Leukemia

The word **Leukemia** comes from the Greek leukos which means "white" and aima which means "blood" (blood cancer). It defines the production of **abnormal leukocytes** (**immature** and **undifferentiated**). As leukaemia progresses, the bone marrow produces more abnormal blood cells and fewer normal blood cells. As the abnormal blood cells build up in the blood, they can spread to the lymph nodes, spleen, liver, lungs and kidneys. Without treatment, many of the body's key functions will be increasingly affected.

Based on the rapidity of proliferation, they can be classified as **acute or chronic**, and **myeloid or lymphoid based** on the cell of origin. Predominant subtypes are acute myeloid leukemia (AML) and chronic myeloid leukemia (CML), involving the myeloid lineage; acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL) involving the lymphoid chain.

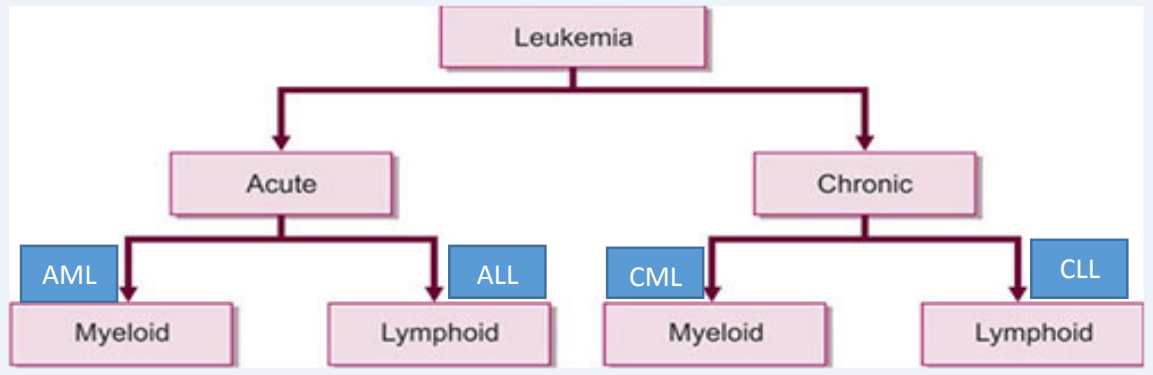


Figure 1 Leukemia classification

Acute leukemia is rapidly progressing diseases that affect cells, which are not fully developed. These cells cannot carry out their normal functions.

Chronic leukemia usually progresses more slowly, and patients have greater numbers of mature cells. In general, these more mature cells can carry out some of their normal functions.

With **myeloid leukemia**, a cancerous change begins in a marrow cell that normally forms certain blood cells—that is, red cells, some types of white cells and platelets.

With **lymphocytic leukemia**, the cancerous change begins in a marrow cell that normally forms lymphocytes (another type of white cell).

Leukemia symptoms

Chronic leukemia symptoms are usually less severe and develop more slowly than those of acute leukemia, which all type participate with these symptoms:

1-Fatigue **2-**Frequent infections **3-**Enlarged lymph nodes **4-**Unexplained fevers **5-**Night sweats **6-**Bruising and excess bleeding **7-**Abdominal pain **8-**Bone and joint pain **9-**Headaches and other neurological symptoms **10-**Weight loss **11-**shortness of breath.

Causes and Risk factors of Leukemia

It is due to a series of **mutations in genes that control the growth of cells** and occur through time, which leads to their uncontrolled growth in the bone marrow. While the exact causes of these mutations are **unknown**, several **risk factors** are varying with the different types of leukemia include:

1-radiation (from atomic bomb exposures to medical radiation) **2-**exposures to chemicals such as benzene and pesticides **3-**previous chemotherapy **4-**smoking **5-**alcoholisim **6-**age **7-**family history of leukemia **8-**down syndrome **9-**some infections

Acute leukemia

It is a blood cancer that develops suddenly and progresses quickly. It starts when the body makes too many **immature white blood cells (blast cells)**, also it is **defined** as the **presence of over 20% of blast cells in the blood**. These abnormal blast cells are known as leukemia cells, they multiply out of control and continue to divide but never mature into normal cells, that include two main types:

1-Acute myeloid leukemia (AML):

It is the most common leukemia **among the adult population** and accounts for **about 80% of all cases**. It is characterized by clonal expansion of immature "blast cells" in the peripheral blood.

Also it is characterized by mutations of the genes involved in hematopoiesis. These mutations result in a clonal expansion of **undifferentiated myeloid precursors (blasts) in the peripheral blood and bone marrow** resulting in ineffective erythropoiesis and bone marrow failure.

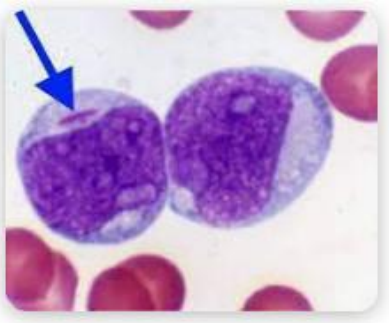
In the 1970s, a group of French, American, and British leukemia experts divided AML into subtypes, from **M0** through **M7**, **based on the type of cell the leukemia develops** from and how mature the cells are. This was based largely on how the leukemia cells looked under the microscope after routine staining and morphology.

AML diagnosis:

1- **CBC** include Hemoglobin, platelets, PCV, RBC count are **decreased**, MCV, MCH, MCHC and RDW is normal. There is normochromic, normocytic anemia, but **WBC count** in CBC is elevated (**$20 – 100 \times 10^9$/L**).
2- The FAB classification describes 8 types of AML depending on the morphology of the blasts.

3- Bone marrow biopsy, a blood test can suggest leukemia, but it usually takes a bone marrow test to confirm the diagnosis.

4- **Auer rods** (or Auer bodies) appear in **blood film** are large, crystalline cytoplasmic inclusion bodies sometimes observed in myeloid blast cells during acute myeloid leukemia, acute promyelocytic leukemia, high-grade myelodysplastic syndromes and myeloproliferative disorders.



Auer Rods

It is Composed of fused lysosomes and rich in lysosomal enzymes, Auer rods are azurophilic and can resemble needles.

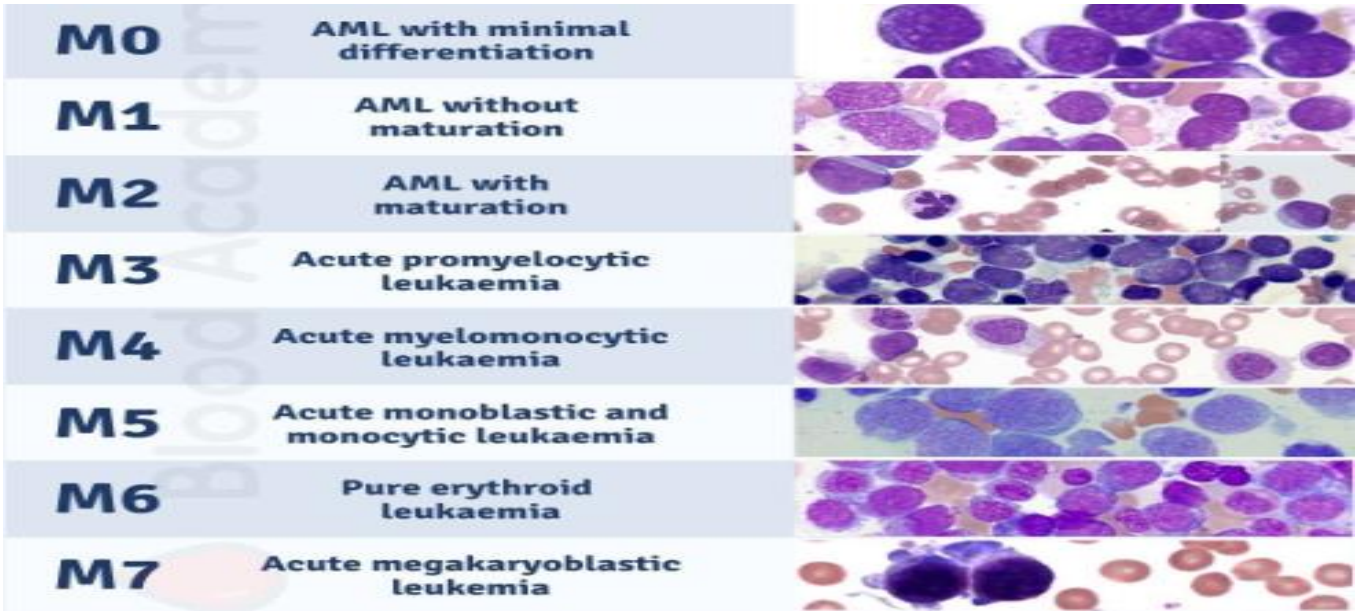


Figure 2 AML leukemia types depend on FAB classification

2- Acute Lymphoblastic Leukemia (ALL):

It is only type of leukemia that affects children more often than adults, and why the risk is different at different ages is **unknown**, and it is responsible for 85% of **childhood** cancers, it is a failure to produce normal lymphocytic cells (more than normal), but there is no enough to kill viruses, fungus and produce antibodies because immature and undifferentiated.

The two main subtypes of **ALL** are B cell, which makes up about 85% of ALL cases, and T cell, which makes up 15%.

ALL diagnosis:

1-CBC include the same parameters in AML.

2- Bone marrow examination shows solidly cellular marrow because replaced by proliferating blasts.

3-Immunophenotyping differentiates the blasts into T and B cells. B cells are CD19+, CD10+ and may show cytoplasmic CD22. T cells are CD2+, CD5+ and CD7+

4- Cytochemistry, Special stains are done to differentiate ALL from AML, these are:

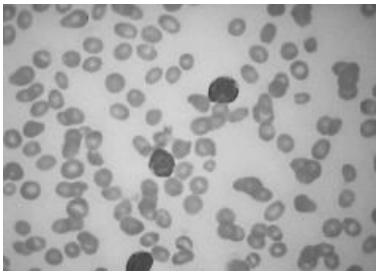
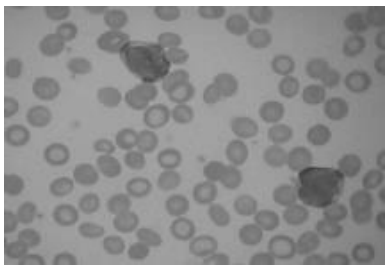
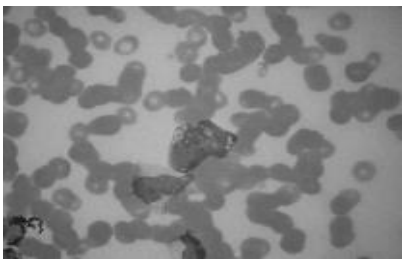
A. Myeloperoxidaes and Sudan Black stains are negative in ALL.

B. Periodic Acid Schiff stain may show positive staining in the cytoplasm of ALL blasts with no differentiation between T and B cells.

5-Biochemical tests show raised serum **uric acid**, **LDH** and **creatinine**.

6-The differential cells in blood film show many blast cells, the FAB classification describes 3 types of ALL depending on the morphology of the blasts, that include:

a-ALL L1 b-ALL L2 c-ALL L3

AL 1 characterized by condensed chromatin and nucleoli are not seen.

AL 2 it has pale blue cytoplasm forms a rim around the nucleus and does not contain any inclusions**.**

AL 3 the cytoplasm is moderate in amount blue in color and there are punched out vacuoles in the cytoplasm and overlying the nucleus.

Chronic Leukemia

It refers to large number of abnormal white blood cells, there will be large numbers circulating in the blood. They crowd out normal white blood cells and **don't fight infection**. This may cause various health problems, such as anemia (from too few red cells) or bleeding. It is caused by changes to one or more of the genes (DNA) that control the growth and development of blood cells. These changes happen over time, but it is not known why they occur in some people and not others.

Chronic leukemia was differing from acute that appearing gradually, and develops slowly over months to years. There are two main types of chronic leukemia, the difference between them is in the type of white blood cells that are affected.

1-Chronic myeloid leukemia (CML): is an acquired malignant disease characterized by over production of cells of the **granulocytic series**, especially the **neutrophilic series**, leading to marked splenomegaly and very high white blood cell counts, **basophilia** and **thrombocytosis** are common.

It is slightly more common in **men than in women** and is **rare in children**, and **median age at diagnosis is approximately 45 to 50 years,**

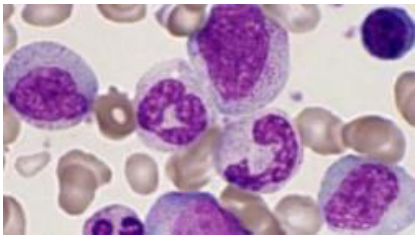
A characteristic cytogenetic abnormality, the **Philadelphia chromosome (Ph)**, is present in the bone marrow cells in more than **95% of CML cases**, shared in **translocation** of chromosome **22** and chromosome **9**, which involves the **ABL1** gene in chromosome **9** and the **BCR** gene in chromosome **22**, As a result of this translocation that called **Philadelphia chromosome chromosomal abnormality**,

The apposition of these two genetic sequences produce a new hybrid gene (BCR/ABL), which code for a novel protein of molecular weight 210,000 KD (P210). The P210 protein is a tyrosine kinase may play a role in triggering the uncontrolled proliferation of (CML cells).

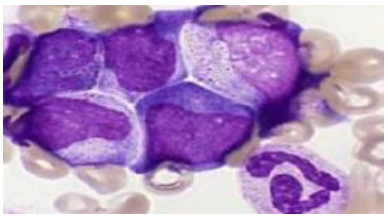
CML phases:

Disease Course of Chronic myelogenous leukemia classically occurs in three phases:

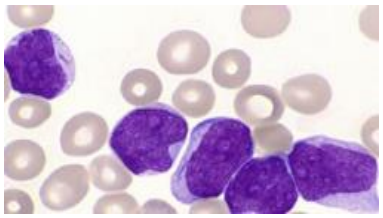
1-A chronic phase (last 4-5 years up to 15 years) asymptomatic or have only mild symptoms of fatigue and the % Of blast is less than 5%.



2-An accelerated phase (last 6-9 months) a gradual increase in blasts in the blood or bone marrow, it is short, may transformed to AML or myelofibrosis, and the percentage of blast is between 5-20%.

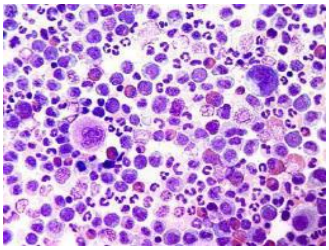


3-Blast crisis (last for3-6 months) rapid progression and short survival, and the percentage of blast is more than 20% in the peripheral blood and bone marrow.



CML diagnosis:

1- **CBC** shows **increased granulocytes** of all types, typically including **mature myeloid** cells, **Basophils and Eosinophils** are almost commonly increased; this feature may help differentiate CML from a leukemia reaction, **RBC, decrease (Anemia), Hb: is low, Platelet count: increase.**



2- **Bone Marrow Study** Hypercellular, increase fibrosis in 30-40%, granulocytic hyperplasia blasts less 10%.

3- **Cytogenetics** that detects the translocation (9;22) which involves the ABL1 gene in chromosome 9 and the BCR gene in chromosome 22, as a result of this translocation.

4- **Biochemistry leukocyte alkaline phosphatase (LAP),** serum lactate dehydrogenase (**LDH**), serum **uric acid** and serum **vitamin B12** all are **increased**.

2-Chronic lymphoblastic leukemia:

The World Health Organization (WHO) includes "**lymphocytic leukemia**" and "**lymphoma**" within one classification. Each of these cancers is the result of a change to a cell that was destined to be a lymphocyte.

However, lymphocytic leukemia and lymphoma originate in different parts of the body. Lymphocytic leukemia develops in the lymphatic tissue within the bone marrow. Lymphoma begins in a lymph node, or another lymphatic structure in the skin, the gastrointestinal tract, or some other site in the body. Chronic lymphocytic leukemia (CLL) and small cell lymphocytic lymphoma (SLL) are often **considered to be one disease because they are similar with regard to incidence, signs and symptoms, genetic features, disease progression and treatment**.

The leukemic lymphocytes and tissue abnormalities that are observed in people with SLL are identical to those observed in patients with CLL. However, in people with SLL, there is more lymph node and lymphoid tissue involvement and less marrow and blood involvement; in people with CLL, the marrow and blood are more affected.

Chronic lymphocytic leukemia (CLL) results from an acquired (not present at birth), 25-50% of patients will be **asymptomatic** at time of presentation, it caused by mutation (change) to the DNA of a single marrow cell that develops into a lymphocyte.

In **95** percent of people with CLL, the change occurs in a **B lymphocyte**. In the other 5 percent of people with CLL, the cell that transforms from normal to leukemic has the features of a T lymphocyte or a natural killer (NK) cell. Thus, any of the three major types of lymphocytes (T cells, B cells or NK cells) can undergo a malignant transformation that causes diseases related to B-cell CLL.

It was effect in adult with age 55-70 years and don't depend on gender that have equal frequent in males than females, also CLL continuous through 2 to 20 years.

CLL diagnosis:

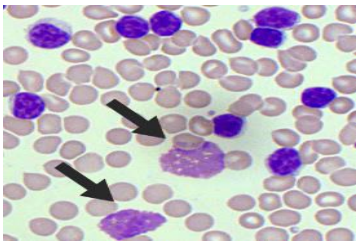
1-**CBC**: Hemoglobin, PCV, RBC count are mildly decreased, MCV, MCH, MCHC, RDW and Platelet count are **normal**, **but WBC count is elevated (50.0 – 250.0x109/L)** with **lymphocytosis.**

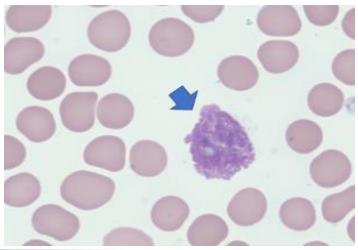
2-**Bone marrow biopsy**, will show an **increase in the number of lymphocytes** in the marrow and often a **decrease in the number of normal marrow cells**.

3-**Biochemistry** tests revealed **increase** serum LDH and uric acid, but **decrease in gamma globulins (γ)**

4-**Blood film** shows leukocytosis but small lymphocytes and **smudge cells** is remnants of cells, without clear cytoplasmic borders and come from damaged lymphocytes .

Figures of smudge cell





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