Acute Leukaemias

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09.11.2026

Acute Leukaemias

- Clonal expansion of malignant haematopoietic precursor cells.

- Generally rapidly fatal unless treated with intensive chemotherapy and/or targeted therapies together with supportive care.

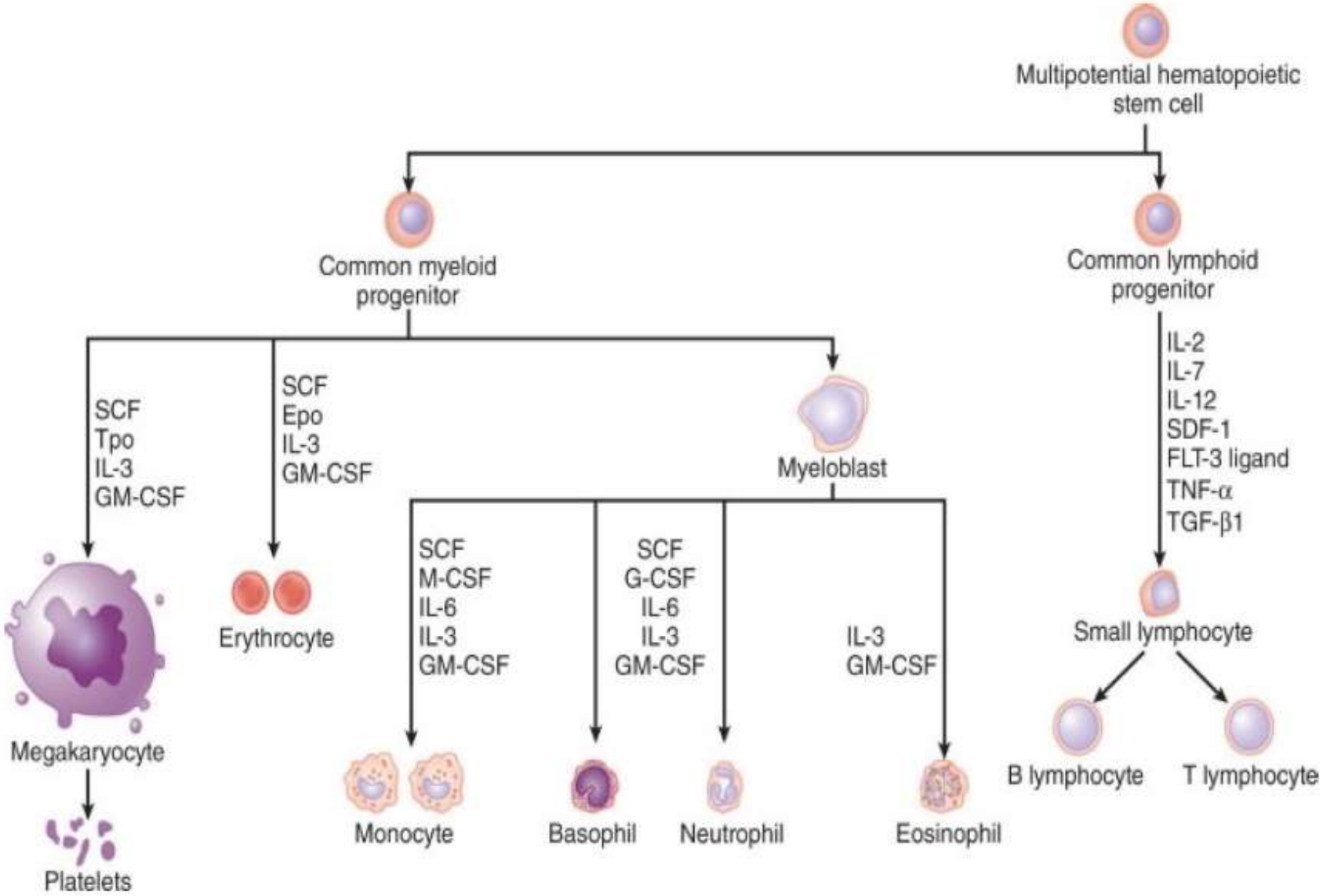

FIGURE 2-4 Hematopoietic growth factors. Factors that act on particular types of progenitors are listed. Epo, erythropoietin; FLT-3, Fms-like tyrosine kinase-3; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; IL, interleukin; M-CSF, monocyte colony-stimulating factor; SCF, stem cell factor (also known as c-KIT ligand); SDF-1, stromal cell-derived factor-1; TGF, transforming growth factor; TNF, tumor necrosis factor; Tpo, thrombopoietin.

Stage of leukaemic transformation:

- Transformation to leukaemia occurring at one of several developmental stages

- Transformation to leukaemia occurring within primitive multipotent cells

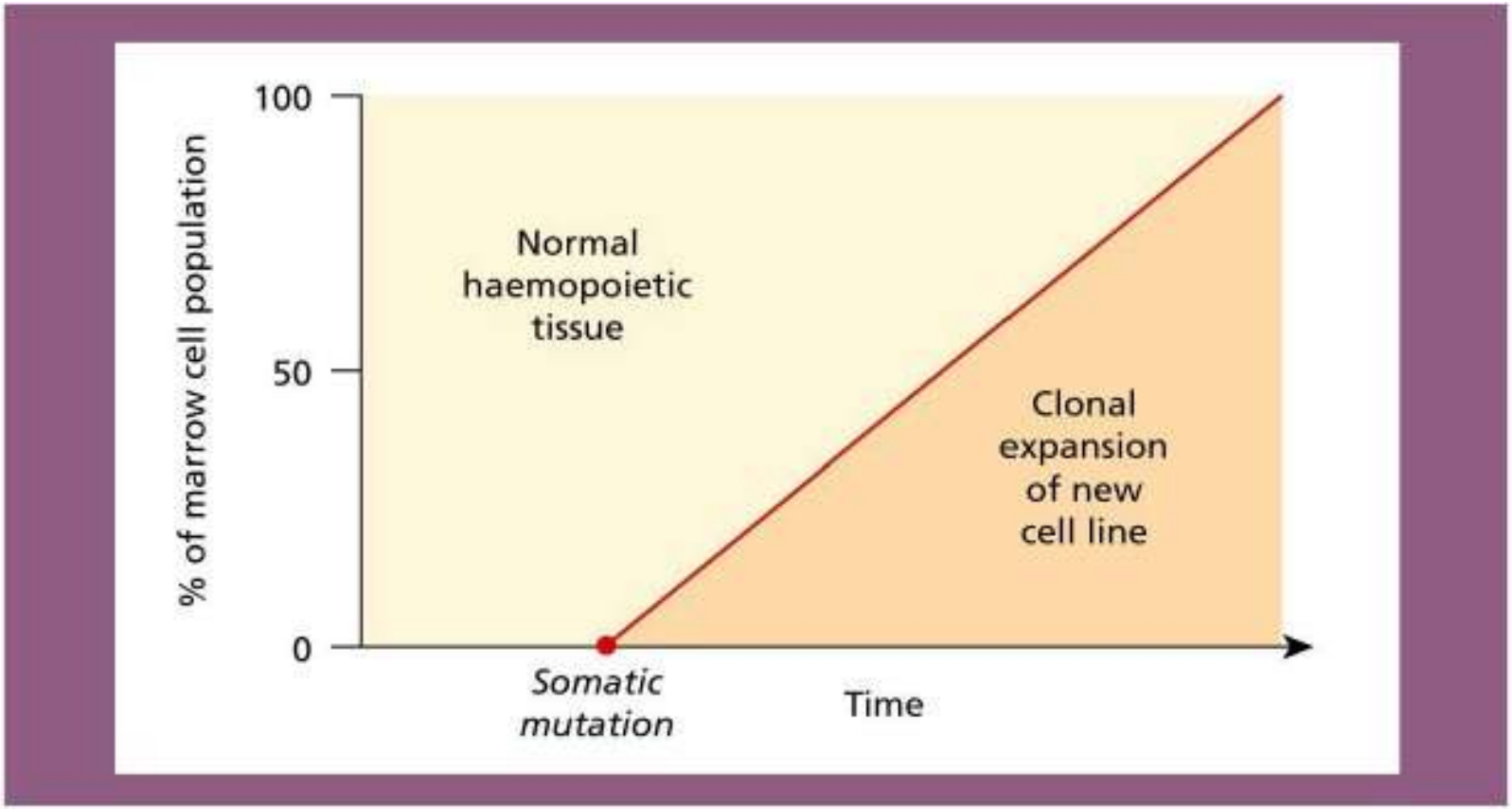

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Figure 11.1 Theoretical graph to show the replacement of normal bone marrow cells by a clonal population of malignant cells arising by successive mitotic divisions from a single cell with an acquired genetic alteration.

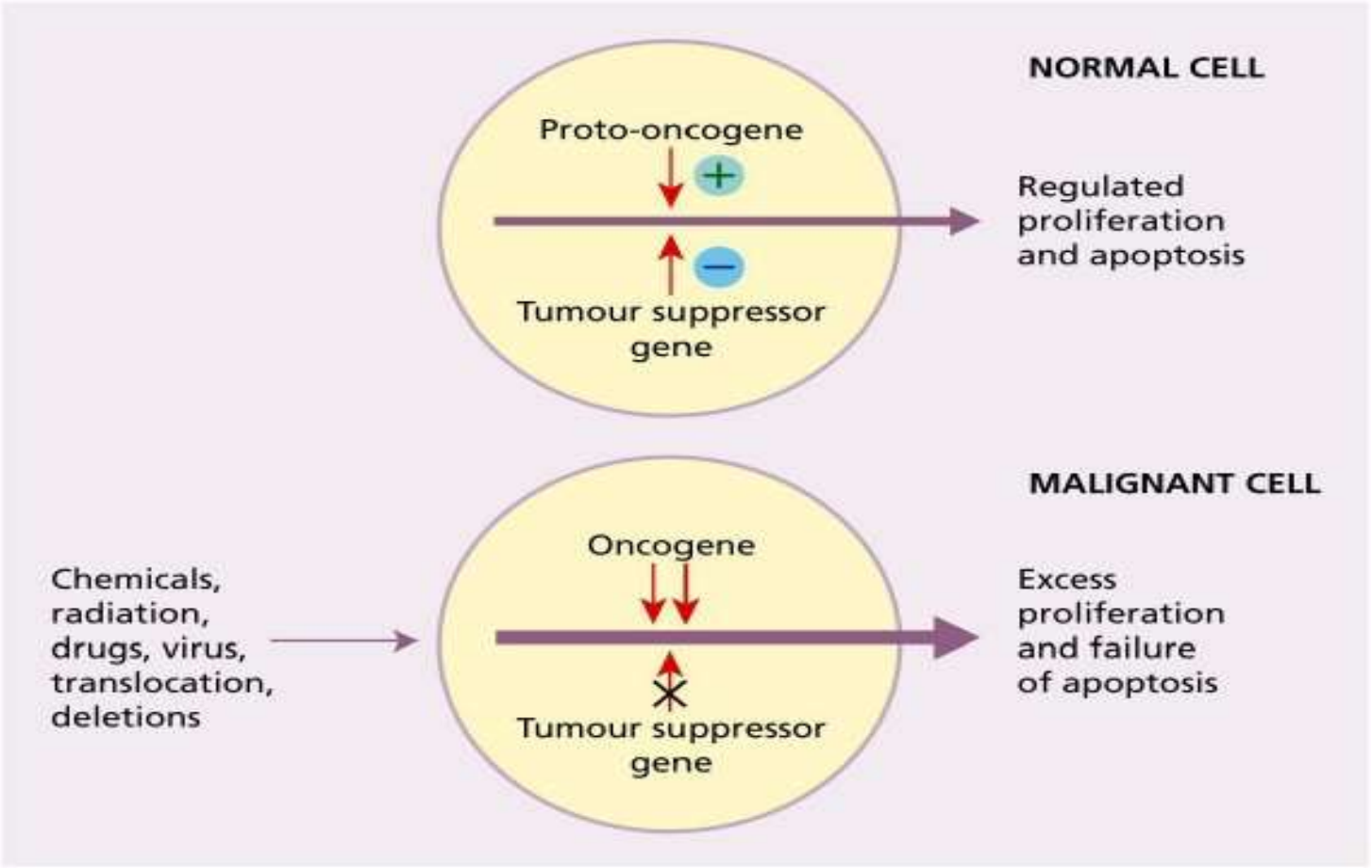

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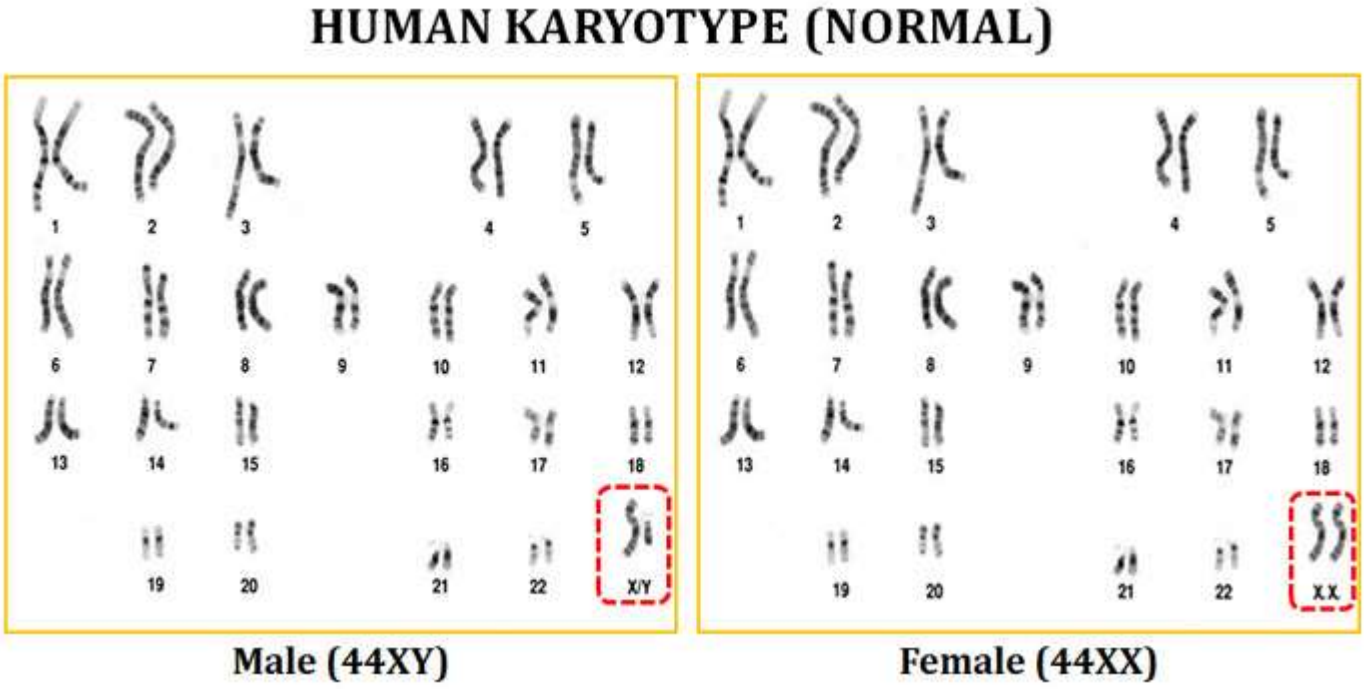
Figure 11.4 Proliferation of normal cells depends on a balance between the action of proto-oncogenes and tumour-suppressor genes. In a malignant cell this balance is disturbed leading to uncontrolled cell division.

Concepts of Cytogenetics

- 46 (22 autosomes pairs and two sex chromosomes)



Concepts of Cytogenetics

Chromosomal Aberrations:

- Numeric

Aneuploidy: Trisomy or Monosomy

- Structural:

Unbalanced: deletions, duplications, or insertions

Balanced: Inversion, translocation

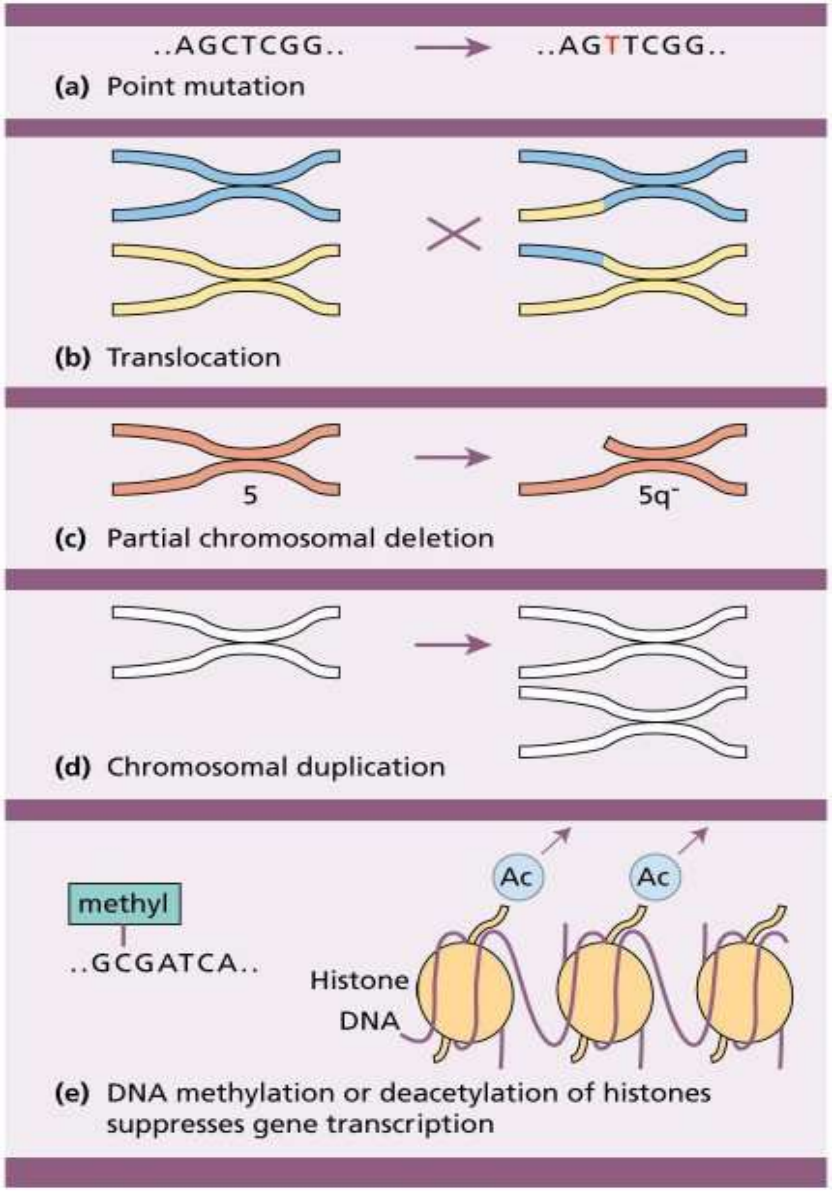


Figure 11.8 Types of genetic abnormality which may lead to haemopoietic malignancy. **(a)** Point mutation; **(b)** chromosomal translocation; **(c)** chromosomal deletion or loss; **(d)** chromosomal duplication; **(e)** DNA methylation or deacetylation of histone tails suppresses gene transcription.

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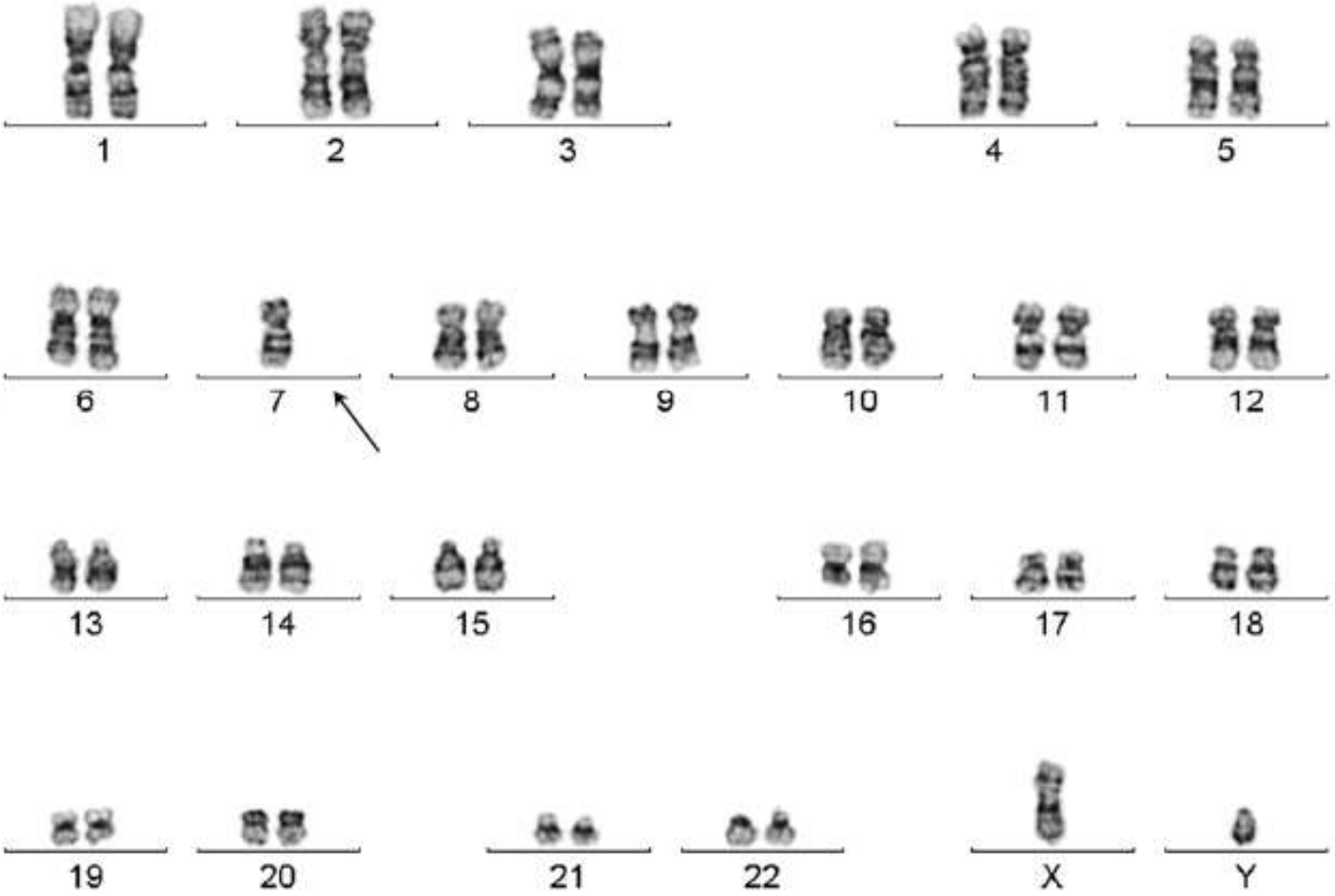

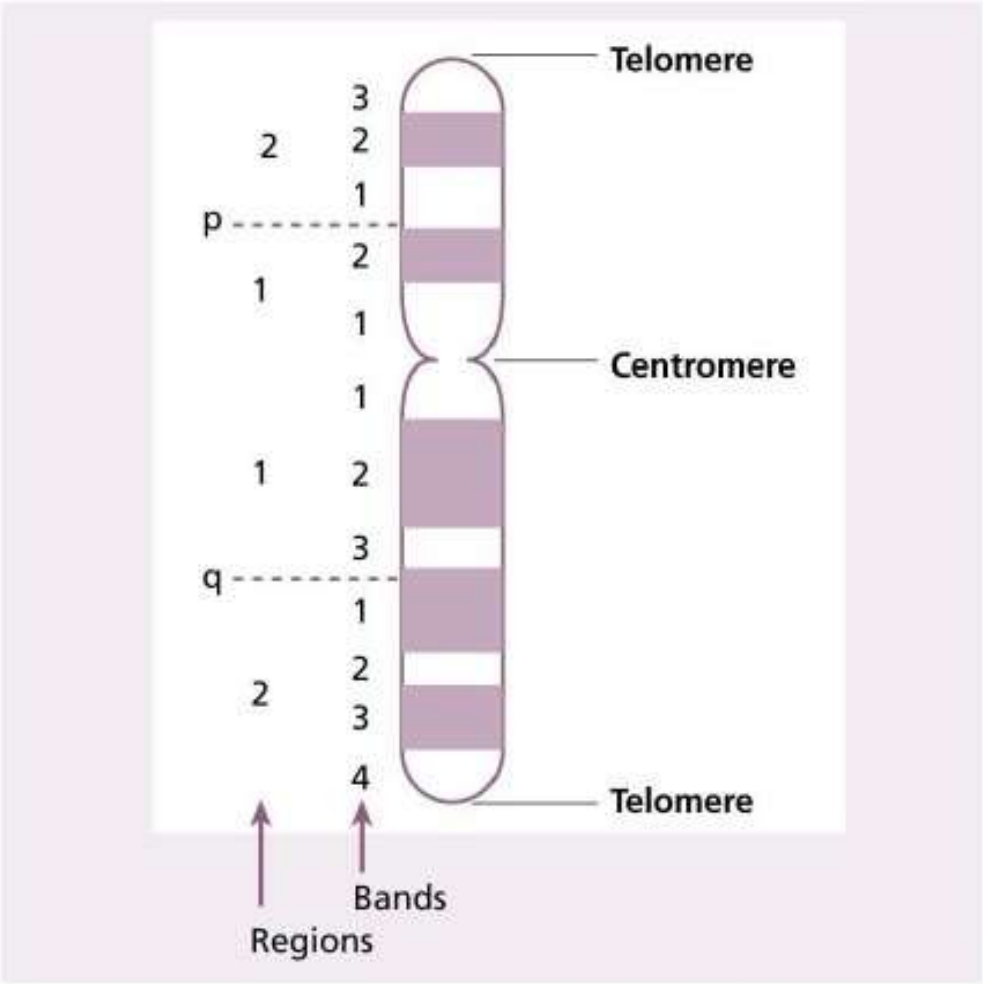

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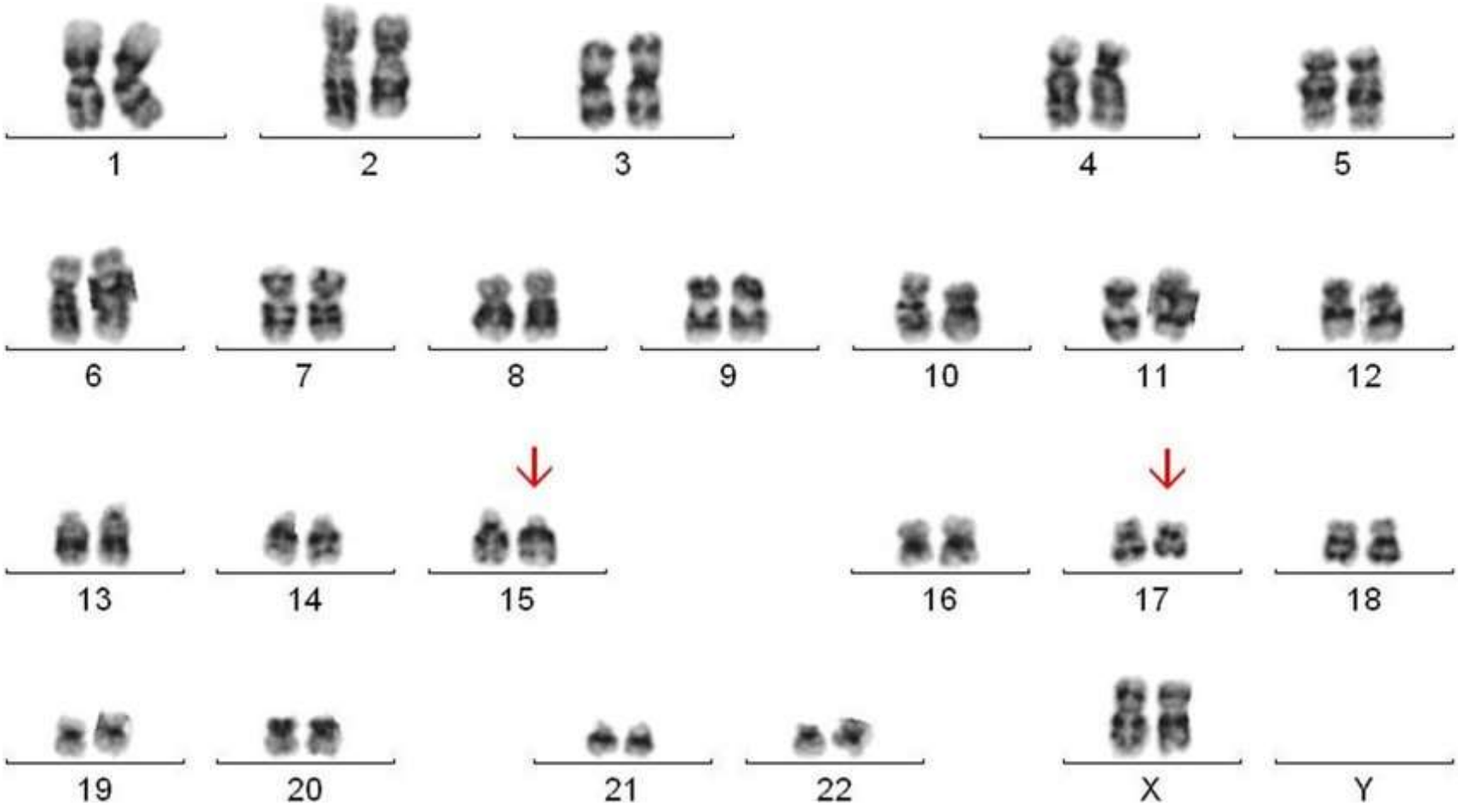
Figure 11.7 A schematic representation of a chromosome. The bands may be divided into subbands according to staining pattern.


46,XX,t(15;17)(q22;q12)
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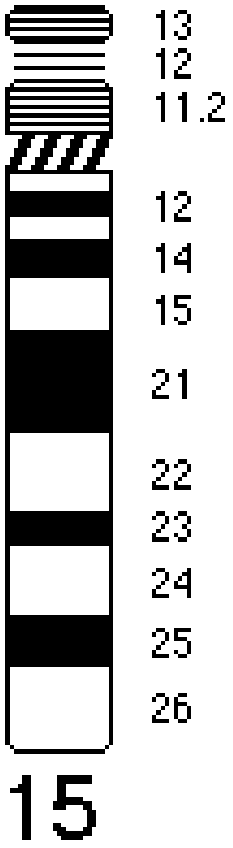
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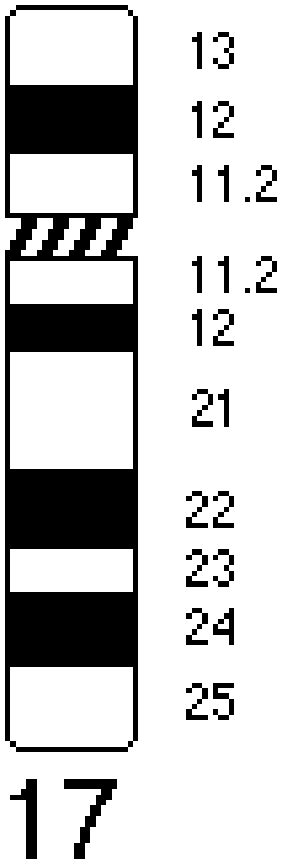
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11.2
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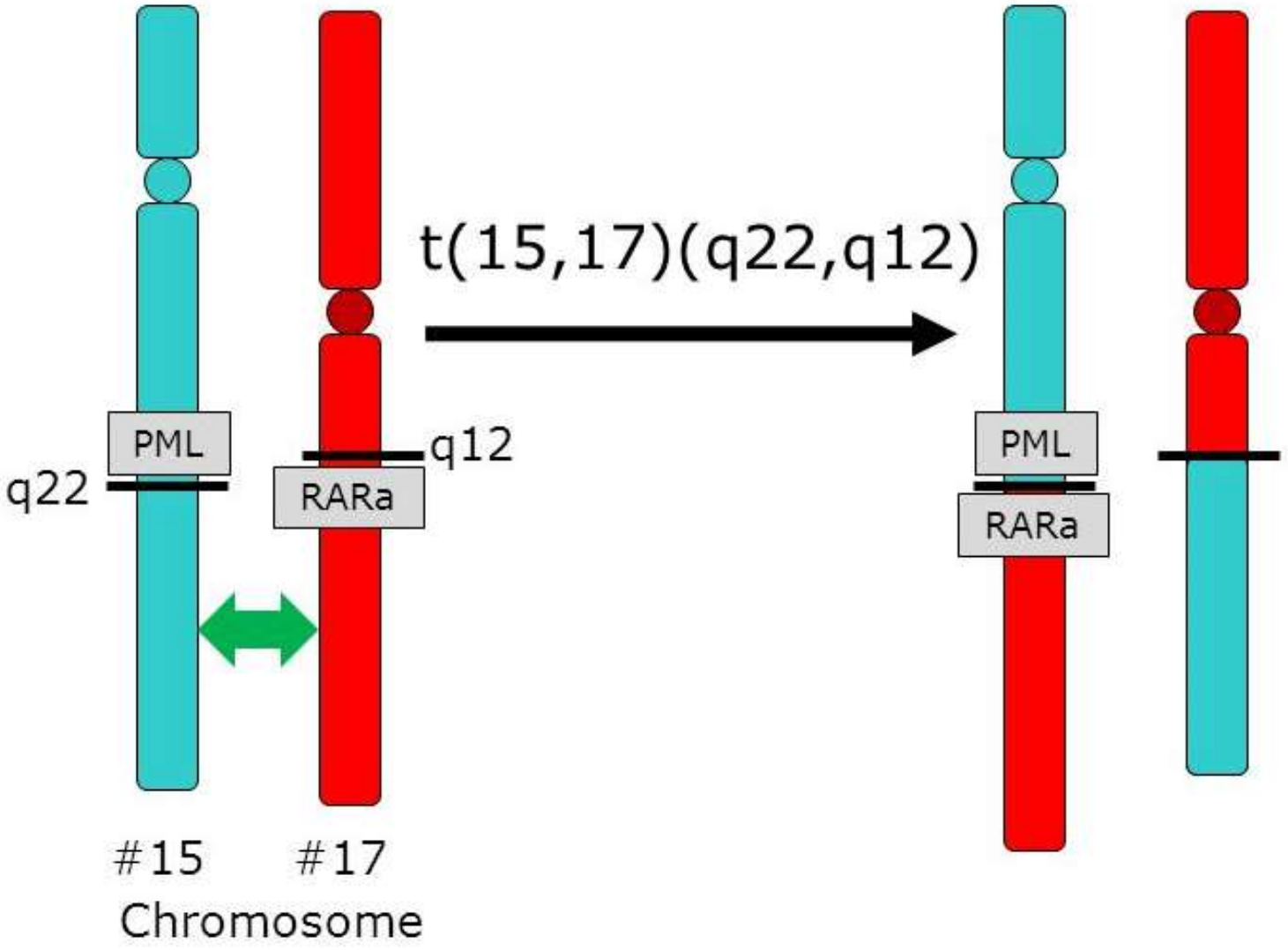
t(15,17)(q22,q12)
PML
RARa
q22
q12
PML
RARa
#15
#17
Chromosome

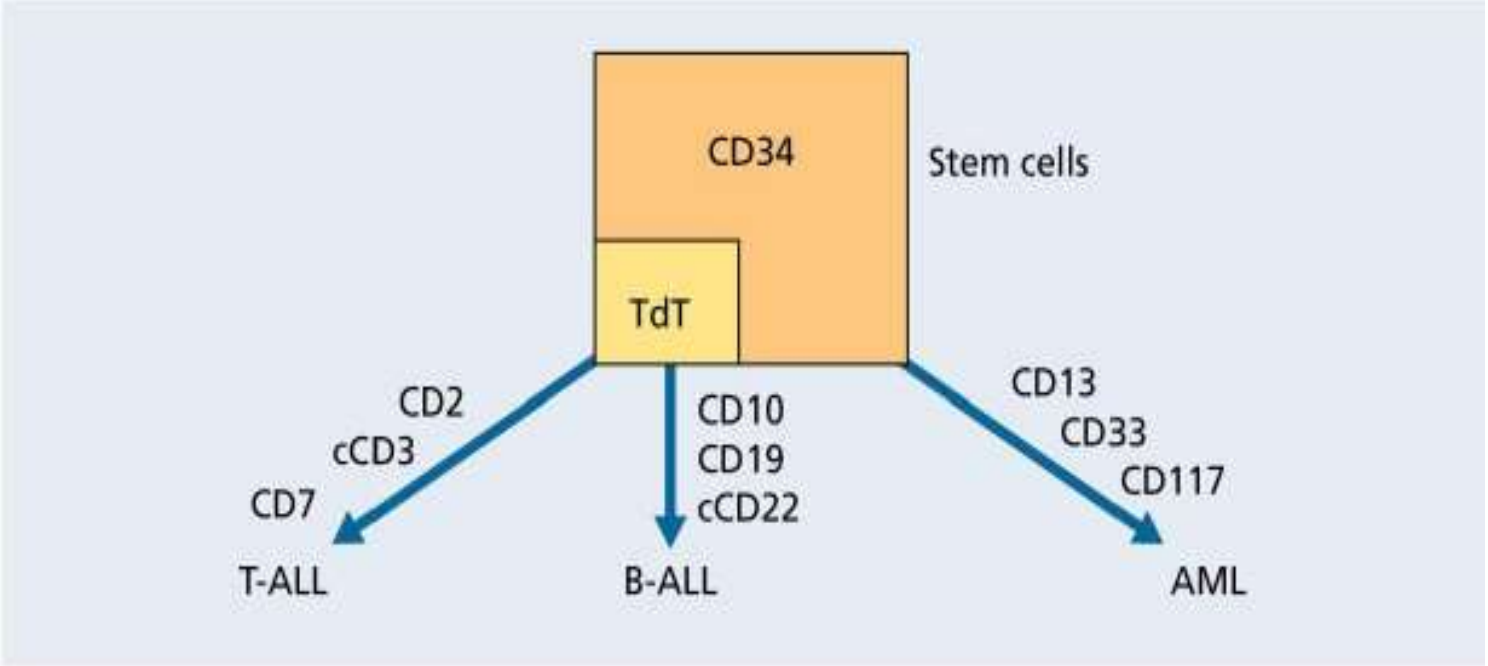

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Figure 13.1 Development of three cell lineages from pluripotential stem cells giving rise to the three main immunological subclasses of acute leukaemia. The immunological characterization using pairs of markers is shown, as well as the three markers characterizing the early 'stem' cells. AML, acute myeloid leukaemia; B-ALL, B-cell acute lymphoblastic leukaemia; c, cytoplasmic; HLA, human leucocyte antigen; T-ALL, T-cell acute lymphoblastic leukaemia; TdT, terminal deoxynucleotidyl transferase.

Acute Myeloid Leukaemia

- Most common acute leukemia in adults. Incidence is 3 to 5 cases per 100,000 population.

- The median age at diagnosis is approximately 65 years with 1/3 > at age of ≥ 75 years.

- Risk Factors:

<u>Environmental:</u>

exposure to chemicals, radiation, tobacco, chemotherapy (alkylating agents, topoisomerase inhibitors and purine analogues), and retroviruses.

<u>Antecedent haematological disease:</u>

myelodysplastic syndrome, myeloproliferative neoplasms, paroxysmal nocturnal haemoglobinuria, aplastic anaemia

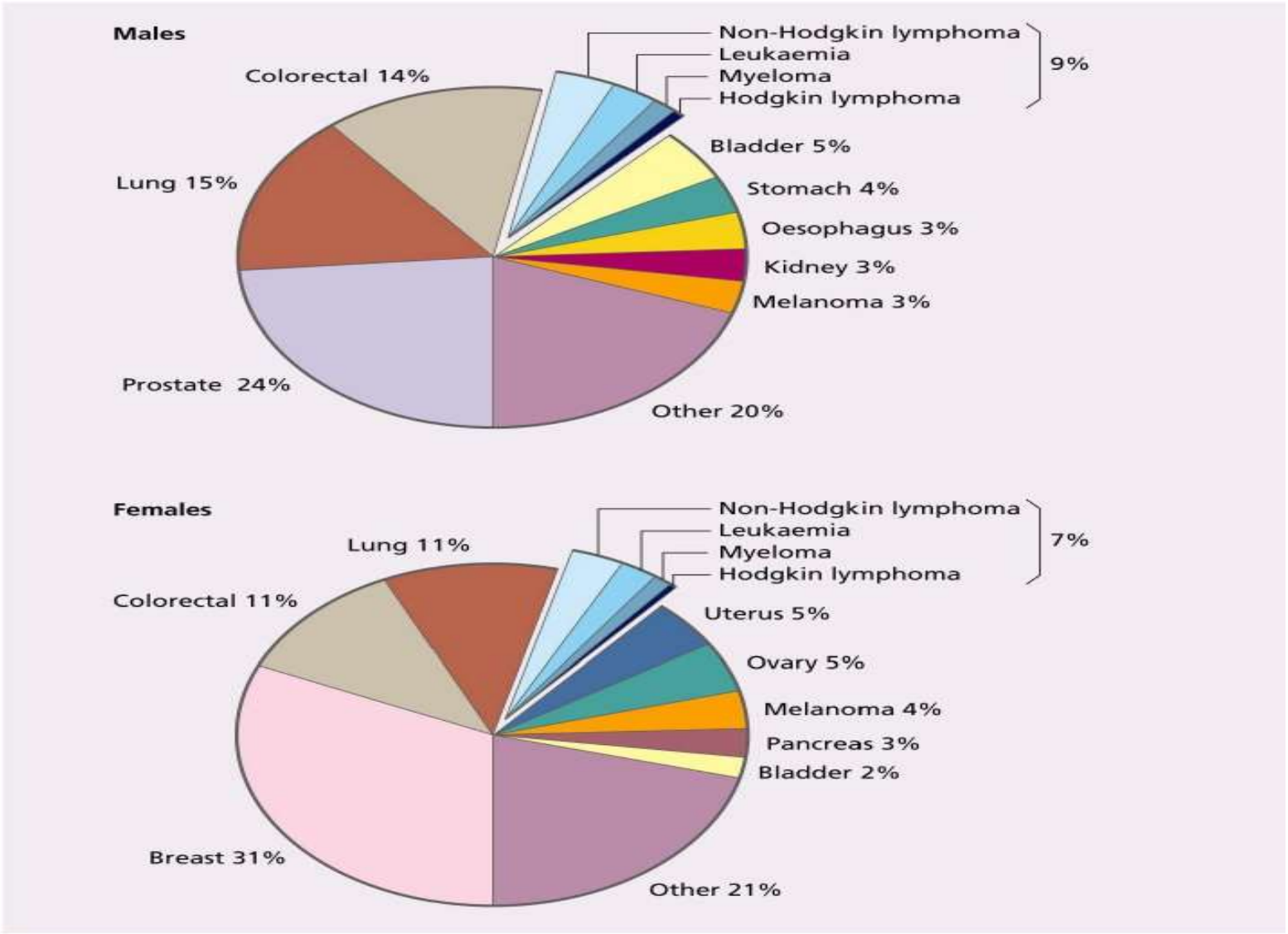

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Figure 11.2 The relative frequency of the haematological malignancies as a proportion of malignant disease. (From Smith A. *et al.* (2009) *Br J Haematol* **148**,739–53, with permission.)

Presentation:

- Symptoms of Pancytopenia
- Fatigue is the most common symptom.
- Sternal and bone pain; expansion of medullary cavity by leukaemic process.
- Fever- prompt antibiotic therapy.
- Skin- leukaemic cutis
- CNS manifestiations (headaches, visual changes and cranial nerves palsies)
- Gingival hypertrophy
- Hepato- splenomegaly: ~10%
- Myeloid Sarcoma: ~1% of AML cases. Sites of isolated myeloid sarcoma include bone, periosteum, soft tissues, and lymph nodes, and less commonly the orbit, intestine, mediastinum, epidural region, uterus, and ovary
- Hyperleukocytosis
- DIC
- Electrolyte/Metabolic abnormalities

Electrolyte/Metabolic abnormalities:

High turnover of proliferating leukaemic cells.

Hyperuricaemia, Hyperphosphataemia, Hypocalcaemia, Hyper and Hypokalemia.

Tumor lysis syndrome:

Rapid death of leukaemic cells.

Risk Factors: Hyperleukocytosis, impaired KFT at baseline, hyperuricaemia.

Release of large amounts of phosphate from lysed blasts, which co precipitates with calcium in the kidneys

hyperphosphatemia, hypocalcemia, hyperuricemia, hyperkalemia, and renal insufficiency.

Others




A
B

Laboratory :

Peripheral Blood:

Haemoglobin:

Anaemia, usually normocytic

Platelets: usually low.

75% less than 100

25% less than 25

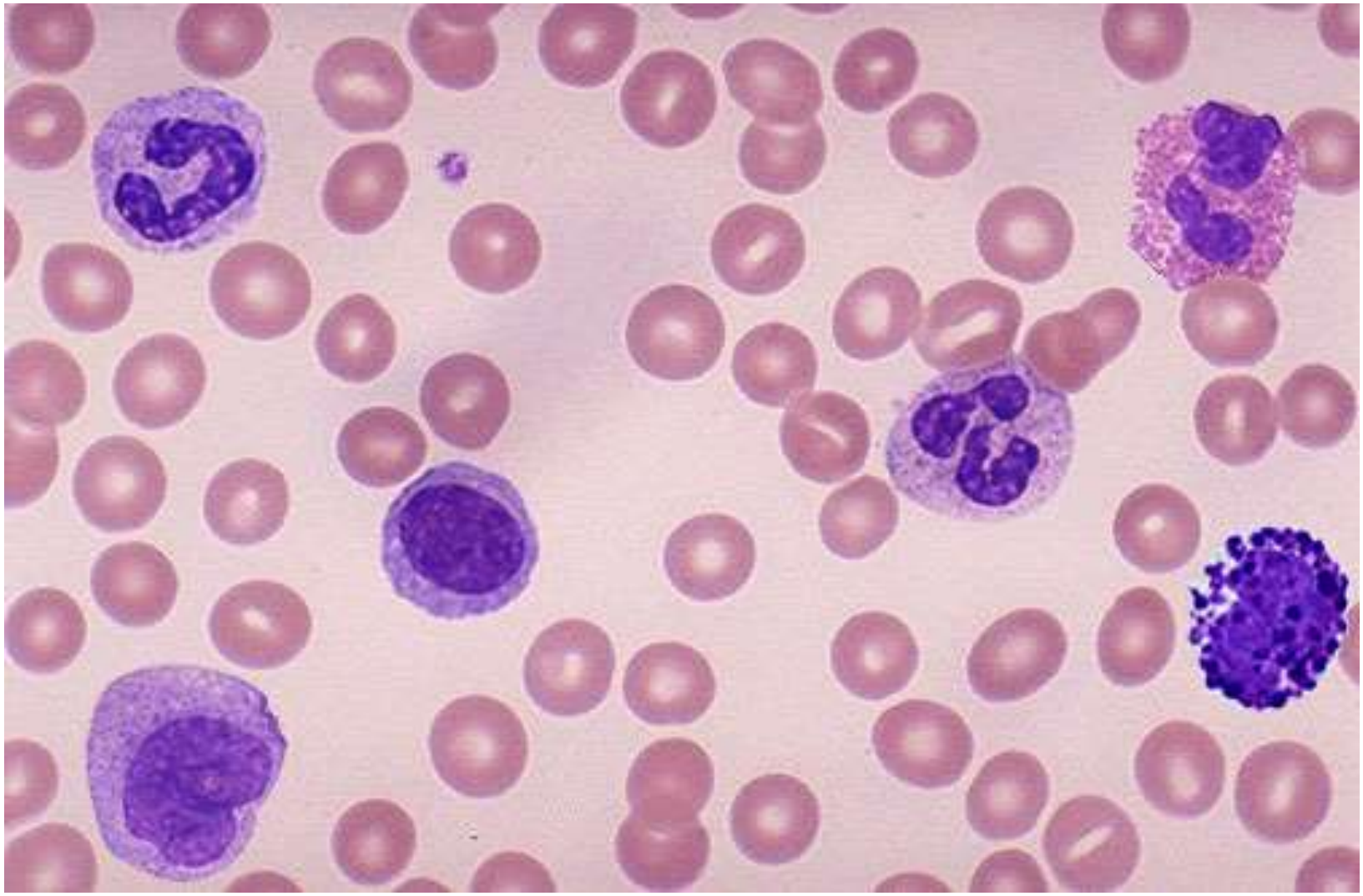
WBCs:

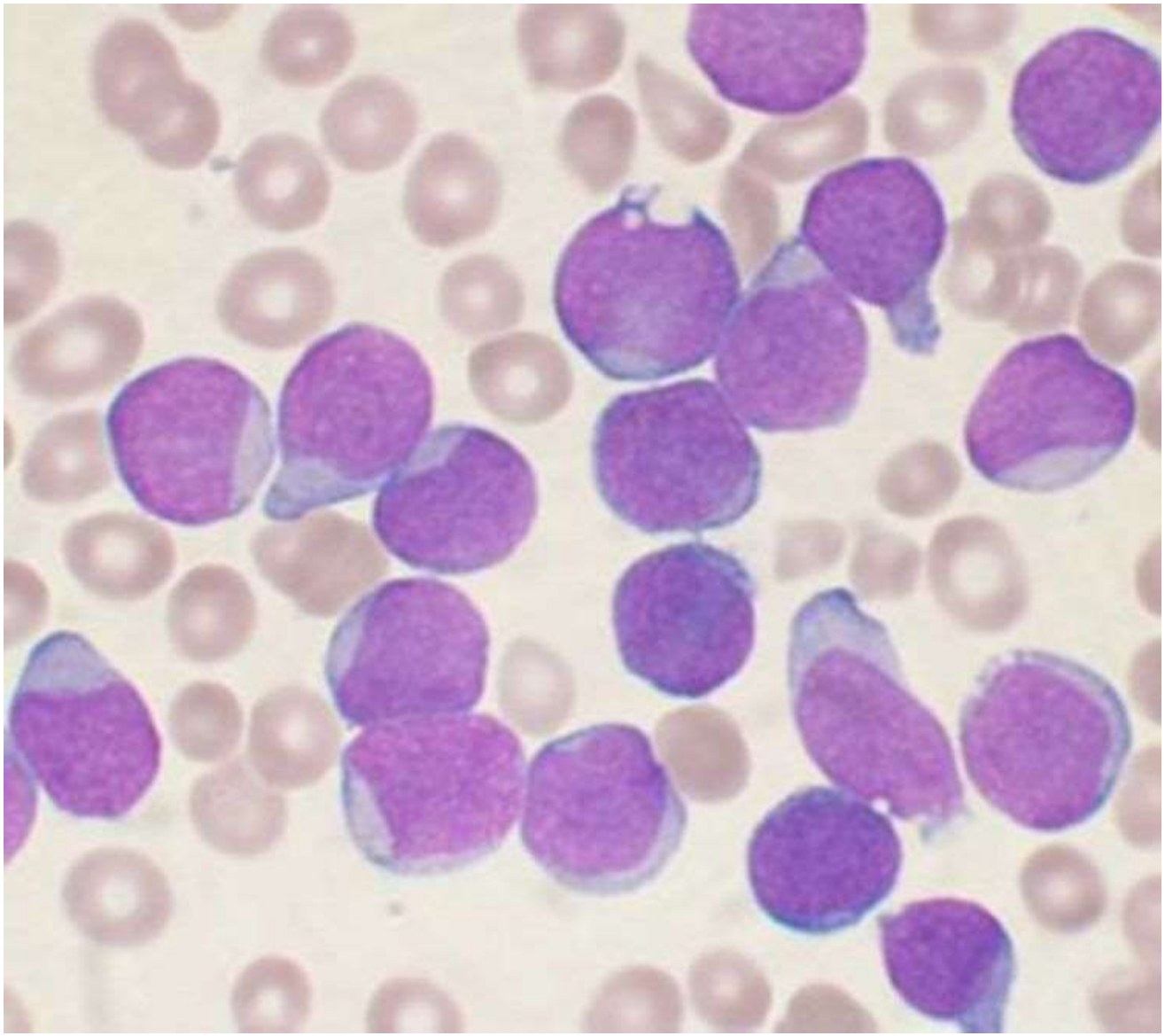
Median: 15

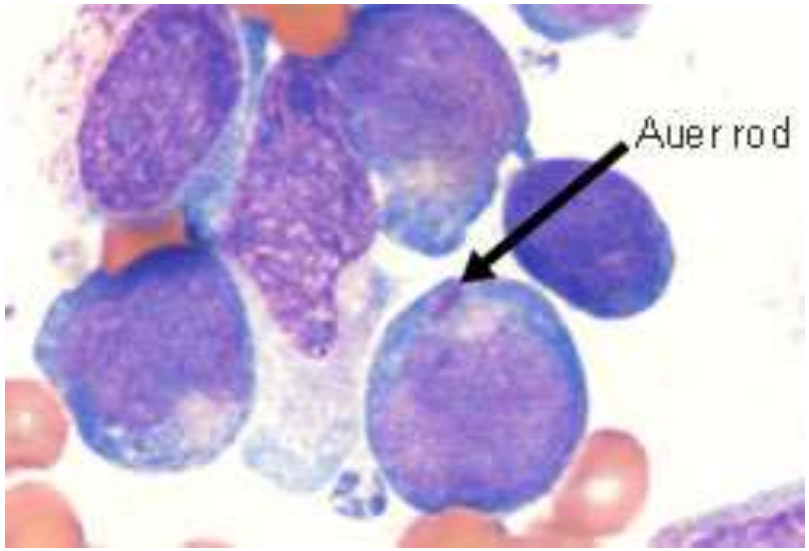
20% more than 100

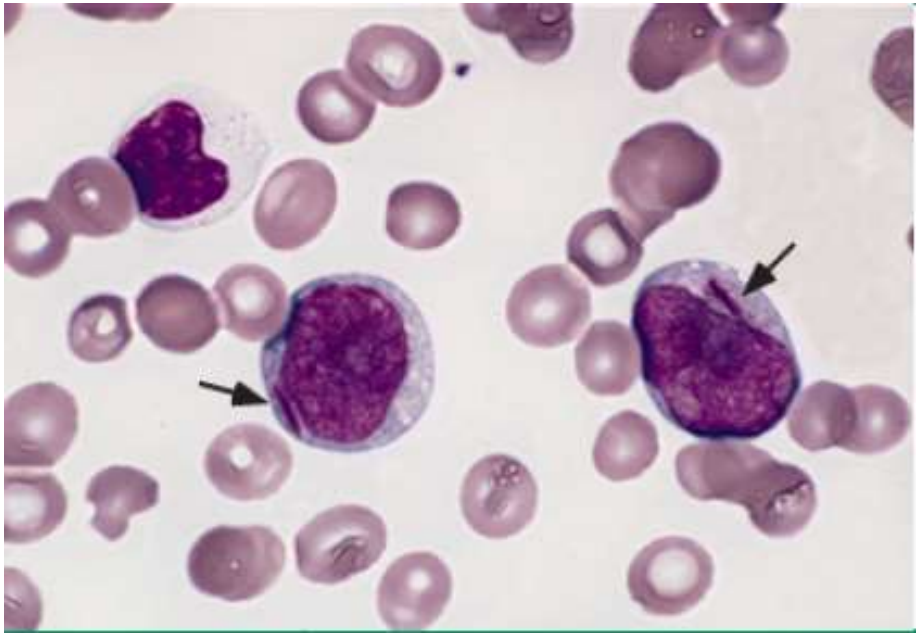
25-40% less than 5

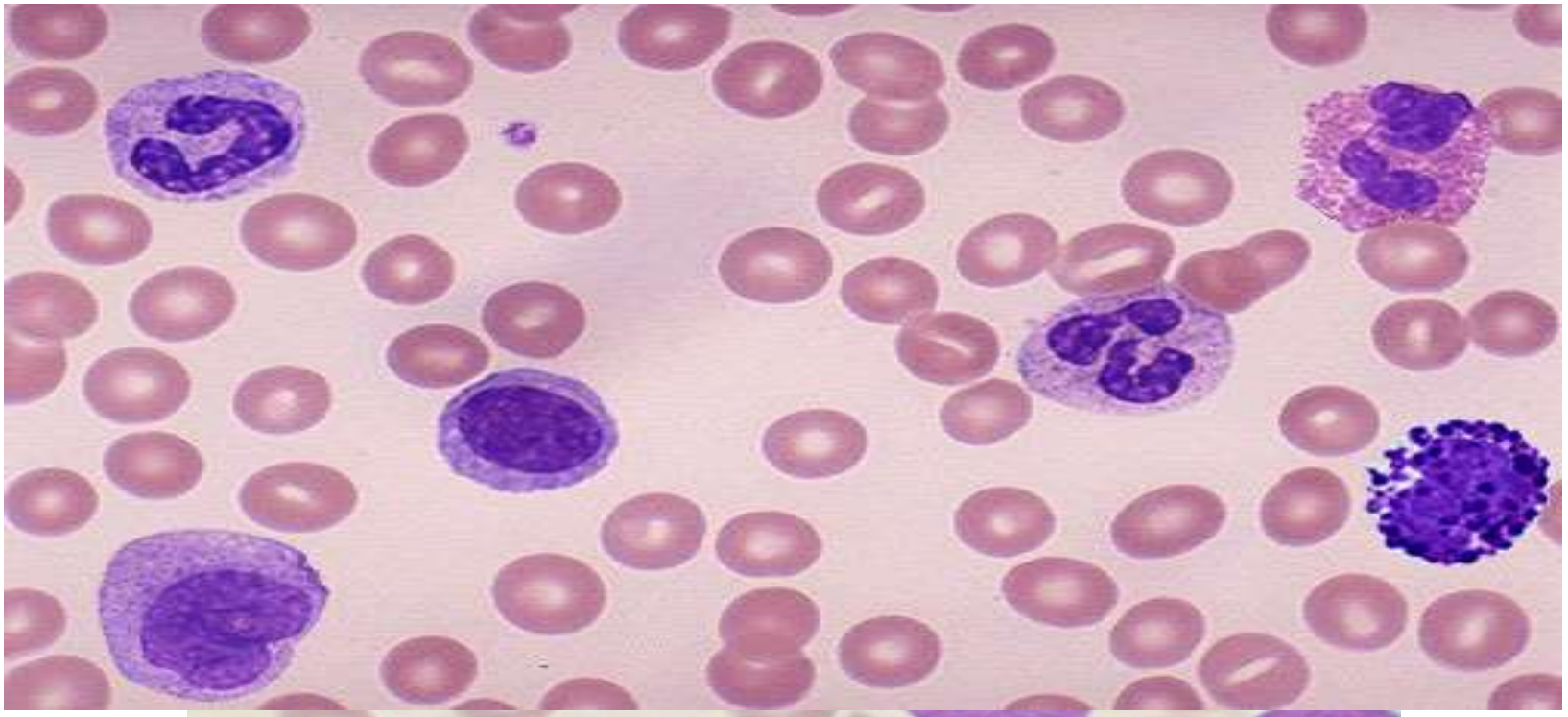
95% with blasts.

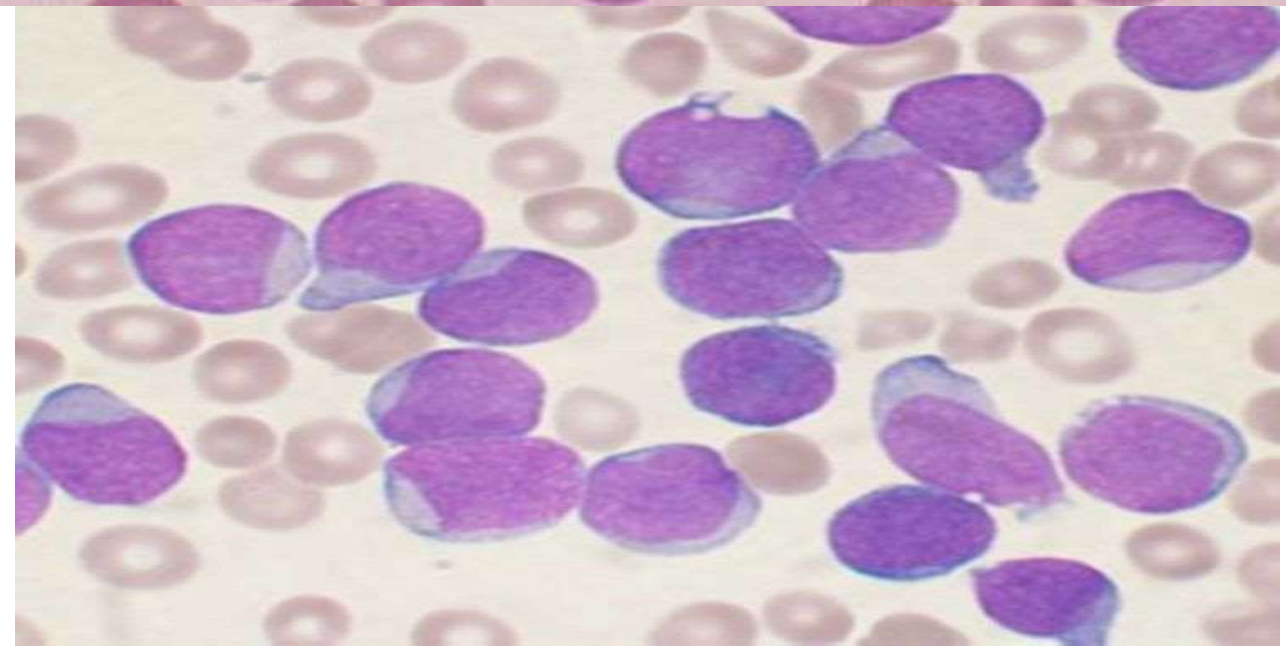





Auer rod







Laboratory :

Bone Marrow:

- Usually hypercellular
- Presence of dysplasia or fibrosis suggest an antecedent bone marrow disease
- Blast count is essential to perform

To Diagnose AML:

- Presence of ≥ 20% of blasts in PB or BM
- Those blasts are of myeloid lineage
- Myeloid Sarcoma or certain genetic aberrations are enough on their own to diagnose AML regardless of blast count (t8:21, inv16, t15:17)

Laboratory :

Blasts are of myeloid lineage:

- Flow cytometry: CD34, HLA-DR, CD117, CD13, and CD33.
- Presence of Auer rod cells.
- Positive MPO stain.

Genetic aberrations: Karyotyping, FISH, molecular tests.

Cytogenetic abnormalities in acute myeloid leukemia

Cytogenetic finding	Affected genes	Clinical features	Prognosis	Approximate incidence in de novo AML
t(8;21)	*RUNX1/RUNX1T1*	Younger adults (average age 30 years) AML with maturation (FAB M2) Auer rods usually present	Favorable	5 to 7%
t(15;17)	*PML/RARA*	Younger adults (average age 40 years) Atypical promyelocytes with bilobed nucleus and granules (APL, FAB M3) Disseminated intravascular coagulation common	Favorable; high cure rate with all-trans retinoic acid-based therapy	5 to 8%
t(11;17)	*ZBTB16/RARA*	Similar to APL but with sparser granules and absence of the typical bilobed nucleus	Poor response to all-trans retinoic acid-based treatment	<1%
abn(16q22)	*CBFB/MYH11*	Younger adults (average age 35 to 40 years) Acute myelomonocytic leukemia (FAB M4) with eosinophilia	Favorable; high reinduction rate post relapse	5%
abn(11q23)	*MLL* and many partners	Older adults (average age >50 years) Acute monoblastic and monocytic leukemia (FAB M5) Hyperleukocytosis and extramedullary disease common	Poor, except t(9;11)	3%

Cytogenetic abnormalities in acute myeloid leukemia

Cytogenetic finding	Affected genes	Clinical features	Prognosis	Approximate incidence in de novo AML
+8		Older adults (average age >60 years) Varied morphology Often associated with other chromosomal additions and deletions	Poor	3 to 10%
del 5, del 7, 5q-, 7q-, or combinations		Older adults (average age >60 years) Varied morphology, common in acute erythroid leukemia (FAB M6) Common in patients with secondary AML and prior MDS	Poor	15 to 20%
Inv 3	*RPN1/MECOM*	Morphologically abnormal megakaryocytes; increased platelet count Other abnormalities common (del 5,7)	Poor	<1%
abn(p17)	*TP53*	Younger adults (average age <60 years) Varied morphology Other abnormalities common (del 5,7, complex karyotype)	Poor	5%
+13		Older adults (average age >60 years) Varied morphology, sometimes undifferentiated, high frequency of hybrid features	Poor	Approximately 1 to 2%
t(6;9)(p2;q34)	*DEK/NUP214*	AML with maturation (FAB M2)/Acute myelomonocytic leukemia (FAB M4) with prominent basophilia	Poor	<1 to 2%

Cytogenetic abnormalities in acute myeloid leukemia

Cytogenetic finding	Affected genes	Clinical features	Prognosis	Approximate incidence in de novo AML
t(9;22)	*BCR/ABL1*	Older adults (average age >50 years) Usually AML with minimal differentiation (FAB M1), prominent splenomegaly, possible transformation of unrecognized CML	Poor	Approximately 1%
t(1;22)	*RBM15/MKL1*	Infants (aged 0 to 3 years) Often acute megakaryoblastic leukemia (FAB M7), prominent organomegaly	Poor	<1%
t(8;16)	*KAT6A/CREBBP*	Acute myelomonocytic leukemia (FAB M4) and acute monoblastic and monocytic leukemia (FAB M5), erythrophagocytosis	Poor	<1%

Prognosis:

Age

Performance status

Secondary AML

Genetic aberrations

Eastern Cooperative Oncology Group (ECOG, Zubrod, World Health Organization) performance scale

Performance status	Definition
0	Fully active; no performance restrictions.
1	Strenuous physical activity restricted; fully ambulatory and able to carry out light work.
2	Capable of all self-care but unable to carry out any work activities. Up and about >50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair >50% of waking hours.
4	Completely disabled; cannot carry out any self-care; totally confined to bed or chair.

Adapted from: Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982; 5:649.

Graphic 72901 Version 10.0

Mortality during induction chemotherapy in acute myeloid leukemia

Patient age	Performance status*	Death by day +28 (percent)
<50	<3	5
50-59	<3	7
60-69	<3	10
70-79	<3	13
>79	<3	30
<50	≥3	39
50-69	≥3	46
>69	≥3	57

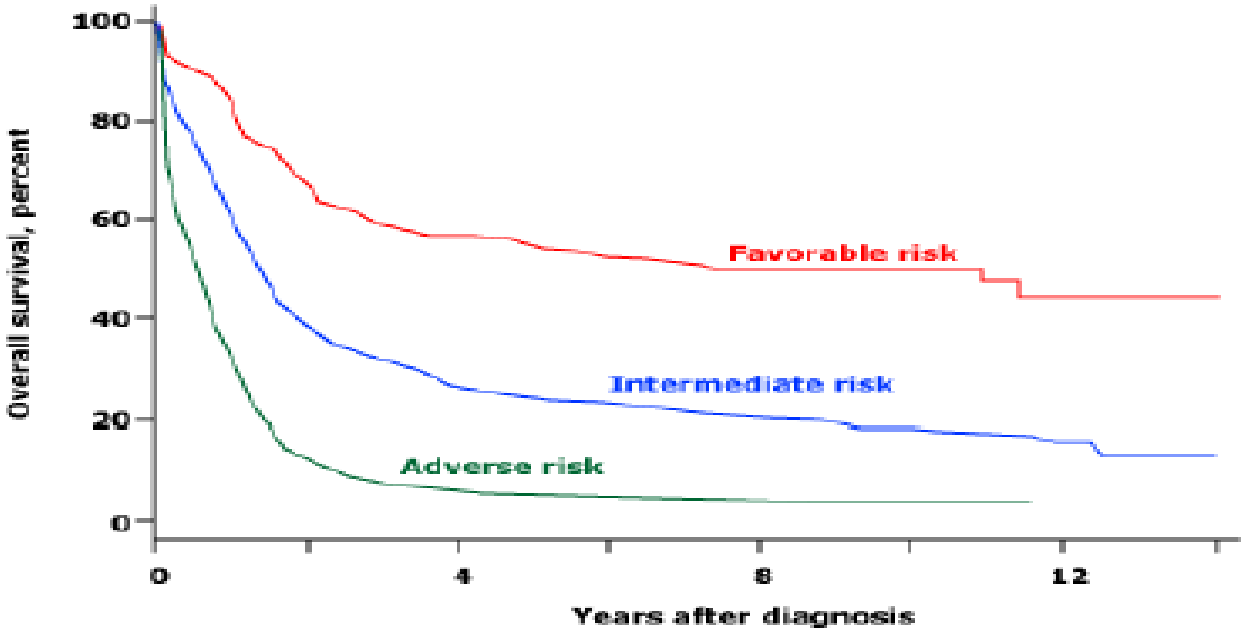
* Zubrod (ECOG) performance status at the onset of treatment. A score of <3 is seen in a patient who is either asymptomatic or symptomatic and is in bed <50 percent of the time. A score of 3 or greater means that the patient is symptomatic and in bed >50 percent of the time.

Data from Estey, EH. Cancer 2001; 92:1059.

2017 European LeukemiaNet risk stratification of acute myeloid leukemia by genetics

Risk category*	Genetic abnormality
Favorable	t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
	inv(16)(p13.1;q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
	Mutated *NPM1* without *FLT3-ITD* or with *FLT3-ITD*^{low}¶
	Biallelic mutated *CEBPA*
Intermediate	Mutated *NPM1* and *FLT3-ITD*^{high}¶
	Wild type *NPM1* without *FLT3-ITD* or with *FLT3-ITD*^{low}¶ (without adverse-risk genetic lesions)
	t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*$^{\Delta}$
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); *DEK-NUP214*
	t(v;11q23.3); *KMT2A* rearranged
	t(9;22)(q34.1;q11.2); *BCR-ABL1*
	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOM*(*EVI1*) –5 or del(5q); –7; –17/abn(17p)
	Complex karyotype,$^{\diamond}$ monosomal karyotype§
	Wild type *NPM1* and *FLT3-ITD*^{high}¶
	Mutated *RUNX1*¥
	Mutated *ASXL1*¥
	Mutated *TP53*‡

Overall survival in acute myeloid leukemia

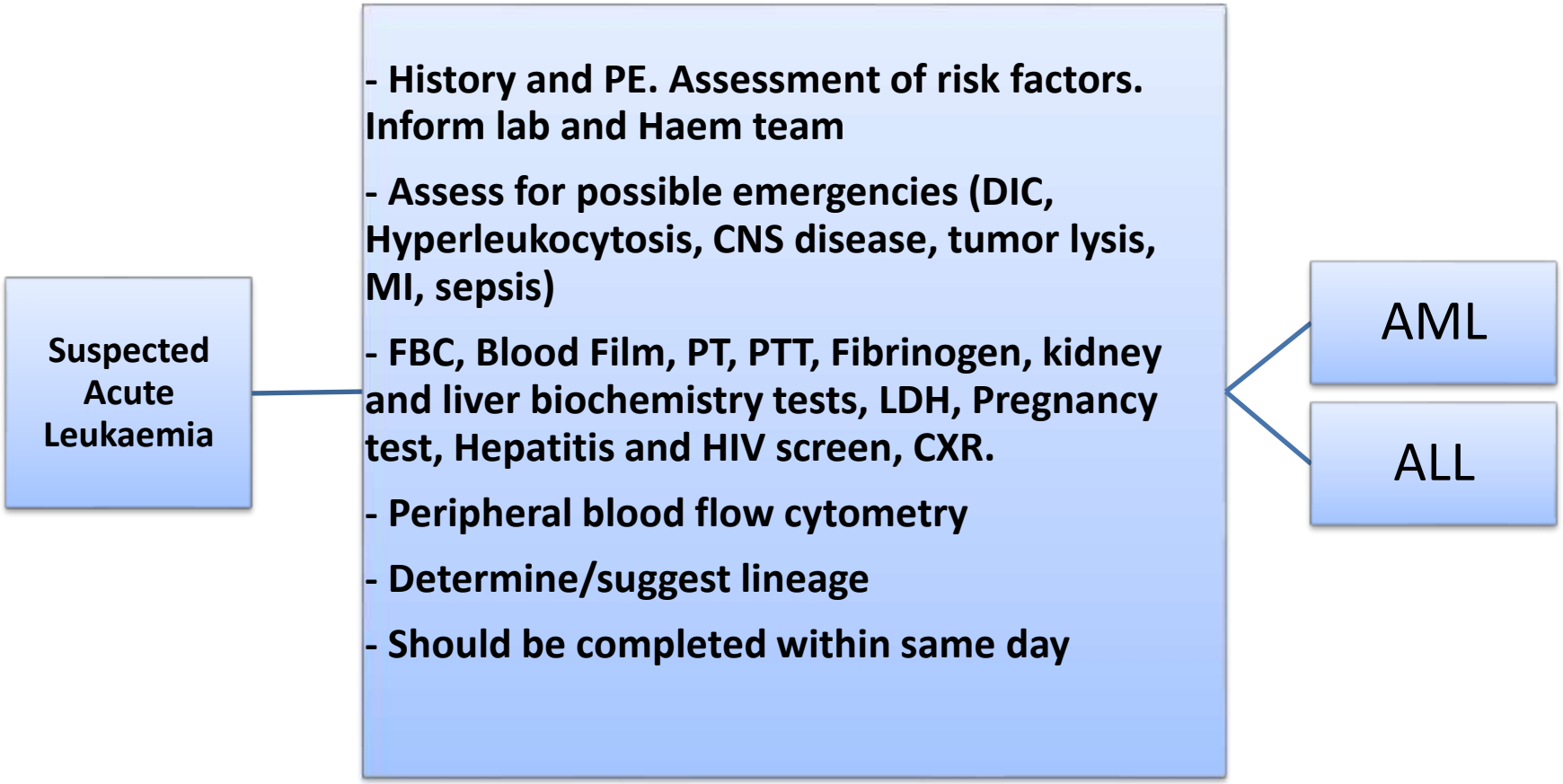


This figure illustrates overall survival in adult subjects with acute myeloid leukemia (AML, age range 15 to 86 years, median 52 years), according to the following cytogenetic risk categories: Favorable risk (median survival 7.6 years): t(8;21); inv(16) or t(16;16); del(9q). Intermediate risk (median survival 1.3 years): normal karyotype; -Y; del(5q); loss of 7q; t(9;11); +11; del(11q); abn(12p); +13; del(20q); +21. Adverse risk (median survival 0.5 years): complex karyotype (≥3 abnormalities); inv(3) or t(3;3); t(6;9); t(6;11); -7; +8 (sole abnormality); +8 with one other abnormality other than t(8;21), t(9;11), inv(16), or t(16;16); t(11;19)(q23;p13.1).

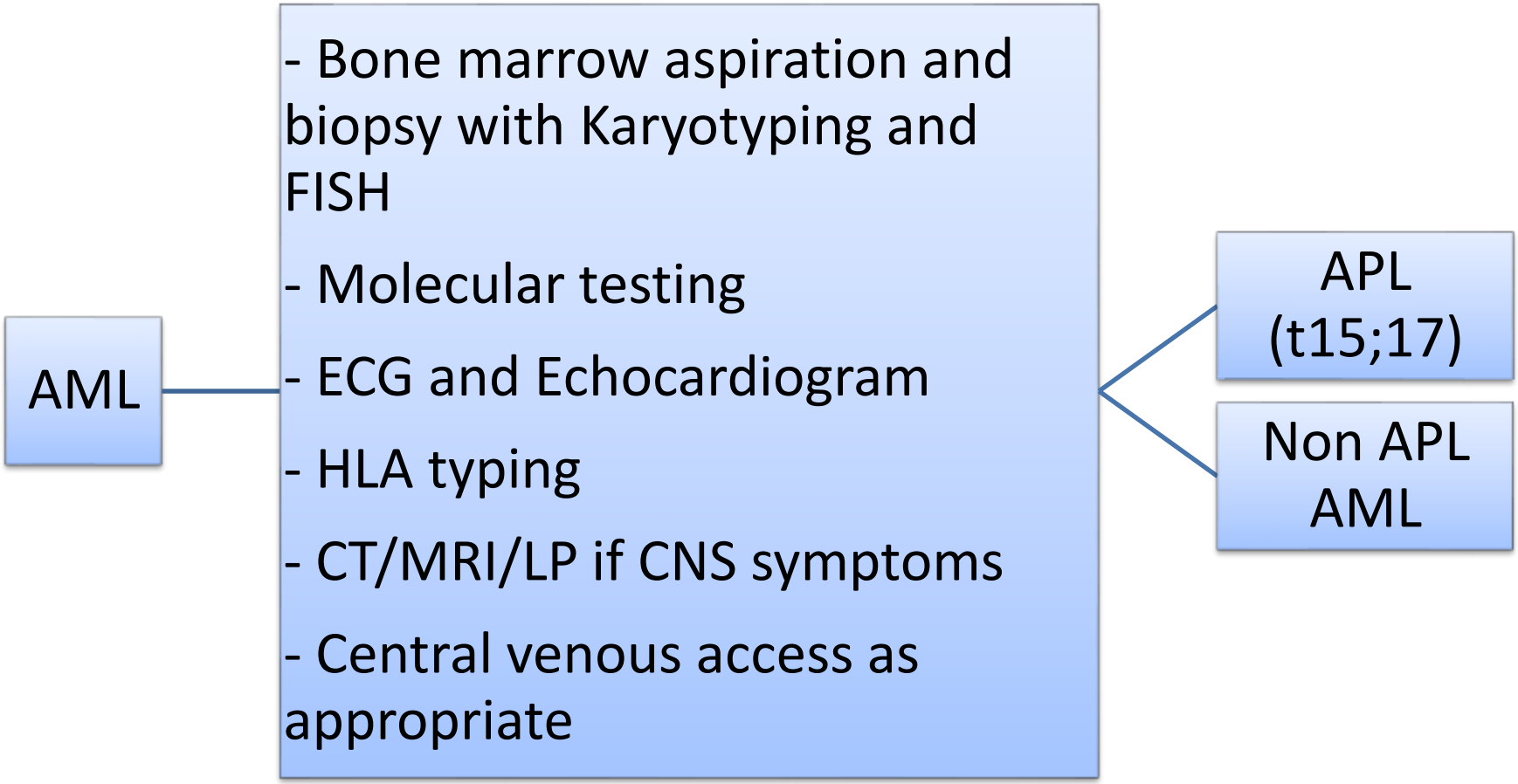
Data from Byrd, JC, et al. Pretreatment cytogenetic abnormalities are predictive of induction success, cumulative incidence of relapse, and overall survival in adult patients with de novo acute myeloid leukemia: Results from Cancer and Leukemia Group B (CALGB 8641). Blood 2002; 100:4325.

Graphic 65190 Version 3.0

Management


Suspected Acute Leukaemia
- History and PE. Assessment of risk factors. Inform lab and Haem team
- Assess for possible emergencies (DIC, Hyperleukocytosis, CNS disease, tumor lysis, MI, sepsis)
- FBC, Blood Film, PT, PTT, Fibrinogen, kidney and liver biochemistry tests, LDH, Pregnancy test, Hepatitis and HIV screen, CXR.
- Peripheral blood flow cytometry
- Determine/suggest lineage
- Should be completed within same day
AML
ALL

Management


AML
- Bone marrow aspiration and biopsy with Karyotyping and FISH
- Molecular testing
- ECG and Echocardiogram
- HLA typing
- CT/MRI/LP if CNS symptoms
- Central venous access as appropriate
APL (t15;17)
Non APL AML

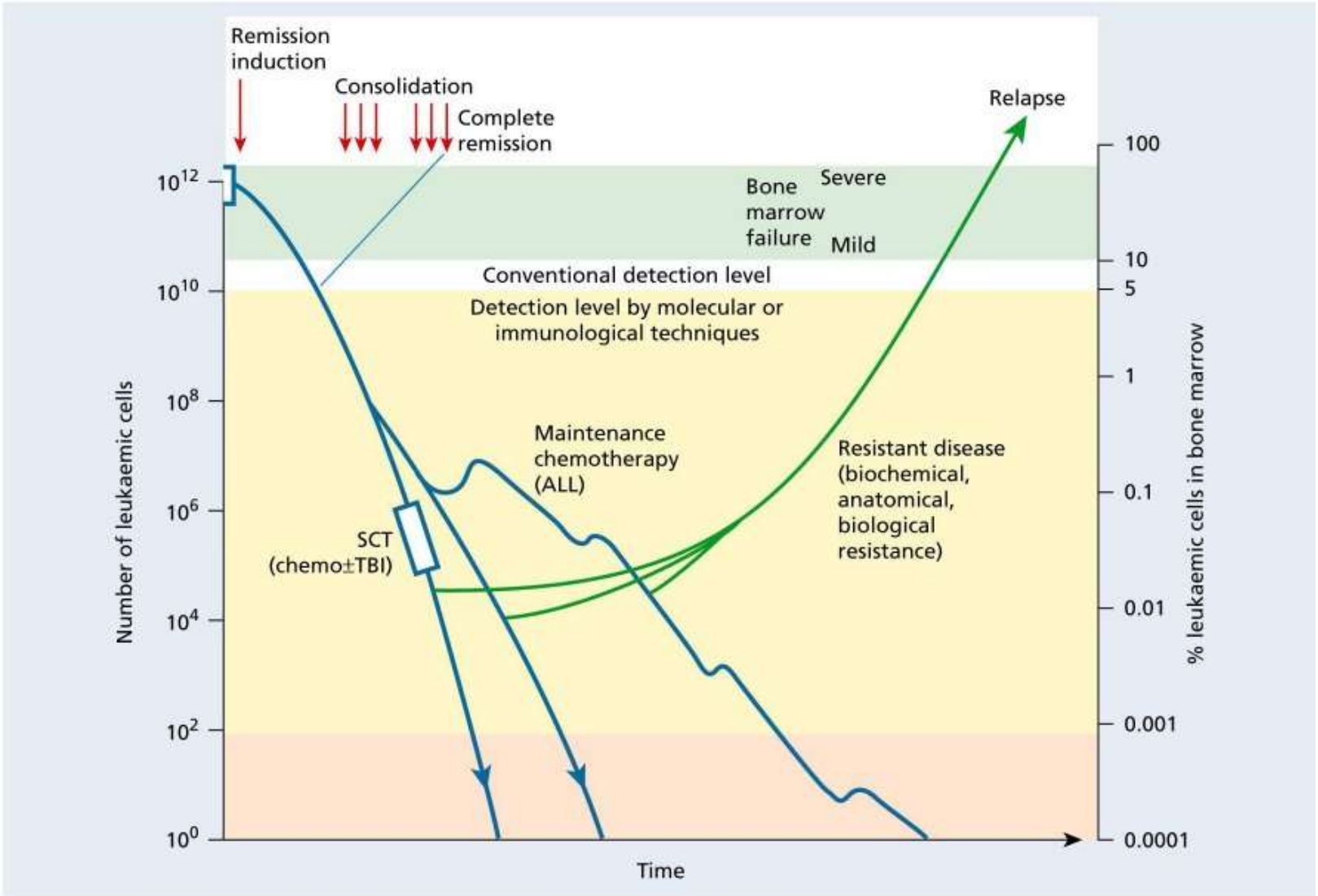
Management

- Treatment should be started as soon as possible. Some data suggest treatment delay beyond 5 days is associated with reduced CR rates.
- Patients with fever or infective symptoms should be treated promptly as neutropenic sepsis.
- Prophylaxis: Antiviral and antifungal should be started:

  Aciclovir 400 mg BD, Fluconazole 200 mg OD t to start and continue until unsupported ANC count of 1.0.
- Allopurinol to start one day before chemotherapy and continue until WBCs is less than 1.0. Rasbiuricase should be used in high risk situations, check G6pd status if planned.
- Anti-emetic s and other supportive medications should be discussed in details with the fellow. Different protocols have different emetogenic potentials.
- Routine use of GCSF is discouraged. Generally, GCSF should be avoided within 24 hours of completing chemotherapy and 48 hours before the next cycle.

Management

- Induction treatment: aim of induction is to reduce disease burden and restore normal haematopoiesis.
- 60-80% patients will achieve CR after induction.
- Post-remission therapy aims to destroy leukaemic cells that survived induction chemotherapy but are undetectable by conventional studies (Consolidation)
- Almost all patients will relapse if not consolidated within 4-8 months of induction.
- Consolidation can be by additional cycles of chemotherpy or bone marrow transplantation.



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Management

- APL should be identified as induction should include all-trans retinoic acid which is able to iduce proliferation of leukaemic cells. APL is divided into low and high risk and patients with WBCs count of > 10 are considered high risk for differentiation syndrome and bleeding.

- ATRA should be started if APL is suspected until diagnosis is confirmed. It can be stopped if APL is excluded.

Management

- Patients with AML are grouped as younger and older patients (usual cut off age is 60).
- Younger patients are treated with standard induction (Cytarabine and an anthracycline) regimens (7+3, DA 10+3, etc)
- Response is assessed with a bone marrow biopsy and cytogenetics/molecular tests.
- Different recommendations as to when to assess response.

Management

- Patient achieving remission after induction are consolidated.
- Consolidation is usually additional cycles of chemotherapy for favourable risk group and bone marrow transplant for other risk groups.
- Patients who are not fit for a bone marrow transplant or don’t have a matched sibling donor should be offered autologous transplant or consolidation chemotherapy.

Management

- Older patients can be treated with less intensive regimens such as hypomethylating agents, hydroxycarbamide, low dose cytarabine or supportive care.

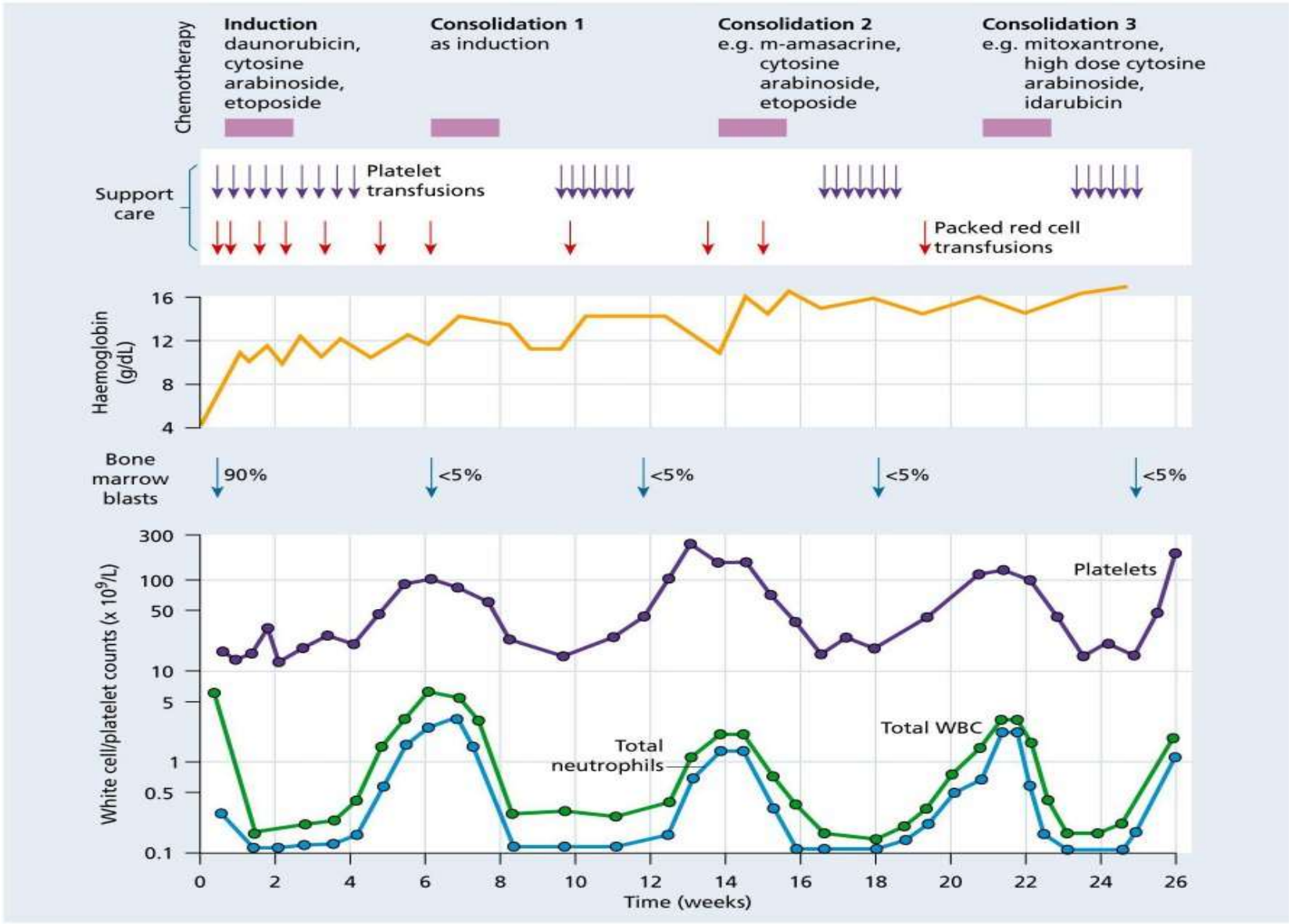

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Figure 13.10 Typical flow chart for the management with chemotherapy of acute myeloid leukaemia. WBC, white blood cells.

Acute Lymphoblastic Leukaemia

- Incidence: 1.58 / 100 000 individuals per year
- Most common acute leukaemia in children: 75-80%.
- 57.2% of cases < 20 yrs

  26.8% of cases > 45 yrs

  11% of cases > 65 yrs

- Risk Factors:

  Age, exposure to chemotherapy or radition therapy, genetic disorder (particularly down syndrome),

Acute Lymphoblastic Leukaemia

- 5-year OS:

  Children: 86-89%

  AYA (15-39 yrs) : 42-63%

  Adults (40-59 yrs): 24%

  Adults (60 or older): 17%

Table 24.1 Immunological classification, corresponding cytogenetic and molecular aberrations and frequencies in adult ALL.

	*Adults (%)**	*Surface marker*	*Cytogenetics†*	*Molecular genetics†*
B-lineage		HLA-DR$^+$, TdT$^+$, CD19$^+$ and/or CD79a$^+$ and/or CD22$^+$		
Pro B-ALL	11	No further differentiation markers	t(4;11)	*ALL1(MLL)–AF4*
Common-ALL	50	CD10$^+$	t(9;22)	*BCR–ABL*
Pre B-ALL	12	CD10$^{+/-}$, cyIgM$^+$	t(9;22), t(1;19)	*BCR–ABL, E2A–PBX1*
B-ALL	5	CD10$^{+/-}$, sIgM$^+$	t(8;14)	*MYC–IGH*
T-lineage		TdT$^+$, cyCD3$^+$ or sCD3$^+$		
Early T-ALL	6	cyCD3$^+$, CD7$^+$, CD5$^{+/-}$, CD2$^{+/-}$	t(11;14)	*LMO1*–TCRα/δ
Cortical T-ALL (Thy ALL)	10	cyCD3$^+$, CD7$^+$, CD1a$^+$, sCD3$^{+/-}$	t(10;14)	*HOX11*–TCRα/δ
Mature T-ALL	6	sCD3$^+$, CD1a$^-$		

*Frequencies according to central immunophenotyping of the GMALL Study Group; personal communication of Professor E. Thiel and Dr S. Schwartz, Free University of Berlin, Germany.

†Most frequent, typical aberrations.

cyIgM, cytoplasmic IgM; sIgM, surface IgM; cyCD3, cytoplasmic CD3; sCD3, surface CD3; TdT, terminal deoxynucleotidyltransferase.

Presentation:

Investigations:

Additional:

CT scans, CSF examination, testicular exam

Table 24.2 Symptoms and clinical signs at diagnosis in adult ALL patients.*

	T-lineage (%)	*B-precursor (%)*	*Mature B (%)*
Gender			
Male	73	54	78
Female	27	46	22
Age			
15–20 years	22	19	8
20–50 years	67	58	64
>50 years	11	24	27
Bleeding	28	28	30
Infections	22	29	37
Lymphadenopathy	77	40	61
Hepatomegaly	45	41	56
Splenomegaly	55	43	47
Mediastinal tumour	62	1	5
CNS involvement	8	3	13
Other organ involvement	15	4	32

*$N = 640$ patients of GMALL studies 03/87 and 04/89.

Table 24.3 Blood counts at the time of diagnosis in adult ALL.*

	T-lineage (%)	*B-precursor (%)*	*Mature B (%)*
Leucocytes or WBC			
$<10 \times 10^9$/L	18	40	37
$10–50 \times 10^9$/L	36	31	42
$>50 \times 10^9$/L	46	29	20
Granulocytes			
$<0.5 \times 10^9$/L	13	28	3
$>0.5 \times 10^9$/L	87	72	97
Platelets			
$<25 \times 10^9$/L	21	32	29
$>25 \times 10^9$/L	79	68	71
Hb			
<8 g/dL	16	29	17
>8 g/dL	84	71	83

*N = 640 patients of GMALL studies 03/87 and 04/89.

Adverse prognostic clinical features:

Older Age (>35 yr)
High WBCs (>30 for B-cell and >100 for T-Cell)
Race (Hispanic or Black)
Male sex

RISK GROUPS	CYTOGENETICS
Good risk	Hyperdiploidy (51–65 chromosomes; cases with trisomy of chromosomes 4, 10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22): *ETV6-RUNX1*
Poor risk	Hypodiploidy (<44 chromosomes); *KMT2A* rearranged (t[4;11] or others); t(v;14q23)/IgH; t(9;22)(q34;q11.2): *BCR-ABL1* (defined as high risk in the pre-TKI era); complex karyotype (5 or more chromosomal abnormalities); Ph-like ALL; intrachromosomal amplification of chromosome 21 (iAMP21)

Table 1. Common Chromosomal and Molecular Abnormalities in ALL

Cytogenetics	*Gene*	*Frequency in Adults*	*Frequency in Children*
Hyperdiploidy (>50 chromosomes)	--	7%	25%
Hypodiploidy (<44 chromosomes)	--	2%	1%
t(9;22)(q34;q11): Philadelphia chromosome (Ph)	*BCR-ABL1*	25%	2%–4%
t(12;21)(p13;q22)	*ETV6-RUNX1 (TEL-AML1)*	2%	22%
t(v;11q23) [eg, t(4;11), t(9;11)], t(11;19)	*KMT2A (MLL)*	10%	8%
t(1;19)(q23;p13)	*TCF3-PBX1 (E2A-PBX1)*	3%	6%
t(5;14)(q31;q32)	*IL3-IGH*	<1%	<1%
t(8;14), t(2;8), t(8;22)	*c-MYC*	4%	2%
t(1;14)(p32;q11)	*TAL-1*[a]	12%	7%
t(10;14)(q24;q11)	*HOX11 (TLX1)*[a]	8%	1%
t(5;14)(q35;q32)	*HOX11L2*[a]	1%	3%
t(11;14)(q11) [eg, (p13;q11), (p15;q11)]	*TCRα and TCRδ*	20%–25%	10%–20%
BCR-ABL1-like	*various*[b]	10%–30%	15%
ETP	*various*[a]	2%	2%
Ikaros	*IKZF1*	25%–35%	12%–17%

[a]Abnormalities observed exclusively in T-cell lineage ALL; all others occur exclusively or predominately in B-cell lineage ALL. [b]See text for more details.

AYA patients:

- Regimens based on data from multi-institutional or cooperative group studies:
  - CALGB 10403 regimen: daunorubicin, vincristine, prednisone, and pegaspargase (ongoing study in patients aged <40 years)[15,f]
  - COG AALL0232 regimen: daunorubicin, vincristine, prednisone, and pegaspargase (patients aged ≤21 years)[16,f]
  - COG AALL0434 regimen with nelarabine (for T-ALL): daunorubicin, vincristine, prednisone, and pegaspargase; nelarabine added to consolidation regimen[17,f]
  - DFCI ALL regimen based on DFCI Protocol 00-01: doxorubicin, vincristine, prednisone, high-dose methotrexate, and pegaspargase (ongoing study in patients aged <50 years)[18,f]
  - GRAALL-2005 regimen: daunorubicin, vincristine, prednisone, pegaspargase, and cyclophosphamide (patients aged <60 years), with rituximab for CD20-positive disease[19,f]
  - PETHEMA ALL-96 regimen: daunorubicin, vincristine, prednisone, pegaspargase, and cyclophosphamide (patients aged <30 years)[20,f]
- Regimens based on data from single-institution studies:
  - Hyper-CVAD ± rituximab: hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine; with or without rituximab for CD20-positive disease[21]
  - USC ALL regimen based on CCG-1882 regimen: daunorubicin, vincristine, prednisone, and methotrexate with augmented pegaspargase (patients aged 18–57 years)[22,f]
  - Linker 4-drug regimen: daunorubicin, vincristine, prednisone, and pegaspargase[23]

Adult patients: Treatment of Older Patients (≥65 y) with ALL (ALL-D 6 of 6)

- CALGB 8811 Larson regimen: daunorubicin, vincristine, prednisone, pegaspargase, and cyclophosphamide; for patients aged ≥60 years, reduced doses for cyclophosphamide, daunorubicin, and prednisone[24]
- GRAALL-2005 regimen: daunorubicin, vincristine, prednisone, pegaspargase, and cyclophosphamide (patients aged <60 years) with rituximab for CD20-positive disease[19,e]
- Hyper-CVAD ± rituximab: hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine; with or without rituximab for CD20-positive disease[21,25]
- Linker 4-drug regimen: daunorubicin, vincristine, prednisone, and pegaspargase[23]
- MRC UKALLXII/ECOG2993 regimen: daunorubicin, vincristine, prednisone, and pegaspargase (induction phase I); and cyclophosphamide, cytarabine, and 6-MP[c] (induction phase II)[26]

Maintenance regimen:

- Weekly methotrexate + daily 6-MP[c] + monthly vincristine/prednisone pulses (duration based on regimen)

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Maintenance regimen:

- Weekly methotrexate + daily 6-MP[c] + monthly vincristine/prednisone pulses (duration based on regimen)

Table 24.4 Overall treatment results in adult ALL in larger studies.

Study	*N*	*Median age (range)*	*SCT*	*CR (%)*	*Early death (%)*	*Survival*
LALA 87, France (Thiebaut *et al.* 2000)	572	33 (15–60)	PO	76	9	27% at 10 years
NILG 08/96, Italy (Bassan *et al.* 2001)	121	35 (15–74)	PR	84	8	48% at 5 years
GMALL 05/93, Germany (Gökbuget *et al.* 2001)*	1163	35 (15–65)	PR	83	NR	35% at 5 years
JALSG-ALL93, Japan (Takeuchi *et al.* 2002)	263	31 (15–59)	PO	78	6	30% at 6 years
UCLA, USA (Linker *et al.* 2002)	84	27 (16–59)	PR	93	1	47% at 5 years
Sweden (Hallbook *et al.* 2002)	153	42 (16–82)	PR	75	NR	28% at 5 years
GIMEMA 0288, Italy (Annino *et al.* 2002)	767	28 (12–60)	NR	82	11	27% at 9 years
MD Anderson, USA (Kantarjian *et al.* 2004)	288	40 (15–92)	Ph+	92	5	38% at 5 years
EORTC ALL-3, Europe (Labar *et al.* 2004)	340	33 (14–79)	PO	74	NR	36%† at 6 years
LALA 94, France (Thomas *et al.* 2004)	922	33 (15–55)	PR	84	5	36% at 5 years
GOELAL02, France (Hunault *et al.* 2004)	198	33 (15–59)	HR	86	2	41% at 6 years
MRC XII/ECOG E 2993, UK–USA (Rowe *et al.* 2005)	1521	15–59	PO	91	NR	38% at 5 years
GIMEMA 0496, Italy (Mancini *et al.* 2005)*	450	16–60	NR	80	NR	33% at 5 years
Pethema ALL-93, Spain (Ribera *et al.* 2005)	222	27 (15–50)	HR	82	6	34% at 5 years
JCOG-9004 (Tobinai *et al.* 2007)	143	41 (<64)	PO	83	10	32% at 5years
GMALL 07/03 (Gökbuget *et al.* 2007)*	713	34 (15–55)	PR	89	5	54% at 5years
NILG 09/00 (Bassan *et al.* 2009)	280	38 (16–66)	PR	84	8	34% at 5years
Weighted mean	7405			84	7	35%

*Abstract.

†Survival of patients in CR.

PO, prospective stem cell transplantation (SCT) in all patients with donor (type a); Ph+, SCT in Ph-positive ALL (type b); PR, SCT according to prospective risk model (type c); HR, prospective SCT in a study for high-risk patients only; NR, not reported.

Thank you