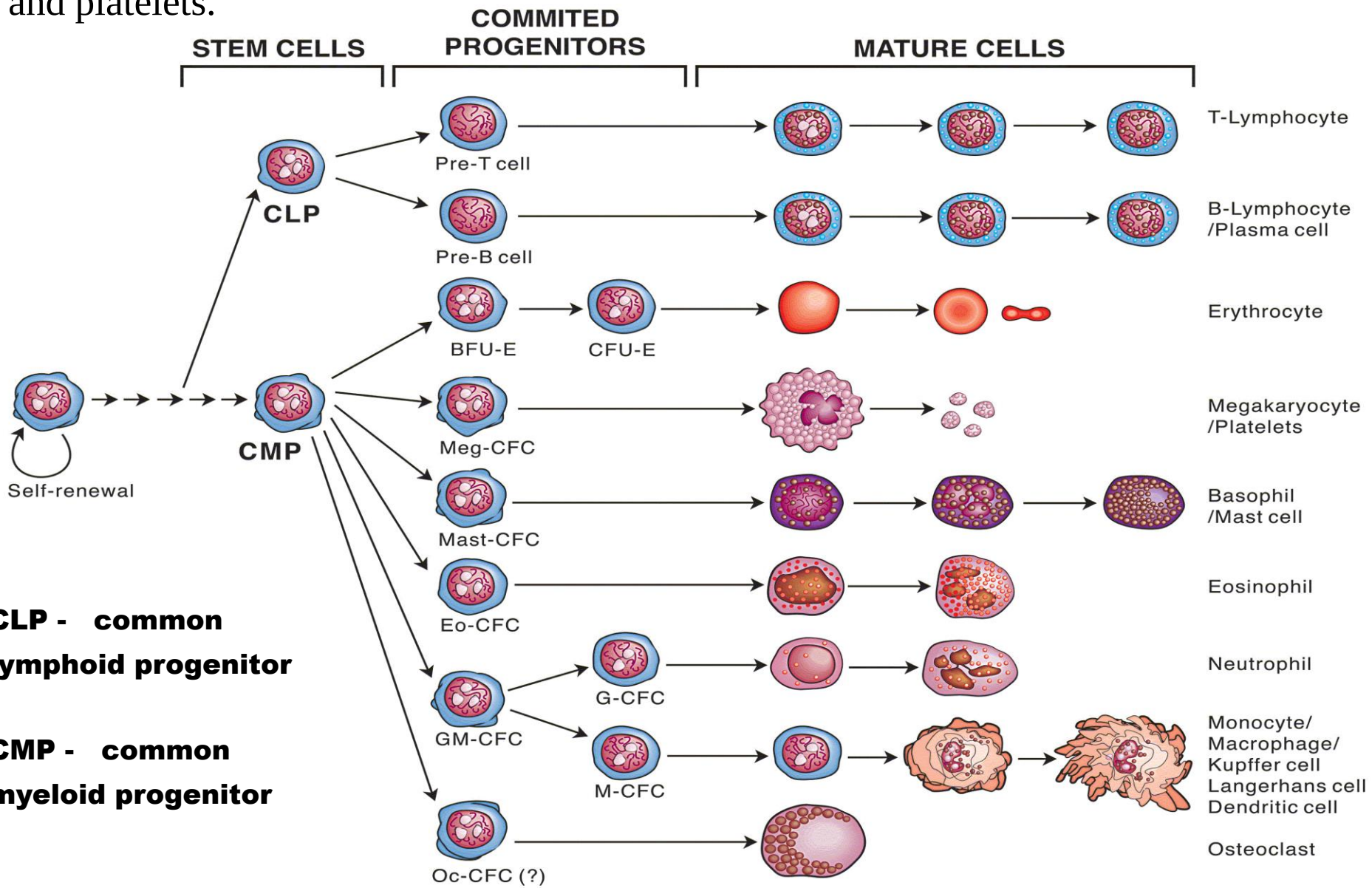
Acute leukemia

Hematopoietic stem cells divide to form more blood-forming stem cells, or they mature into one of three types of blood cells: white blood cells, red blood cells and platelets.



CLP - common lymphoid progenitor

CMP - common myeloid progenitor

Acute leukemia occurs when a hematopoietic stem cell undergoes malignant transformation (clonal) into a primitive, undifferentiated cell with abnormal longevity.

If these cells are lymphocytes we diagnose acute lymphocytic leukemia [ALL]; if these cells are myeloid cells we diagnose acute myelocytic leukemia [AML].

In acute leukemia cells proliferate abnormally, replacing normal marrow tissue and hematopoietic cells.

Acute leukemia during the diagnosis is disseminated cancer with 10^{12} leukemic cells (approx. 1 kg of leukemic cells).

Because they are bloodborne, they can infiltrate various organs and sites, including the liver, spleen, lymph nodes, CNS, kidneys, and gonads.

Etiopathogenesis

The etiopathogenesis of acute leukemia is not yet known. The underlying pathophysiology in acute leukemia consists of a maturational arrest of bone marrow cells in the earliest stages of development – leukemic transformation. The mechanism of this arrest involves the activation of abnormal genes through chromosomal translocations and other genetic abnormalities.

The known causes of leukemic transfomation are:

- viruses,
- substances which acts as cofactors:
    - radiation exposure
    - chemicals (benzen and derivatives)
    - drugs (Melfalan)

History

Patients with acute leukemia present with symptoms resulting from bone marrow failure, organ infiltration with leukemic cells, or both. The time course is variable. Some patients, particularly younger ones, present with acute symptoms over a few days to 1-2 weeks.

Symptoms of bone marrow failure are related to anemia, neutropenia, and thrombocytopenia.

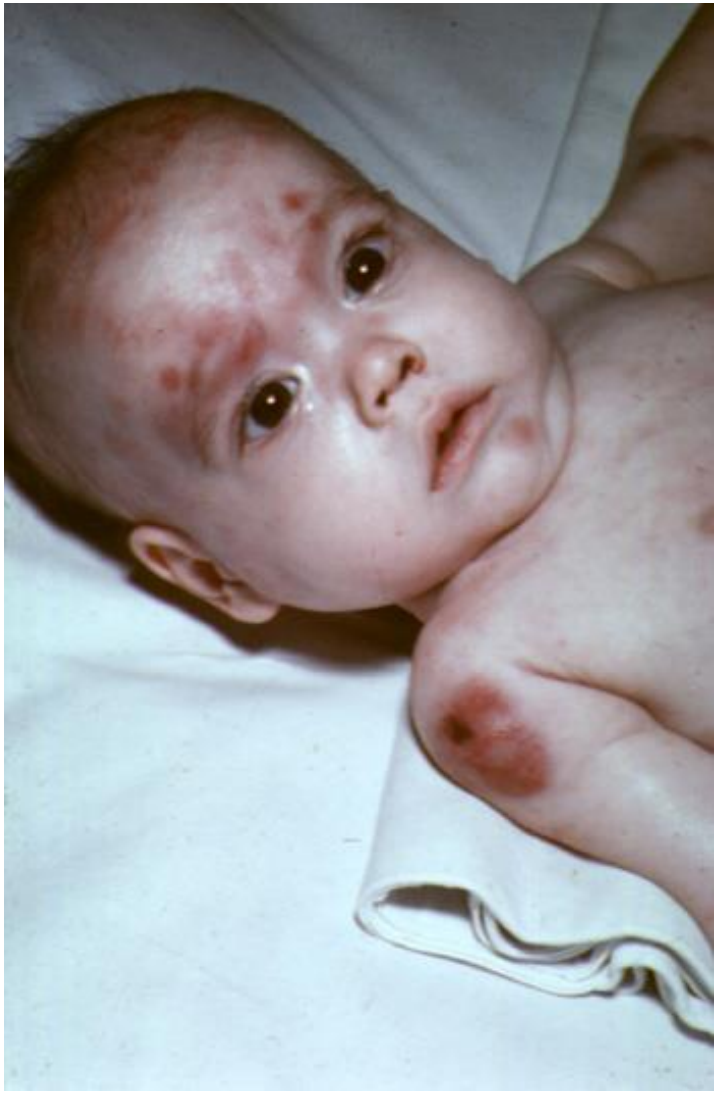
The most common symptom of anemia is fatigue, dyspnea upon exertion, dizziness.

Patients often have decreased neutrophil levels despite an increased total white blood cell (WBC) count. Patients have the highest risk of infection and present with fever.

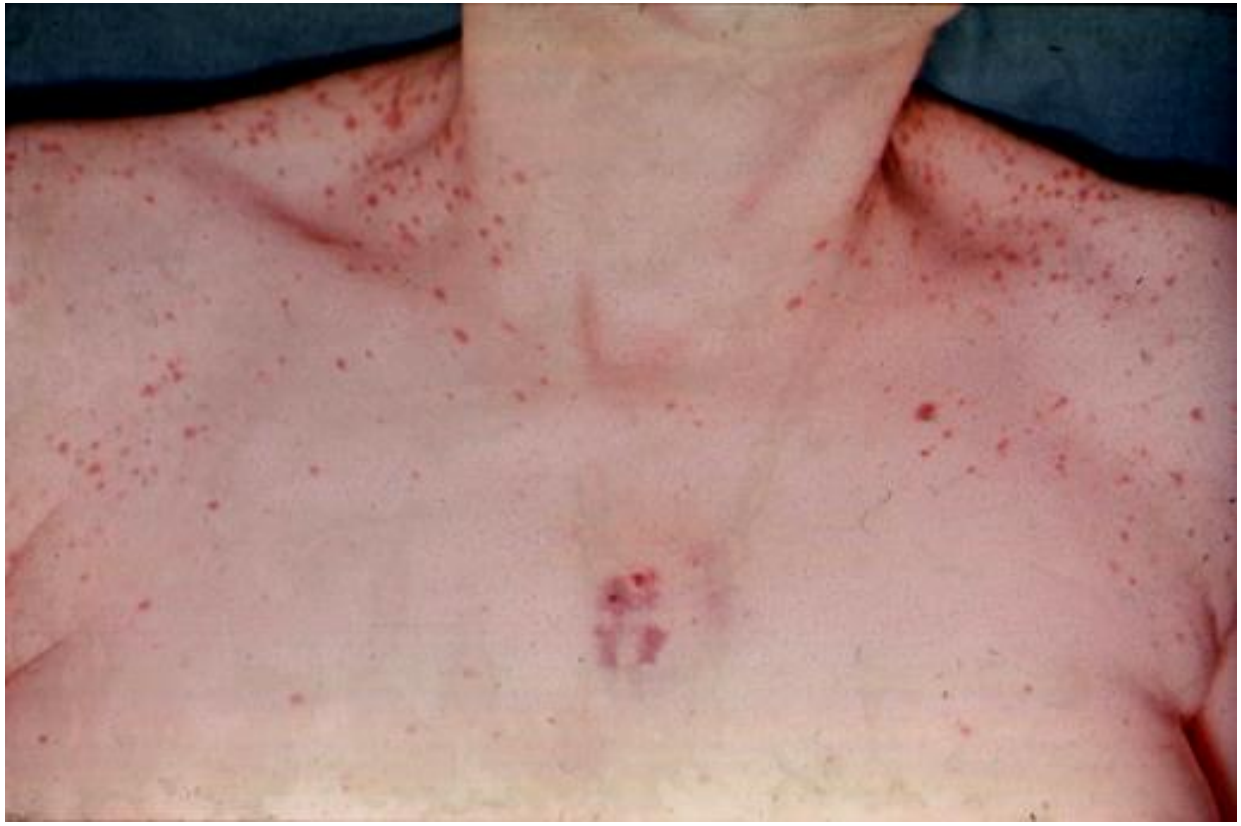
Patients often present with bleeding gums and multiple ecchymoses. Bleeding may be caused by thrombocytopenia, coagulopathy that results from disseminated intravascular coaguloation (DIC), or both.

Symptoms of organ infiltration with leukemic cells

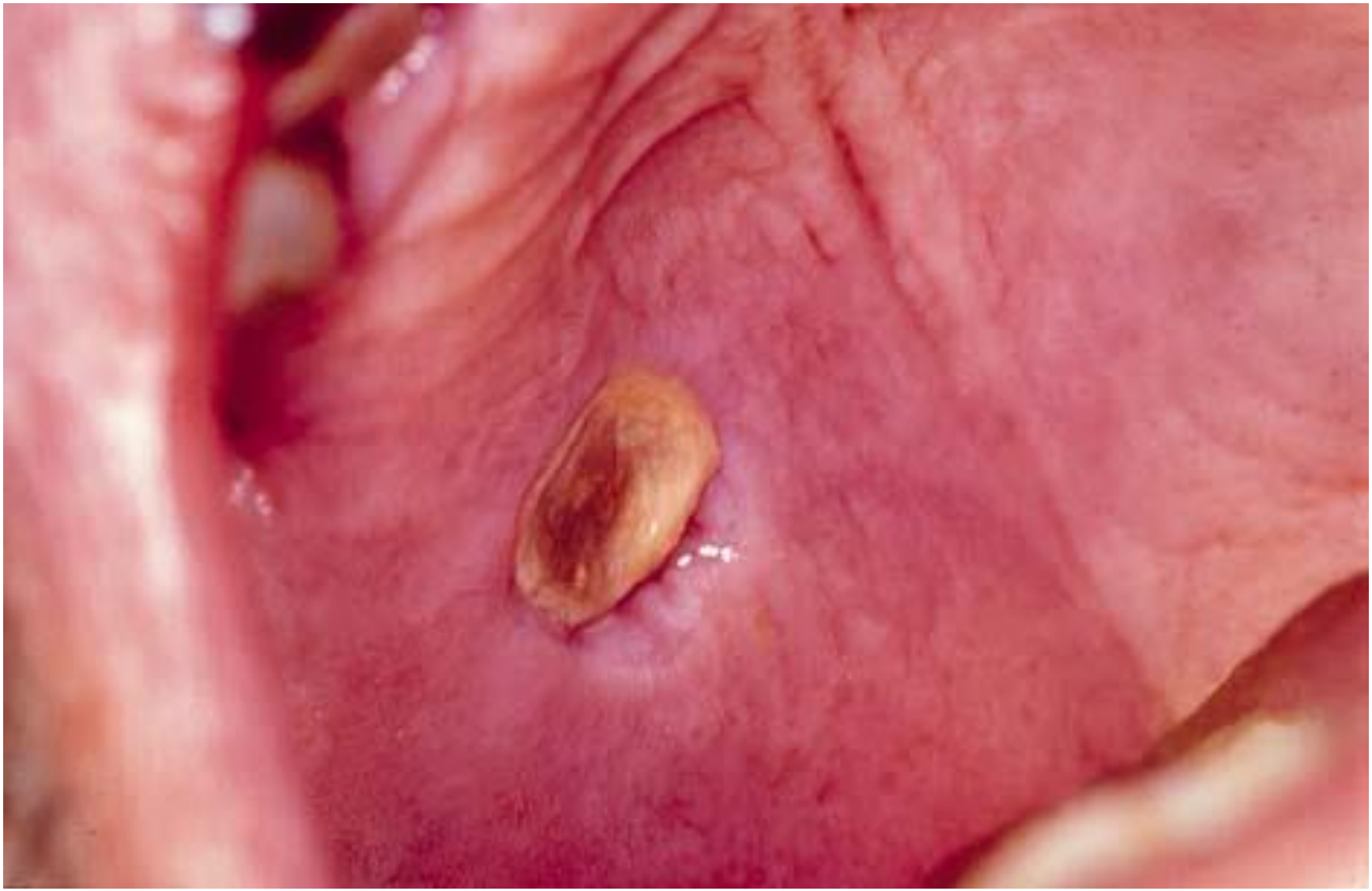
- The most common sites of infiltration include the spleen, liver, gums, and skin. Infiltration occurs most commonly in patients with the monocytic subtypes of acute myelogenous leukemia (AML).
- Patients with splenomegaly note fullness in the left upper quadrant and early satiety.
- Patients with gum infiltration often present to their dentist first. Gingivitis due to neutropenia can cause swollen gums, and thrombocytopenia can cause the gums to bleed.
- Patients with markedly elevated WBC counts (>100,000 cells/μL) can present with symptoms of leukostasis (ie, respiratory distress and altered mental status). Leukostasis is a medical emergency that requires immediate intervention.
- Patients with a high leukemic cell burden may present with bone pain caused by increased pressure in the bone marrow.

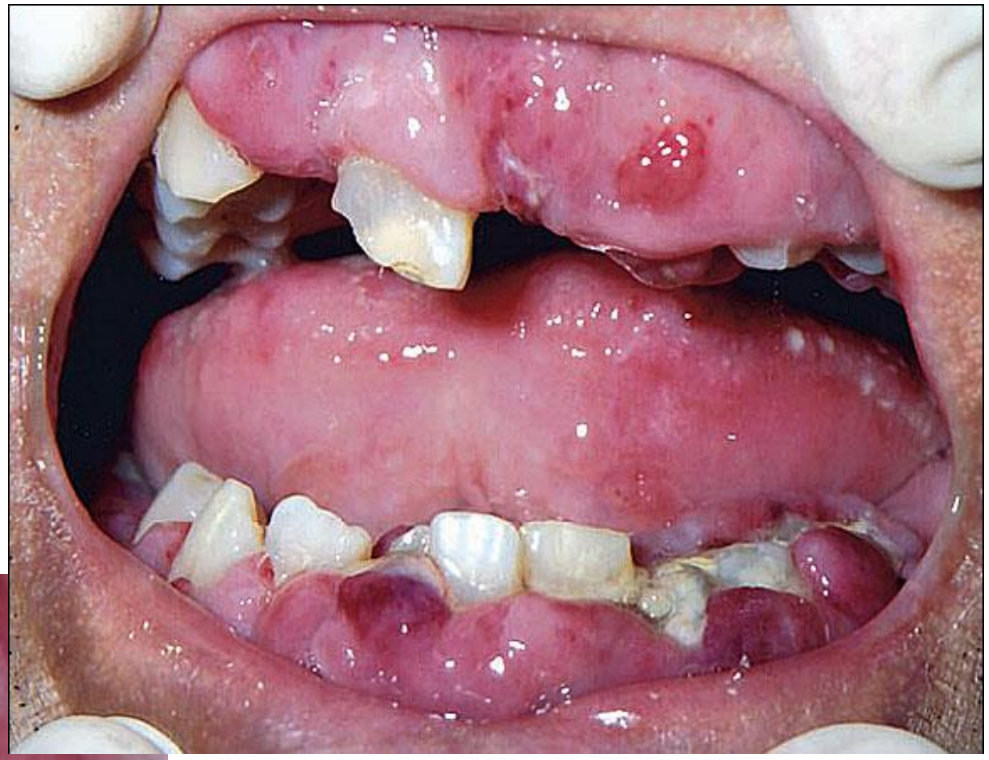


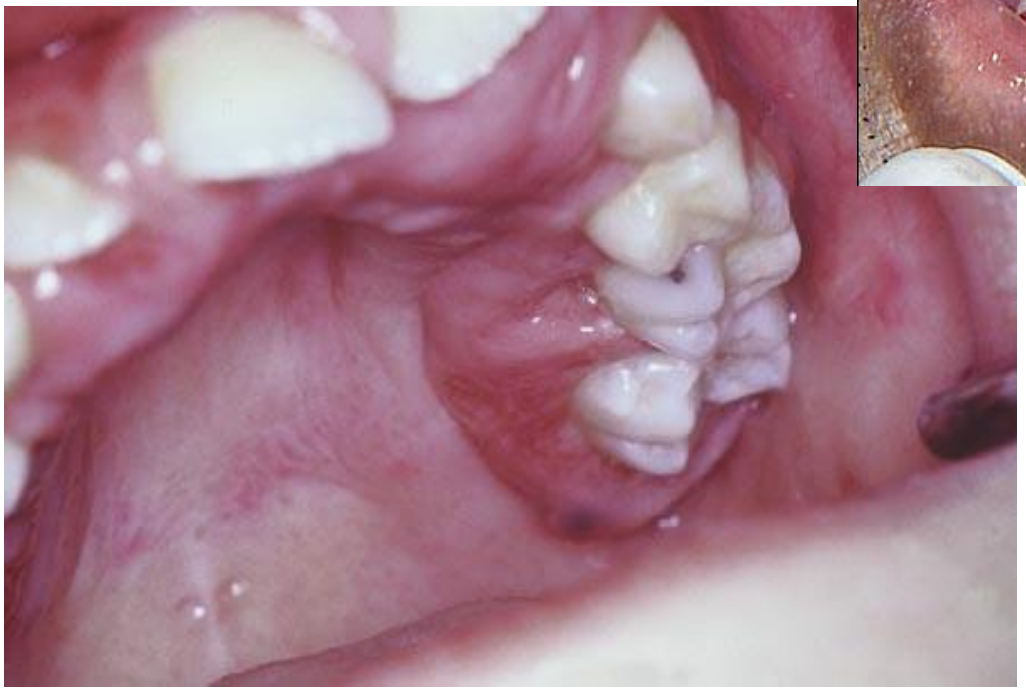
Acute lymphoblastic leukemia ALL. Pale skin and bruises- thrombocytopenia.



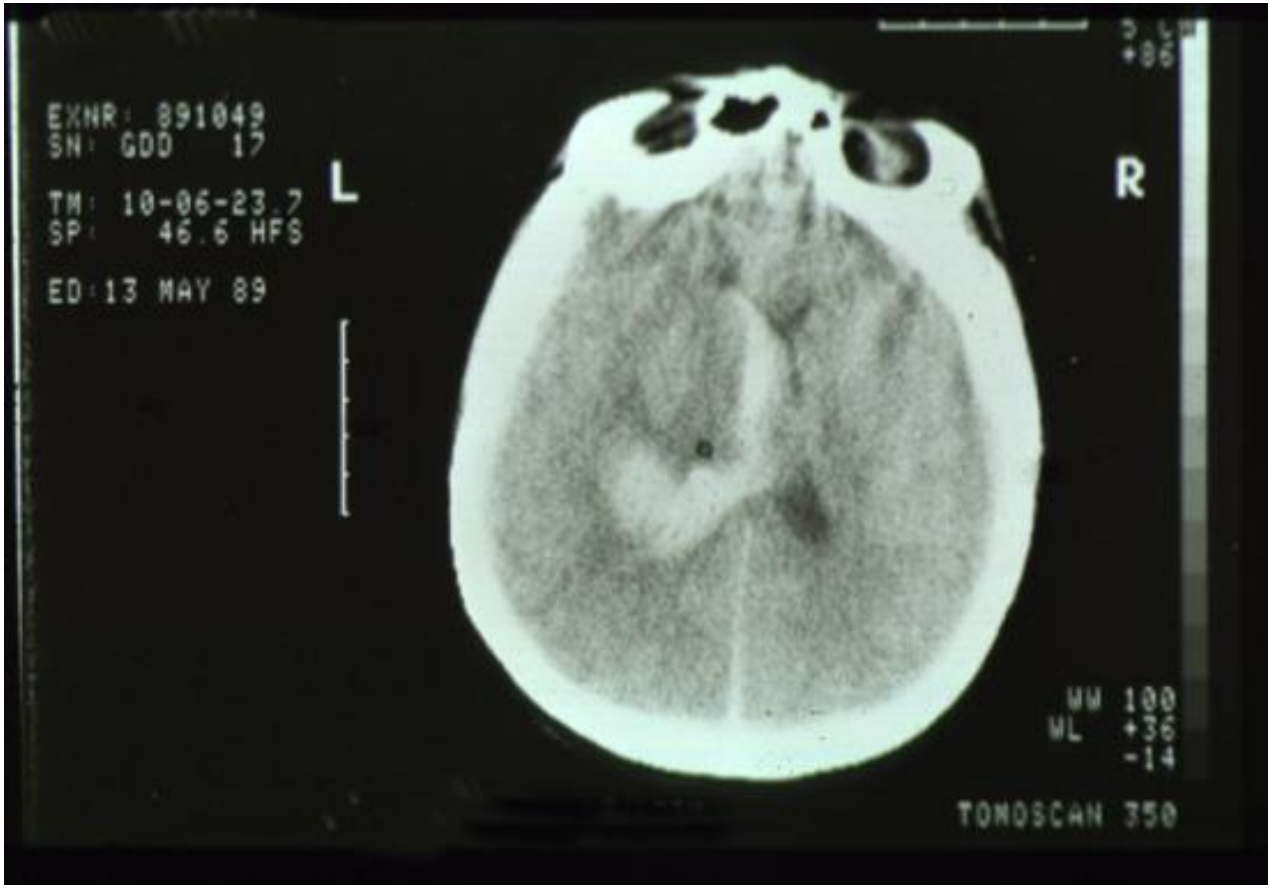
Patient with AML- Pale skin and petechiae



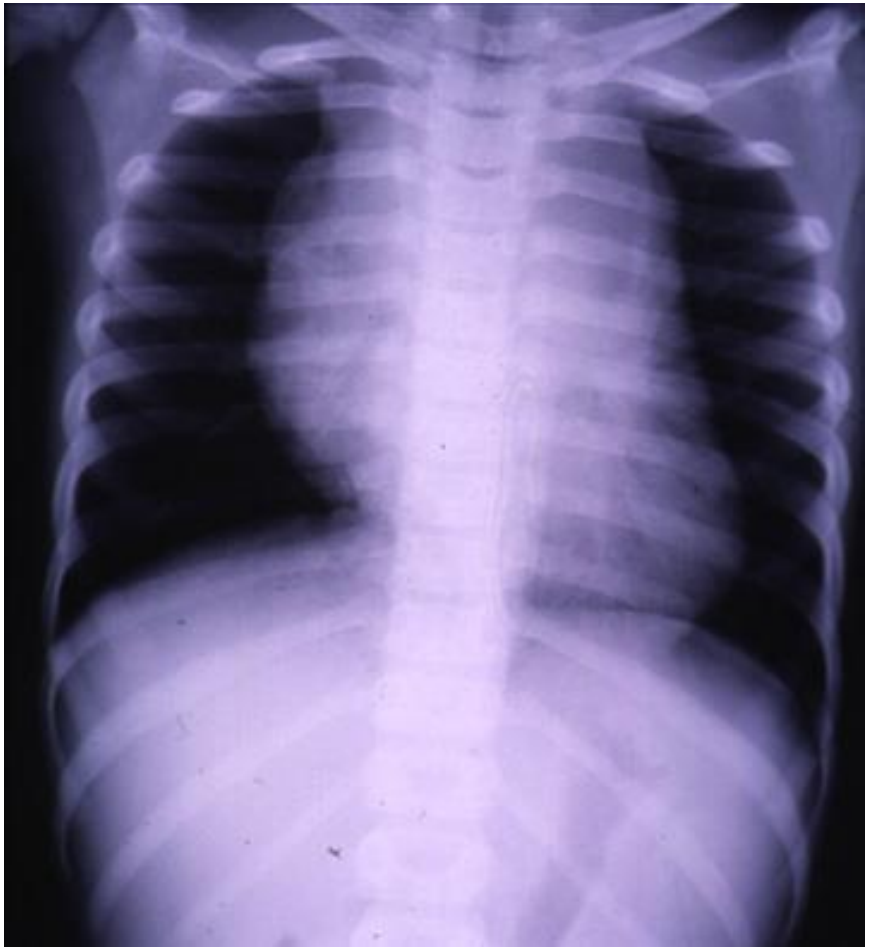




Prominent gingival hyperthrophy - Acute monocytic leukemia



Acute promielocytic leukemia- CT- intra cranial hemorrhage with DIC



ALL enlarged intrathoracic nodes

Diagnosis

Is done with the use of:

- Complete blood cell (CBC) and peripheral smear
- Bone marrow examination
- Histochemical studies, cytogenetics, immunophenotyping, and molecular biology studies
- Imaging

Complete blood cell (CBC) count:

1. pancytopenia
    - anaemia
    - thrombocytopenia
    - elevated, normal or deminished white blood cell

Blasts in peripheral smear suggest acute leukemia.

- *hiatus leucaemicus*

WBC		58.57	10^3/uL	(4.0	- 10.0	)
RBC		1.99	10^6/ul	(4.0	- 5.5	)
HGB		6.1	g/dL	(12	- 16	)
HCT		18.6	%	(37	- 47	)
MCV	93.0		fL	(81	- 99	)
MCH	30.6		pg	(27	- 34	)
MCHC	32.9		g/dL	(31	- 37	)
CHCM	33.4		g/dL	(31	- 37	)
RDW		17.6	%	(11.5	- 14.5	)
HDW		3.34	g/dL	(2.2	- 3.2	)
PLT	142		10^3/uL	(130	- 350	)
MPV	9.7		fL	(7.0	- 12.0	)
PCT	0.14		%	(0.12	- 0.36	)
PDW	59.8		%	(40.0	- 60.0	)

Anisocytosis	+
Makrocytosis	+
Hypochromia	+

Samodzielny Publiczny Szpital Kliniczny
Akademii Medycznej w Białymstoku
Zakład Diagnostyki Hematologicznej
PRACOWNIA CYTOLOGII
tel. 746-87-24

Data 04-09-22

Oddz. 41

Imię [redacted]

Nazwisko [redacted]

kom. blastyczne i kom. z szeregu monocytoidalnego

Wzór krwinek białych

Granulocyty	66	Mieloblasty	
	8	Promielocyty	
	2	Mielocyty	
	13	Metamielocyty	
		Pałeczkowate	
		Podzielone	
		Kwasochłonne	
		Zasadochłonne	
Limfocyty		Limfoblasty	
		Prolimfocyty	
	9	Limfocyty	
		Monocyty	
		Kom. plazmat.	

Opis dość znaczna anizocytoza, mieszana polichromatofilia, ne 100 leukocytów znaleziono 178 cytoblastów

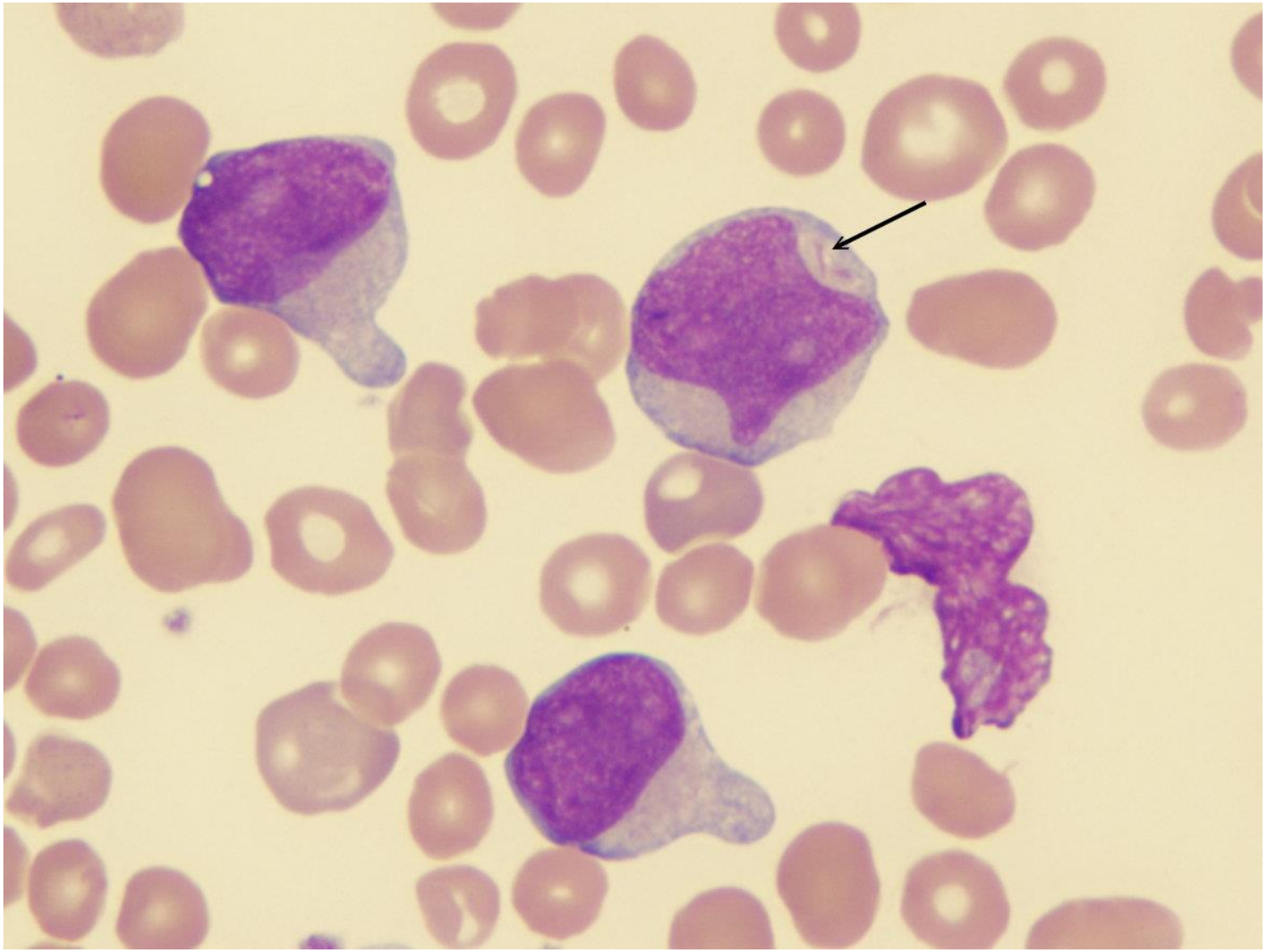
Wykonujący Wiesława Mejsak st. lab. diagnostyki med

Kierownik

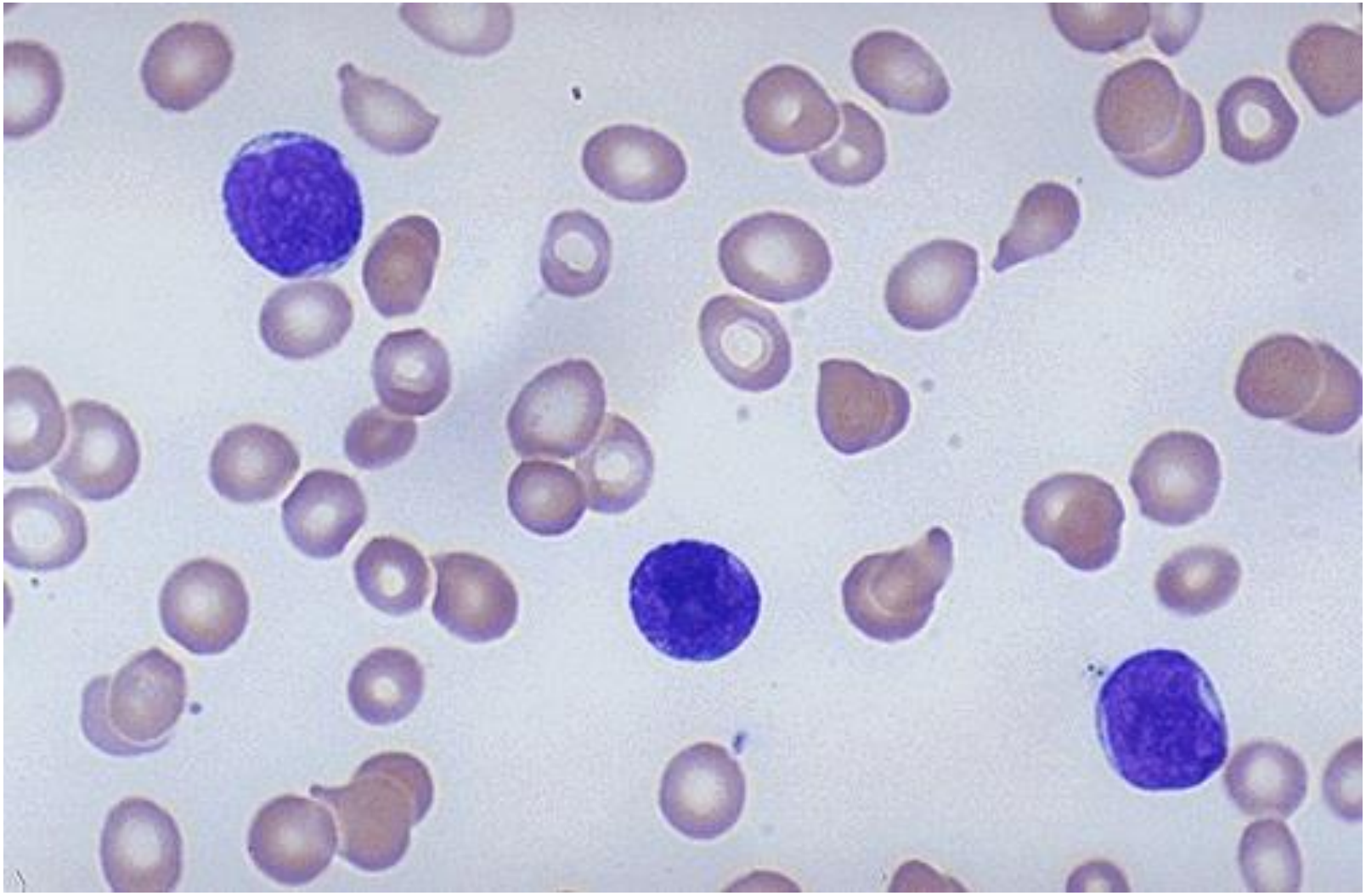
Retikulocyty 39 ‰

AML

-CBC and blood smear



AML blood - Auer’s rods



ALL blood smear

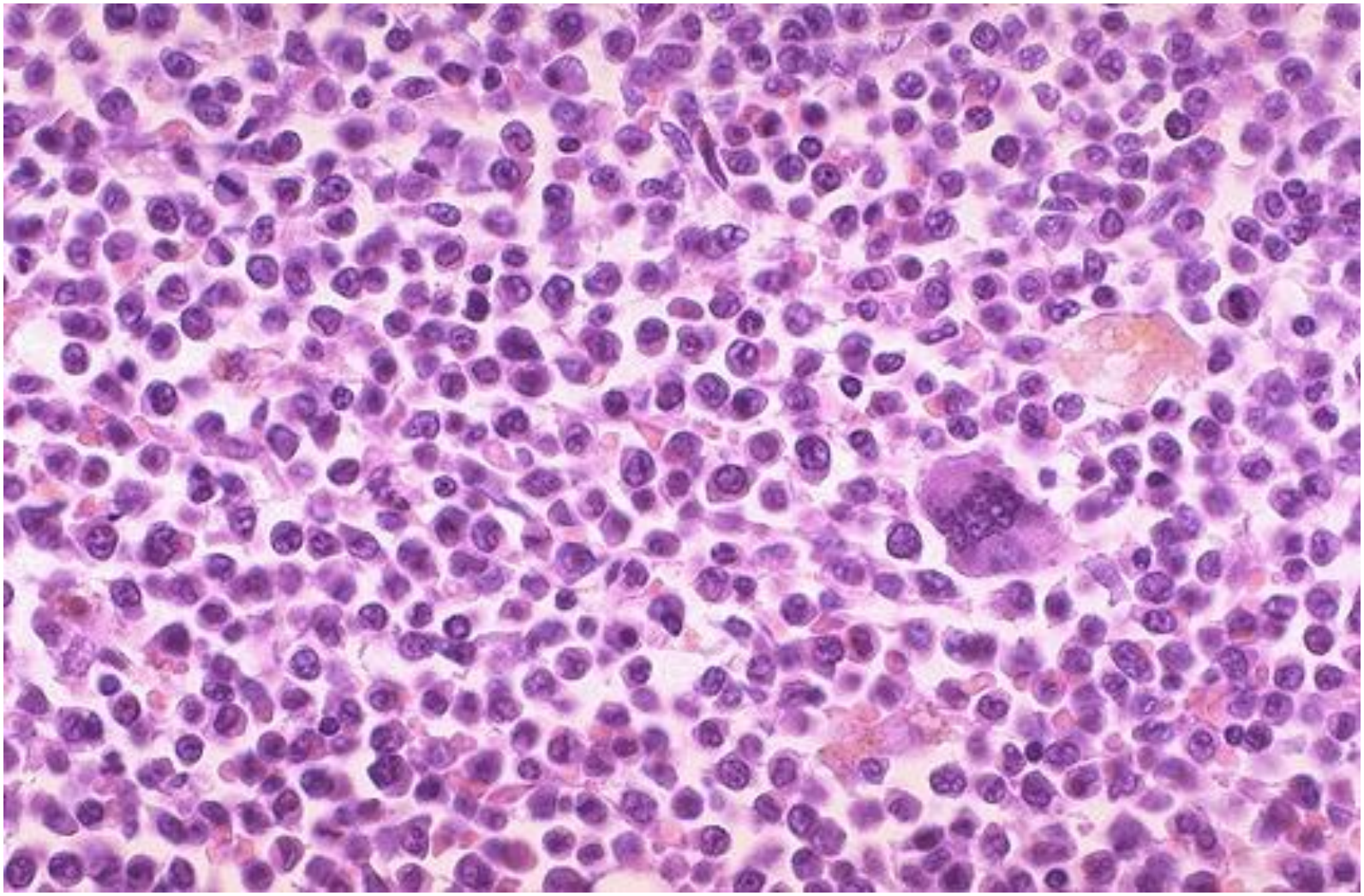
Bone marrow aspiration

A blast count can be performed with bone marrow aspiration. Historically, by French-American-British (FAB) classification, acute leukemia was defined by the presence of more than 30% blasts in the bone marrow.

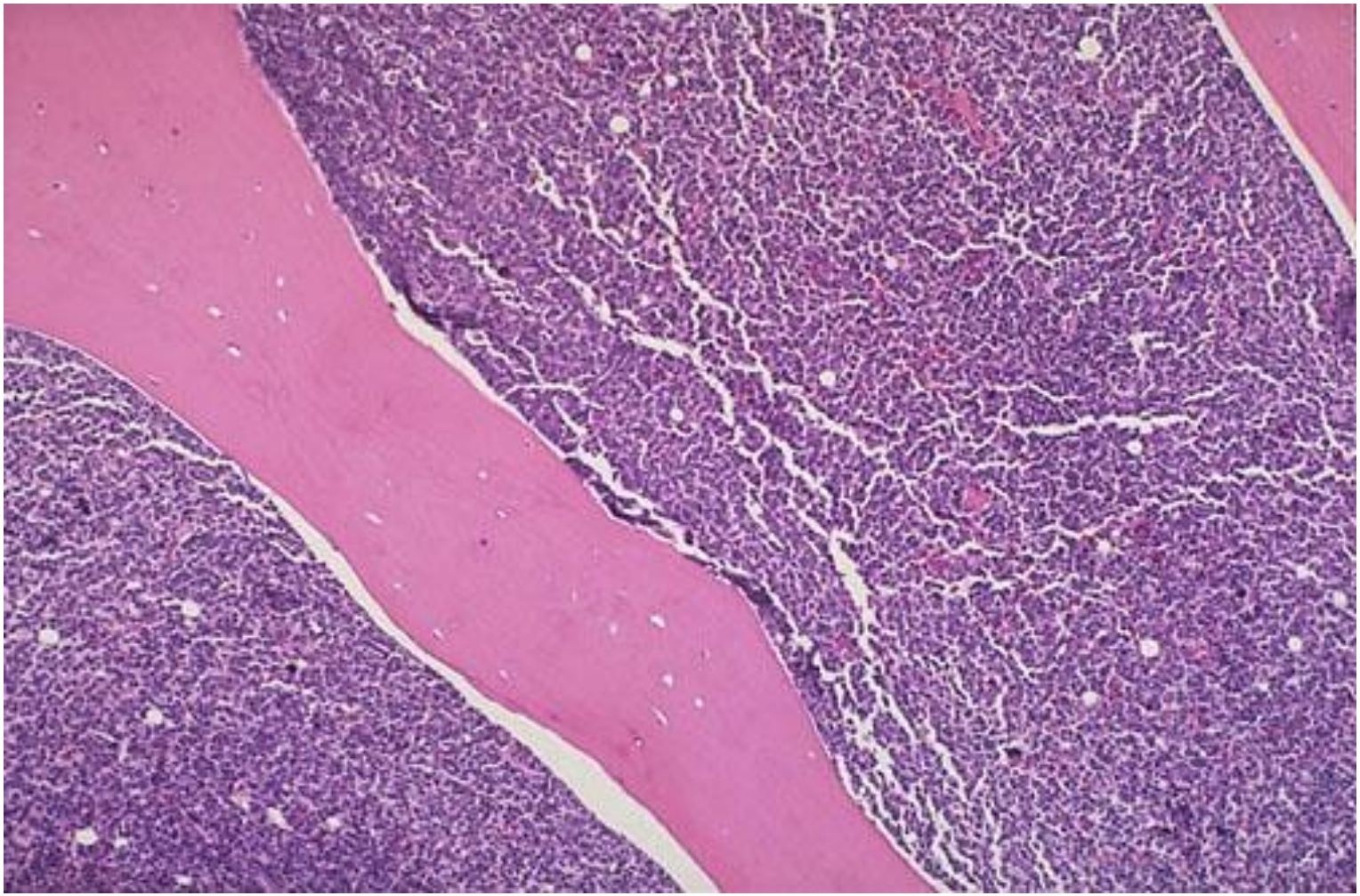
In the newer World Health Organization (WHO) classification, AML is defined as the presence of greater than 20% blasts in the marrow.

The bone marrow aspirate also allows evaluation of the degree of dysplasia in all cell lines.

- Histochemical studies
- Immunophenotyping studies
- Cytogenetical evaluation
- Molecular biology studies



AML bone marrow



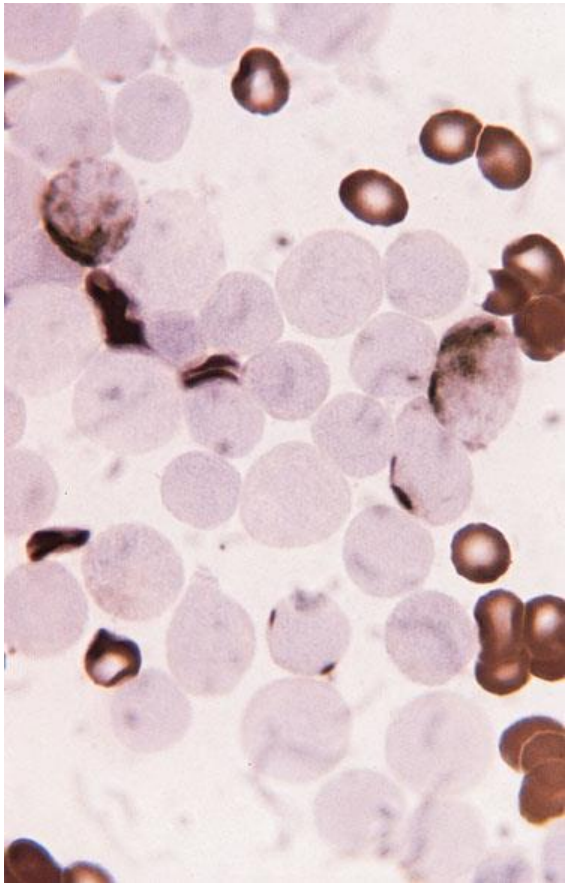
ALL – hypercellularity – with excess blasts

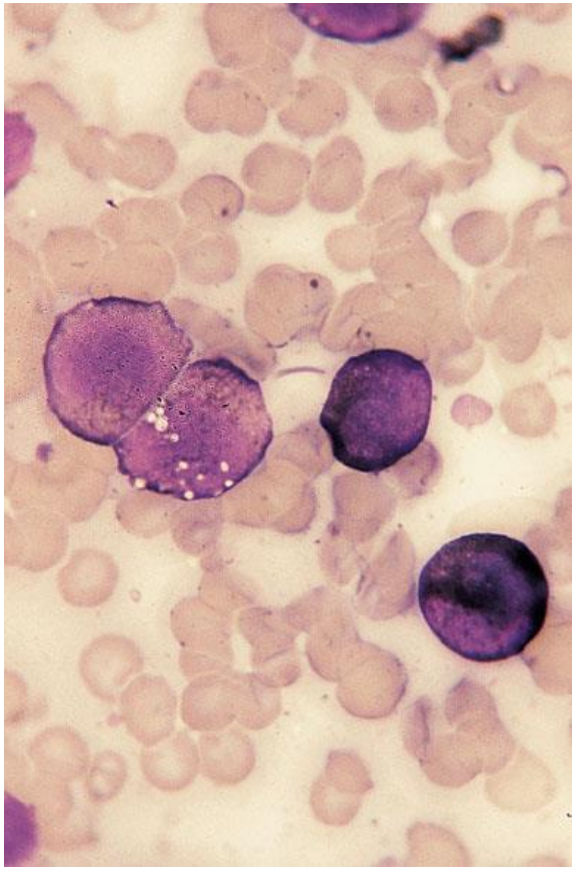
Histochemical studies

Staining of peripheral and bone marrow cells can help to distinqiushed the myeloid and lymphoid cancers cell.

Cytochemical differentiation of acute leukemia

Reaction	AML M1-M5	M_6	ALL
POX (mieloperoksydase)	+	-	-
Sudan B	+	-	-
Non specific esterase	+ (M_4, M_5)	-	-
PAS	+	+	+
Phosphatase	-	-	+





Left AML myeloperoxydase M1

Right AML Sudan B M4

Immunophenotyping with the use of flow cytometry can be used to help distinguish acute myelogenous leukemia (AML) from acute lymphoid leukemia (ALL) and further classify the subtype of AML. The immunophenotype correlates with prognosis in some instances.

Markers of *B cells*	Markers of *T cells*	Markers of myeloid line
CD 10 CD 19 CD 20 CD 22 Cygl Smlg	CD 1 CD 2 CD 3 CD 4 CD 5 CD 7 CD 8	CD 13 CD 15 CD 33 Cdw 65
Markers of platelets	**Markers of erythroid line**	**Markers of monocytic line**
Cdw 41 Cdw 42	GpA – glicophorin A	CD 11 b CD 14

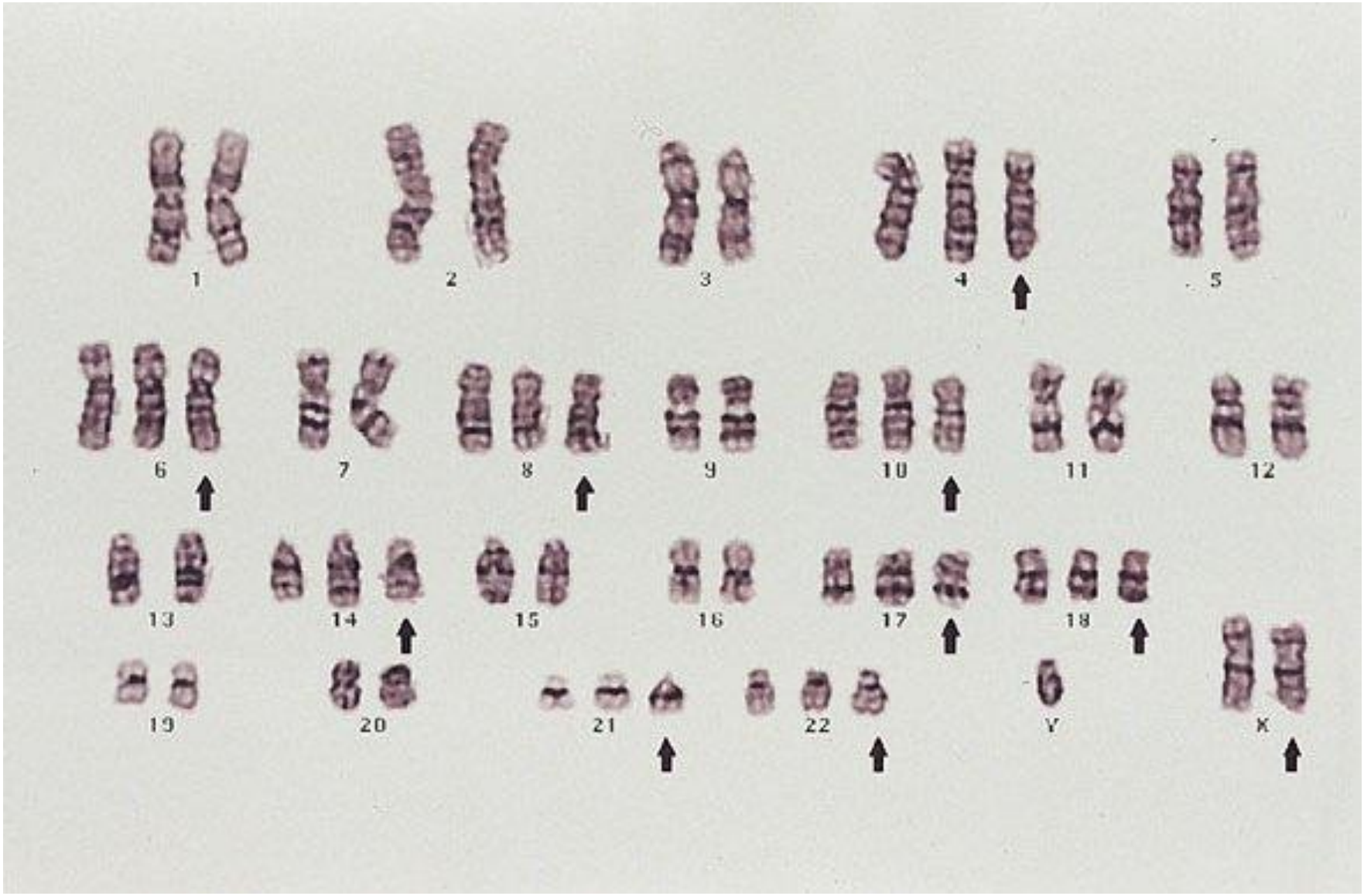
Marker	Lineage
CD13	Myeloid
CD33	Myeloid
CD34	Early precursor
HLA-DR	Positive in most AML, negative in APL
CD11b	Mature monocytes
CD14	Monocytes
CD41	Platelet glycoprotein IIb/IIIa complex
CD42a	Platelet glycoprotein IX
CD42b	Platelet glycoprotein Ib
CD61	Platelet glycoprotein IIIa
Glycophorin A	Erythroid
TdT	Usually indicates acute lymphocytic leukemia, however, may be positive in M0 or M1
CD11c	Myeloid
CD117 (c-kit)	Myeloid/stem cell

Cytogenetic studies

Cytogentic studies performed on bone marrow provide important prognostic information and are useful to confirm a diagnosis of APL, which bears the t(15;17) chromosome abnormality and is treated differently.

Table.
Common Cytogenetic Abnormalities in AML

Abnormality	Genes Involved	Morphology	Response
t(8;21)(q22;q22)	***AML/ETO***	**M2**	**Good**
inv(16)(p13;q22)	***CBFb/MYH11***	**M4eo**	**Good**
Normal	**Multiple**	**Varies**	**Intermediate**
-7	**Multiple**	**Varies**	**Poor**
-5	**Multiple**	**Varies**	**Poor**
+8	**Multiple**	**Varies**	**Intermediate-poor**
11q23	***MLL***	**Varies**	**Intermediate-poor**
Miscellaneous	**Multiple**	**Varies**	**Intermediate-poor**
Multiple complex*	**Multiple**	**Varies**	**Poor**



ALL hyperdiploidia- common ALL

Molecular diagnosis is performed for:

- Evaluation for marker gens for specific luekemia
- Evaluation of expresion of gens for specific cytokines and their regulatory mechanisms
- Evaluation for drug resistance
- Evaluation for human leukocyte antigen system (*HLA*) HLA for peripheral blood stem cell (*PBSC*) transplantation

OMÓWIENIE WYNIKÓW

Preparaty wybitnie bogatokomórkowe.

W obrazie dominują komórki blastyczne i promielocyty (na ogół średniej wielkości, o regularnym kształcie jądra i cytoplazmy). W cytoplazmie niektórych komórek blastycznych obecna jest ziarnistość azurochłonna, co stwarza trudność w różnicowaniu komórek na szczeblu komórka blastyczna – promielocyt.

Ocena fenotypu komórek blastycznych i promielocytów szpiku metodą cytometrii przepływowej wykazała obecność dwóch populacji komórek:

1 – populacja stanowiąca około 60% populacji komórek blastycznych i promielocytów o fenotypie: CD33, CD13, HLA-DR, koekspresja CD7, słaba ekspresja CD14

CD33	-około 96% komórek
CD13	-około 50,5% komórek
HLA-DR	-około 79,5% komórek
CD7/CD33	-około 58% komórek
CD14	-około 36% komórek,

2 - populacja stanowiąca około 40% populacji komórek blastycznych i promielocytów o fenotypie: CD33, CD13; brak ekspresji HLA-DR, CD7 i CD14

CD33	-około 97,5% komórek
CD13	-około 49% komórek

W obu populacjach komórek blastycznych i promielocytów stwierdzono brak ekspresji antygenów linii limfoidalnej: CD10, CD3, CD5, CD19, CD20, CD22 oraz antygenu CD34.

Badania cytochemiczne komórek blastycznych i promielocytów szpiku wykazały:
-reakcja peroksydazowa – dodatnia lub silnie dodatnia w blisko 100% komórek,
-reakcja na obecność esterazy nieswoistej – słabo dodatnia lub dodatnia w około 15% komórek,
-reakcja PAS na obecność glikogenu – ujemna.

Układ czerwonokrwinkowy sięga dolnej granicy normy. Erytropoeza normoblastyczna z komórkami o cechach megaloidalnych.

Odsetek limfocytów w granicach normy.

Na 1000 komórek jądrzastych szpiku nie znaleziono megakariocytów.

Histologic Findings

The older, more traditional, FAB classification of acute myelogenous leukemia (AML) is as follows:

M0 - Undifferentiated leukemia

M1 - Myeloblastic without differentiation

M2 - Myeloblastic with differentiation

M3 - Promyelocytic

M4 - Myelomonocytic

- M4eo - Myelomonocytic with eosinophilia

M5 - Monoblastic leukemia

- M5a - Monoblastic without differentiation
- M5b - Monocytic with differentiation

M6 - Erythroleukemia

M7 - Megakaryoblastic leukemia

The newer WHO classification is as follows :

- Acute myelogenous leukemia (AML) with recurrent genetic abnormalities
  - AML with t(8;21)(q22;q22), (*AML1/ETO*)
  - AML with abnormal bone marrow eosinophils and inv(16)(p13q22) or t(16;16)(p13)(q22), *(CBFB/MYH11)*
  - APL with t(15;17)(q22;q12), *(PML/RARa)* and variants
  - AML with 11q23 *(MLL)* abnormalities
- AML with multilineage dysplasia
  - Following MDS or MDS/myeloproliferative disease (MPD)
  - Without antecedent MDS or MDS/myeloproliferative disease (MPD) but with dysplasia in at least 50% of cells in 2 or more lineages
- AML and MDS, therapy related
  - Alkylating agent or radiation-related type
  - Topoisomerase II inhibitor type
  - Others
- AML, not otherwise classified
  - AML, minimally differentiated
  - AML, without maturation
  - AML, with maturation
  - Acute myelomonocytic leukemia
  - Acute monoblastic or monocytic leukemia
  - Acute erythroid leukemia
  - Acute megakaryoblastic leukemia
  - Acute basophilic leukemia
  - Acute panmyelosis and myelofibrosis
  - Myeloid sarcoma

Treatment of acute leukemia

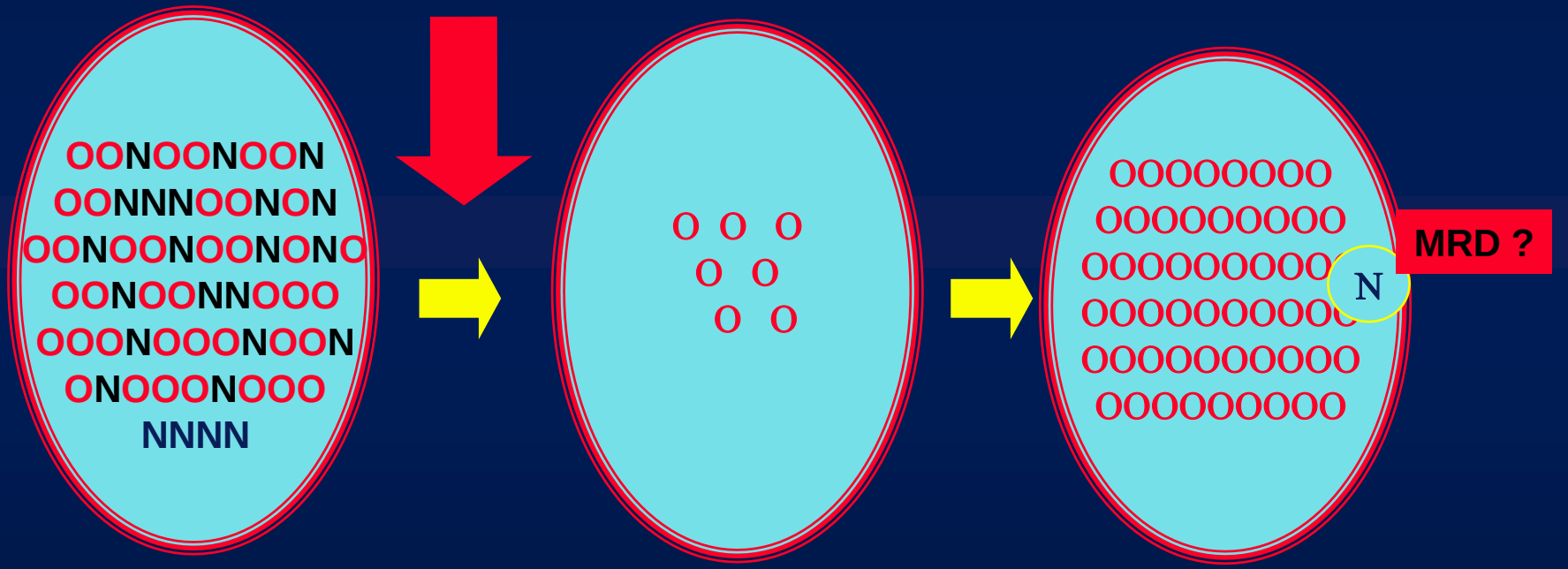
Theoreticaly knowing the genetical defect cousing the leukemic transformation giving the selectively acting drug we should undo or diminish the genetical damage and/or it`s consequences.

Treatment of acute leucemia consists of:

1. Chemotherapy
2. Supportive care
3. Peripheral blood stem cell (*PBSC*) transplantation

Oncological treatment

CHEMOTHERAPHY



PATIENT WITH CANCER

BONE MARROW APLASIA

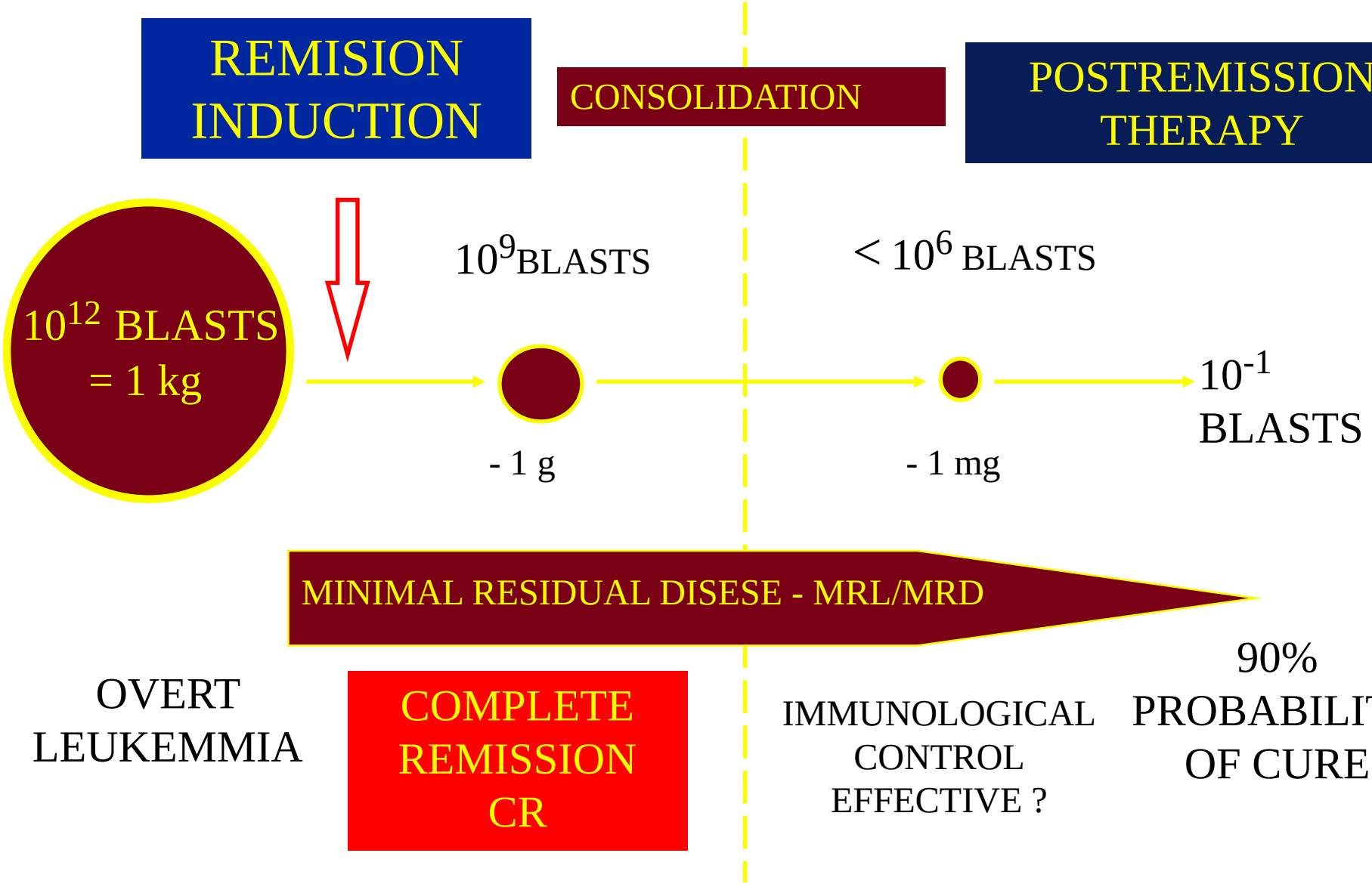
TOTAL REMISION

The goal of treatment is complete remission, including resolution of abnormal clinical features, restoration of normal blood counts and normal hematopoiesis with < 5% blast cells, and elimination of the leukemic clone. Although basic principles in treating ALL and AML are similar, the drug regimens differ.

Basic principles in treating acute leukemia

- Induction therapy
- Consolidation therapy
- Supportive care

THERAPY OF ACUTE LEUKEMIA - GENERAL POLICY



HOLOWIECKI 1997

THERAPY OF ACUTE MYELOBLASTIC LEUKEMIA AML GENERAL PRINCIPLES

INDUCTION 4-6 weeks "REMOVAL OF TUMOR MASS"	CONSOLIDATION 3-6 Mo 'REMOVAL OF MRD'	POSTREMISSION THERAPY
• INTENSIVE CARE UNIT •SUPPORTIVE THERAPY • 1. ARA-C - 200mg/m2 7 days •2. DNR 45-60 mg/m2 iv 3 days *(IdR 12 mg/m2,)* • *3. +/- cladribine* - CNS : Mtx / Ara-C i.t.	• HD Ara-C (2- 6 g/m2/d x3-4. or • HD/ID Ara-C +Mitox or • HD/ID Ara-C + AMSA " + Antr+Vep " + IdR • Therapy like remission induction? - CNS: Mtx/Ara-C i.t.	**1.** MAINTANANCE every 4-6 weeks sequentialy up to 2 yrs: a. Ara-C sc +DNR b. Ara-C sc + 6TG. **2.** HCT TRANSPLANT: BMT OR ABMT/BCT +/- Immunotheraphy? **3.** 'Wait and watch' • CNS prophyl.: Mtx / Ara-C ev. 6 Mo.
50-70% CR	mortality<7%	DFS 5 y: 1.=10-15% 2. = 45-60%

I. Induction therapy

- “REMOVAL OF TUMOR MASS”

according to PALG in patients aged 60 years or younger, treatment options for induction therapy include:

- ‘’3+7’’ 3 days of daunarubicine, 5 days of Ara-C,

- ‘’3+7’’+ cladribine.

Alternative options for elderly patients

1. ‘’2+5’’ Daunarubicin for 2 days and Ara-C for 5 days
2. Hydroxyurea
3. Novel agents
   - Tipifarnib (a farnesyl transferase inhibitor)
   - Cloretazine is a novel alkylating agent
   - Clofarabine is a purine analogue
   - The hypomethylating agents, azacytidine and decitabine

II. Consolidation therapy

- removal of minimal residual disease (MRD)- in patients aged 60 years or younger, treatment options for consolidation therapy include:

- high-dose Ara-C,

- autologous stem cell transplantation,

- allogeneic stem cell transplantation.

III. POSTREMISSION THERAPY

The third- last – is remission maintenance treatment aiming towards cure with use of polychemotheraphy regiments.

Stem cell transplantation in AML

Patients with high-risk cytogenetics findings are rarely cured with chemotherapy and should be offered transplantation in first remission.

The hematopoietic stem cells are found in:

• the **bone marrow**,

• the bloodstream **- peripheral blood stem cells** (PBSCs),

• the **umbilical cord.**

Cells from any of these sources can be used in transplants.

Bone marrow transplantation (BMT), peripheral blood stem cell transplantation (PBSCT) and transplantation from hematopoietic stem cells from umbilical cord are procedures that restore stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy.

To understand more about why BMT and PBSCT are used, it is helpful to understand how chemotherapy and radiation therapy work.

Chemotherapy and radiation therapy generally affect cells that divide rapidly. They are used to treat cancer because cancer cells divide more often than most healthy cells. However, because bone marrow cells also divide frequently, high-dose treatments can severely damage or destroy the patient's bone marrow.

Without healthy bone marrow, the patient is no longer able to make the blood cells needed to carry oxygen, fight infection, and prevent bleeding. BMT and PBSCT replace stem cells that were destroyed by treatment. The healthy, transplanted stem cells can restore the bone marrow's ability to produce the blood cells the patient needs.

There are three types of transplants:

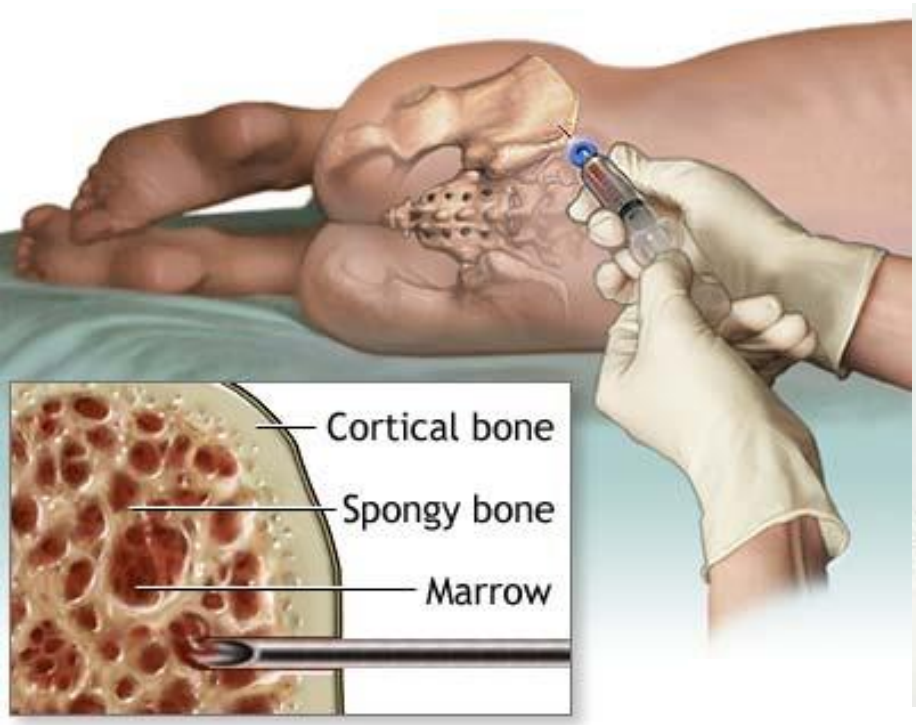
- In **autologous transplants**, patients receive their own stem cells.
- In **syngeneic transplants**, patients receive stem cells from their identical twin.
- In **allogeneic transplants**, patients receive stem cells from their brother, sister, or parent. A person who is not related to the patient (an unrelated donor) also may be used.

BMT and PBSCT are most commonly used in the treatment of leukemia and lymphoma. They are most effective when the leukemia or lymphoma is in remission (the signs and symptoms of cancer have disappeared). BMT and PBSCT are also used to treat other cancers such as neuroblastoma (cancer that arises in immature nerve cells and affects mostly infants and children) and multiple myeloma. Researchers are evaluating BMT and PBSCT in clinical trials (research studies) for the treatment of various types of cancer.

The procedure for obtaining bone marrow is called “harvesting” and is similar for all three types of BMTs (autologous, syngeneic, and allogeneic).

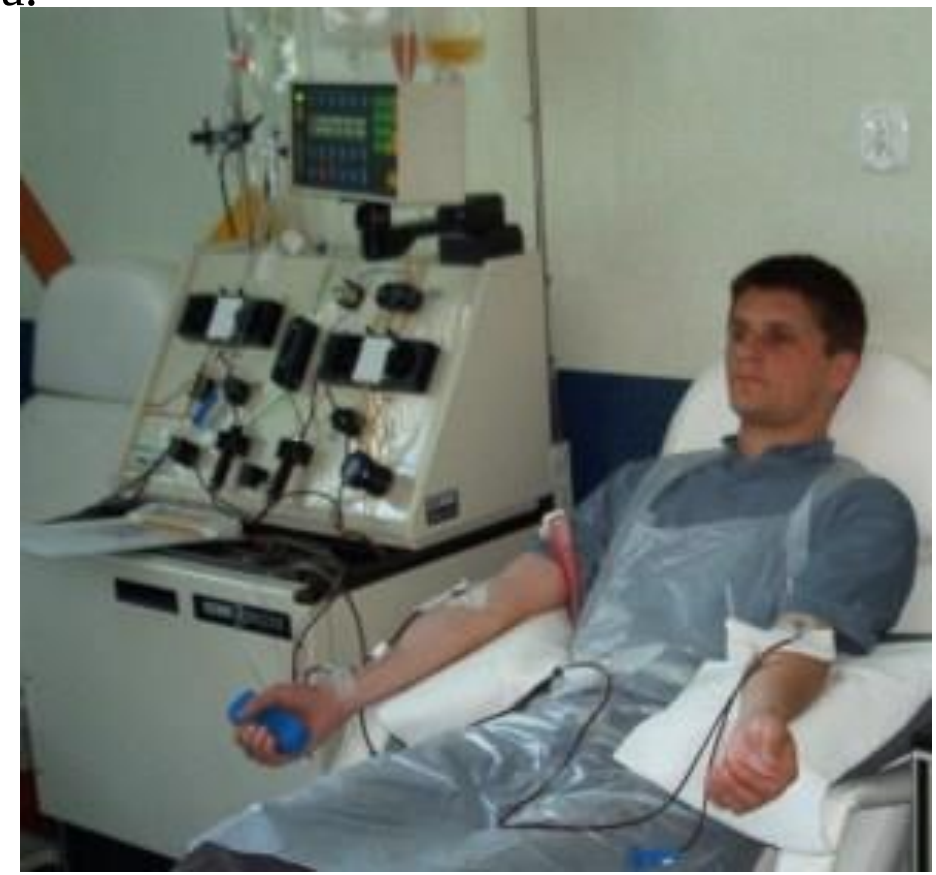
The donor is given either general anesthesia, which puts the person to sleep during the procedure, or regional anesthesia, which causes loss of feeling below the waist. Needles are inserted through the skin over the pelvic (hip) bone or, in rare cases, the sternum (breastbone), and into the bone marrow to draw the marrow out of the bone. Harvesting the marrow takes about an hour.

The harvested bone marrow is then processed to remove blood and bone fragments. Harvested bone marrow can be combined with a preservative and frozen to keep the stem cells alive until they are needed.



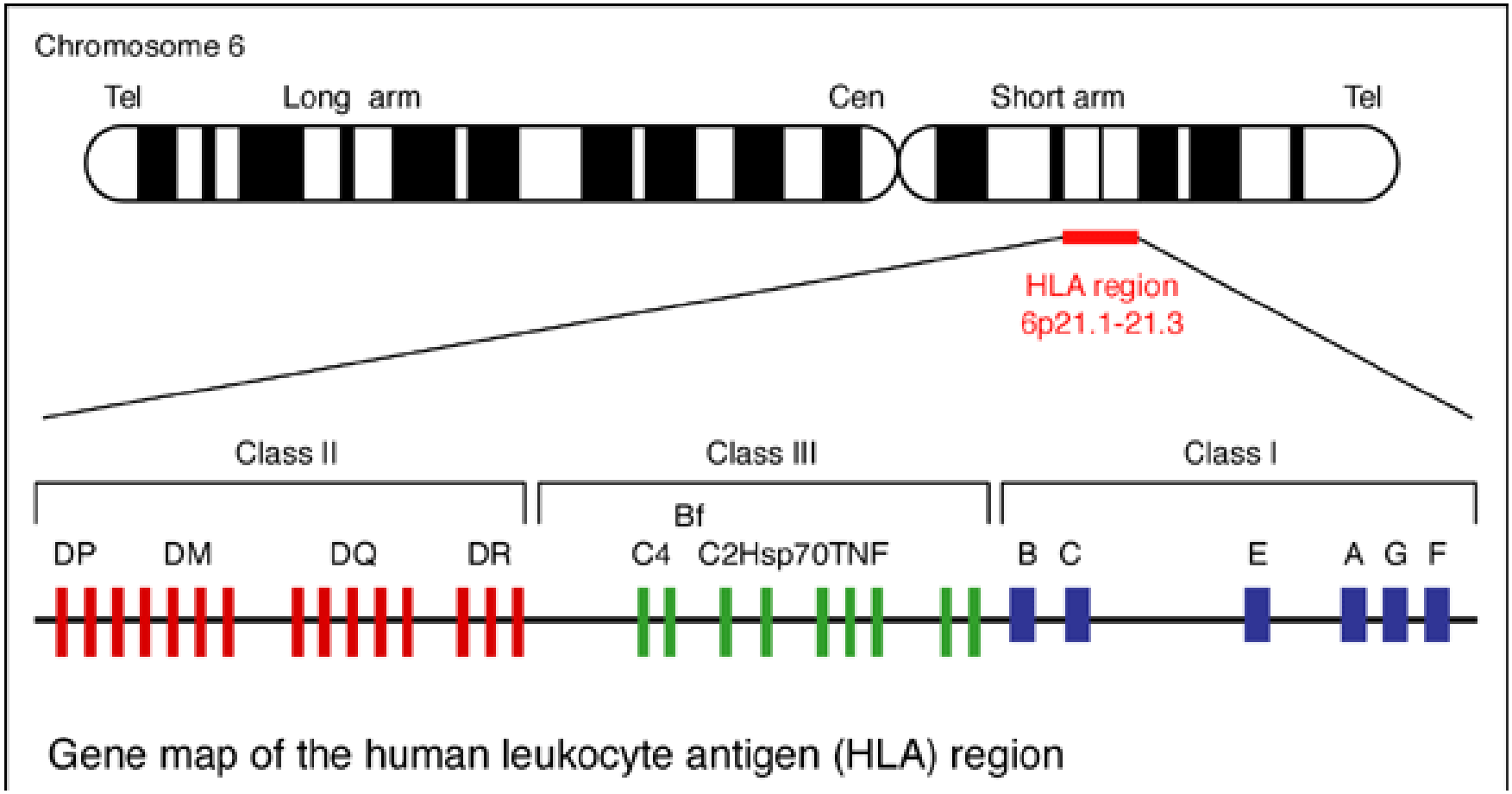
The stem cells used in PBSCT come from the bloodstream. A process called apheresis or leukapheresis is used to obtain PBSCs for transplantation. For 4 or 5 days before apheresis, the donor may be given G-CSF or GM-CSF to increase the number of stem cells released into the bloodstream. In apheresis, blood is removed through a large vein in the arm or a central venous catheter placed in a large vein in the neck, chest, or groin area.

The blood goes through a machine that removes the stem cells. The blood is then returned to the donor and the collected cells are stored. Apheresis typically takes 4 to 6 hours. The stem cells are then frozen until they are given to the recipient.



To minimize potential side effects, we use transplanted stem cells that match the patient's own stem cells as closely as possible. People have different sets of proteins, called human leukocyte-associated (HLA) antigens, on the surface of their cells. The set of proteins, called the HLA type, is identified by a special blood test.

In most cases, the success of allogeneic transplantation depends in part on how well the HLA antigens of the donor's stem cells match those of the recipient's stem cells. The higher the number of matching HLA antigens, the greater the chance that the patient's body will accept the donor's stem cells. In general, patients are less likely to develop a complication known as graft-versus-host disease (GVHD) if the stem cells of the donor and patient are closely matched.



Gene map of the human leukocyte antigen (HLA) region. The HLA region spans 4×10^6 nucleotides on chromosome 6p21.1 to p21.3, with class II, class III and class I genes located from the centromeric (Cen) to the telomeric (Tel) end. **HLA class I** molecules restrict $CD8^+$ cytotoxic T lymphocyte function and mediate immune responses against 'endogenous' antigens and virally infected targets, whereas **HLA class II** molecules are involved in the presentation of 'exogenous' antigens to T helper cells. The **HLA class III** region contains many genes encoding proteins that are unrelated to cell-mediated immunity but that nevertheless modulate or regulate immune responses in some way, including tumour necrosis factor (TNF), heat shock proteins (Hsps) and complement proteins (C2, C4)

REGIONALNE CENTRUM
KRWIODAWSTWA I KRWIOLECZNICTWA
- SP ZOZ W BIAŁYMSTOKU
ul. M. Skłodowskiej – Curie 23; 15-950 Białystok
tel. (85) 744-70-02; fax (85) 744-71-33
www.rckik.bialystok.pl sekretariat@rckik.bialystok.pl

Certyfikat ISO 9001 : 2000
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WYNIK

badania antygenów HLA klasy I

testem limfocytotoksyczności

Nazwisko i imię	wiek	A	A	B	B	C	C
MAGDALENA	24	1	24	7	8	7	-
MARTA	25	2	24	7	44	7	-
ANNA	21	2	24	7	44	7	-
AGNIESZKA	17	2	3	44	41	2	7
WERONIKA	14	1	24	7	8	7	-

Badanie wykonał Sławomir Ziarko
mgr analityki med

Sprawdził: *mgr Alina Juchnowicz*
7213
diagnosta laboratoryjny
specjalista analityki klinicznej

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WYNIK

badania antygenów HLA PCR SSP

klasa II

Nazwisko i imię		DRB1	DRB1	DR	DR	DQB1	DQB1
Magdalena	lat 24	*12	*15	51	52	*03	*06
Weronika - siostra	lat 14	*12	*15	51	52	*03	*06

Badanie wykonał Sławomir Ziarko
mgr analityki med

Sprawdził: *mgr Alina Juchnowicz*
diagnosta laboratoryjny
specjalista analityki klinicznej

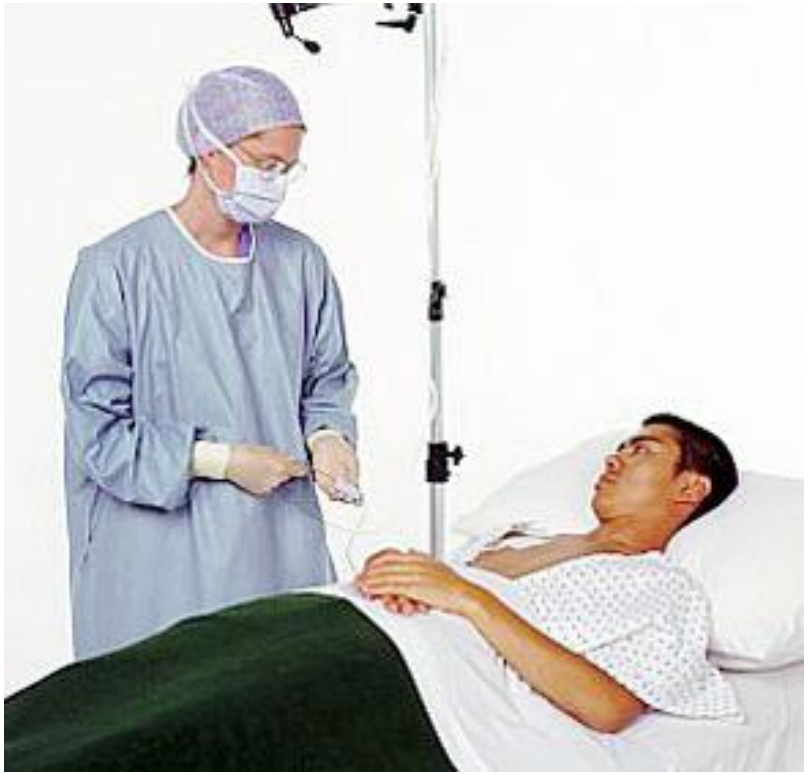
Data badania: 2005-02-01

Close relatives, especially brothers and sisters, are more likely than unrelated people to be HLA-matched. However, only 25 to 35 percent of patients have an HLA-matched sibling. The chances of obtaining HLA-matched stem cells from an unrelated donor are slightly better, approximately 50 percent. Among unrelated donors, HLA-matching is greatly improved when the donor and recipient have the same ethnic and racial background. Although the number of donors is increasing overall, individuals from certain ethnic and racial groups still have a lower chance of finding a matching donor. Large volunteer donor registries can assist in finding an appropriate unrelated donor.

Because identical twins have the same genes, they have the same set of HLA antigens. As a result, the patient’s body will accept a transplant from an identical twin. However, identical twins represent a small number of all births, so syngeneic transplantation is rare.

After being treated with high-dose anticancer drugs and/or radiation, the patient receives the stem cells through an intravenous (IV) line just like a blood transfusion. This part of the transplant takes 1 to 5 hours.

After entering the bloodstream, the stem cells travel to the bone marrow, where they begin to produce new white blood cells, red blood cells, and platelets in a process known as “engraftment.” Engraftment usually occurs within about 2 to 4 weeks after transplantation.



Patient is given a bone marrow transplant directly into the bloodstream through a catheter.

Complete recovery of immune function takes much longer, however—up to several months for autologous transplant recipients and 1 to 2 years for patients receiving allogeneic or syngeneic transplants.

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The major risk of destruction of stem cells by high doses of chemotherapy and/or radiation therapy is an increased susceptibility to infection and bleeding.

The antibiotics are given to prevent or treat infection. The patients may also be given transfusions of platelets to prevent bleeding and red blood cells to treat anemia.

Patients who undergo BMT and PBSCT may experience short-term side effects such as nausea, vomiting, fatigue, loss of appetite, mouth sores, hair loss, and skin reactions.

Potential long-term risks include complications of the pretransplant chemotherapy and radiation therapy, such as infertility, cataracts (clouding of the lens of the eye, which causes loss of vision); secondary new cancers; and damage to the liver, kidneys, lungs, and/or heart.

With allogeneic transplants, a complication known as **graft-versus-host disease (GVHD)** sometimes develops. GVHD occurs when white blood cells from the donor (the graft) identify cells in the patient's body (the host) as foreign and attack them. The most commonly damaged organs are the skin, liver, and intestines. This complication can develop within a few weeks of the transplant (acute GVHD) or much later (chronic GVHD). To prevent this complication, the patient may receive medications that suppress the immune system.

Additionally, the donated stem cells can be treated to remove the white blood cells that cause GVHD in a process called “T-cell depletion.” If GVHD develops, it can be very serious and is treated with steroids or other immunosuppressive agents. GVHD can be difficult to treat, but some studies suggest that patients with leukemia who develop GVHD are less likely to have the cancer come back. Clinical trials are being conducted to find ways to prevent and treat GVHD.

A **“mini-transplant”** (also called a **non-myeloablative** or **reduced-intensity transplant**) is a type of allogeneic transplant. This approach is being studied in clinical trials for the treatment of several types of cancer, including leukemia, lymphoma, multiple myeloma, and other cancers of the blood.

A mini-transplant uses lower, less toxic doses of chemotherapy and/or radiation to prepare the patient for an allogeneic transplant. The use of lower doses of anticancer drugs and radiation eliminates some, but not all, of the patient’s bone marrow. It also reduces the number of cancer cells and suppresses the patient’s immune system to prevent rejection of the transplant.

Unlike traditional BMT or PBSCT, in **“mini-transplant”,** cells from both the donor and the patient may exist in the patient’s body for some time after a mini-transplant. Once the cells from the donor begin to engraft, they may cause the **graft-versus-tumor** (GVT) effect and work to destroy the cancer cells that were not eliminated by the anticancer drugs and/or radiation. To boost the GVT effect, the patient may be given an injection of their donor’s white blood cells. This procedure is called a **“donor lymphocyte infusion”**.

A **“tandem transplant”** is a type of autologous transplant. This method is being studied in clinical trials for the treatment of several types of cancer, including multiple myeloma and germ cell cancer. During a tandem transplant, a patient receives two sequential courses of high-dose chemotherapy with stem cell transplant. Typically, the two courses are given several weeks to several months apart.

Treatment of APL

APL is a special subtype of acute myelogenous leukemia (AML).

APL is most commonly associated with coagulopathy due to DIC and fibrinolysis.

Currently, the most standard approach is the combination of ATRA and anthracycline-based chemotherapy and aggressive supportive care.

Supportive care

- Replacement of blood products

  Packed red blood cells,

  Platelets.

  Fresh frozen plasma should be given to patients with a significantly prolonged prothrombin time,

  Cryoprecipitate should be given if the fibrinogen level is less than 100 g/dL.
- Antibiotics – intravenous antibiotics should be given to all febrile patients. At minimum, antibiotics should include broad-spectrum coverage such as that provided by a third-generation cephalosporin with or without vancomycin.
- Growth factors

Other

- hiperurycemia - Allopurinol
- vomiting- Metoklopramid, Navoban, Zofran;
- hypokaliemia - Elkinton II i.v., Kalium effervescens

New drugs in treatment of (AML).

Class	Agent	Target
Antibodies/ Immunoconjugates	Gemtuzumab ozogamicin	CD33
MDR inhibitors	PSC833, Zosuquidar	P-gp
Fernysyl Transferase inhibitors	Tipifarnib (Zarnestra)	Lamin A, HJJ-2 Rho B, CENP-E and CENP-F, lamins A and B
FLT3 inhibitors	PKC-412, CEP-701, MLN518, SU11248	FLT3 ITD
Histone deacetylase cytarabine (HDAC) inhibitors	Valproic acid, SAHA, depsipeptide	HDAC
Antiangiogenic agents	Bevacizumab	VEGF
Apoptosis inhibitors	Genasense	BCL-2
Deoxyadenosine analogs	Clofarabine	DNA