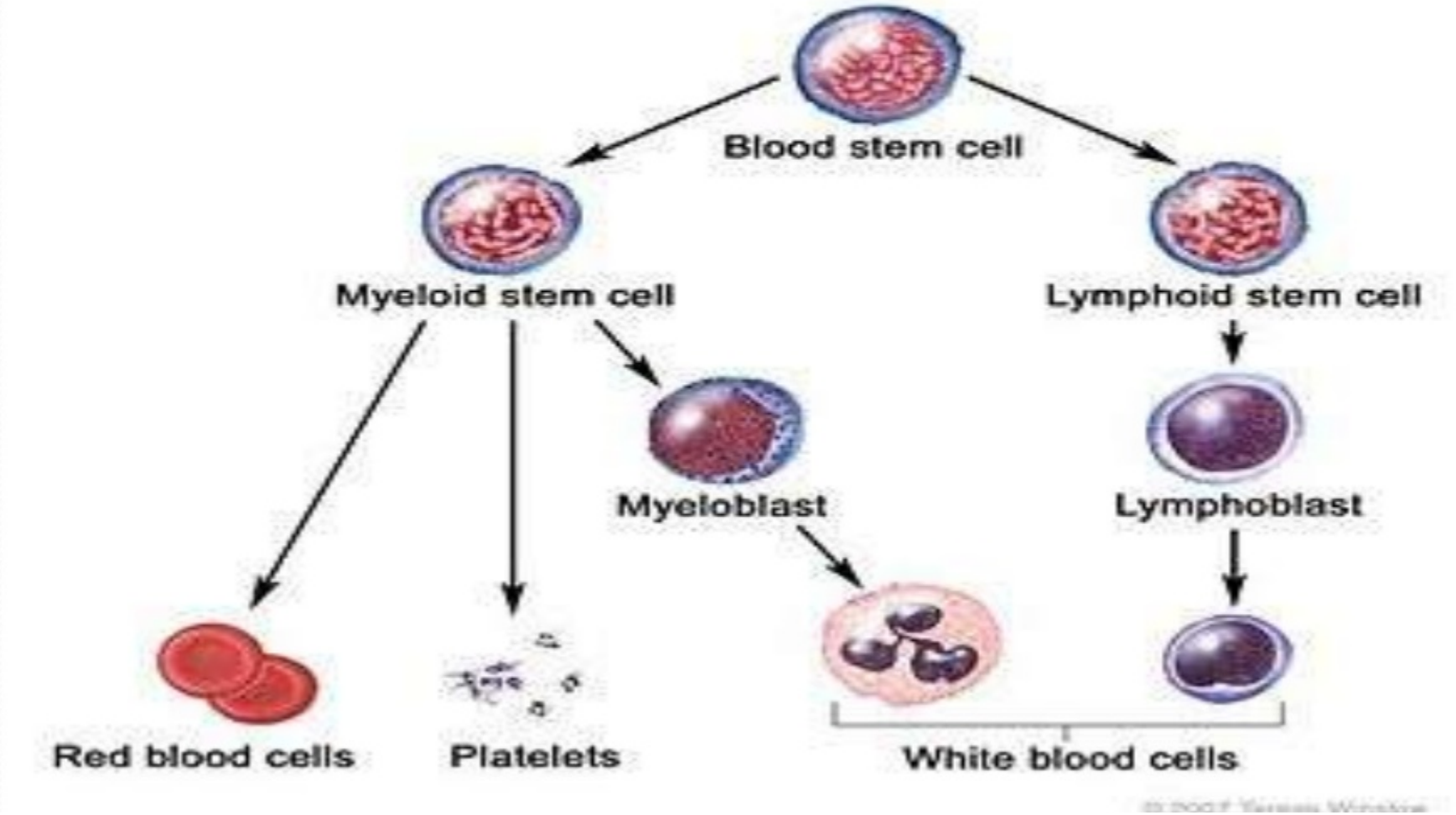
Definition

It is a group of malignant disorder, affecting the blood and blood –forming tissue of the bone marrow lymph system and spleen.

- The word Leukemia comes from the Greek *leukos* which means "white" and *aima* which means "blood".

- The stem cells are committed to produce specific types of blood cells. Lymphoid stem cells produce either T or B **lymphocytes.**
- Myeloid stem cells differentiate into three broad cell types: RBCs, WBCs, and platelets.

PATHOPHYSIOLOGY



etiology

- Combination of predisposing factors including genetic and environmental influences.
- Chronic exposure to chemical such as benzene
- Radiation exposure.
- Cytotoxic therapy of breast, lung and testicular cancer.

- Congenital anomaly
- The presence of primary immunodeficiency and infection with the human T –cell leukemia virus type-1

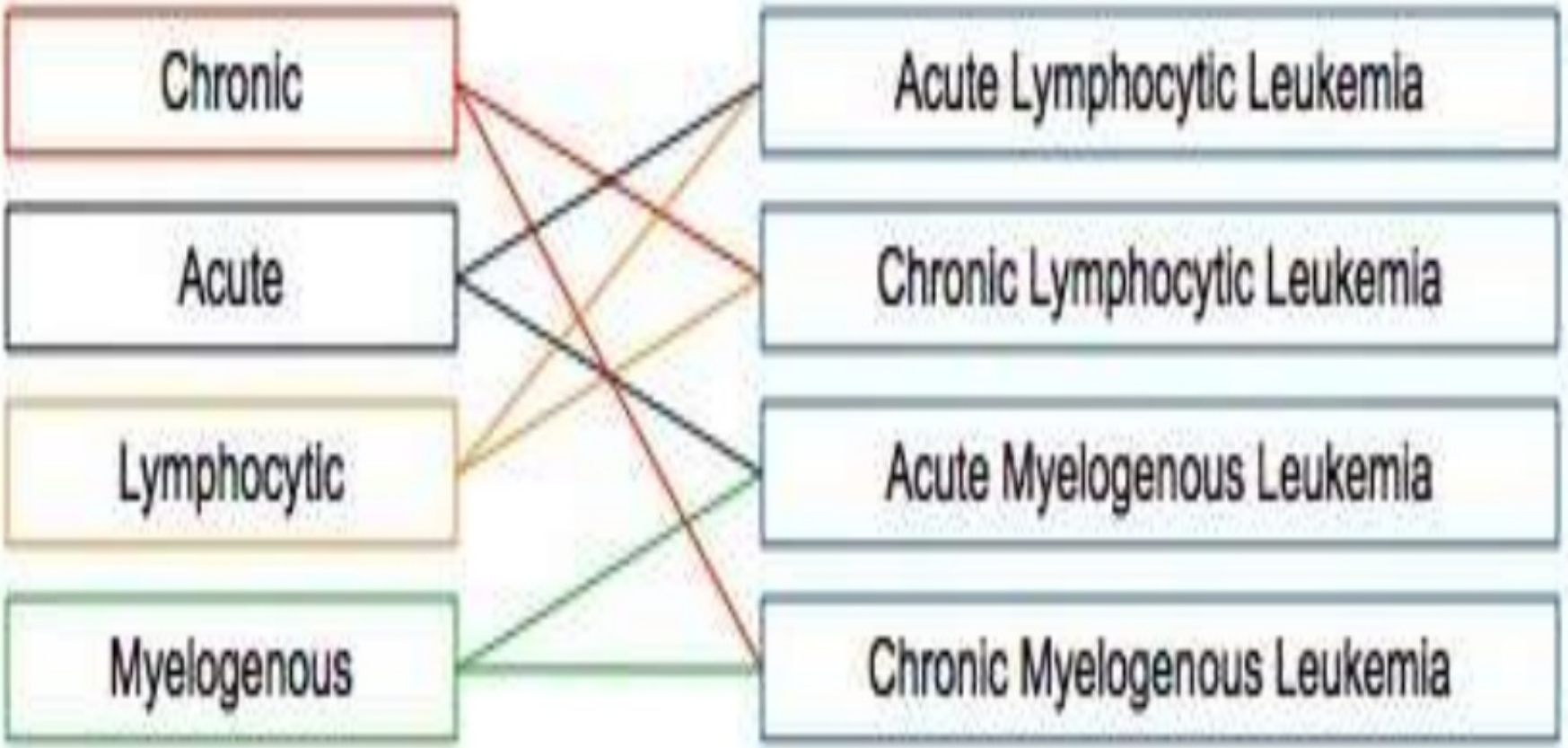
- The lack of control causes –
- nomal bone marrow to be replaced by immature and undifferentiated leukocytes or blat cells . –
- abnormal immature leukocytes then circulates in the blood and infiltrate the blood forming organs (liver , spleen, lymph nodes) and other sites throughout the body.

Different types of leukemia

- It may be acute or chronic. Acute leukemia gets worse very fast and may make feel sick right away. Chronic leukemia gets worse slowly and may not cause symptoms for years.

- Lymphocytic and Myelogenous Leukemias are also subdivided into the type of affected blood cell. If the cancerous transformation occurs in the type of marrow that makes lymphocytes, the disease is called *lymphocytic leukemia*.

- If the cancerous change occurs in the type of marrow cells that produce red blood cells, other types of white cells, and platelets, the disease is called *myelogenous leukemia*

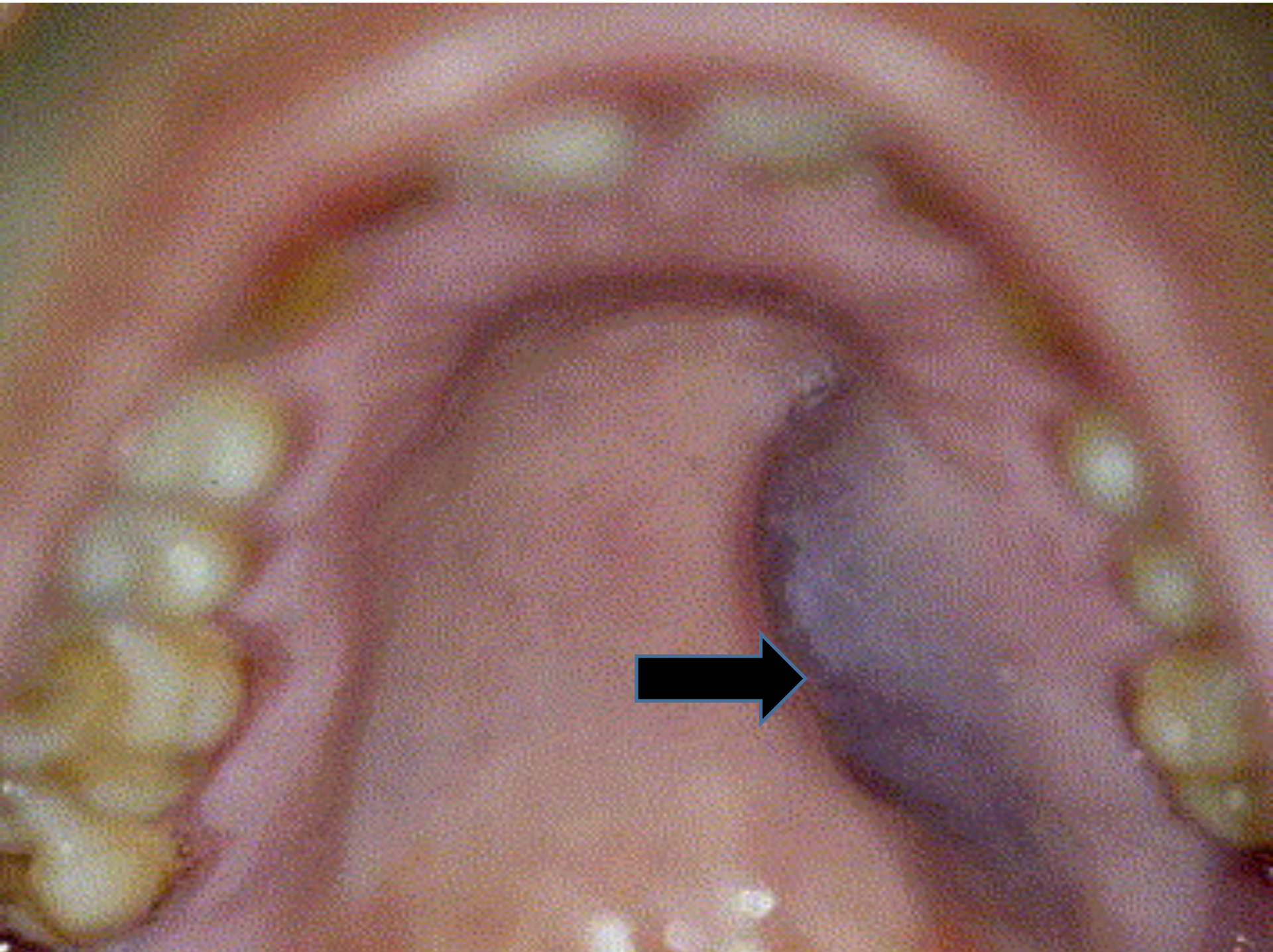

Chronic
Acute
Lymphocytic
Myelogenous
Acute Lymphocytic Leukemia
Chronic Lymphocytic Leukemia
Acute Myelogenous Leukemia
Chronic Myelogenous Leukemia

INCIDENCE—

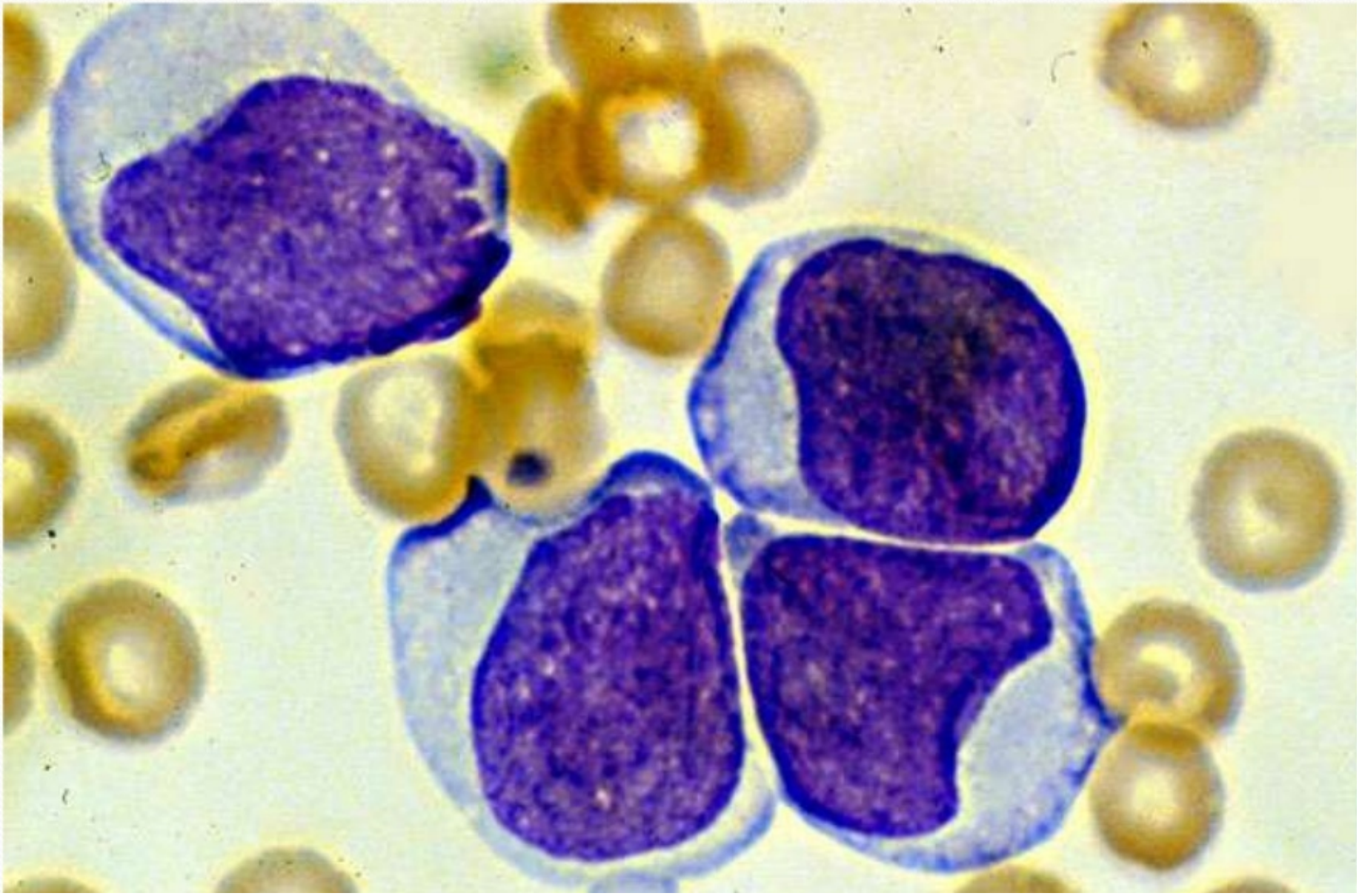
- In adults, chronic lymphocytic leukemia (CLL) and acute myelogenous leukemia (AML) are the most common leukemias.
- In children, the most common leukemia is acute lymphoblastic leukemia (ALL). Childhood leukemias also include acute myelogenous leukemia (AML) and other myeloid leukemias, such as chronic myelogenous leukemia (CML) and juvenile myelomonocytic leukemia (JMML).

- 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)



ALL Histology



Classification of leukaemia

1. **1. Acute lymphatic leukaemia (ALL)**

   Usually occurs before 14 years of age peak incidence is between 2-9 years of age, older adu

Pathophysiology

It arising from a single lymphoid stem cell, with impaired maturation and accumulation of the malignant cells in the bone marrow.

Acute lymphatic leukaemia Cont.

Signs and symptoms

Anaemia, bleeding, lymphadenopathy, infection

Clinical manifestation	Clinical manifestation
▪Fever ▪Pallor ▪Bleeding ▪Anorexia ▪Fatigue	▪Weakness ▪Bone, joint and abdominal pain ▪Increase intracrania press.

Acute lymphatic leukaemia Cont.

Diagnosis

- Low RBCs count, Hb, Hct, low platelet count , low normal or high WBC count.
- Blood smear show immature lymph blasts.

Bone marrow aspirate and biopsy: more than 20% lymphoblast in bone marrow.

Bone marrow in acute leukemia

- Necessary for diagnosis
- Useful for determining type
- Useful for prognosis
- Acute leukemias are defined by the presence of > 20% blasts in bone marrow (% of nucleated marrow cells)

- Generalized lymphadenopathy
- Infection of respiratory tract
- Anaemia and bleeding of mucus membrane
- Weight lossa
- Mouth sore

Treatment:

Chemotherapy

Induction

Consolidation

Maintenance

Intrathecal cytotoic drugs and /or craniospinal radiation.

Hematopoietic Stem cell transplantation (Bone marrow transplantation).

Acute lymphatic leukaemia Cont.

Treatment Cont.

- Avoid infection (hand washing, avoid crowds),injury
- Take measure to decrease nausea and t promote appetite, smoking and spicy and hot foods.
- Maintain oral hygiene.

Acute Myeloid Leukemia

(AML)

It occurs at any age but occurs most often at adolescence and after age of 55

Pathophysiology

Characterized by the development of immature myeloblasts in the bone marrow.

Clinical manifestation

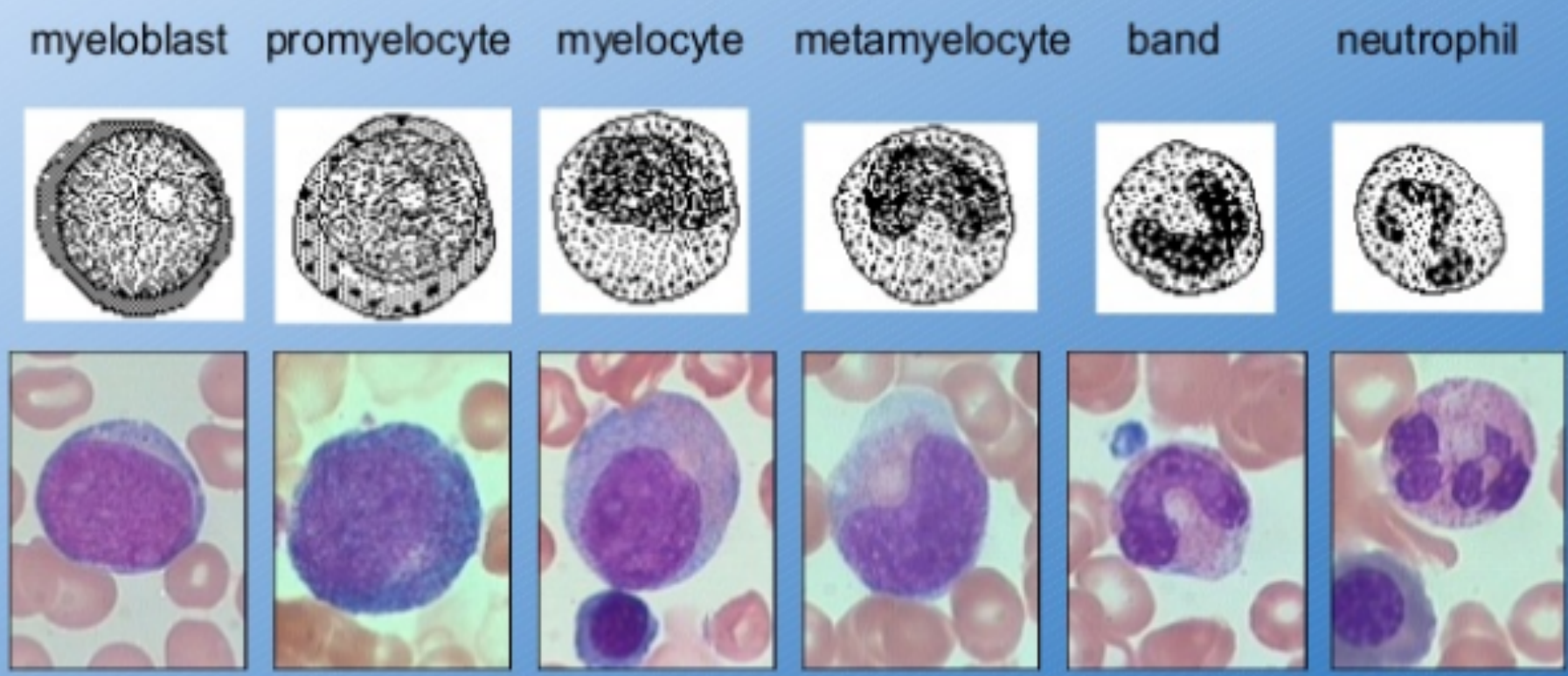
Similar to ALL plus sternal tenderness.

Management

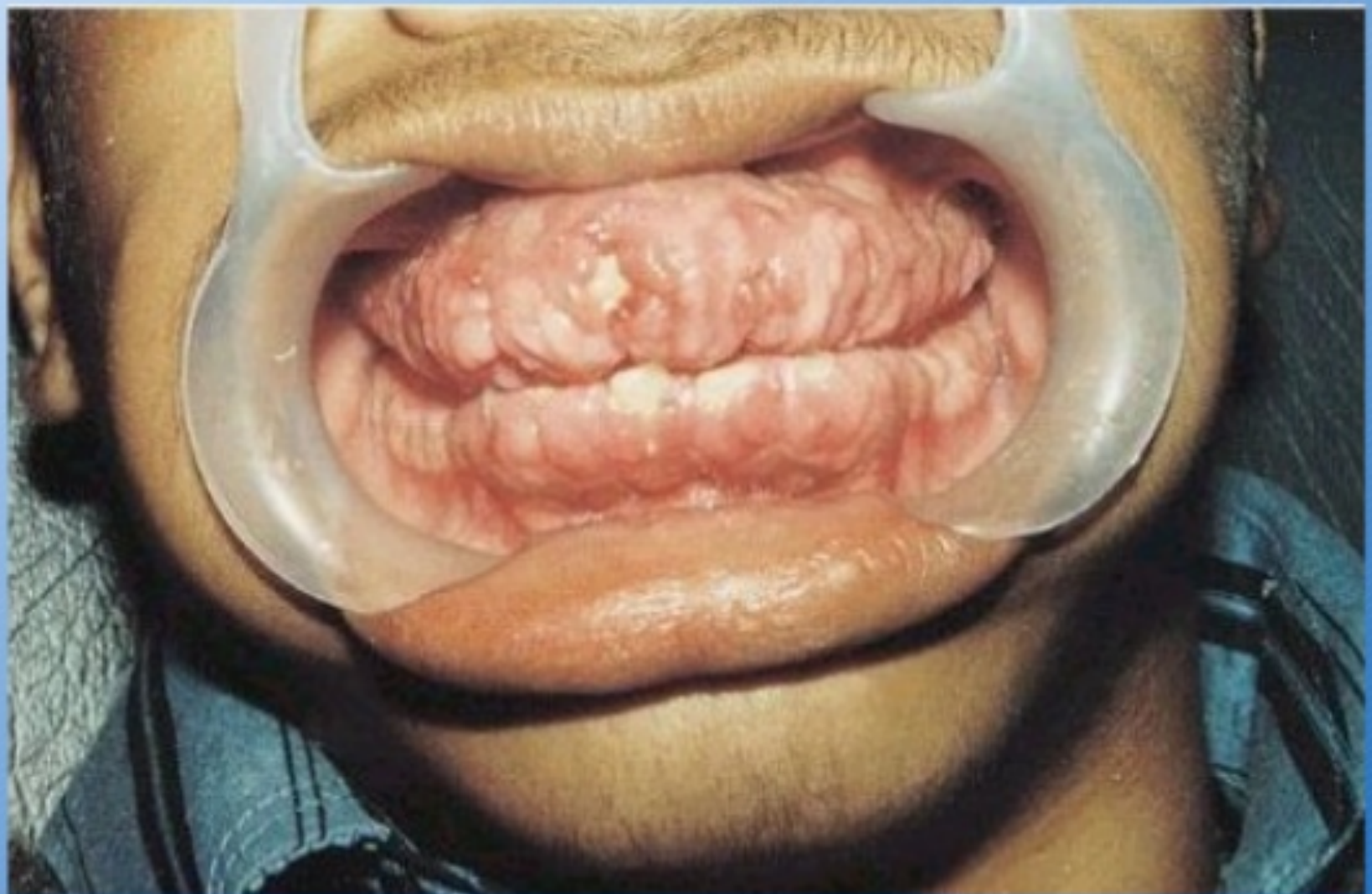
Diagnosis

Low RBC, Hb, Hct, low platelet count, low to high WBC count with myeloblasts.

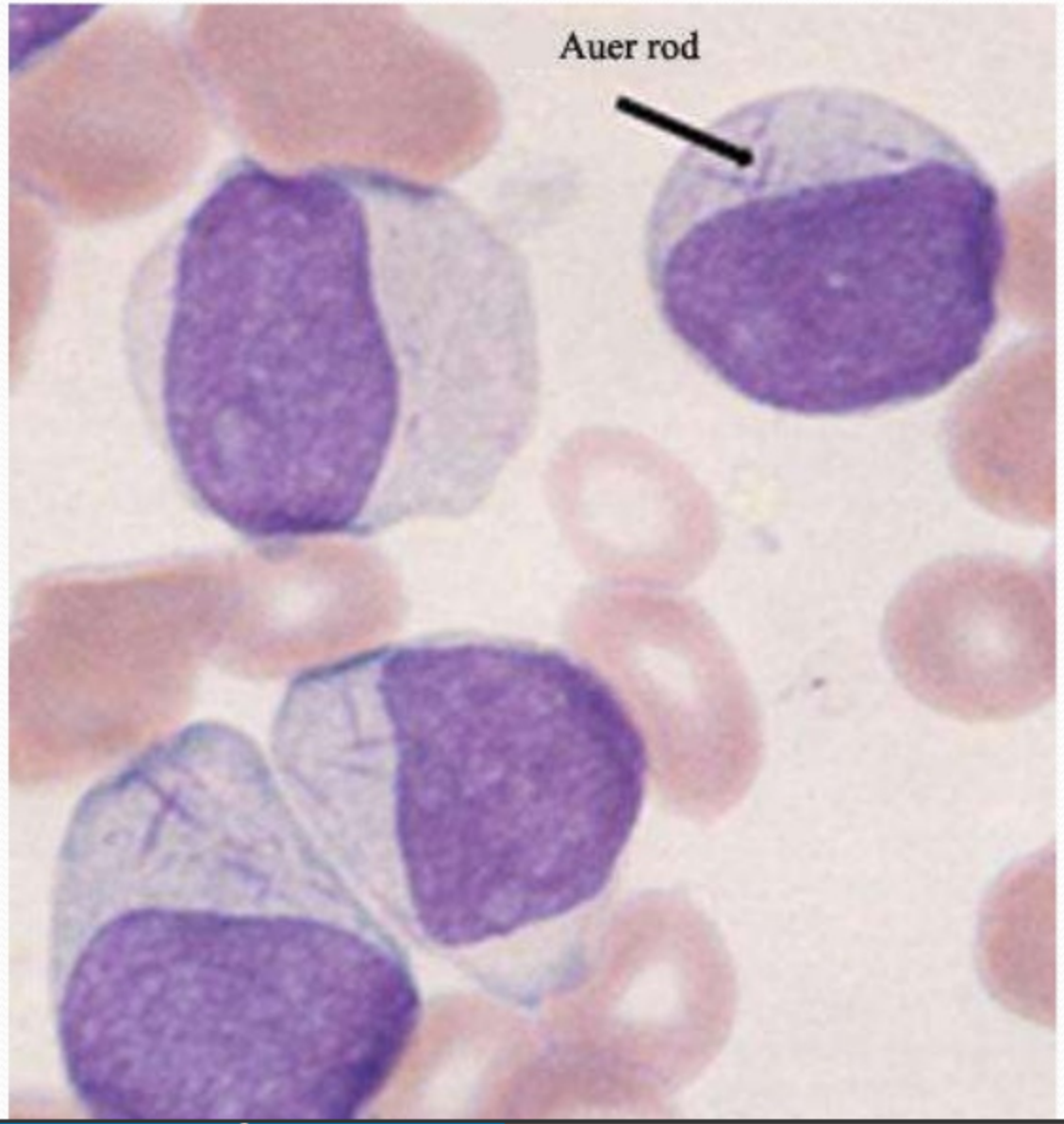
Myeloid maturation



Gum hypertrophy



AML Histology



Complete remission

CR is defined-

- Blood neutrophil count -1000/L
- Platelet count 100,000/L.
- Circulating blasts - absent.
- The bone marrow <5% blasts
- Auer rods -absent.
- Extramedullary leukemia -absent

Chronic Lymphocytic Leukemia

(CLL)

The incidence of CLl increases with age and is rare under the age of 35.It is common in men.

Pathophysiology

- It is characterized by proliferation of small, abnormal , mature B lymphocytes, often leading to decreased synthesis of immunoglobulin and depressed antibody response.
- The number of mature lymphocytes in peripheral blood smear and bone marrow are greatly increased

Chronic lymphocytic Leukaemia (CLL) Cont

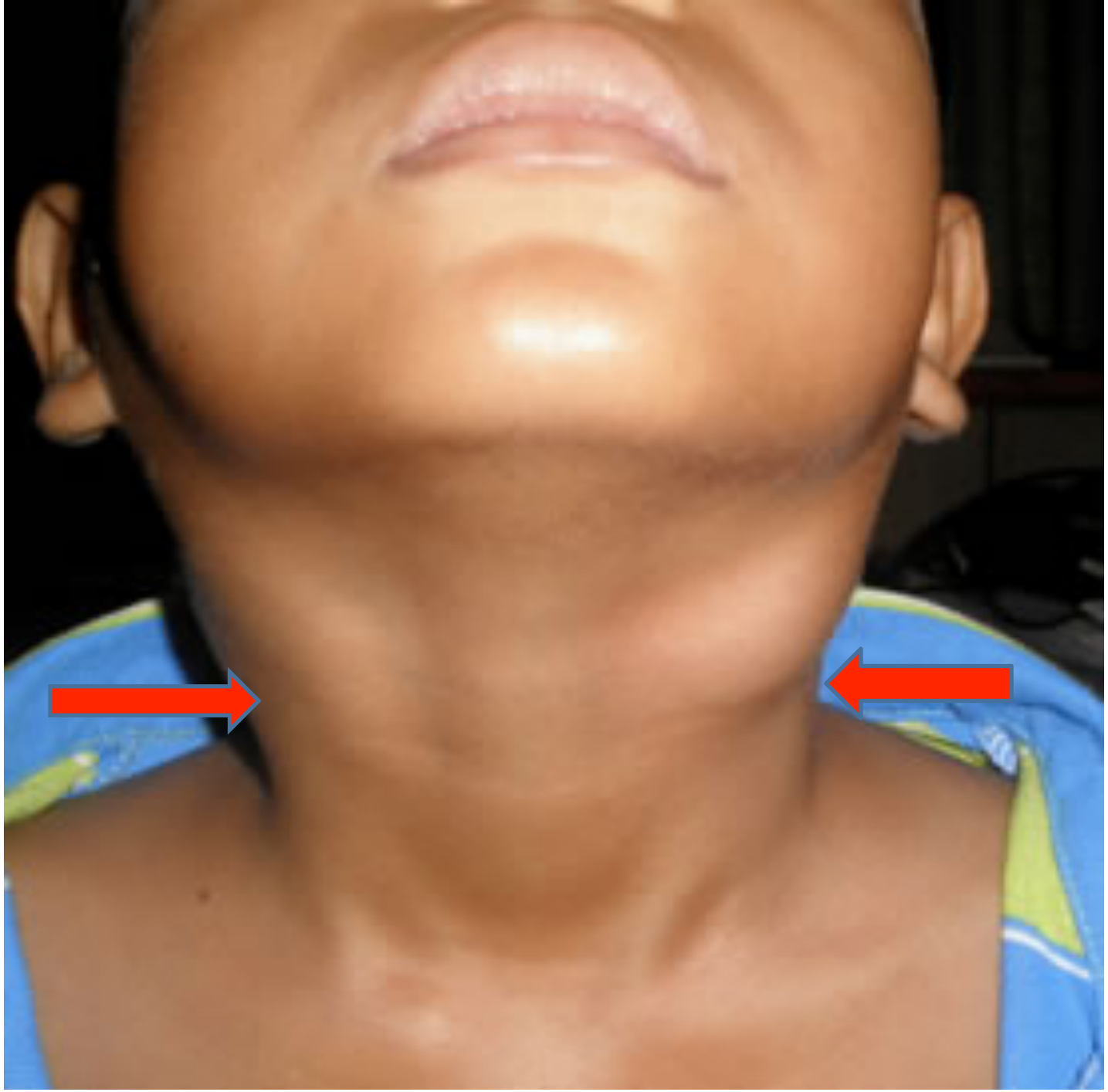
Clinical Manifestation

Usually there is no symptoms.

Chronic fatigue , weakness , anorexia, splenomegaly , lymphadenopathy, hepatomegaly.

Signs and Symptoms

- Pruritic vesicular skin lesions .
- Anaemia
- Thrombocytopenia.
- The WBC count is elevated to a level between 20,000 to 100,000.
- Increase blood viscosity and clotting episode.



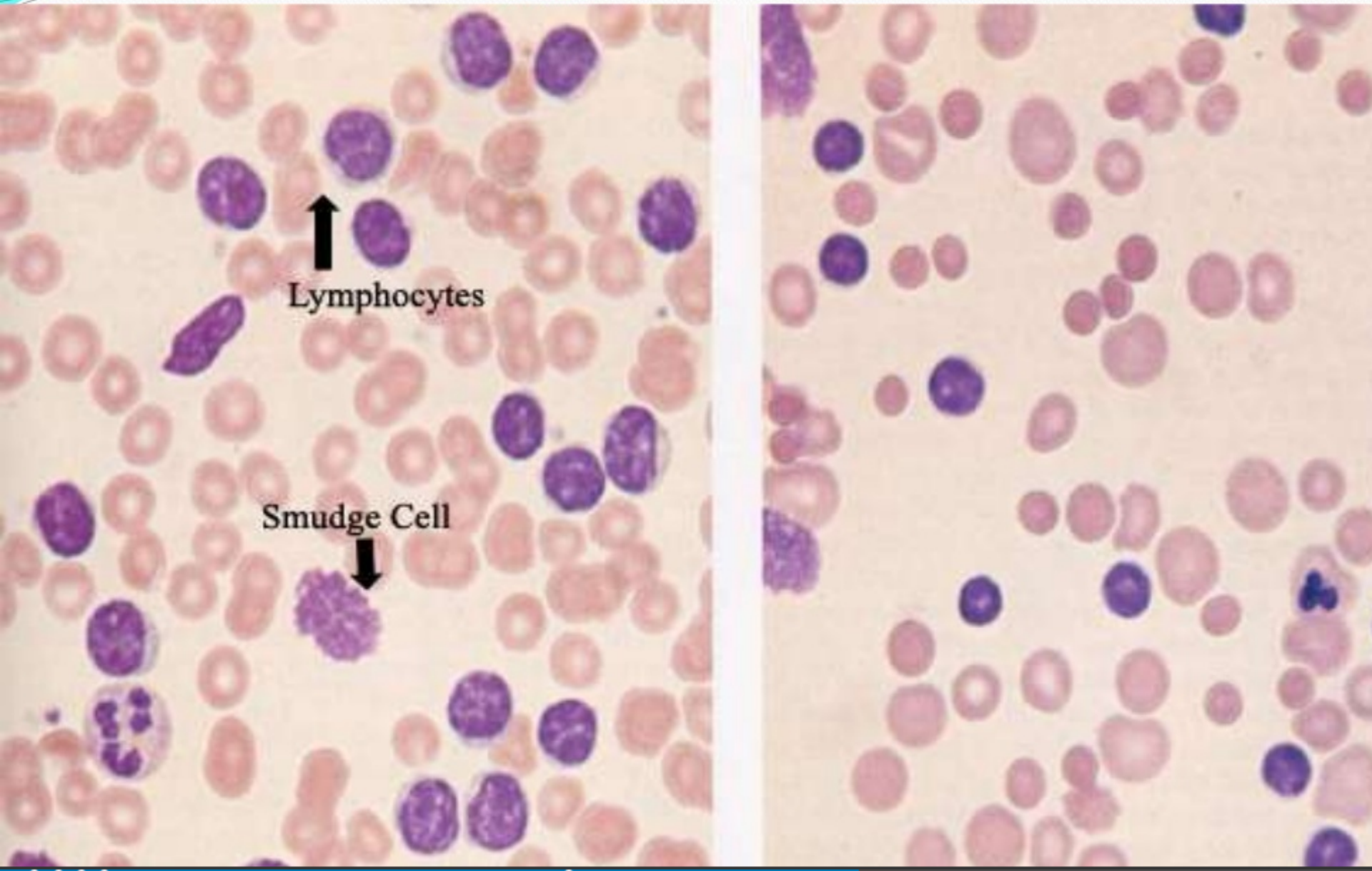
Chronic lymphocytic Leukaemia (CLL) Cont

Management

I. Persons are treated only when symptoms, particular anaemia , thrombocytopenia , enlarged lymph nodes and spleen appear.

I. Chemotherapy agents such as chlorambucil , and the glucocorticoids.

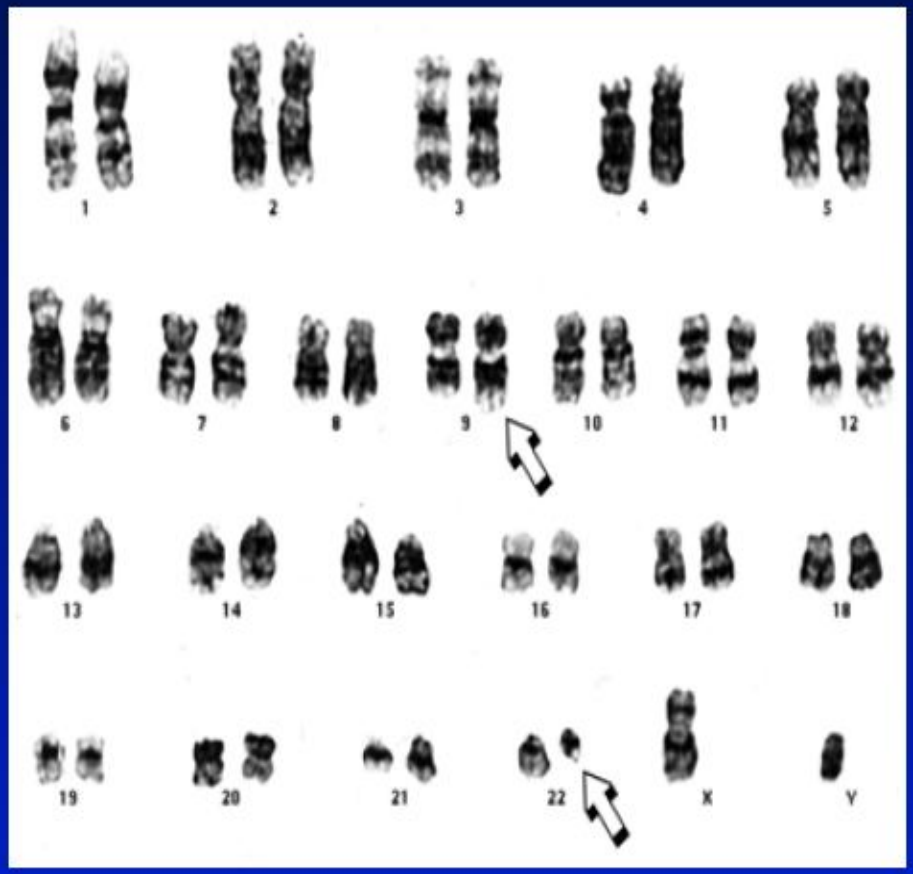
CLL Histology

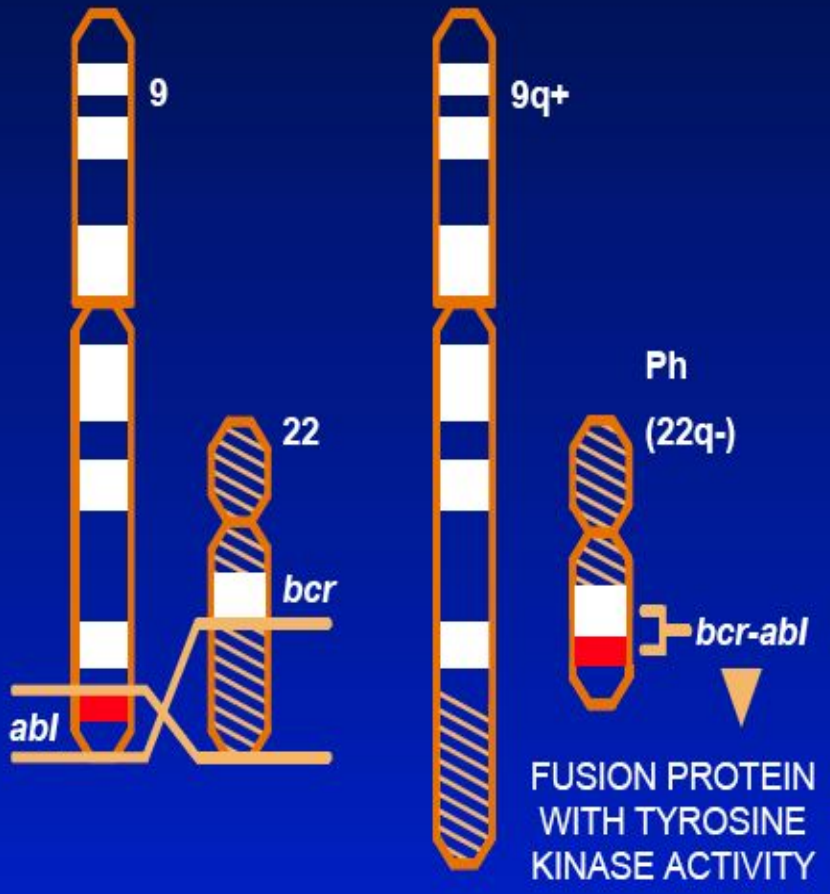


Chronic Myelogenous Leukaemia(CML)

- *Philadelphia chromosome*
  - The chromosome abnormality that causes chronic myeloid leukemia

CML: Linked to a Single Molecular Abnormality





The Philadelphia (Ph) Chromosome: t(9;22) Translocation

Occurs between 25-60 years of age. Peak 45 year

It is caused by benzene exposure and high doses of radiation.

Clinical Manifestation

- There is no symptoms in disease. The classic symptoms, include:
- Fatigue, weakness, fever.
- Weight loss, joint & bone pain.

Chronic Phase

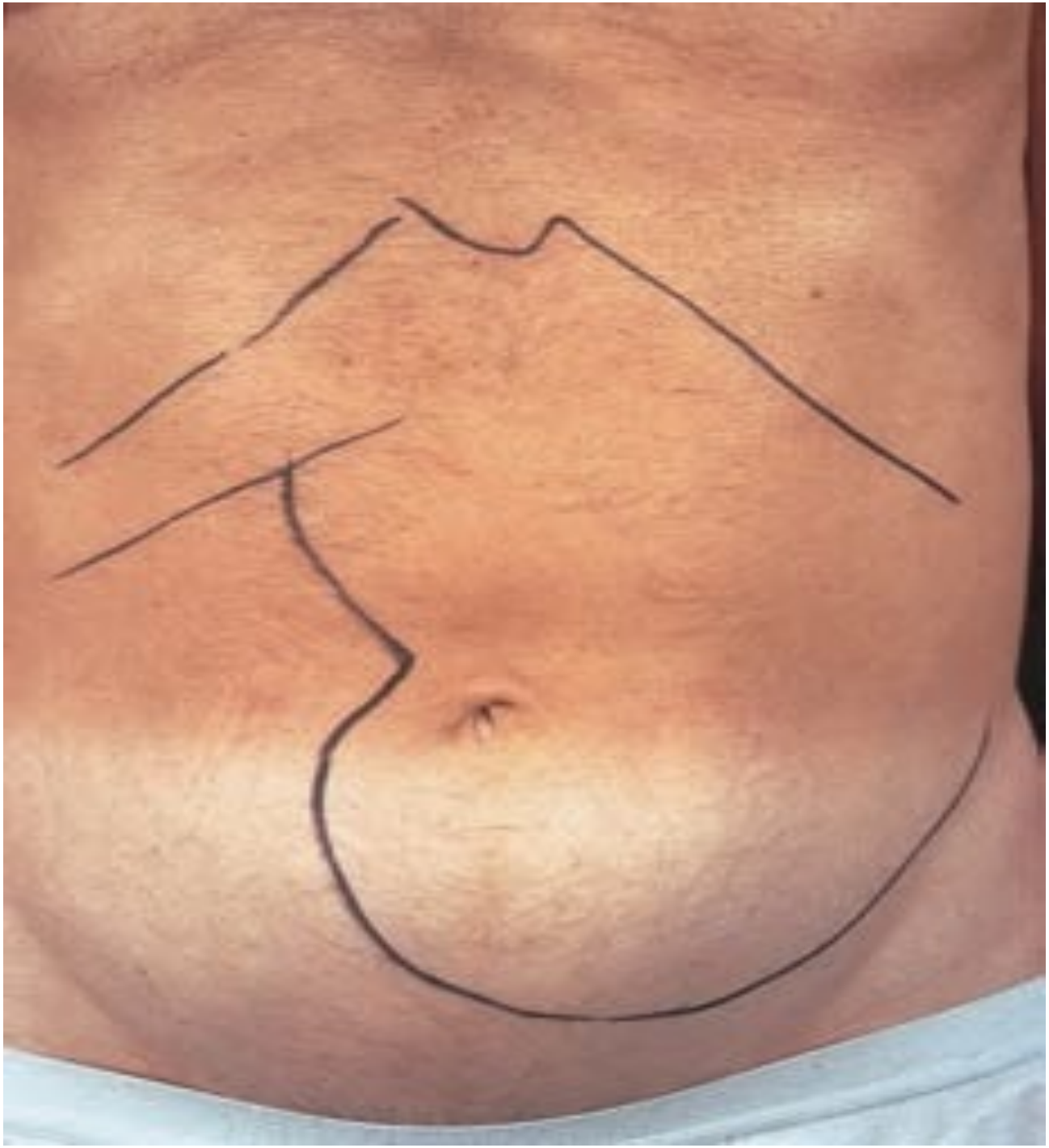
Accelerated Phase

Blast Phase

Chronic Myelogenous Leukaemia(CML) Cont.

Clinical Manifestation Cont.

- Massive splenomegaly
- The accelerated phase of disease(blostic phase) is characterized by increasing number of granulocytes in the peripheral blood.
- There is a corresponding anaemia and thrombocytopenia.



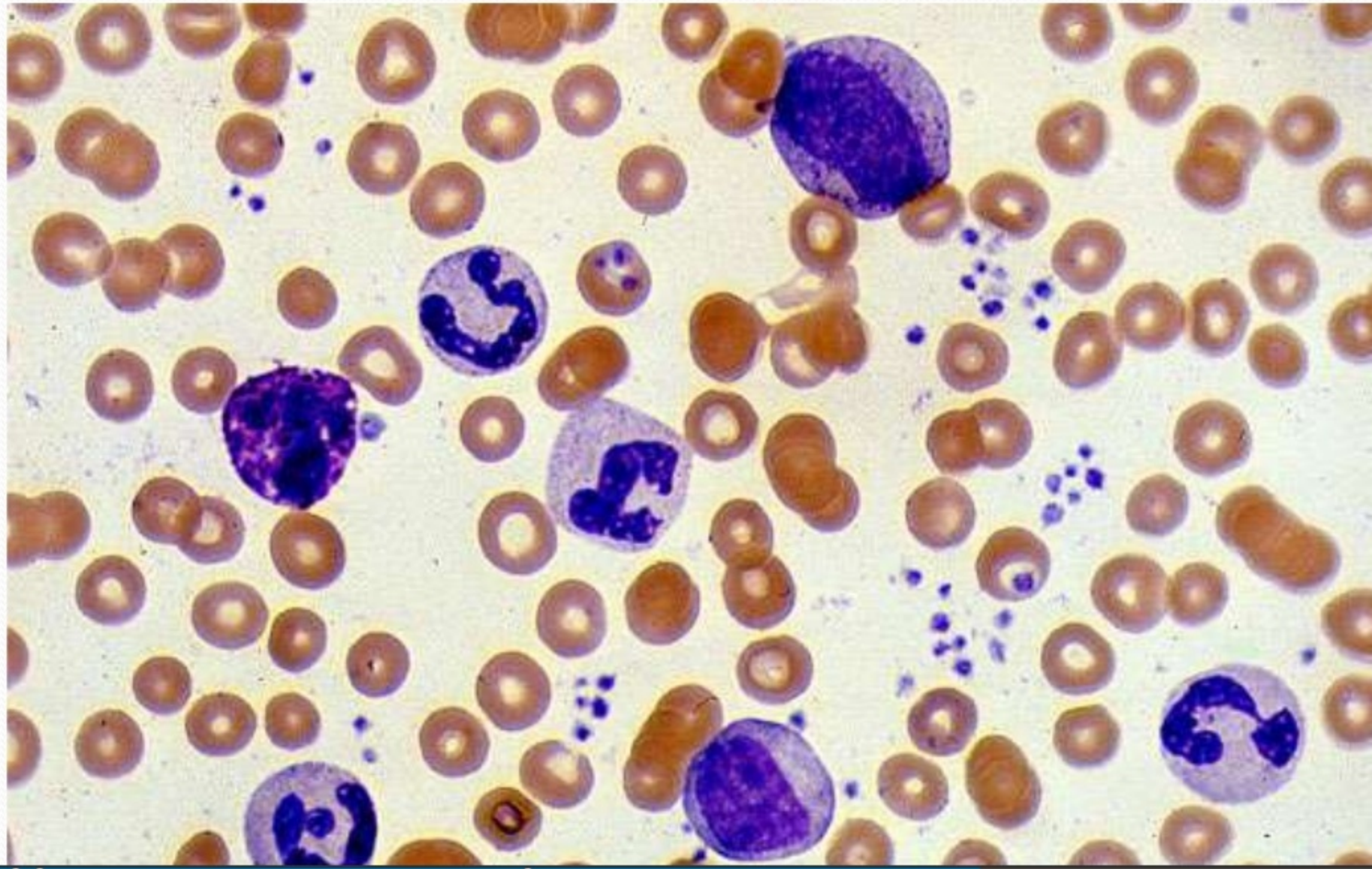
Chronic Myelogenous Leukaemia(CML) Cont.

Diagnosis

Lower RBC count, Hb, Hct, high platelet count early, lower count later.

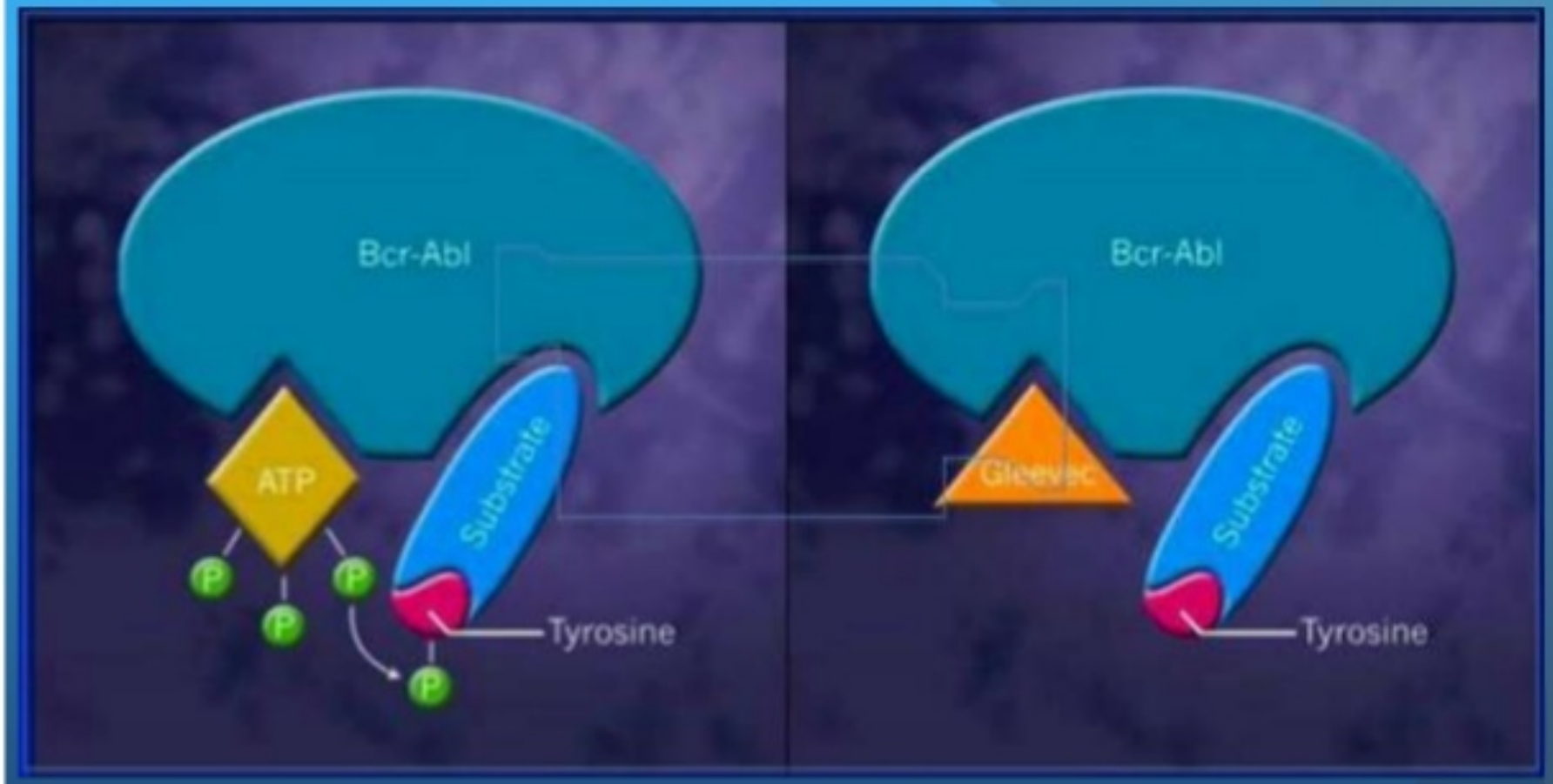
Normal number of lymphocytes and normal or low number of monocytes in WBC .

CML HISTOLOGY



Gleevec® (Imatinib)

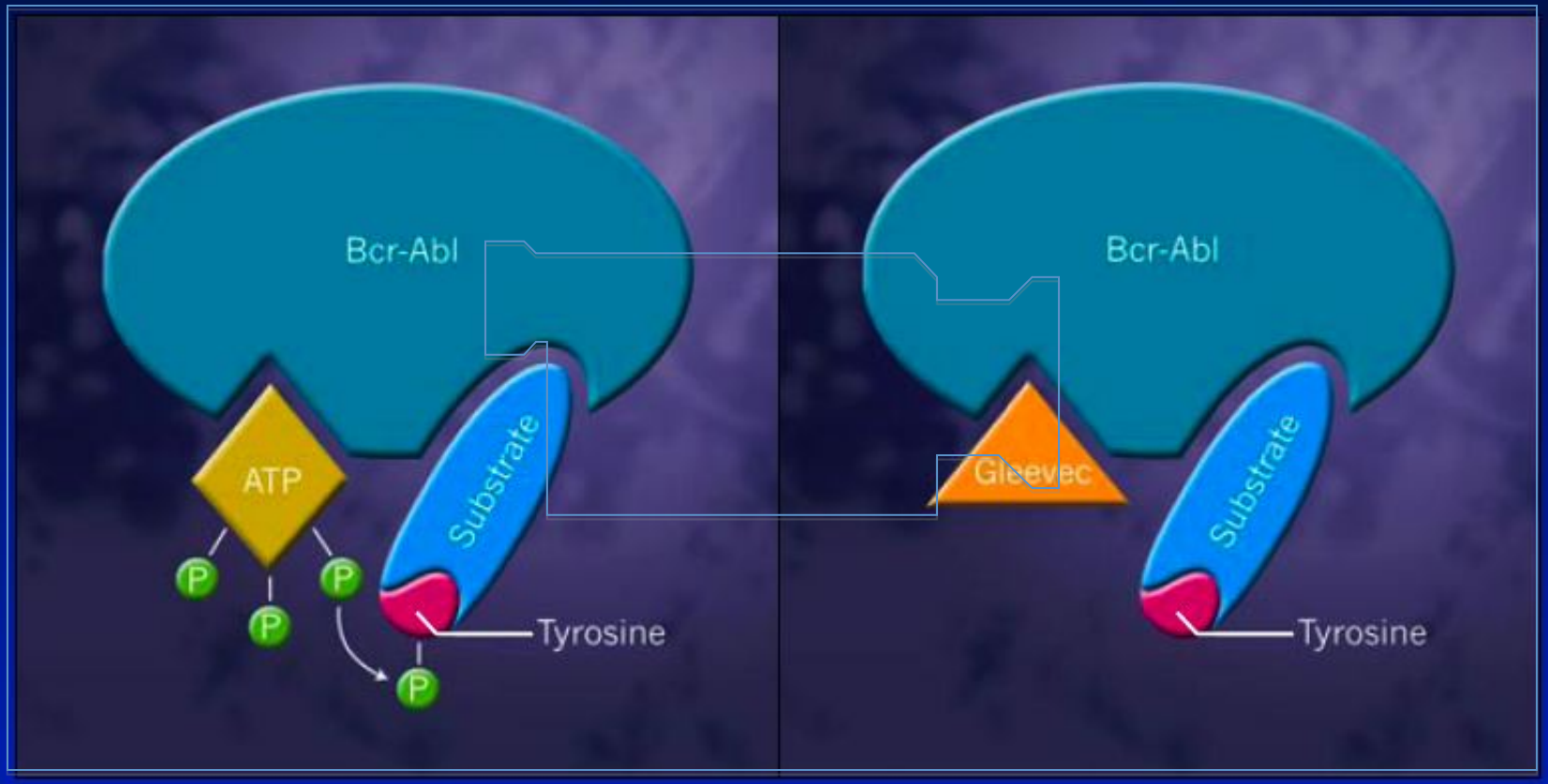
- A tyrosine Kinase Inhibitor developed in the late 1990's to treat Chronic Mylogenous Leukemia which is a cancer of the lymphatic system and bone. [1]
- CML is caused by a translocation of the 9th and 22nd chromosomes.[1]
  - Causes the Bcr-Abl oncogene to be created.[1]
  - Responsible for the activation of many signal transduction pathways that cause the characteristics of CML.



(Figure 2. shows the binding of Bcr/Abl to ATP and then to Gleevec®.)

http://www.pitt.edu/~super1/lecture/lec45951/004.htm

Gleevec® Targets the Cause of CML



- Gleevec—a specific inhibitor of a small family of tyrosine kinases, including Bcr-Abl, Kit, and PDGF receptor