Leukemia

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Leukemia

- A group of malignant disorders affecting the blood and blood-forming tissues of
  - Bone marrow
  - Lymph system
  - Spleen
- Occurs in all age groups

Leukemia

- Results in an accumulation of dysfunctional cells because of a loss of regulation in cell division
- Fatal if untreated
  - Progressive

Leukemia

- Often thought of as a childhood disease
- The number of adults affected with leukemia is 10 times that of children

Leukemia

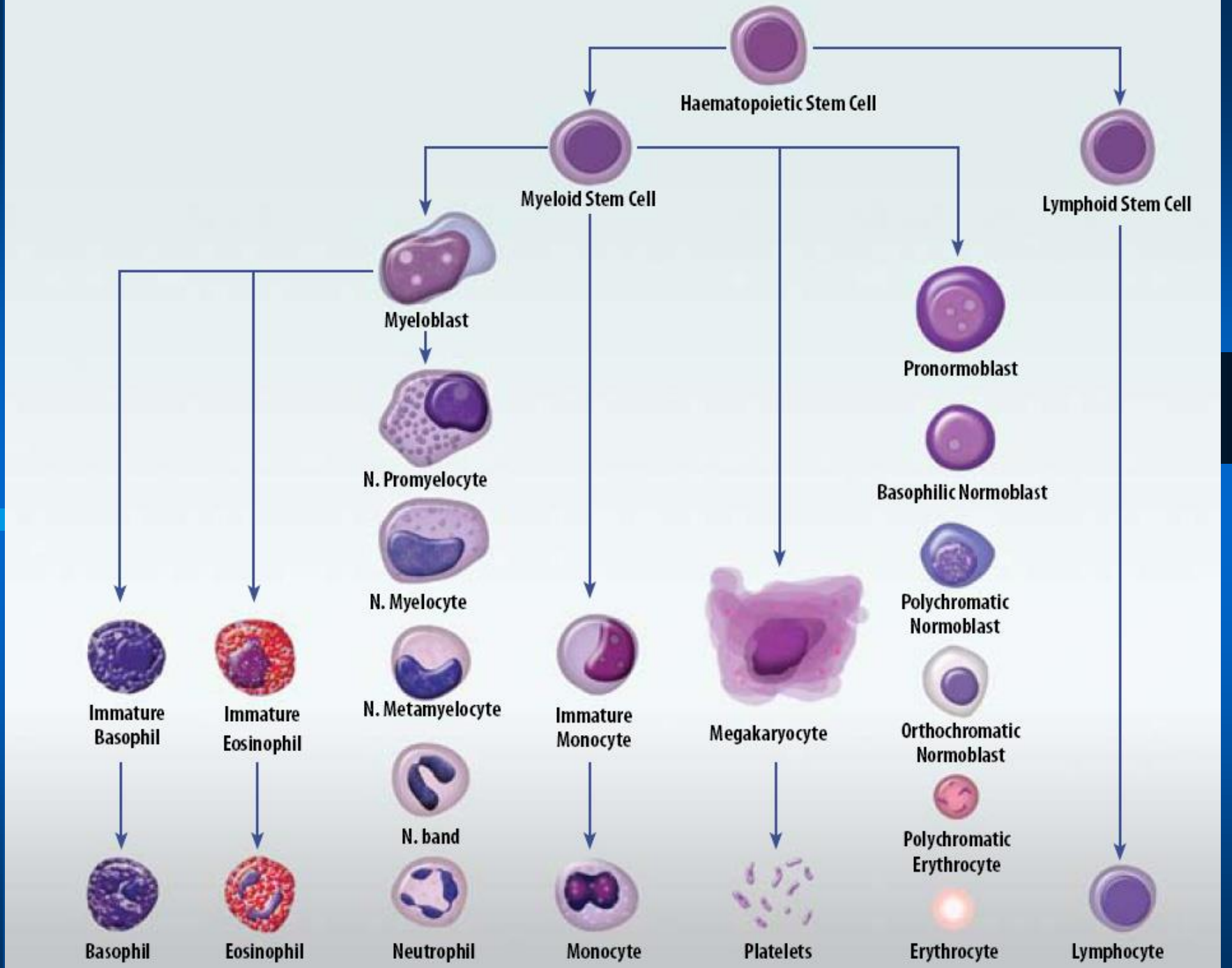
Etiology and Pathophysiology

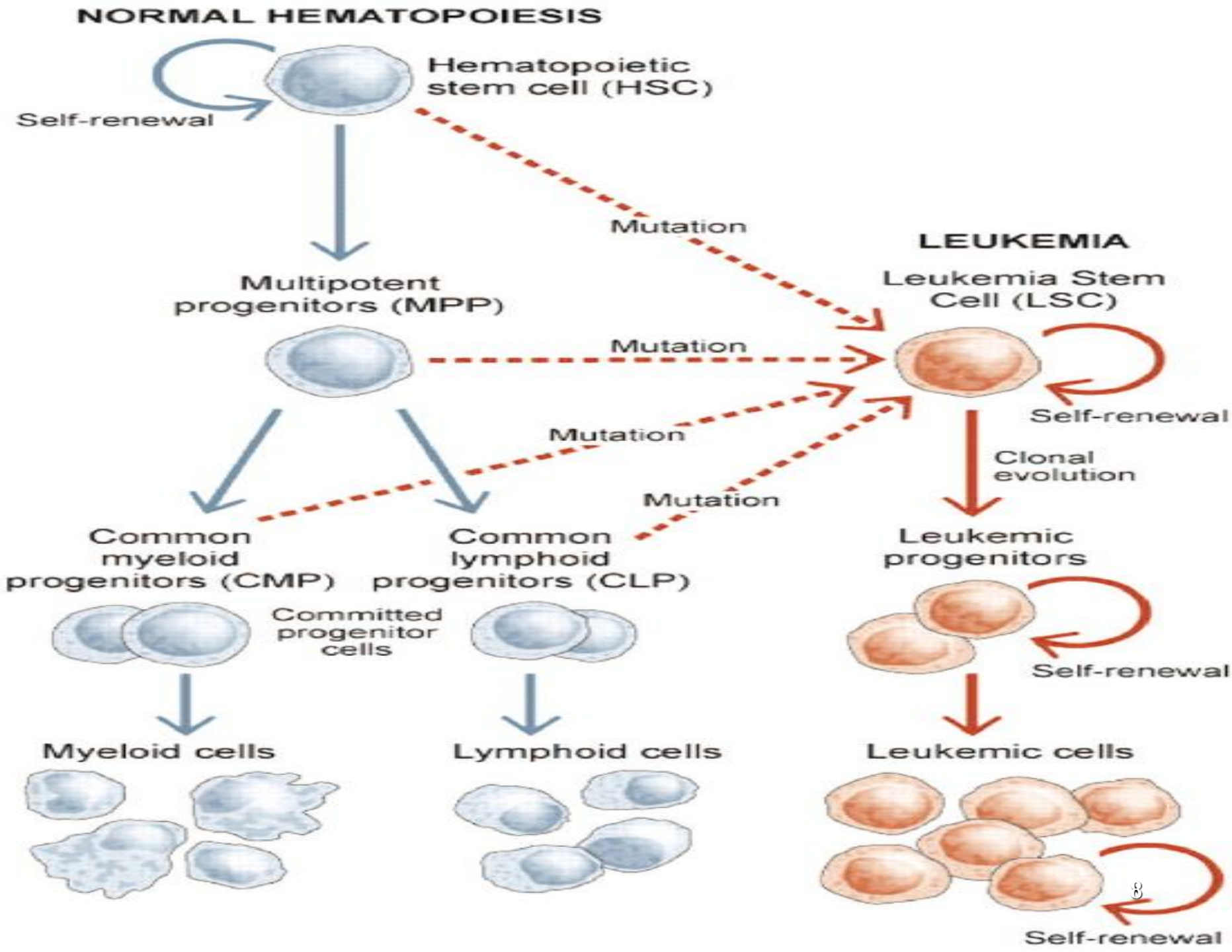
- No single causative agent
- Most from a combination of factors
  - Genetic and environmental influences

Leukemia

Etiology and Pathophysiology

- **Associated with the development of leukemia**
  - **Chemical agents**
  - **Chemotherapeutic agents**
  - **Viruses**
  - **Radiation**
  - **Immunologic deficiencies**


Haematopoietic Stem Cell
Myeloid Stem Cell
Lymphoid Stem Cell
Myeloblast
N. Promyelocyte
N. Myelocyte
N. Metamyelocyte
N. band
Pronormoblast
Basophilic Normoblast
Polychromatic Normoblast
Orthochromatic Normoblast
Polychromatic Erythrocyte
Immature Basophil
Immature Eosinophil
Immature Monocyte
Megakaryocyte
Basophil
Eosinophil
Neutrophil
Monocyte
Platelets
Erythrocyte
Lymphocyte


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 leukemias

Two major types (4 subtypes) of leukemias

Acute leukemias

- Acute lymphoblastic leukemia (ALL)
- Acute myelogenous leukemia (AML)
  (also "myeloid" or "nonlymphocytic")

Chronic leukemias

- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)

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

Leukemia

Classification

- **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**

Myelogenous Leukemia

- Leukemia characterized by proliferation of myeloid tissue (as of the bone marrow and spleen) and an abnormal increase in the number of granulocytes, myelocytes, and myeloblasts in the circulating blood

Myelogenous Leukemia

- Myeloid tissue is a biologic tissue with the ability to perform hematopoiesis. 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).

Myelogenous Leukemia

- Granulocytes are a category of white blood cells characterized by the presence of granules in their cytoplasm.[1] They are also called polymorphonuclear leukocytes (PMN or PML) because of the varying shapes of the nucleus, which is usually lobed into three segments.
- The myeloblast is a unipotent stem cell, which will differentiate into one of the actors of the granular series.

Acute Myelogenous Leukemia (AML)

- Leukemia characterized by proliferation of myeloid tissue (as of the bone marrow and spleen) and an abnormal increase in the number of granulocytes, myelocytes, and myeloblasts in the circulating blood
- One fourth of all leukemias
  - 85% of the acute leukemias in adults
- Abrupt, dramatic onset
  - Serious infections, abnormal bleeding
- Uncontrolled proliferation of myeloblasts
  - 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

Acute Lymphocytic Leukemia

- 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

Chronic Myelogenous Leukemia

- *Philadelphia chromosome*
  - The chromosome abnormality that causes chronic myeloid leukemia (CML) (9 &22)
  - Genetic marker
- Chronic, stable phase followed by acute, aggressive (blastic) phase

Chronic Lymphocytic Leukemia (CLL)

- Production and accumulation of functionally inactive but long-lived, mature-appearing lymphocytes
- B cell involvement
- Lymph node enlargement is noticeable throughout the body
  - ↑ incidence of infection

Chronic Lymphocytic Leukemia

- Complications from early-stage CLL is rare
  - May develop as the disease advances
  - Pain, paralysis from enlarged lymph nodes causing pressure

Hairy Cell Leukemia

- 2% of all adult leukemias
- Usually in males > 40 years old
- Chronic disease of lymphoproliferation
  - B lymphocytes that infiltrate the bone marrow and liver

Hairy Cell Leukemia

- Cells have a “hairy” appearance
- Symptoms from
  - Splenomegaly, pancytopenia, infection, vasculitis
- Treatment
  - alpha-interferon, pentostatin, cladribine

Unclassified Leukemias

- 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

Differential Diagnosis

1. Aplastic anemia
2. Myelodysplastic syndromes
3. Multiple myeloma
4. Lymphomas
5. Severe megaloblastic anemia
6. Leukemoid reaction

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

Leukemia

Clinical Manifestations

- Relate to problems caused by
  - Leukemic cells infiltrate patient's organs
    - Splenomegaly
    - Hepatomegaly
    - Lymphadenopathy
    - Bone pain, meningeal irritation, oral lesions (chloromas)

Leukemia

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

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

What is remission?

The main aim of treatment for acute lymphoblastic leukaemia is to give a remission. This means that the abnormal, immature white cells or blasts can no longer be detected in the blood or bone marrow, and normal bone marrow has developed again.

- For many people with acute lymphoblastic leukaemia the remission lasts indefinitely and the person is said to be cured.

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

Leukemia

Collaborative Care

- Chemotherapeutic treatment (cont.)
  - 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 treatment
  - 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**

Leukemia - *Bone Marrow and Stem Cell Transplantation*

- 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

Case 1

- 17 ys lady presented to th Er with CBC : WBCs 50,000 HGB 10 PLT 15000
- Abnormal circulating blasts 30%

How to proceed with diagnosis and ttt

Diagnosis and Risk stratification

- **1- Peripheral blood morphology**
- **Abnormal blasts**
- **2- Peripheral blood flowcytometry**
- **30 % blasts with CD 33 , CD 34 +ve**
- **3- BMBx for**
- **Morphology (myeloblasts)**
- **Cytogenetics (t 8:22)**
- **Flowcytometry (50% blasts express M antigens)**
- **Molecular (FLT 3 –ITD +ve)**

Treatment

- Goals
- 1- Remission induction (chemo for 28 days)
- 2-Response assessment (D 28)
- 3-Consolidation (chemo / SCT)
- 4- Maintinence.

RECOMMENDED BOOKS

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

BEST WISHES