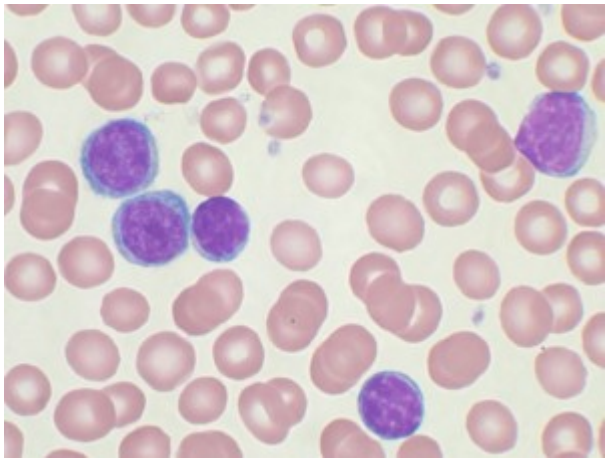
Types of Leukemia

See online here

Leukemia is blood cancer, this condition is characterized by exceeded amount of immature white blood cells in the blood stream (blasts), which normally remain in the bone marrow for their further maturity or sent to special organs (spleen, thymus) to get ready for their proper functioning. White blood cells are responsible for the adequate immune reaction of the body to various antigens (infections, malignant cells, foreign bodies, allergens); hence, immature cells cannot cover this function fully and fail to perform in the way m proper white cell do. Thus, the body easily contracts different infections as it is not capable to fight them, as the disease advances the bone morrow becomes exhausted shooting even more damaged cells or stops producing blood cells at all (hemogenic collapse).



Types of Leukemia

Classification

Acute leukemias which can be of myeloid or lymphoid lineage

- Acute lymphoblastic leukemia (ALL)
- Acute myeloid leukemia (AML)

Chronic leukemias which can be of myeloid or lymphoid lineage

- Chronic myelogenous leukemia
- Chronic lymphocytic leukemia

Acute Lymphocytic Leukemia

This is the most common form of leukemia in children between 2 and 4 years of age. This form rarely affects adults, though another incidence occurs after the age of 45 years. The

immature lymphocytes, mostly B-cells produced by the bone marrow, are not capable to maintain their direct function, namely, to provide immunity for the body. Thus, their young forms get to different organs and tissues and develop the symptoms of the disease.

Acute lymphoblastic leukemia, B-cell origin is the most common hematopoietic malignancy in children, with 80% of those cases showing B-cell lineage as confirmed by expression of CD19, CD79, and cyCD22 as well as lack of definitive myeloid differentiation. The leukemic form must pertain to more than 20% of the lymphoblasts in the bone marrow, with or without more than 20% in the peripheral blood.

Almost all cases show extensive replacement of marrow by neoplastic lymphoblasts, with reduction of normal hematopoietic elements. Note, in the case of a hypercellular marrow, more than 80% of the cells are represented by lymphoblasts. Patients present with any of the signs and symptoms of marrow failure, such as pallor and fatigue caused by anemia, petechiae and ecchymoses caused by thrombocytopenia, and fever related to granulocytopenia.

	Pre-B ALL	**Pre-T ALL**
Frequency	80%	20%
Age of onset	Childhood	Adolescence
Site	Blood/BM	Mediastinal mass
WBC count	Low-Normal	High
Prognosis	Good	Poor
Symptoms	Pancytopenia, neurologic symptoms, bone pain	

Acute Myeloid Leukemia (nonlymphocytic leukemia)

This is a very aggressive, fast-growing blood and bone marrow cancer. The bone marrow suddenly begins production of immature blood cells of all types—red, white, platelets—which, with time, crowd the normal ones, so that the normal immune response to the infections is not possible.

The tumor is thought to arise from several causes such as:

- Genetic influence
- Radiation exposure
- Chemical exposure such as benzene
- Drugs that induce secondary malignancies have been implicated in the development of AML
- Smoking and other occupational exposures such as exposure to petroleum products, paint, embalming fluids, ethylene oxide, herbicides, and pesticides, have also been associated with an increased risk of AML

There are subtypes of this kind of leukemia, according to the prevalence of the affected blood cells:

- Myeloblastic (M0) – on a special analysis
- Myeloblastic (M1) – without maturation
- Myeloblastic (M2) – with maturation
- Promyelocytic (M3)
- Myelomonocytic (M4)
- Monocytic (M5)
- Erythroleukemia (M6)

- Megakaryocytic (M7)

Chronic Lymphocytic Leukemia

It is a slowly growing blood and bone marrow cancer, which disturbs production and maturation of lymphocytes and spreads to the lymph nodes, liver, and spleen. **Thus, the tumor mostly presents with:**

- May be asymptomatic
- Splenomegaly typical
- Lymphocytosis > 5000/uL
- Mature appearance of lymphocytes
- Co-expression of CD19, CD5

Sometimes, it takes years for the disease to manifest as all pathogenic processes are indolent. However, it can turn into an acute form and then the prognosis aggravates accordingly.

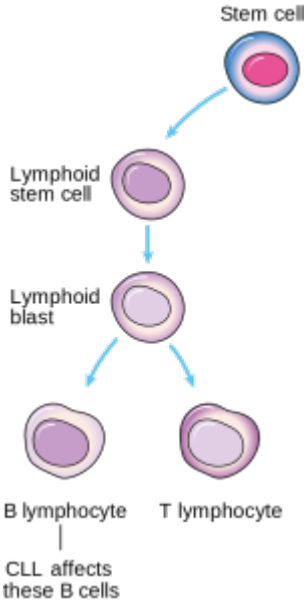


Image: “Diagram showing the cells CLL afects” by Cancer Research UK. License: CC BY-SA 4.0

B-cell chronic lymphocytic leukemia is the most common chronic leukemia in adults in Western countries. Most cases involve blood and bone marrow with or without the involvement of lymph nodes, spleen, liver, and other organs. The neoplastic lymphocytes are small but slightly larger than normal small lymphocytes.

They show scant cytoplasm and round, to slightly irregular, nuclei, containing clumped chromatin. Nucleoli are small to indistinct. A characteristic morphologic feature is a presence of “smudge” or “basket” cells, which are essentially neoplastic cells that got “smudged” during slide preparation because of the fragile nature of these cells. Compare the cell size of CLL cells with a single large granular lymphocyte.

Chronic Myeloid Leukemia

CML, unlike the other types of leukemia, has a distinguishing feature which makes this condition stand out from among this group.

The age-adjusted incidence is higher in men than in women (1.7 versus 1.0). The incidence of CML increases slowly with age until the middle forties, when it starts to rise rapidly. Chronic myelogenous leukemia (CML) accounts for 20% of all leukemias affecting adults.

CML is associated with an abnormal chromosome known as the Philadelphia chromosome (Ph chromosome-abnormal cancer chromosome). It occurs when a piece of chromosome 22 breaks off and joins to the end of chromosome 9, which also breaks off and reattaches to chromosome 22. This type of leukemia, just like the other ones, affects the blood and the bone marrow.

Chronic myelogenous leukemia is a clonal chronic myeloproliferative disorder. It results in absolute increase in cells of the granulocytic lineage, including neutrophils, eosinophils, and basophils. It is caused by the fusion of a portion of the BCR gene on chromosome 22q, with a portion of the ABL1 gene translocated from chromosome 9q34, thus forming what is known as the Philadelphia chromosome. The resulting fused tyrosine kinase protein BCR-ABL has constitutive proliferative activity. The marrow is markedly hypercellular, with an elevated myeloid to erythroid ration often exceeding 10:1.

Differentiating Leukemias

	ALL	**AML**	**CML**	**CLL**
Age	Children	Young adults	Middle-age	Elderly
Onset	Abrupt/Acute		Chronic/Insidious	
Symptoms	Cytopenias, bone pain		Non-specific, fatigue, weakness, etc.	
Prognosis	Excellent (2/3 cured)	Moderate (30% cured)	OK with imatinib; otherwise poor	Poor, but slowly progressing

Hairy Cell Leukemia

This is a rare subtype of chronic lymphocytic leukemia (CLL). It’s an indolent form of blood cancer. The whole essence of the condition is that the bone marrow produces far too many B-lymphocytes, which crowd the other types of blood cells. Being immature, the B-cells are not able to protect the body from infectious invaders.

The name of the disease comes from the specific appearance of the cells under a microscope. This illness is very peculiar as at the initial stages it might not require any treatment since there are no severe symptoms. However, as the disease progresses, treatment is cannot be evaded.

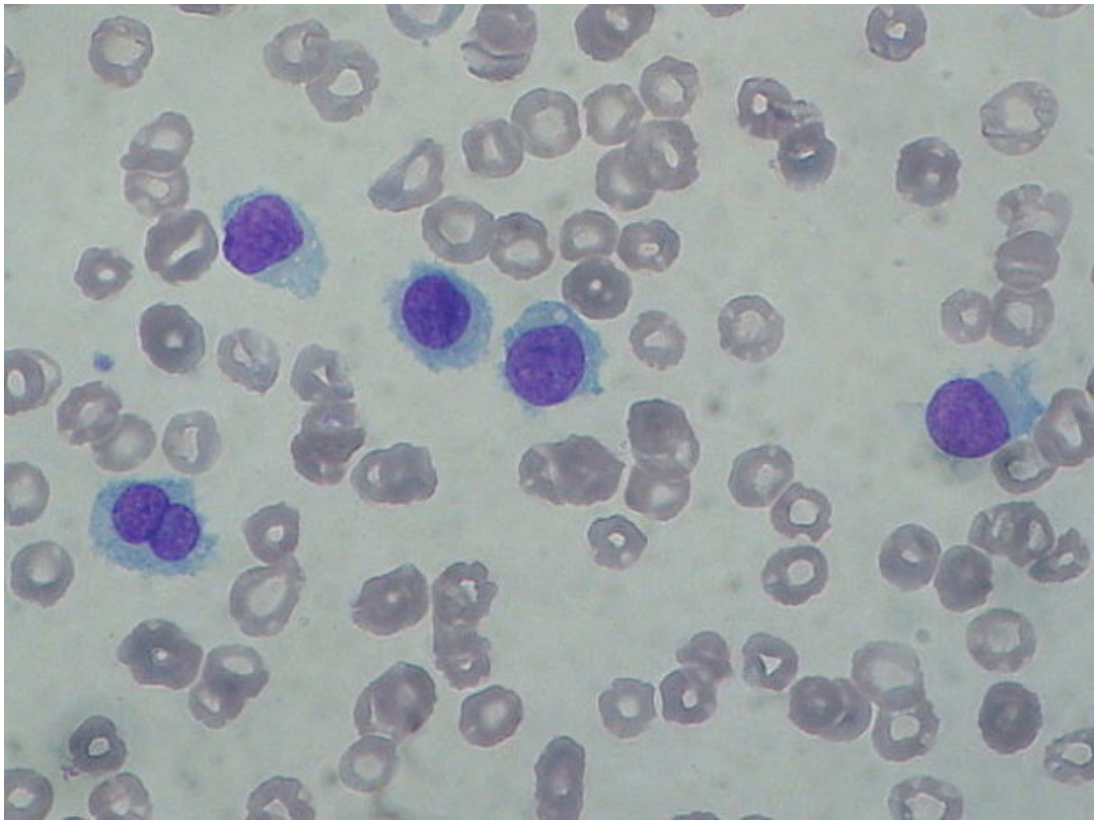
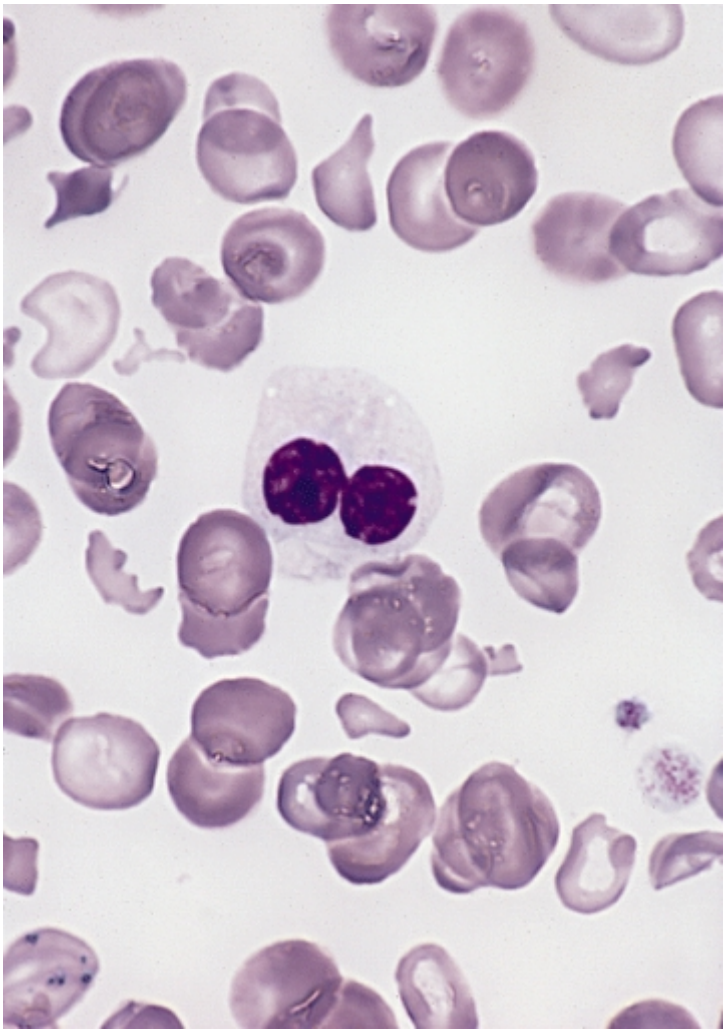


Image: “Hairy cell leukemia: abnormal B cells look “hairy” under a microscope because of radial projections from their surface.” by Paulo Henrique Orlandi Mourao. License: CC BY-SA 3.0

Figure: Hairy cell leukemia (HCL) is a rare, mature B-cell neoplasm, which involves bone marrow and spleen, but generally, only few circulating cells are seen on peripheral blood smears. Bone marrow involvement can be interstitial, patchy or diffuse (as in this case) depending on the extent of involvement. Because of marrow involvement, most patients present with pancytopenia and splenomegaly. Monocytopenia is also common. Absolute lymphocytosis may occur in up to 25% of the patients. Lymphadenopathy and hepatomegaly may also occur.

Myelodysplastic Syndromes

The bone marrow produces far too few blood cells of all types. They look dysplastic under microscope (getting the name for the condition), thus they are not able to perform their assumed functions in the body. Sometimes, this disease is called preleukemia, however, the true leukemia never develops from this condition. Myelodysplastic syndromes are associated with severe bleedings and infections.



Bone marrow: Therapy-related myelodysplastic Syndrome: Blood smear from an adult female with a myelodysplastic syndrome related to radiotherapy and chemotherapy for Hodgkin disease. A hypogranular neutrophil with a pseudo-Pelger-Huet nucleus is shown. The red blood cells show marked poikilocytosis, in part related to post-splenectomy status. (Wright-Giemsa stain)

Etiology and Risk Factors

- Predisposing hematological disorder (myelodysplastic syndrome)
- Family history of malignant blood disease
- Receiving chemotherapy or radiotherapy treatment
- Exposure to aggressive cancerogenous chemicals (benzene or radiation)
- Smoking
- Down syndrome and Fanconi anemia
- Having sibling with leukemia

However, patients may not be exposed to any of the risk factors mentioned above.

Epidemiology

Leukemia incidence is highest among Caucasians and lowest among the Chinese, Japanese and Koreans. Males are predisposed to developing blood cancer, namely leukemia. There is a 50% higher incidence in men than women. Also, elderly age contributes to the danger of contracting this disease. Leukemia is diagnosed in about 29,000 adults and 2,000 children in the United States annually. In childhood leukemia,

the most affected kids are Filipinos, followed by white Hispanics, non-Hispanic whites and blacks, accordingly.

Most Common Symptoms and Signs

- Fatigue
- Night sweats
- Sudden high-grade fever
- Sound pallor
- Bruising or bleeding after an insignificant injury. Petechiae (flat, pinpoint spots under the skin, usually follow acute forms)
- Significant weight loss
- Absence of appetite
- Breathlessness (lymphoblastic forms)
- Bone or stomach pain (ALL)
- Full feeling or pain below the ribs (ALL, CML)
- Diffuse lymphadenopathy, non-painful lumps in the neck, under the arms, stomach or groin (lymphoblastic forms), though there may be painful, swollen lymph nodes (CLL)

Review Questions

The correct answers can be found below the references.

1. A 3-years-old white boy suffers from severe infections. Recently, he has had impetigo of his face and upper limbs. His body temperature may rise up to 40C without any obvious reason; the skin is covered with a dot-like rash of brown color. The mother of the child complains about frequent nose bleedings occurring without any obvious trauma. Her elder son suffers from acute lymphocytic leukemia. The child is weak and sleepy. What is the most probable primary diagnosis for this set of symptoms and history data?

A. Acute Lymphocytic Leukemia
B. Acute Myeloid Leukemia
C. Chronic Lymphocytic Leukemia
D. Chronic Myeloid Leukemia
E. Hairy Cell Leukemia
F. Myelodysplastic Syndromes

2. What abnormal chromosome is responsible for the development of chronic myeloid leukemia?

A. Philadelphia Chromosome
B. Chromosome 13
C. Chromosome 22
D. Down chromosome
E. None of the above

3. Which type of leukemia is associated with the total disruption of all blood cells' production (immaturity, absence of red and white cells together with platelets in the bone marrow and the blood, consequently)?

A. Acute Lymphocytic Leukemia
B. Acute Myeloid Leukemia

C. Chronic Lymphocytic Leukemia
D. Chronic Myeloid Leukemia
E. Hairy Cell Leukemia
F. Myelodysplastic Syndromes

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Notes