# Leukemia 2

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# 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 ALLplus sternal tenderness. Splenomegaly and lymphadenopathy generally are less prominent than in ALL, but on rare occasions AML mimics a lymphoma by manifesting as a discrete tissue mass

## Management

### Diagnosis

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

# FRENCH-AMERICAN-BRITISH (FAB) CLASSIFICATION LEUKEMIA

The diagnosis and classification of AML are based on morphologic, histochemical, immunophenotypic, and karyotypic findings. Of these, the karyotype is most predictive of outcome

## Acute leukemia: morphological classification

### Acute Myeloid (AML)

$M_0$: minimally differentiated
$M_1$: without maturation
$M_2$: with maturation
$M_3$: hypergranular promyelocytic
$M_4$: myelomonocytic
$M_5$: (a) monoblastic, (b) monocytic
$M_6$: erythroleukemia
$M_7$: megakaryoblastic
Rare types (e.g. eosinophilic, natural killer)

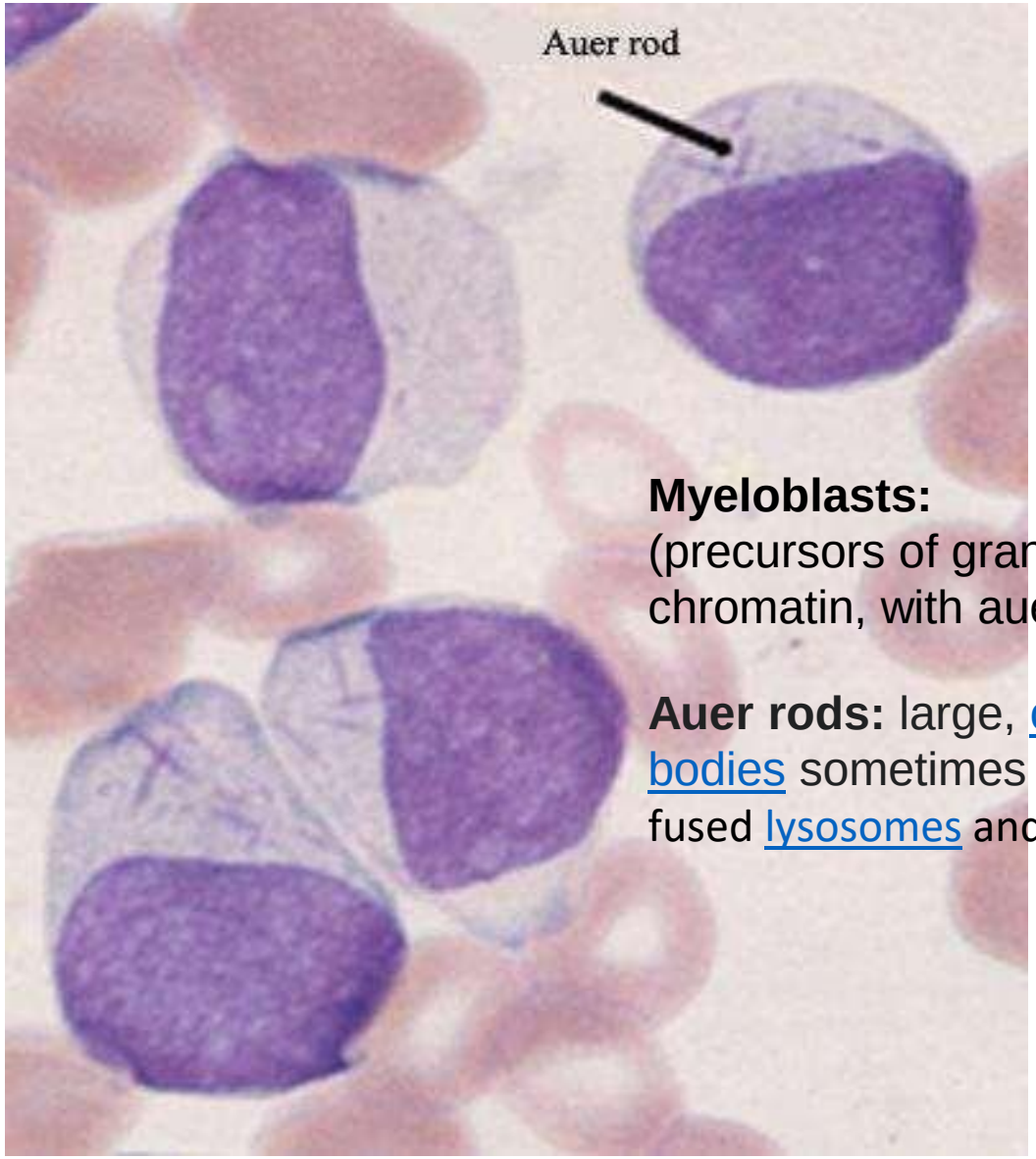
### Acute Lymphoblastic (ALL)

$L_1$: small, monomorphic
$L_2$: large, heterogeneous
$L_3$: Burkitt-cell type

- **Most AMLs harbor mutations in genes encoding transcription factors that are required for normal myeloid cell differentiation.** These mutations interfere with the differentiation of early myeloid cells, leading to the accumulation of myeloid precursors (blasts) in the marrow.
- Of particular interest is the (15;17) translocation in acute promyelocytic leukemia, which results in the fusion of the retinoic acid receptor α *(RARA)* gene on chromosome 17 and the *PML* gene on chromosome 15. The chimeric gene produces a PML/RARA fusion protein that blocks myeloid differentiation at the promyelocytic stage, probably in part by inhibiting the function of normal retinoic acid receptors.

- AMLs without translocations involving *RARA* do not respond to all-*trans* retinoic acid (ATRA). More recently, it has been noted that the combination of ATRA and arsenic trioxide, a salt that induces the degradation of the PML/RARA fusion protein, is even more effective than ATRA alone, producing cures in more than 80% of patients.
- This is an important example of a highly effective therapy targeted at a tumor-specific molecular defect.

# AML Histology




**Myeloblasts:**
(precursors of granulocytes) have delicate nuclear chromatin, with auer rods

**Auer rods:** large, crystalline cytoplasmic inclusion bodies sometimes observed in myeloid blast. Composed o fused lysosomes and rich in lysosomal enzymes

# Chronic lymphocytic Leukaemia (CLL)

The incidence of CLL increases with age more than 60 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 (more than 5x10^9) with or without nodal involvement (SLL)

# Chronic lymphocytic Leukaemia (CLL) Cont

**Clinical Manifestation**

Usually there is no symptoms.

Chronic fatigue, weakness, anorexia, splenomegaly, lymphadenopathy, hepatomegaly and pruritic vesicular skin lesions .

Laboratory findings:

- Anemia
- Thrombocytopenia.
- The WBC count is elevated to a level between 20,000 to 100,000 with lymphocytosis

# Chronic lymphocytic Leukaemia (CLL) Cont

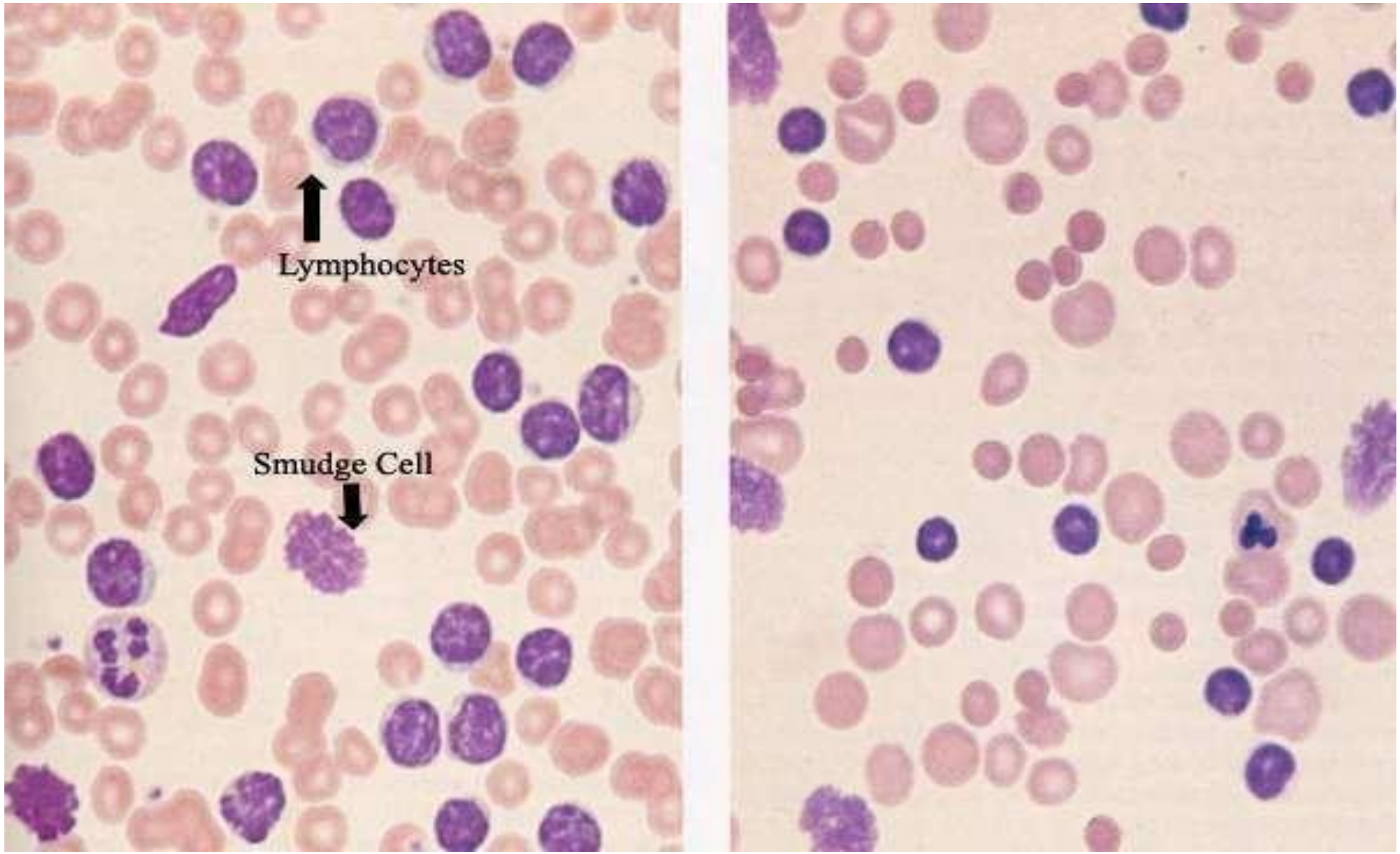
**Management**

- Persons are treated only when symptoms, particular anaemia, thrombocytopenia.

- Chemotherapy agents such as chlorambucil, and glucocorticoids.

- Patient and family education is that describe for ALL.

# CLL Histology



# Chronic Myelogenous Leukaemia (CML)

- **CML is distinguished from other myeloproliferative neoplasms by the presence of a chimeric *BCR-ABL* gene derived from portions of the *BCR* gene on chromosome 22 and the *ABL* gene on chromosome 9.**

*Philadelphia chromosome:* (the chromosome abnormality that causes CML).

- Although the Ph chromosome is highly characteristic of CML, it also is present in 25% of adult B cell–ALLs and a small subset of AMLs.

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

CML principally affects adults between 25 and 60 years of age.

The peak incidence is in the **fourth and fifth** decades of life

## Clinical Manifestation

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

# 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 .

## Treatment

The commonly drugs are hydroxyurea and busulfan (monitor of WBC count needed with therapy).

The only potential curative therapy of CML is the bone marrow transplant.

## Nursing Intervention

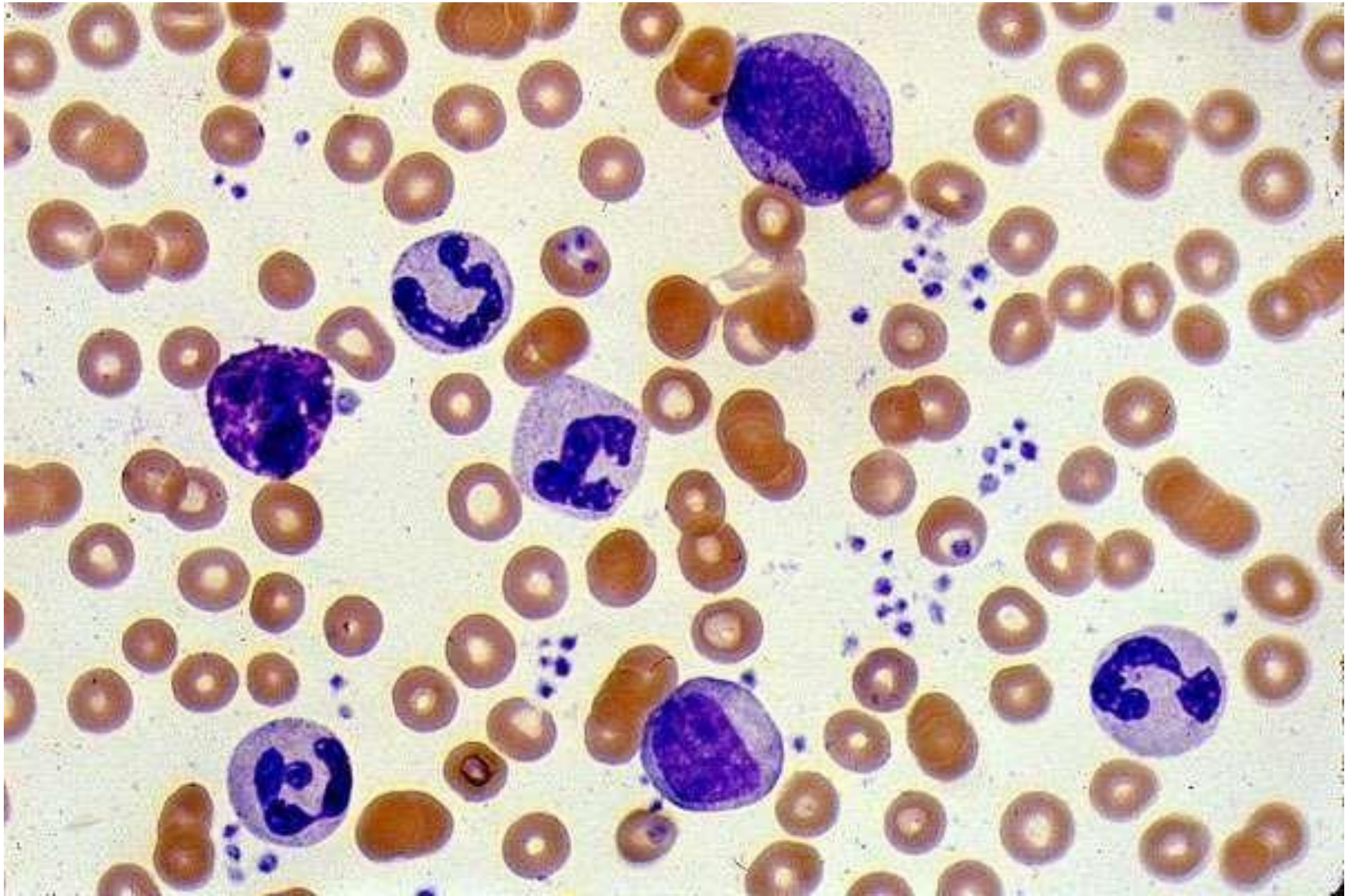
Taking measures to prevent infection.

Providing oral hygiene.

Patient and family education as ALL and AML.

- The peripheral blood findings are highly characteristic. The leukocyte count is elevated, often exceeding 100,000 cells/µL.
- **The circulating cells are predominantly neutrophils, metamyelocytes, and myelocytes**, but **basophils** and **eosinophils** are also prominent and platelets are usually increased.
- The bone marrow is hypercellular owing to increased numbers of maturing granulocytic and megakaryocytic precursors.
- The red pulp of the enlarged spleen resembles bone marrow because of the presence of extensive **extramedullary hematopoiesis.**

# CML HISTOLOGY



- The natural history of CML initially is one of slow progression. Even without treatment, the median survival is 3 years. After a variable (and unpredictable) period, approximately half of CML cases enter an accelerated phase marked by increasing anemia and new thrombocytopenia, the appearance of additional cytogenetic abnormalities, and finally transformation into a picture resembling acute leukemia (blast crisis).
- In the remaining 50% of cases, blast crisis occurs abruptly, without an accelerated phase. Of note, in 30% of cases the blast crisis resembles precursor-B cell ALL. In the remaining 70% of cases, the blast crisis resembles AML. Less commonly, CML progresses to a phase of extensive bone marrow fibrosis resembling primary myelofibrosis.

# MANAGEMENT

watchful waiting,
chemotherapy,
targeted therapy,
radiation therapy, and
stem cell transplant.

# Treatment

## The choice of treatment depends mainly on the following:

The type of leukemia (acute or chronic) and whether leukemia cells were found in cerebrospinal fluid

# WATCHFUL WAITING

- Chronic leukemia without symptoms, may not need cancer treatment right away.
- Watch for health closely so that treatment can start when it begin to have symptoms.

# chemotherapy

- People with acute leukemia need to be treated right away.
- The goal of treatment is to destroy signs of leukemia in the body and make symptoms go away, this is called a **remission**.
- After people go into remission, more therapy may be given to prevent a **relapse**.

# STEM CELL TRANSPLANT

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

# TYPES OF STEM CELL TRANSPLANTATION

1. **Allogeneic Stem Cell Transplant**

stem cells are taken from a matching donor. To determine if a donor's stem cells are the right match, the patient undergoes a human leukocyte antigens (HLA) test. Through this test, we compare the patient's blood and tissue type against blood samples from the donor.

## 2. Autologous Stem Cell Transplant

In this type of transplant, stem cells are collected from the patient themselves. The stem cells are then harvested, frozen and stored, and then given back to the patient. This type of transplant is rare for leukemia patients and is typically used in select cases of AML.

## Nutrition and Physical Activity

It's important for you to take care of eating well and staying as active.

Right amount of calories to maintain a good weight. Enough protein. Eating well may help to feel better and have more energy.

## Follow-up Care

regular checkups after treatment for leukemia.