

ACUTE AND CHRONIC LEUKEMIA

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

2017-2018 Spring Semester

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Plan of the lecture



- Leukaemia' General Overview
- Major kinds of leukemia (acute myelogenous & lymphoblastic, chronic myelogenous & lymphocytic)
- Abbreviations
- Diagnostic guidelines

Definition

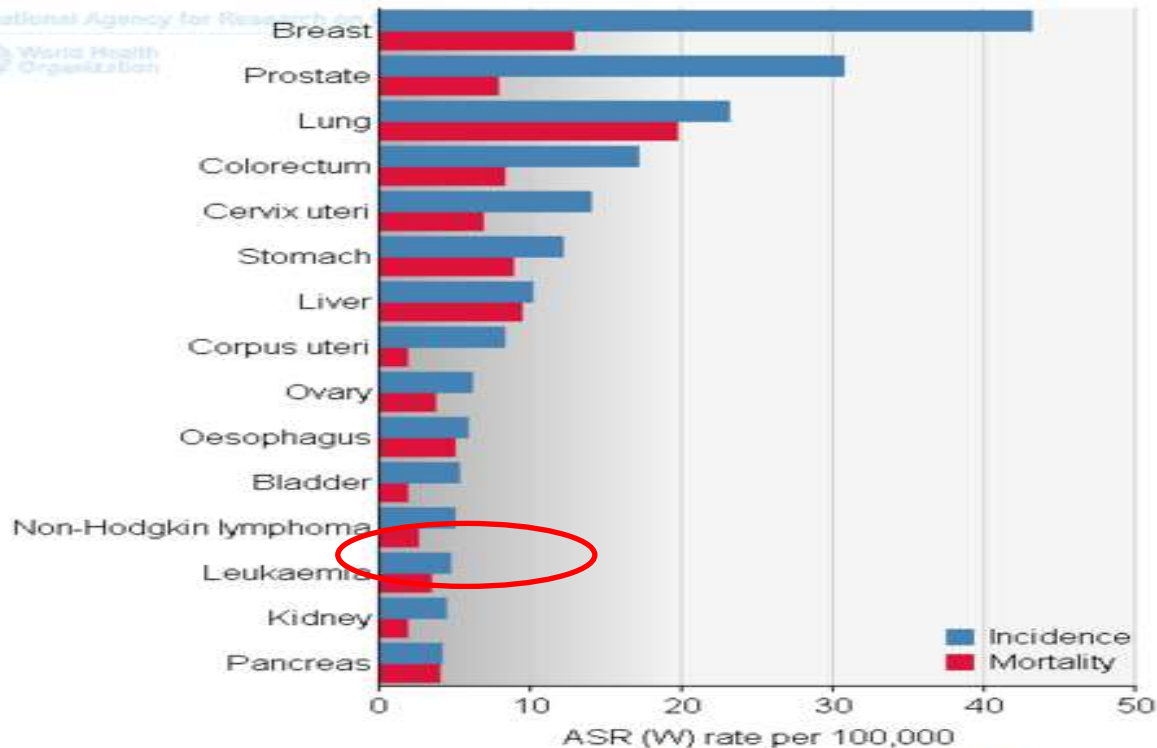
Leukemia (leukaemia) is a group of progressive, malignant neoplasms (cancers) of the blood-forming organs, marked by diffuse replacement of the bone marrow development of leukocytes and their precursors in the blood and bone marrow, accompanied by a reduced number of erythrocytes and blood platelets, and resulting in anemia, increased susceptibility to infection and hemorrhage with weakness and malaise, fever, pain in the joints and bones, swelling of the lymph nodes, spleen, and liver.

Epidemiology 1

[Men](#)
[Women](#)
[Both sexes](#)
[Summary statistics](#)

WORLD

Estimated age-standardised incidence and mortality rates: both sexes



Estimated incidence, mortality and 5-year prevalence: both sexes

Risk Factors

Acute leukemia

- Chronic exposure to certain chemicals (for example benzene)
- Long-term treatment with alkylating substances and ionizing radiation
- Mutations in cellular oncogenes, tumor suppressor genes, and transcription factors

Risk Factors

Chronic leukemia

- Sex (men: women is 2:1) and genetic factors (1st degree relatives of patients have a more than 3 times greater chance to develop leukemia)
- East Asian region
- Certain retroviruses (some rare cases of T-cell leukemia are associated with infection of a human retrovirus (HTLV I))

Etiology

- In almost all cases, the etiology is unknown
- Different kinds of leukemia are believed to have different causes
- Abnormalities of chromosomes have been found in various types of leukemia
- Whether chromosomal alterations are primary or secondary is undetermined, but they are at least contributory in the development of leukemia
- There is an increasing body of evidence incriminating viruses in leukemogenesis in man, and they may be a factor in all cases
- Certain chemicals and ionizing radiation may be important etiologic factors in a few cases

Classification 1

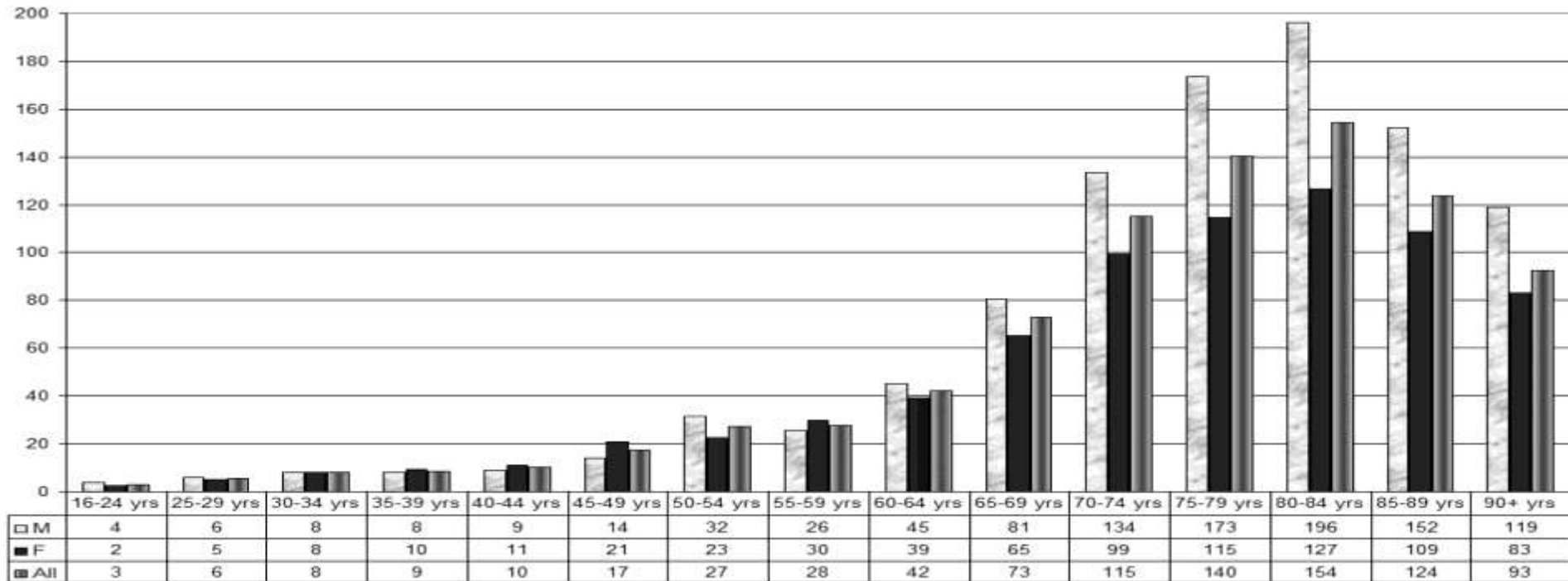
four major kinds of leukemia

Cell type	Acute	Chronic
Myelogenous leukemia ("myeloid" or "nonlymphocytic")	Acute myelogenous leukemia (AML or myeloblastic)	Chronic myelogenous leukemia (CML)
Lymphocytic leukemia (or "lymphoblastic")	Acute lymphoblastic leukemia (ALL)	Chronic lymphocytic leukemia (CLL)

Acute myelogenous leukemia (AML): definition

Acute myelogenous (myeloid, nonlymphocytic) leukemia (AML) represents a group of clonal hematopoietic stem cell disorders in which both a block in differentiation and unchecked proliferation result in the accumulation of myeloblasts at the expense of normal hematopoietic precursors

Acute myelogenous leukemia (AML): epidemiology



AML is the most common acute leukemia affecting adults, and its incidence increases with age

Acute myelogenous leukemia (AML): WHO classification

- AML with certain genetic abnormalities
- AML with myelodysplasia-related changes
- AML related to previous chemotherapy or radiation
- AML not otherwise specified
- Myeloid sarcoma (granulocytic sarcoma or chloroma)
- Myeloid proliferations related to Down syndrome
- Undifferentiated and biphenotypic acute leukemias

Acute myelogenous leukemia (AML): clinical presentation 1

Initial clinical presentations are related to pancytopenia, the reduction of all cell counts, reflecting the leukemic cell replacement of bone marrow and include:

- Headache/disorientation due to abnormal white blood cells infiltrating the central nervous system (CNS)

Acute myelogenous leukemia (AML): clinical presentation 2

- Anemia which is accompanied by pallor, fatigue, malaise, hypoxia, and bleeding, caused by rapidly proliferating leukocytes inhibiting formation of erythrocytes and thrombocytes
- Infections (pneumonia) and mouth/throat ulcerations, caused by increased numbers of immature or abnormal leukocytes which are unable to fight off infections

Acute myelogenous leukemia (AML): clinical presentation 3

- Increased metabolic rate with weakness, pallor, and weight loss, caused by increased leukocyte production which require increased nutrient production
- Hyperuricemia which may lead to renal pain, obstruction, and infection, caused by a great number of leukocytes being destroyed which releases large amounts of uric acid; in late stages, leukocytes infiltrate the kidneys

Acute myelogenous leukemia (AML): clinical presentation 4

- Enlarged organs (spleen, liver), caused by increased number of white blood cells accumulating within liver and spleen causing tissue distension
- Lymphadenopathy and bone pain, caused by excessive number of white blood cells accumulating in lymph nodes and bone marrow
- Bone discomfort (especially in ribs, sternum, and tibia)
- Older adults may experience delirium, and progressive weakness

Acute myelogenous leukemia (AML): clinical presentation 5



Unexplained
bruising

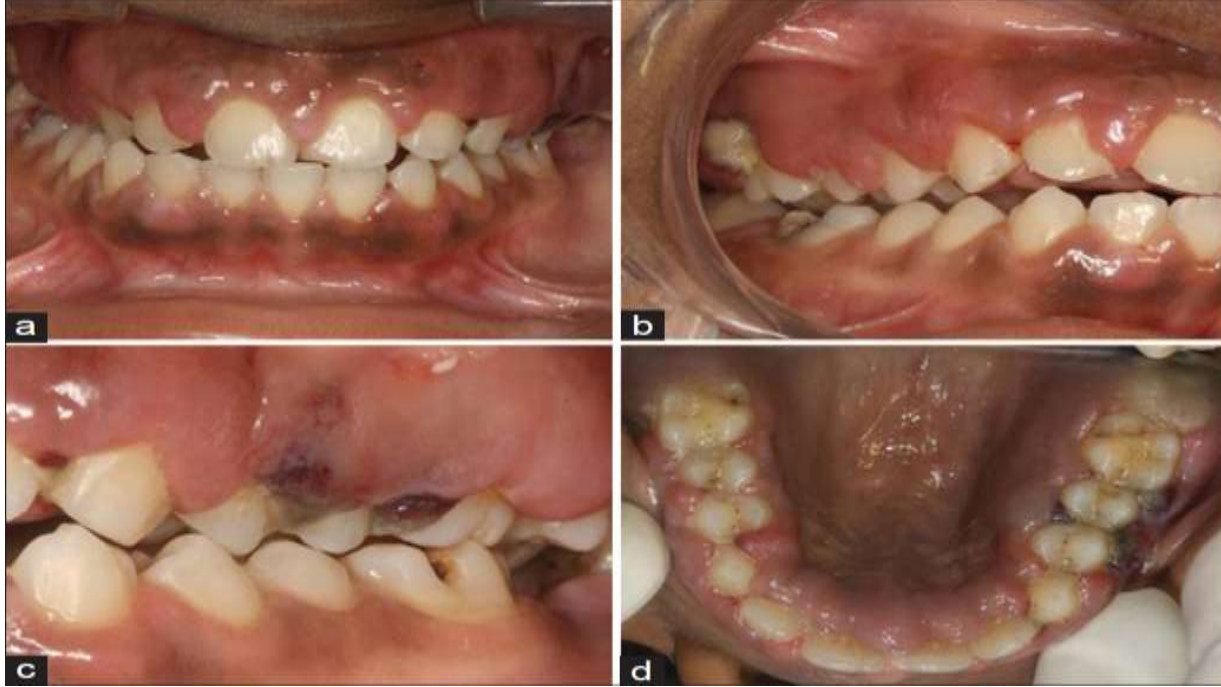


Paleness of
skin



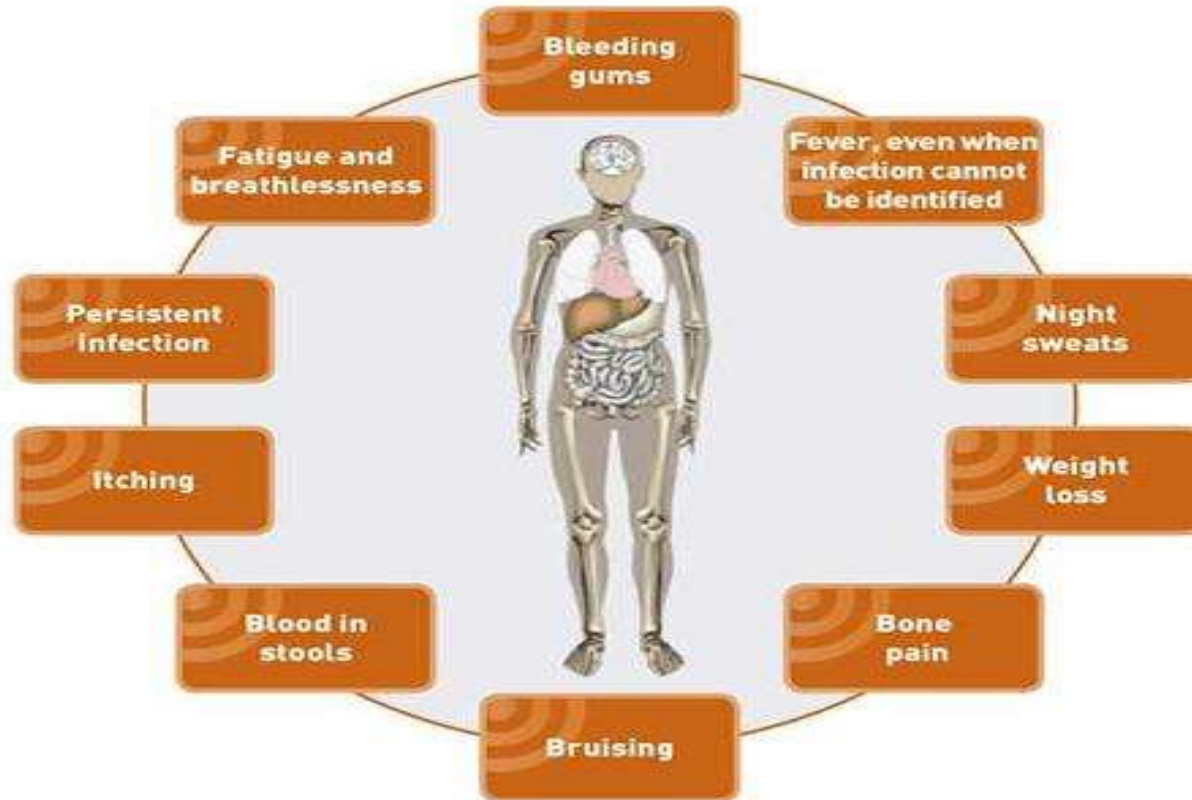
Petechiae

Acute myelogenous leukemia (AML): clinical presentation 6



Severe generalized gingival overgrowth with localized necrosis and sloughing involving the interdental papilla

Acute myelogenous leukemia (AML): clinical presentation 7

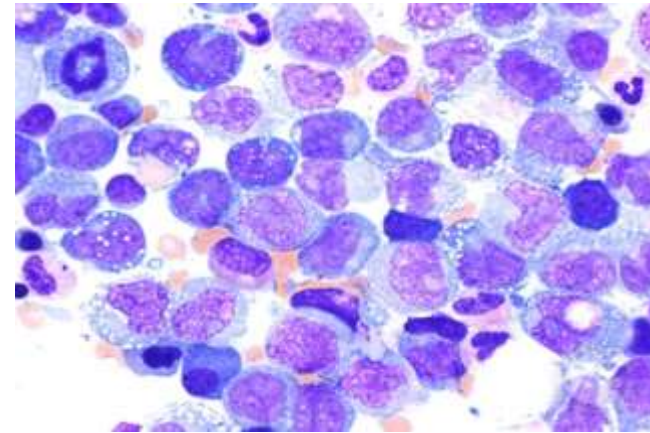
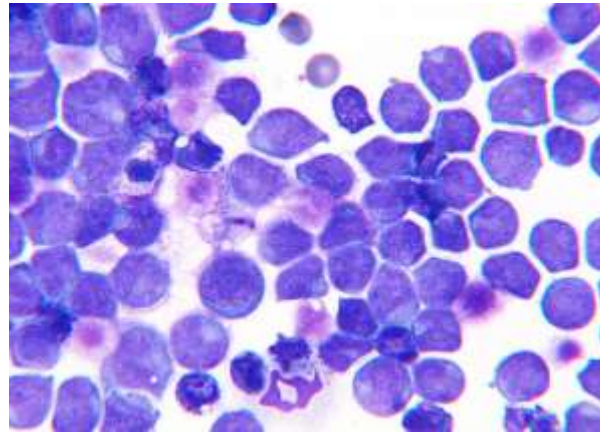
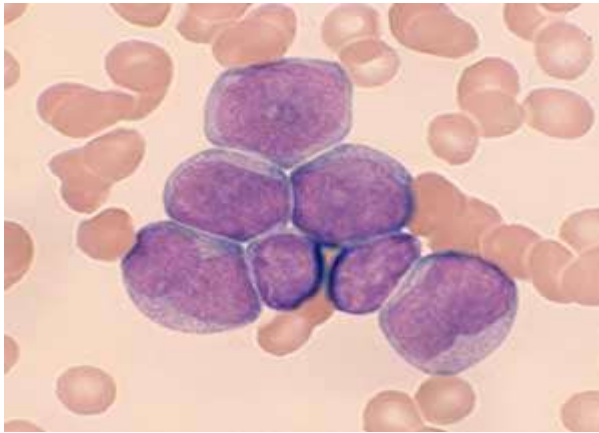


Signs and symptoms of acute myeloid leukemia

Acute myelogenous leukemia (AML): diagnosis 1

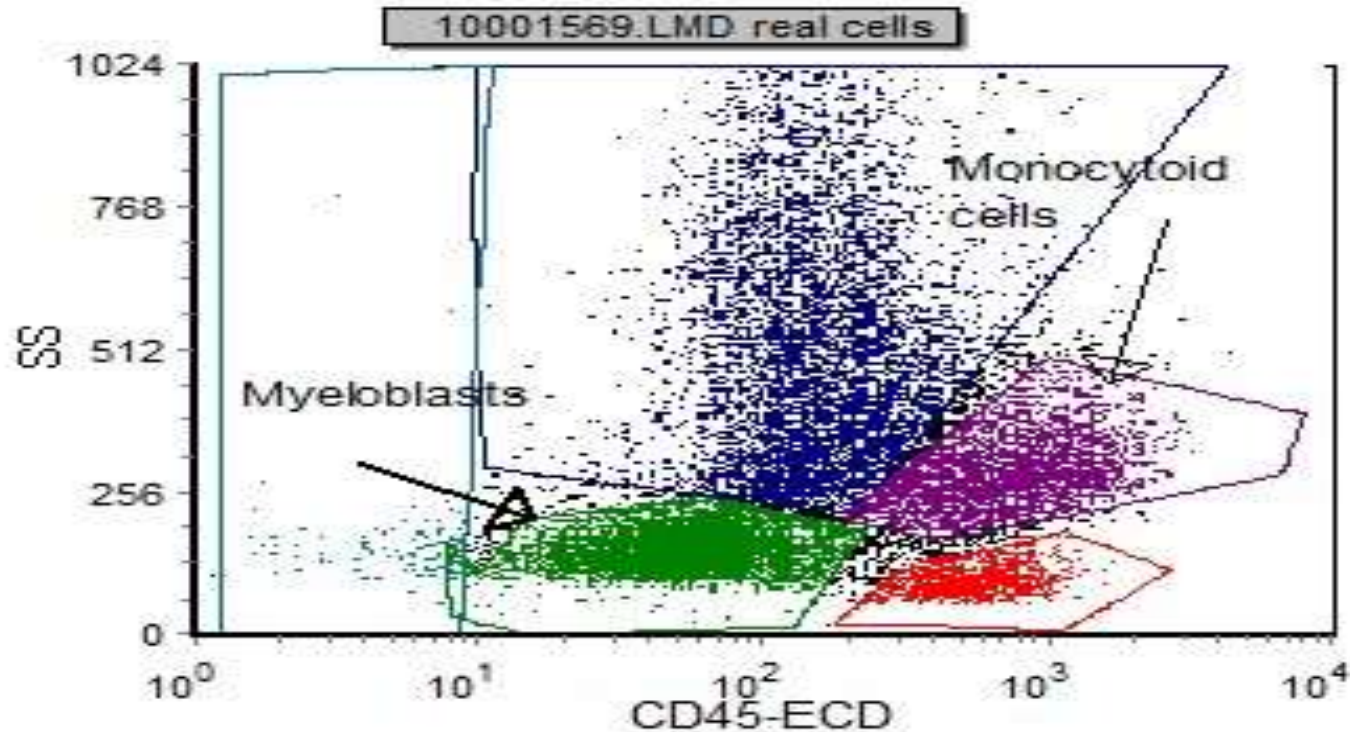
- History and Physical Examination
- Blood Test: leukocytosis, sometimes leukemic blasts, isolated decreases in platelets, red blood cells, or even with a low white blood cell count (leukopenia)
- Bone marrow biopsy and aspiration: to diagnose the presence of leukemia, to differentiate AML from other types of leukemia
- Immunophenotyping: to determine the subtype of AML by comparing the cancer cells to normal cells in the immune system

Acute myelogenous leukemia (AML): diagnosis 2



Malignant myeloid cells

Acute myelogenous leukemia (AML): diagnosis



Immunophenotyping

Acute myelogenous leukemia (AML): treatment 1

There are 4 types of standard treatments:

- 1) Chemotherapy: systemic, intrathecal (the spinal canal, the subarachnoid space), or regional drugs usage depends of the AML subtype
- 2) Radiation
- 3) Stem Cell Transplant
- 4) Targeted Therapy: monoclonal antibodies or other substances to destroy specific cancer cells without harming the patient's normal cells

Acute myelogenous leukemia (AML): treatment 2

The primary treatment is chemotherapy (three phases):

- The first (Induction) phase clears the blood of leukemia cells and reduces the number of blasts in the bone marrow
- The second (Consolidation) phase is administered after a rest period where the patient recovers from the first phase with the goal to kill the leukemia cells that are still present
- The third (Maintenance) phase is necessary in only certain types of leukemia and includes giving low doses of a chemo drug for months or years after the consolidation phase

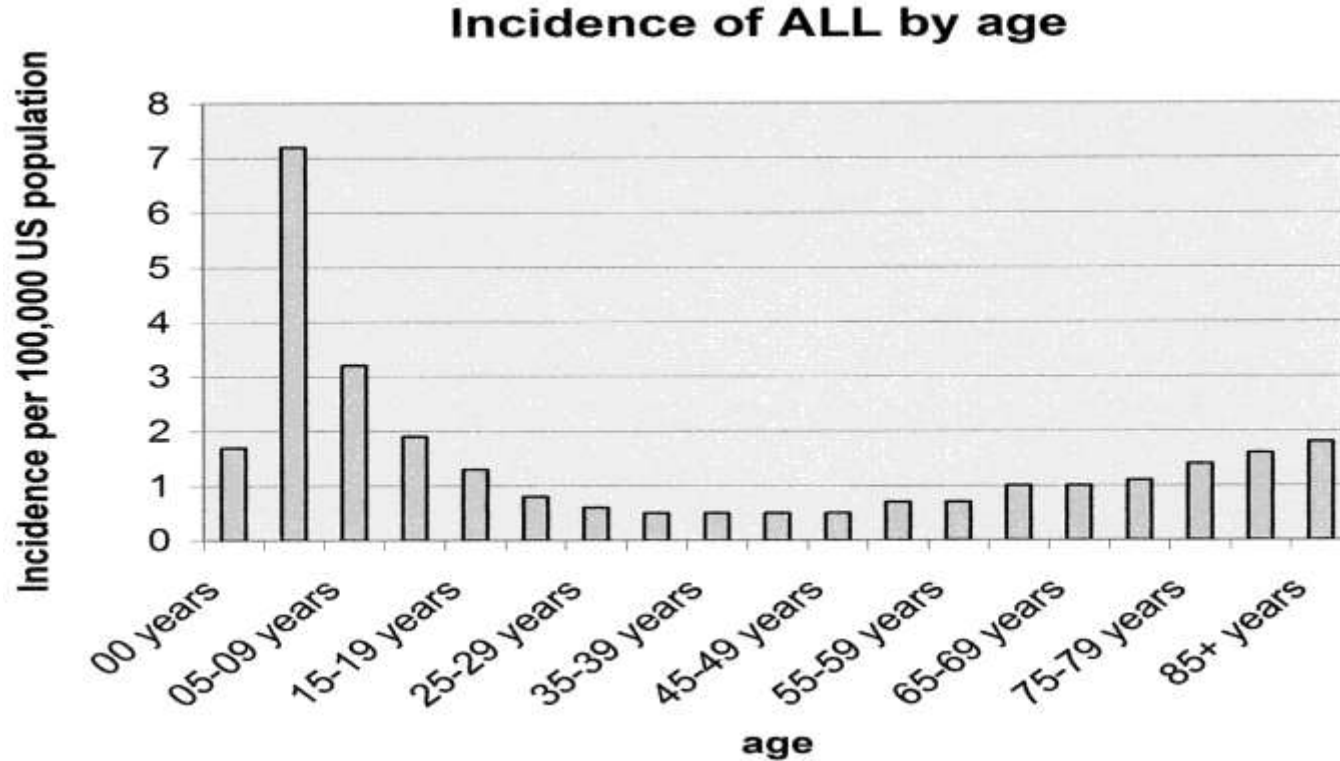
Acute myelogenous leukemia (AML): prognosis

- Acute myeloid leukemia is a curable disease, and the chance of cure for a specific patient depends on a number of prognostic factors
- Increasing age is an adverse factor, because older patients more frequently have a previous antecedent hematologic disorder along with comorbid medical conditions that compromise the ability to give full doses of chemotherapy
- A previous antecedent hematologic disorder is associated with a poor outcome to therapy

Acute lymphoblastic leukemia (ALL): definition

Acute lymphoblastic (lymphocytic, lymphoid) leukemia (ALL) represents a group of clonal hematopoietic stem cell disorders in which both a block in differentiation and unchecked proliferation result in the accumulation of lymphoblasts at the expense of normal hematopoietic precursors

Acute lymphoblastic leukemia (ALL): epidemiology



Incidence of acute lymphoblastic leukemia (ALL) by age

Acute lymphoblastic leukemia (ALL): WHO classification

Precursor lymphoid neoplasms

B-cell lymphoblastic leukemia/lymphoma, not otherwise specified

B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities

B-cell lymphoblastic leukemia/lymphoma with t(9;22)(q34;q11.2); *BCR-ABL1*

B-cell lymphoblastic leukemia/lymphoma with t(v;11q23); *MLL* rearranged

B-cell lymphoblastic leukemia/lymphoma with t(12;21)(p13;q22);

TEL-AML1 (ETV6-RUNX1)

B-cell lymphoblastic leukemia/lymphoma with hyperploidy

B-cell lymphoblastic leukemia/lymphoma with hypoploidy (hypodiploid ALL)

B-cell lymphoblastic leukemia/lymphoma with t(5;14)(q31;q32); *IL3-IGH*

B-cell lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3);

E2A-PBX1 (TCF3-PBX1)

T-cell lymphoblastic leukemia/lymphoma

WHO = World Health Organization

Swerdlow SH, Campo E, Harris NL, et al (eds): WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon, France: IARC Press; 109–138, 2009.

Acute lymphoblastic leukemia (ALL): clinical presentation 1

- Anemia
- Dizziness, weakness
- Fatigue
- Shortness of breath
- Frequent or unexplained fever and infection
- Weight loss and/or loss of appetite
- Bleeding from the gums and/or nose
- Pale skin

Acute lymphoblastic leukemia (ALL): clinical presentation 2

- Excessive and unexplained bruising due to low platelet levels
- Swollen lymph nodes (neck, underarm, groin, stomach)
- Bone pain, joint pain (the spread of "blast" cells from the marrow cavity)
- Pitting edema (swelling) in the lower limbs and/or abdomen

Acute lymphoblastic leukemia (ALL): clinical presentation 3



Unexplained
bruising

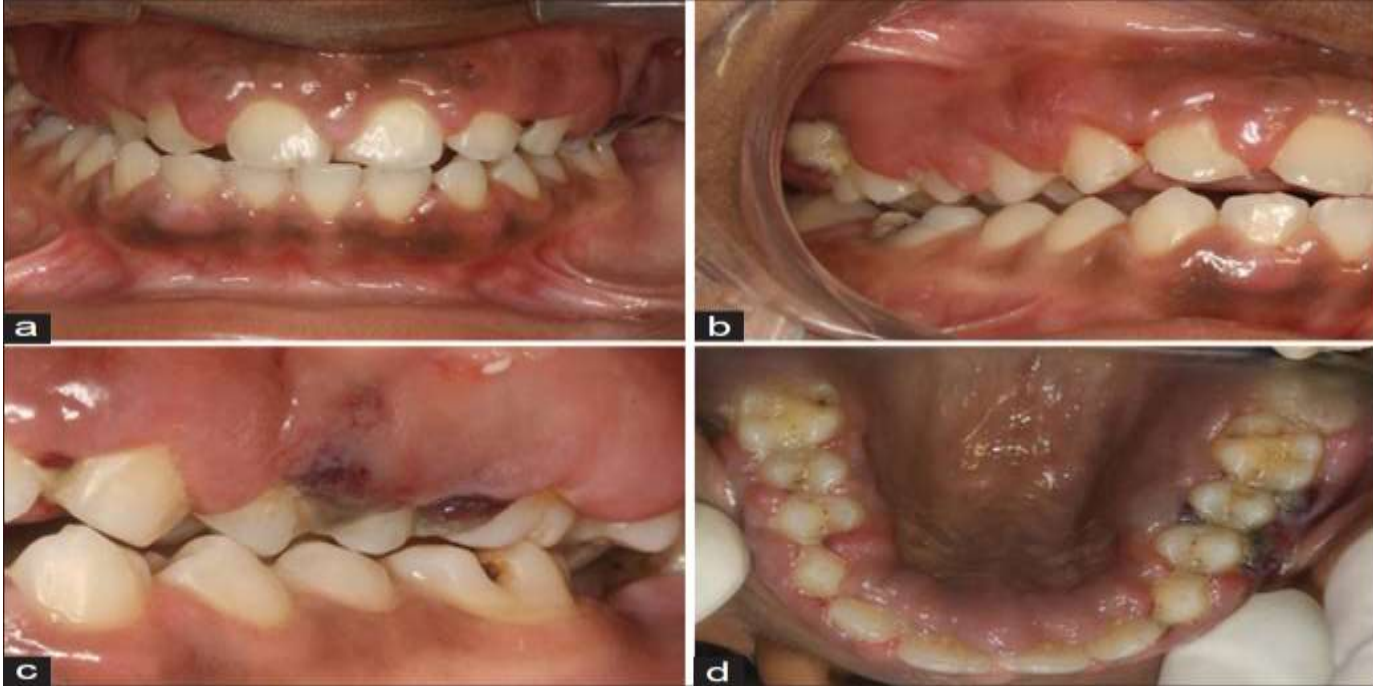


Paleness of
skin



Petechiae

Acute lymphoblastic leukemia (ALL): clinical presentation 4

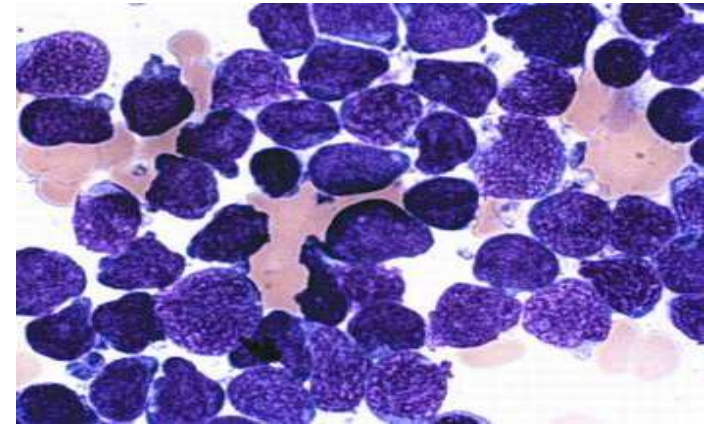
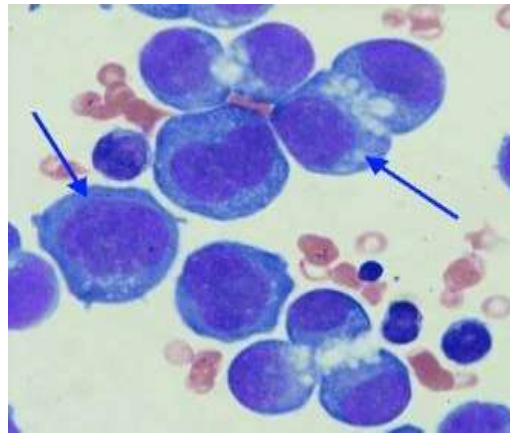
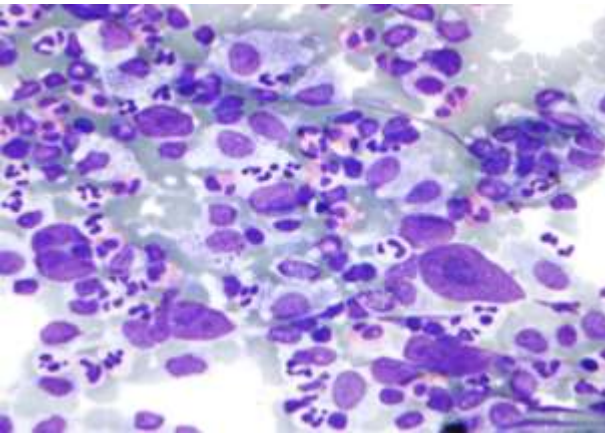


Severe generalized gingival overgrowth with localized necrosis and sloughing involving the interdental papilla

Acute lymphoblastic leukemia (ALL): diagnosis 1

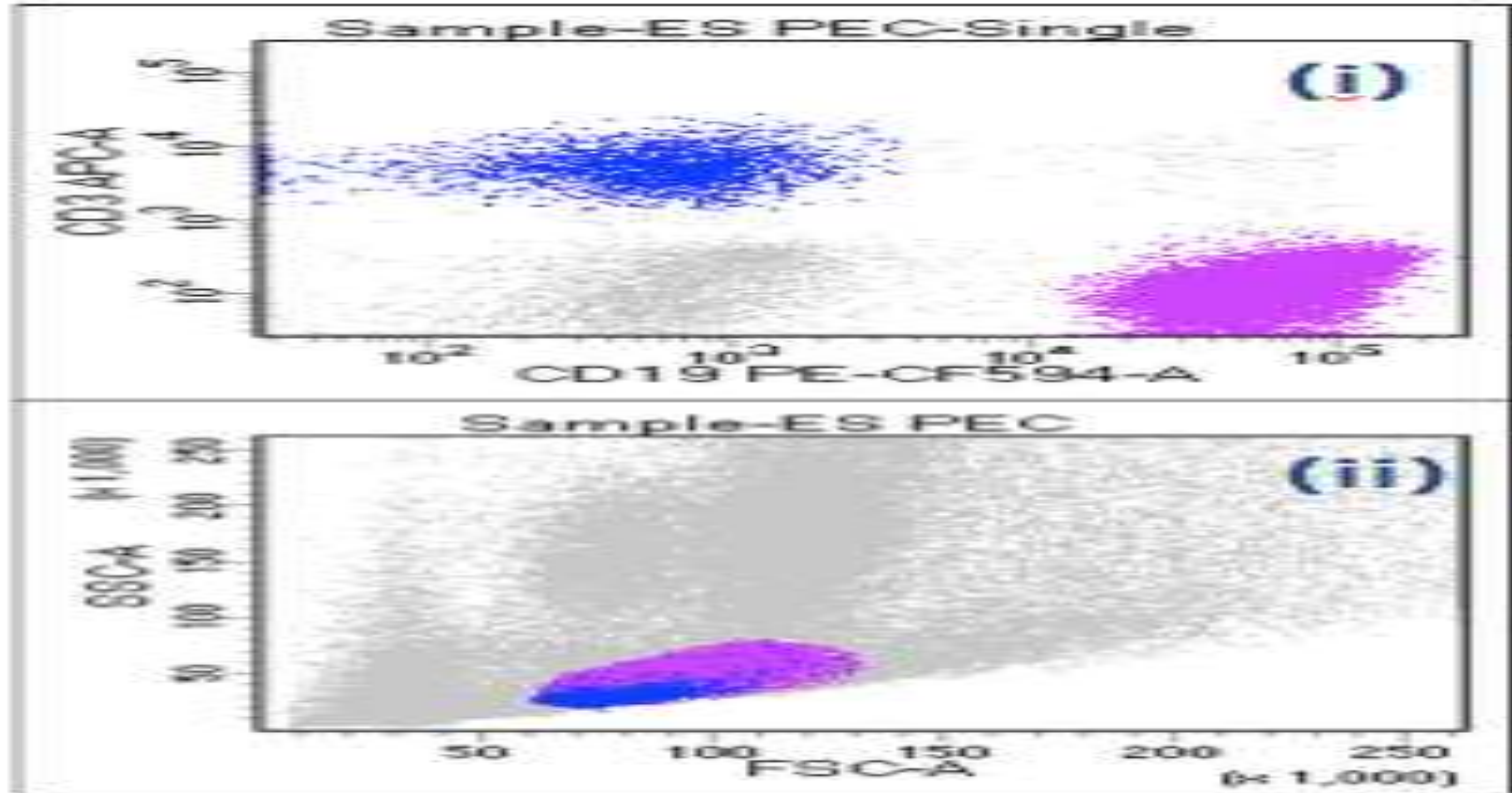
- History and Physical Examination
- Blood Test: leukocytosis, sometimes leukemic blasts, isolated decreases in platelets, red blood cells, or even with a low white blood cell count (leukopenia)
- Bone marrow biopsy and aspiration: the presence of leukemia, differentiation ALL from other types of leukemia
- Immunophenotyping: to determine the subtype of ALL by comparing the cancer cells to normal cells in the immune system

Acute lymphoblastic leukemia (ALL): diagnosis 2



Malignant lymphoblastic cells

Acute lymphoblastic leukemia (ALL): diagnosis 3



Immunophenotyping

Acute lymphoblastic leukemia (ALL): treatment 1

Four phases:

1. Induction therapy with the purpose to achieve remission by killing most of the cancer cells
2. Consolidation (post-remission) therapy with the goal to destroy any remaining leukemia cells in the central nervous system (4 - 8 weeks)
3. Maintenance (low dose) therapy is given to prevent cancer cell re-growth (4 weeks)
4. Preventive therapy to the spinal cord (chemotherapy drugs are injected directly into the spinal cord fluid)

Acute lymphoblastic leukemia (ALL): treatment 2

Four main types of the specific treatments :

- Chemotherapy to kill any leukemia cells that may have spread to the brain and spinal cord)
- Targeted drug therapy to attack specific abnormalities that cause the cancer cell growth
- Radiation therapy is typically used when the cancer has spread to the central nervous system
- Stem cell transplant (SCT) may be used for patients at risk or currently going through a relapse

Acute lymphoblastic leukemia (ALL): treatment 3

Physical Therapy and exercise:

- Up to 15 minutes of walking 5x per week
- Strength training combined with aerobic exercises 3x per week, twice daily, for 30 minutes
- Pain management (transcutaneous electrical nerve stimulation (TENS), hot packs, cold packs, massage, etc.
- Stretching (sustained stretch, active and passive range of motion (ROM), splinting, etc.)

Acute lymphoblastic leukemia (ALL): treatment 4

Medications:

- Chemotherapy: L - asparaginase, Vincristine
- Steroid: Dexamethasone, Hydrocortisone
- Drugs for high-risk patients: Daunorubicin, Cytarabine
- Other drugs: Methotrexate, 6-mercaptopurine

Novel approaches:

- The proteasome, in combination with chemotherapy
- Chimeric antigen receptors (CARs)

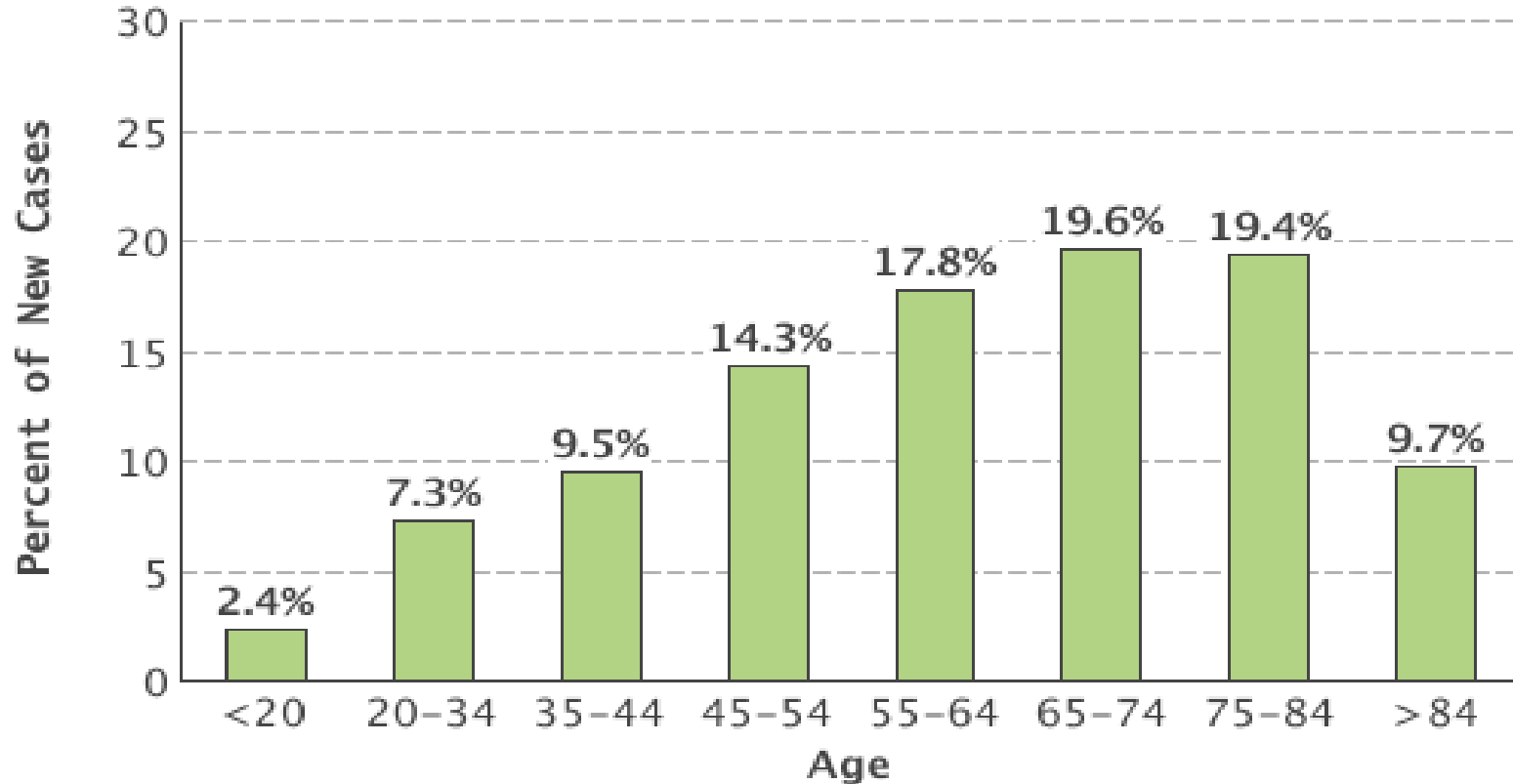
Acute lymphoblastic leukemia (ALL): prognosis

- Acute lymphoblastic leukemia is a curable disease, and the chance of cure for a specific patient depends on a number of prognostic factors
- The 5-year survival rate has improved from zero six decades ago, to 85% currently, largely because of clinical trials on new chemotherapeutic agents and improvements in SCT technology

Chronic myelogenous leukemia (CML): definition

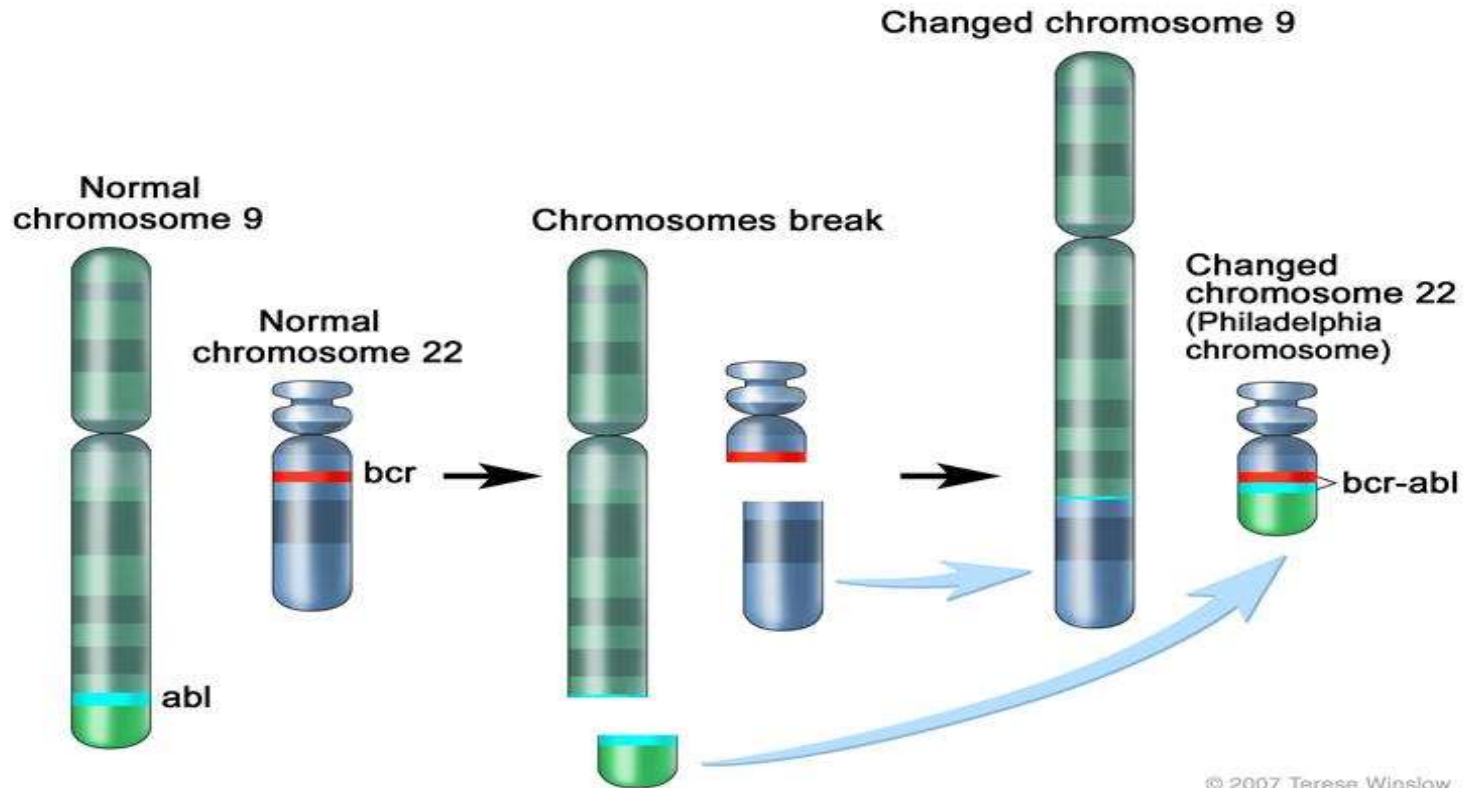
Chronic myelogenous (myeloid, myelocytic, granulocytic) leukemia (CML) is the clonal hematopoietic stem cell disorder with an abnormal increase in mature and immature granulocytes (as neutrophils, eosinophils, and myelocytes) especially in bone marrow and blood, that occurs especially in adults, and that is associated with the presence of the Philadelphia chromosome CML

Chronic myelogenous leukemia (CML): epidemiology



Incidence of CML by age

Chronic myelogenous leukemia (CML): Philadelphia chromosome



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Chronic myelogenous leukemia (CML): classification 1

- Chronic phase: there are few blast cells in the blood and bone marrow and there may be no symptoms of leukemia, this phase may last from several months to several years
- Accelerated phase: there are more blast cells in the blood and bone marrow, and fewer normal cells
- Blastic phase (the blast crisis): more than 30% of the cells in the blood or bone marrow are blast cells and the blast cells may form tumors outside of the bone marrow
- Refractory CML: leukemia cells do not decrease even though treatment is given

Chronic myelogenous leukemia (CML): classification 2

Chronic phase

Untreated

< 15 % blast cells in blood or bone marrow
< 30 % – the sum of blast cells and promyelocytes in blood or bone marrow
< 20 % basophile granulocytes in peripheral blood
Thrombocyte count > $100 \times 10^9/l$

Treated

Normal or close to normal blood values without immature granulocytes in the blood

Chronic myelogenous leukemia (CML): classification 3

Accelerated phase

Blast count between 15–29 % in blood or bone marrow
≥ 30 %, the sum of blast cells and promyelocytes in blood or blood marrow
≥ 20 % basophile granulocytes in blood
Thrombocyte count $< 100 \times 10^9/l$, which cannot be explained by treatment

Often also increasing splenomegaly
new chromosome changes in Ph+ clone

Chronic myelogenous leukemia (CML): classification 4

Blast phase

Characterized by >30 % of the cells in blood or bone marrow are blasts

Patients have symptoms of acute leukemia

Extramedullary illness

Chronic myelogenous leukemia (CML): clinical presentation 1

- Most patients (~90%) are diagnosed during the chronic stage which is most often asymptomatic, and may be diagnosed incidentally with an elevated white blood cell count on a routine laboratory test
- It can also present with symptoms indicative of enlarged spleen and liver and the resulting upper quadrant pain this causes

Chronic myelogenous leukemia (CML): clinical presentation 2

- Mild fever and night sweats due to an elevated basal level of metabolism
- Some (<10%) are diagnosed during the accelerated stage, when fevers are most commonly the result of opportunistic infections
- Some patients are initially diagnosed in the blast phase in which the symptoms are most likely fever, bone pain and an increase in bone marrow fibrosis

Chronic myelogenous leukemia (CML): clinical presentation 3



Splenomegaly in CML

Chronic myelogenous leukemia (CML): diagnosis 1

- CML is often suspected on the basis of a complete blood count, which shows increased granulocytes of all types
- Basophils and eosinophils are almost universally increased; this feature may help differentiate CML from a leukemoid reaction
- A bone marrow biopsy is often performed as part of the evaluation for CML, and CML is diagnosed by cytogenetics that detects the translocation $t(9;22)(q34;q11.2)$ which involves the ABL1 gene in chromosome 9 and the BCR gene in chromosome 22

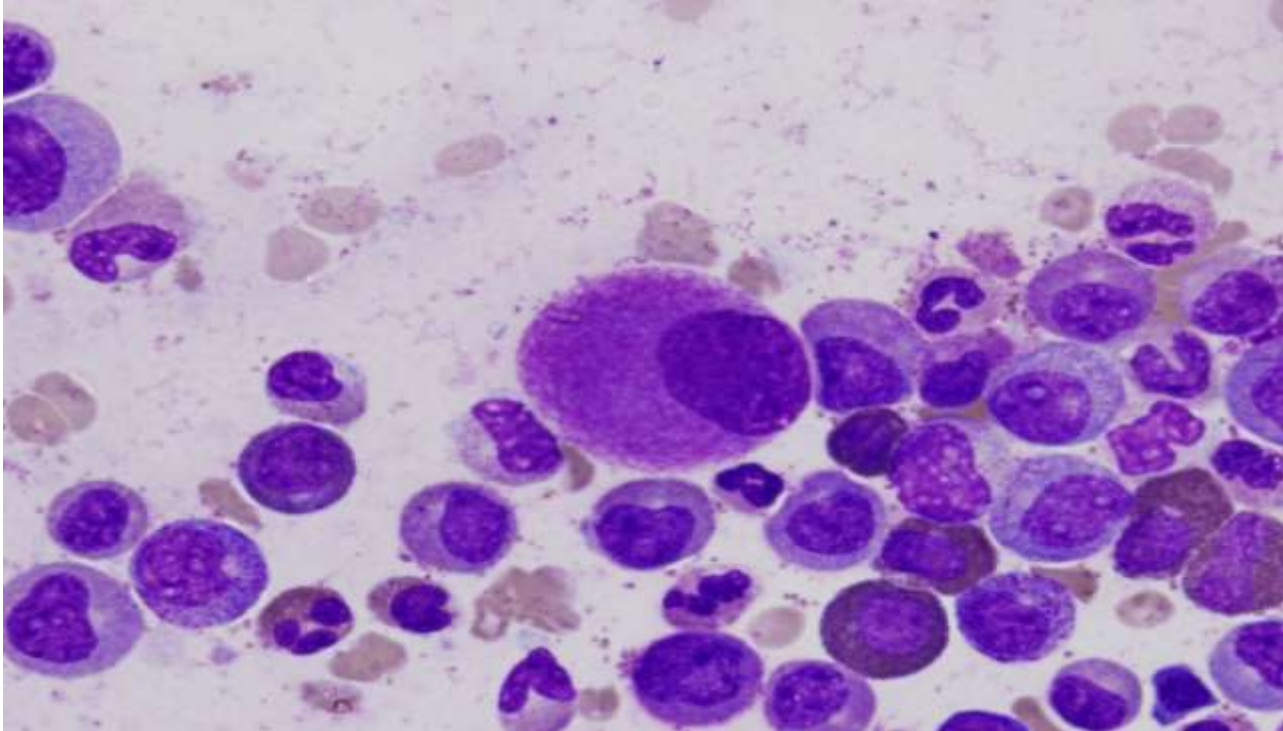
Chronic myelogenous leukemia (CML): diagnosis 2

- Thus, CML can be detected by routine cytogenetics, and the involved genes BCR-ABL1 can be detected by fluorescent in situ hybridization, as well as by polymeric chain reaction (PCR)
- Controversy exists over so-called *Ph-negative* CML, or cases of suspected CML in which the Philadelphia chromosome cannot be detected: many such patients in fact have complex chromosomal abnormalities that mask the (9;22) translocation, or have evidence of the translocation in spite of normal routine karyotyping

Chronic myelogenous leukemia (CML): diagnosis 3

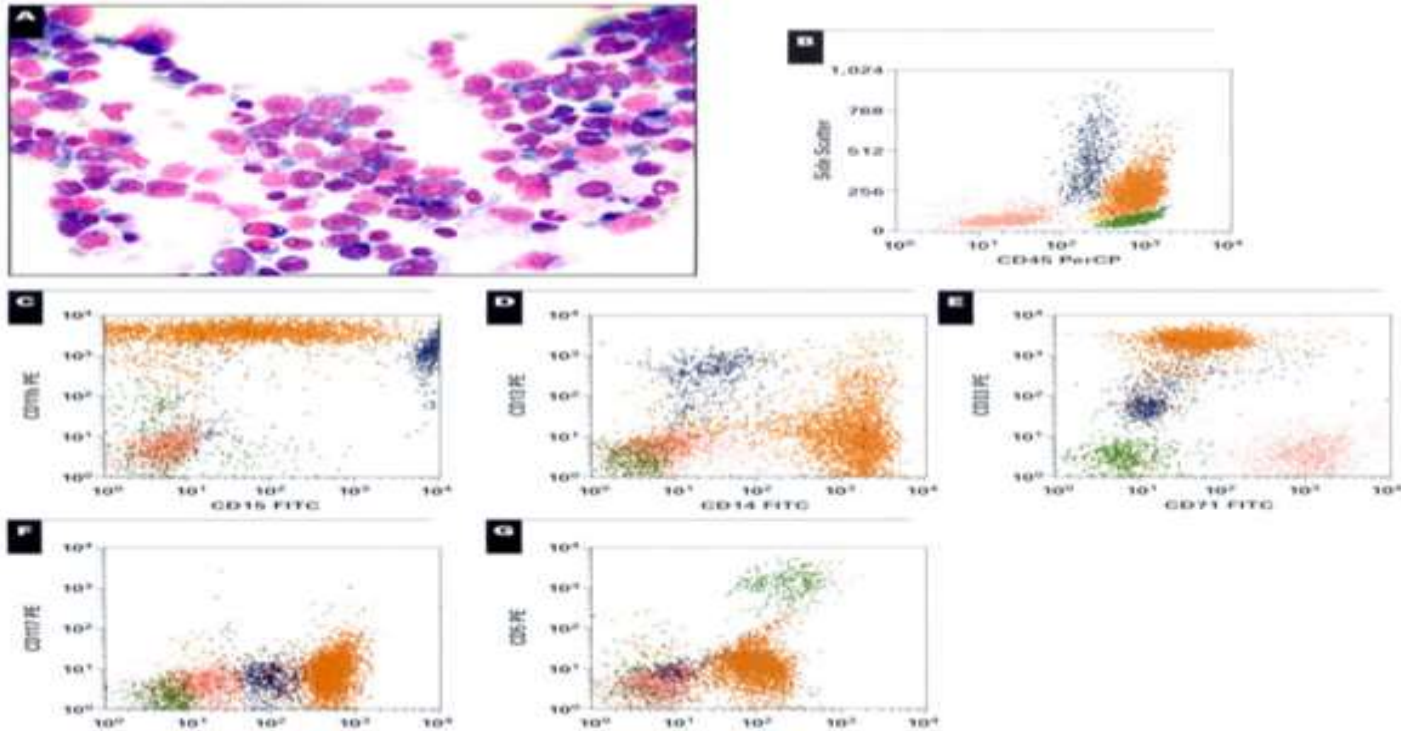
- The small subset of patients without detectable molecular evidence of bcr-abl fusion may be better classified as having an undifferentiated myelodysplastic/myeloproliferative disorder, as their clinical course tends to be different from patients with CML
- CML must be distinguished from a leukemoid reaction, which can have a similar appearance on a blood smear

Chronic myelogenous leukemia (CML): diagnosis 3



A small, hypolobated megakaryocyte (center of field) in a bone marrow aspirate, typically of CML

Chronic myelogenous leukemia (CML): diagnosis 4



Immunophenotyping

Chronic myelogenous leukemia (CML): treatment 1

- The only curative treatment for CML is a bone marrow transplant or an allogeneic stem cell transplant
- Other than this there are four major mainstays of treatment in CML:
 - treatment with tyrosine kinase inhibitors
 - myelosuppressive or leukopheresis therapy (to counteract the leucocytosis during early treatment)
 - splenectomy and interferon alfa-2b treatment

Chronic myelogenous leukemia (CML): treatment 2

Chronic phase

- In the past, antimetabolites (e.g., cytarabine, hydroxyurea), alkylating agents, interferon alfa 2b, and steroids were used as treatments of CML in the chronic phase, but since the 2000s have been replaced by Bcr-Abl tyrosine-kinase inhibitor drugs that specifically target BCR-ABL, the constitutively activated tyrosine kinase fusion protein caused by the Philadelphia chromosome translocation

Chronic myelogenous leukemia (CML): treatment 3

Chronic phase

- Despite the move to replacing cytotoxic antineoplastics (standard anticancer drugs) with tyrosine kinase inhibitors sometimes hydroxyurea is still used to counteract the high WBCs encountered during treatment with tyrosine kinase inhibitors like imatinib; in these situations it may be the preferred myelosuppressive agent due to its relative lack of leukemogenic effects and hence the relative lack of potential for secondary hematologic malignancies to result from treatment

Chronic myelogenous leukemia (CML): treatment 4

Imatinib

- The first of this new class of drugs was imatinib mesylate, approved by the U.S. Food and Drug Administration (FDA) in 2001
- Imatinib was found to inhibit the progression of CML in the majority of patients (65–75%) sufficiently to achieve regrowth of their normal bone marrow stem cell population (a cytogenetic response) with stable proportions of maturing white blood cells

Chronic myelogenous leukemia (CML): treatment 5

Dasatinib, nilotinib and radotinib

- Dasatinib was initially approved in 2007 by the US FDA to treat CML in patients who were either resistant to or intolerant of imatinib
- Nilotinib, was also approved by the FDA for the same indication in 2010
- Radotinib joined the class of novel agents in the inhibition of the BCR-ABL protein and was approved in South Korea in 2012 for patients resistant to or intolerant of imatinib

Chronic myelogenous leukemia (CML): treatment 6

Treatment-resistant CML

- Two approaches were developed to the treatment of CML as a result:
 - In September 2012, the FDA approved a non BCR-ABL targeted agent omacetaxine, administered subcutaneously in patients who had failed with imatinib and exhibited T315I kinase domain mutation
 - In December 2012 , the FDA approved a new pan-BCR-ABL inhibitor Ponatinib which showed efficacy against T315I

Chronic myelogenous leukemia (CML): treatment 7

Vaccination

In 2005, encouraging but mixed results of vaccination were reported with the *BCR/abl* p210 fusion protein in patients with stable disease, with GM-CSF as an adjuvant

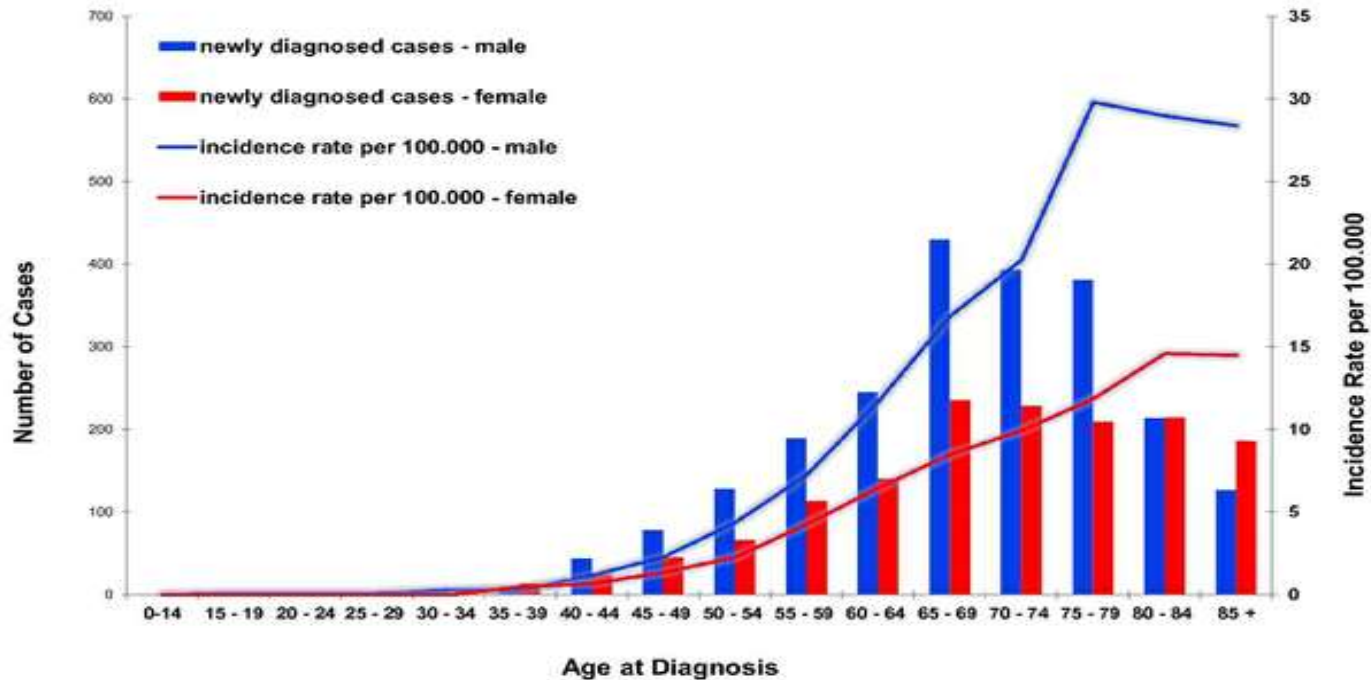
Chronic myelogenous leukemia (CML): prognosis

- The median survival time for CML patients had been about 3–5 years from time of diagnosis
- With the use of tyrosine kinase inhibitors, survival rates have improved dramatically
- A 2006 follow up of 553 patients using imatinib found an overall survival rate of 89% after five years
- A 2011 follow up of 832 patients using imatinib who achieved a stable cytogenetic response found an overall survival rate of 95.2

Chronic lymphocytic leukemia (CLL): definition

Chronic lymphocytic leukemia (CLL) is a monoclonal disorder characterized by a progressive accumulation of small, mature-appearing functionally incompetent lymphocytes in blood, bone marrow, and organs

Chronic lymphocytic leukemia (CLL): epidemiology



Incidence of CLL by age

Chronic lymphocytic leukemia (CLL): classification 1

Stage division of CLL according to Binet			
Criteria	Stage		
	A	B	C
Number of involved lymph node regions	0–2	3–5	0–5
Hemoglobin (g/dl)	>10	>10	<10
Thrombocytes ($10^9/l$)	>100	>100	<100
Survival (years)	>10	5	2.6

Chronic lymphocytic leukemia (CLL): clinical presentation 1

- About 40%-60% of patients are diagnosed in the absence of disease-related symptoms, even with very high numbers of circulating lymphocytes $>100 \times 10^9/l$
- The presence of lymphadenopathy or an abnormal CBC is the only reason to consider the diagnosis
- The remaining patients may present with weakness, fatigue, night sweats, fever, and may be with or without infections or autoimmune diseases
- Physical examination: nontender, painless, and mobile lymphadenopathy, splenomegaly, or hepatomegaly

Chronic lymphocytic leukemia (CLL): clinical presentation 2

- Metabolic abnormalities (e.g., hyperuricemia) or mechanical disorders (e.g., airway obstruction) related to the tumor burden, may also be present
- Manifestations of bone marrow (BM) involvement, particularly significant anemia (hemoglobin $<11\text{g/dl}$) or thrombocytopenia (platelets count $<100 \times 10^9/\text{l}$), are noted at presentation in 15% of CLL patients
- A positive direct antiglobulin test (DAT) is present in about 20% of patients at diagnosis but is not commonly associated with hemolytic anemia

Chronic lymphocytic leukemia (CLL): clinical presentation 3



Zosteriform B-Cell
CLL infiltration



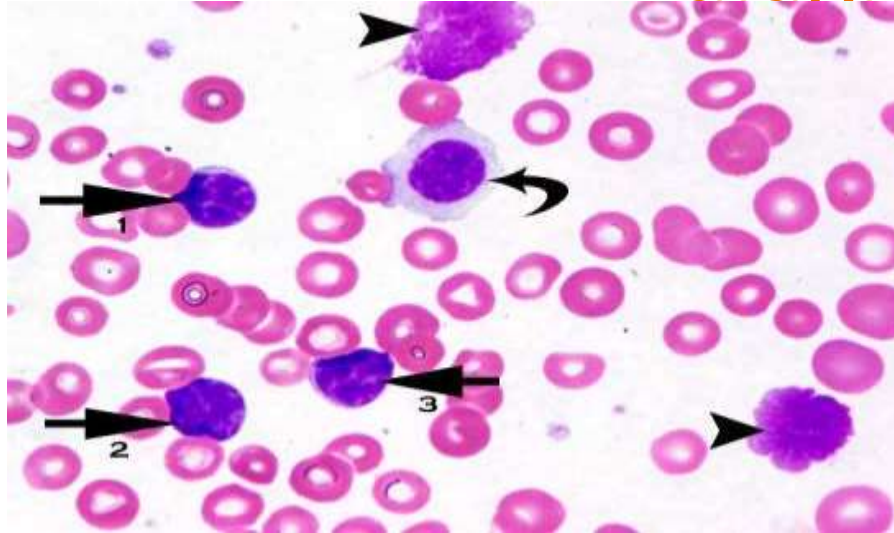
Massive adenopathy involving the neck,
from the level of the mastoid to the
supraclavicular fossa, and large nodal
masses in both axillae

Chronic lymphocytic leukemia (CLL): diagnosis 1

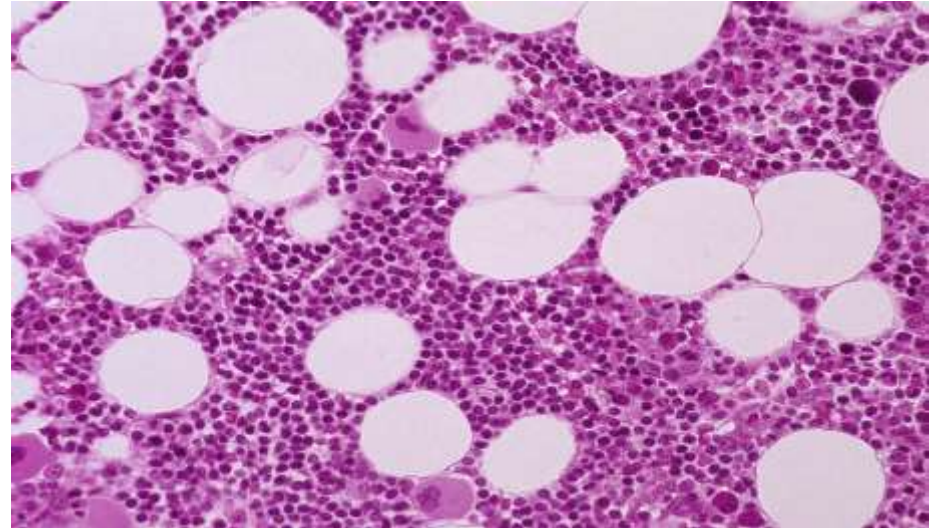
The National Cancer Institute-Sponsored Working Group
diagnosis and response criteria for CLL

- The peripheral blood should exhibit an increase in the number of small mature-appearing lymphocytes to $>5,000/\mu\text{l}$
- The bone marrow (BM) aspirate smear must show $>30\%$ of all nucleated cells to be lymphoid
- BM examination is indicated primarily to evaluate response to treatment or to assess normal elements if there is an unexplained anemia or thrombocytopenia

Chronic lymphocytic leukemia (CLL): diagnosis 2

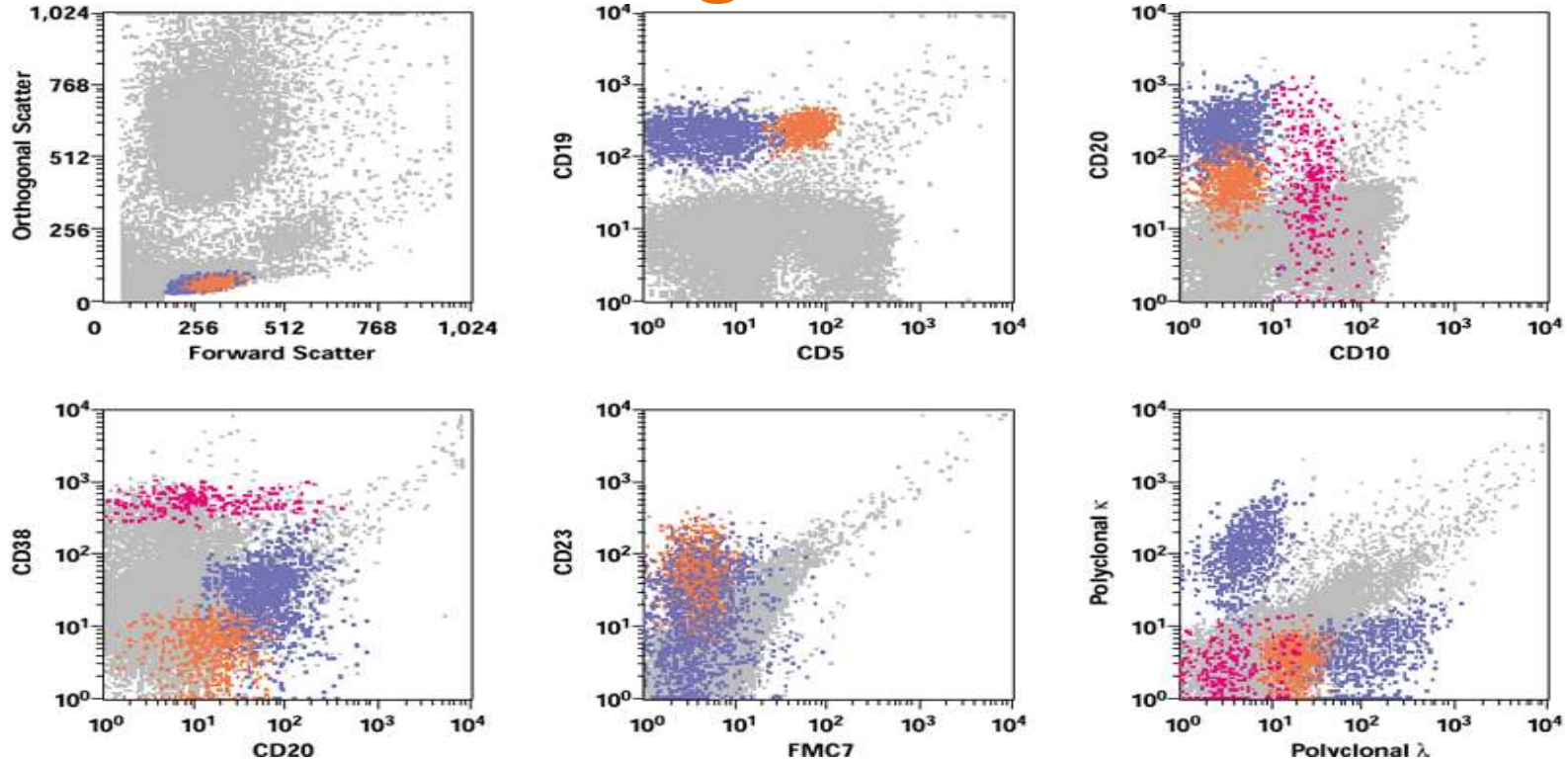


B-cell chronic lymphocytic leukemia: compare the cell size of CLL cells with a single large granular lymphocyte (curved arrow)



The BM biopsy shows a global cellularity within normal range, although somewhat heterogeneous: three cell lines present with maturation

Chronic lymphocytic leukemia (CLL): diagnosis 3



Immunophenotyping

Chronic lymphocytic leukemia (CLL): treatment 1

- CLL treatment focuses on controlling the disease and its symptoms rather than on an outright cure
- CLL is treated by chemotherapy, radiation therapy, biological therapy, or bone marrow transplantation
- Symptoms are sometimes treated surgically (splenectomy removal of enlarged spleen) or by radiation therapy ("de-bulking" swollen lymph nodes)
- An initial treatment: fludarabine, cyclophosphamide, and rituximab

Chronic lymphocytic leukemia (CLL): treatment 2

- Physicians use a “watchful waiting” mode until the disease progressed, 50% of patients have a poor outcome
- Since CLL cells must interact with the stroma in bone marrow or lymphoid tissues to survive, these interactions need to be explored as targets of innovative therapies
- Since as 20% of patients with the worst prognostic markers have stereotypic antigen receptors, they may be valuable points of attack

Chronic lymphocytic leukemia (CLL): prognosis

- Prognosis depends on the subtype
- Some subtypes have a median survival of 6–8 years, while others have a median survival of 22 years (which is a normal lifespan for older patients)
- Telomere length has been suggested to be a valuable prognostic indicator of survival

Prophylaxis

Patients with leukemia in periods of severe granulocytopenia and thrombocytopenia related to the specific antileukemic therapies administered demand secondary prophylaxis with antifungals and antibiotics

Abbreviations

- ALL - acute lymphoblastic leukemia
- AML - acute myelogenous leukemia
- BM – bone marrow
- CALLA - common acute lymphoblastic leukemia antigen
- CARs - Chimeric antigen receptors
- CLL - chronic lymphocytic leukemia
- CML - chronic myelogenous leukemia
- CNS - central nervous system
- DCL - donor cell leukemia
- FAB - French-American-British classification
- FFP - fresh frozen plasma
- ROM - range of motion
- SCT - stem cell transplant
- TdT - terminal deoxynucleotidyl transferase
- TENS - transcutaneous electrical nerve stimulation
- WHO - World Health Organization
- PCR - polymeric chain reaction
- FDA - U.S. Food and Drug Administration

Diagnostic guidelines

- [Peripheral T-Cell Lymphomas: ESMO Clinical Practice Guidelines](#)
- [Diffuse Large B-Cell Lymphoma: ESMO Clinical Practice Guidelines](#)
- [Chronic Lymphocytic Leukaemia: ESMO Clinical Practice Guidelines](#)
- [Hairy Cell Leukaemia: ESMO Clinical Practice Guidelines](#)
- [Philadelphia Chromosome-Negative Chronic Myeloproliferative Neoplasms: ESMO Clinical Practice Guidelines](#)
- [Myelodysplastic Syndromes: ESMO Clinical Practice Guidelines](#)
- [New aspects of the updated guidelines for the diagnosis and treatment of chronic lymphocytic leukemia](#)
- [Leukemia: An Overview for Primary Care](#)