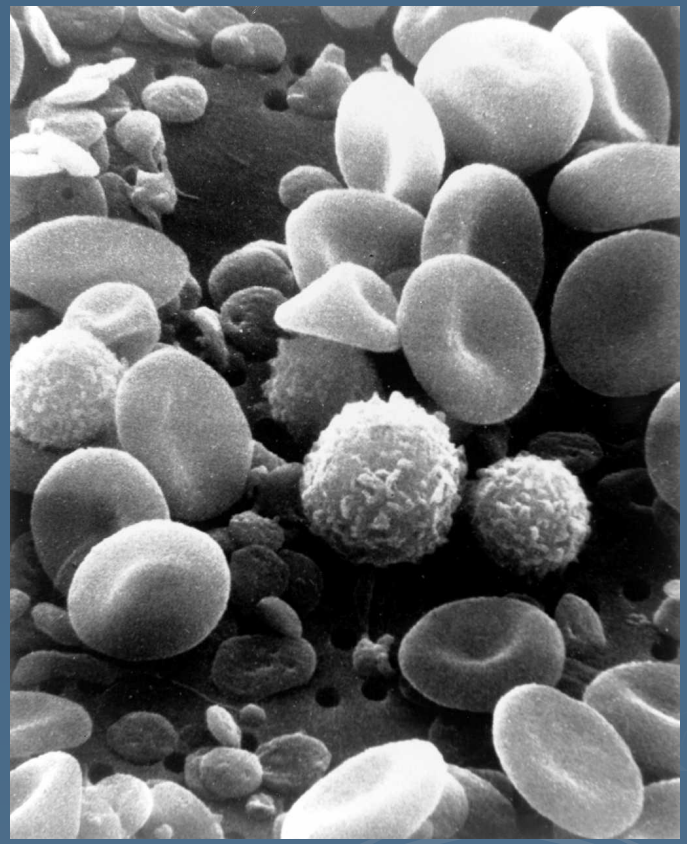
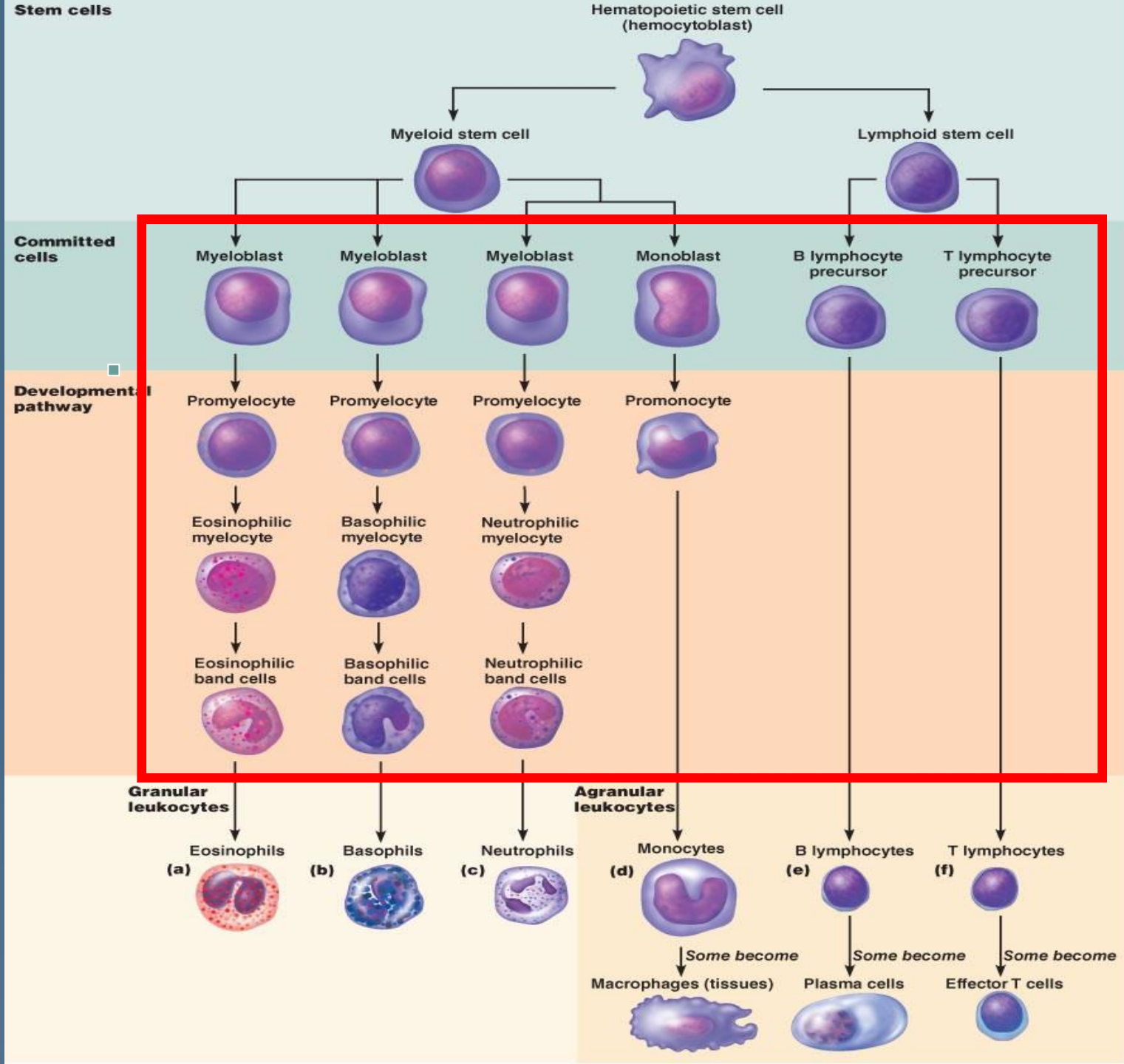
WBC pathology



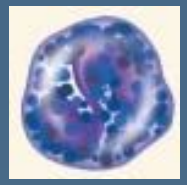
LEUKOPOIESIS



WBC differential count

Leukocytic formula

% correlation between different forms of WBC

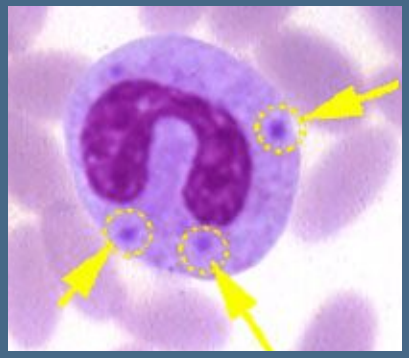
Eosinophils	Basophils	Neutrophils				Lymphocytes	Monocytes
		myelocyte	juvenile	band	segmented		
2-5	0-1	0	0	2-5	50-70	20-40	3-10
							

$$\text{Absolute value} = \frac{\%\ \text{of WBC type} * \text{total WBC count}}{100}$$

Degenerative forms of leukocytes

Neutrophils with hypersegmented nucleus

- ↑ level of glucocorticoids
- B12 deficiency.

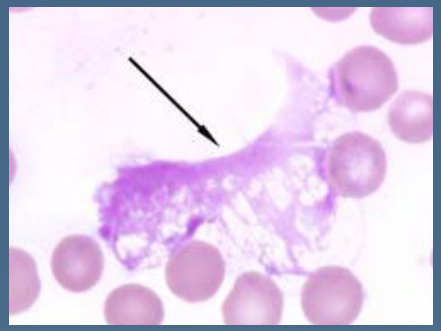


Leukocytes with **Döhle bodies**

- infections
- poisoning
- burns

Leukocytes with **toxic granulation**

- severe inflammation
- tumor necrosis



Gumprecht's cells (shadows)

smudge cells

- cell's partial breakdown during preparation of a smear (CLL)

Leukopenia

- WBC < $4*10^9$ /L High susceptibility to infections

Pancytopenia causes:

- bone marrow tumor
- aplastic state of bone marrow
  - ionizing radiation
  - chemotherapy of tumors (cytostatics)
  - intoxication with benzene, myelotoxic drugs (levomycetine, NSAIDs)
- B12 deficiency
- overactive spleen.

Leukopenia types

Eosinopenia

- after anaphylactic attacks (histaminase)
- severe stress
- ↑ glucocorticoids level

Lymphopenia

- primary immunodeficiency
- immunosuppressive drugs
- measles, poliomyelitis, AIDS (destruction of lymphocytes)

Monocytopenia

- not a distinct disorder

Neutropenia

Lower limit of neutrophils – 1500 -1200/μL (absolute value)

Agranulocytosis – total WBC 1-3*10^9/L
granulocytes < than 750/μL

Clinically - ↓ resistance to infection

- fever
- inflammation of the mouth, nose and eyes
- furunculosis
- pneumonia
- septicemia

Neutropenia reasons

- **Primary** (inherited) - Kostmann syndrome
- **Secondary** (aquired):
  - myelotoxic drugs (phenothiazines)
  - infections (mononucleosis, hepatitis, HIV, rubella, staphylococci, tuberculosis, etc).
  - bone marrow metaplasia
  - autoimmune destruction by cytokines, antibodies (aminopyrine, propylthiouracil, penicillin)

Leukocytosis

WBC > 9 *10^9/L

Absolute leukocytosis –

- activation of leukopoiesis
- release of WBC from bone marrow storage pools.

infection, inflammation, marrow neoplasia

Relative leukocytosis - redistribution of leukocytes in the vessels.

Physiological leukocytosis

Absolute

- **newborns**, - within the first week of life and having protective value.
- **pregnant women**, in the 2nd half of pregnancy.
- on the 2nd week **after delivery**.

Relative:

- physical overload (**myogenic**);
- psychical overload (**emotional**);
- flight over the time zones (**acclimatization**);
- in 1-2 hours after food intake (**alimentary**).

usually neutrophilic

Common causes of leukocytosis

- **Drugs intake** (low doses of corticosteroids, lithium and beta blockers).
- **Splenectomy** – □ of WBC destruction
- **Hemolytic anemia** - leukocytosis occur in association with increased RBC production.
- **Malignancy** - tumor nonspecifically stimulates bone marrow to produce WBC
- In most cases - **inflammation** or **infection**.

Types of leukocytosis

Eosinophilia	Basophilia
>5%	>1%
type 1 allergic reactions	
CML, polycythemia vera	
parasites' invasions	
rheumatoid arthritis, lupus erythematosus	myxedema, thyroiditis, DM type 1

Lymphocytosis

Physiological lymphocytosis - in children from the 4-5th day of life up to 4-5th years.

Absolute pathological lymphocytosis (>40%):

- Acute viral infections (Epstein-Barr v., cytomegalovirus, hepatitis)
- Chronic infections: tuberculosis, brucellosis
- Allergic bronchial asthma
- Lymphoid malignancies

Relative lymphocytosis

- Total WBC count normal or lower
- Leukocytic formula example WBC 4 *10^9/L

Eosinophils	Basophils	Neutrophils				Lymphocytes	Monocytes
		myelocyte	juvenile	band	segmented		
2	**0**	**0**	**0**	**0**	**29**	**60**	**10**

Mechanisms:

- neutrophils migration in the sites of inflammation
- increased granulocytes destruction

Monocytosis

- >10%
- bacterial infections (tuberculosis, syphilis, subacute bacterial endocarditis);
- viral infections, protozoal and rickettsial infections (malaria, typhus);
- convalescence from acute infection;
- hematopoietic disorders (leukemia, myeloma).

Neutrophilia

Aseptic (not-infectious) neutrophilia

- burns, myocardial infarction, intestinal impassability, immunocomplex diseases;
- uremia, diabetic ketoacidosis, thyreotoxocosis, histamine synthesis.

Infectious neutrophilia

- acute infections, caused by pyogenic bacteria (Pneumococcus, Streptococcus, staphylococcus and others);
- marrow tumors (CML, polycytemia vera).

Neutrophils' "Left shift"

Neutrophils nuclear shift

Eosino phils	Baso phils	Neutrophils				Lympho cytes	Mono cytes
		myelo cyte	juvenile	band	segment ed		
4	**0**	**0**	**0**	**8**	**59**	**20**	**9**

Hyporegenerative NNS to the left – □ of band neutrophils %. (easy current of infection/inflammation)

Eosino phils	Baso phils	Neutrophils				Lympho cytes	Mono cytes
		myelo cyte	juvenile	band	segment ed		
4	**0**	**0**	**2**	**8**	**57**	**20**	**9**

Regenerative NNS to the left – ☐ of band neutrophils %, appearance of juvenile cells (moderate nfection/inflammation);

Neutrophils nuclear shift

Eosino phils	Baso phils	Neutrophils				Lympho cytes	Mono cytes
		myelo cyte	juvenile	band	segment ed		
2	**0**	**2**	**7**	**16**	**51**	**18**	**4**

Hyperregenerative NNS to the left - myelogenous type of leukemoid reaction, severe current infection/inflammaion

Eosino phils	Baso phils	Neutrophils				Lympho cytes	Mono cytes
		myelo cyte	juvenile	band	segment ed		
4	**0**	**2**	**7**	**16**	**42**	**20**	**9**

Regenerative- degenerative NNS –severe course of infectious diseases, endogenous intoxications

Leukemoid reaction

- WBC count (> $30*10^9$ / L),

immature WBC in peripheral blood

of WBC is always reversible

Types:

- **myelogenous, lymphocytic**, **monocytic**

Mechanisms:

- output of immature cells
- production of WBC

Reasons

- the same as in leukocytosis

Leukemia

Uncontrolled production of white blood cells caused by the malignancies of the bone marrow.

Features of leukemia:

- abnormal proliferation of leukemic cells;
- organs infiltrations by leukemic cells;
- apoptosis of leukemic cells;
- suppression of normal hemopoiesis.

Etiology of leukemia

- natural or artificial ionizing radiation,
- certain kinds of chemicals (benzene and other aromatic hydrocarbons),
- some viruses (human T-lymphotrophic virus, Epstein-Barr virus),
- genetic predisposition.

Pathogenesis of leukemia

1) mutation of normal hemopoetic cells (**initiation stage**),
2) monoclonal proliferation (**promotion**) - development of primary leukemia of some hemopoetic stem.
3) polyclonal proliferation (**tumor progression stage**) - tumor obtains malignant character.

Manifestations of leukemia

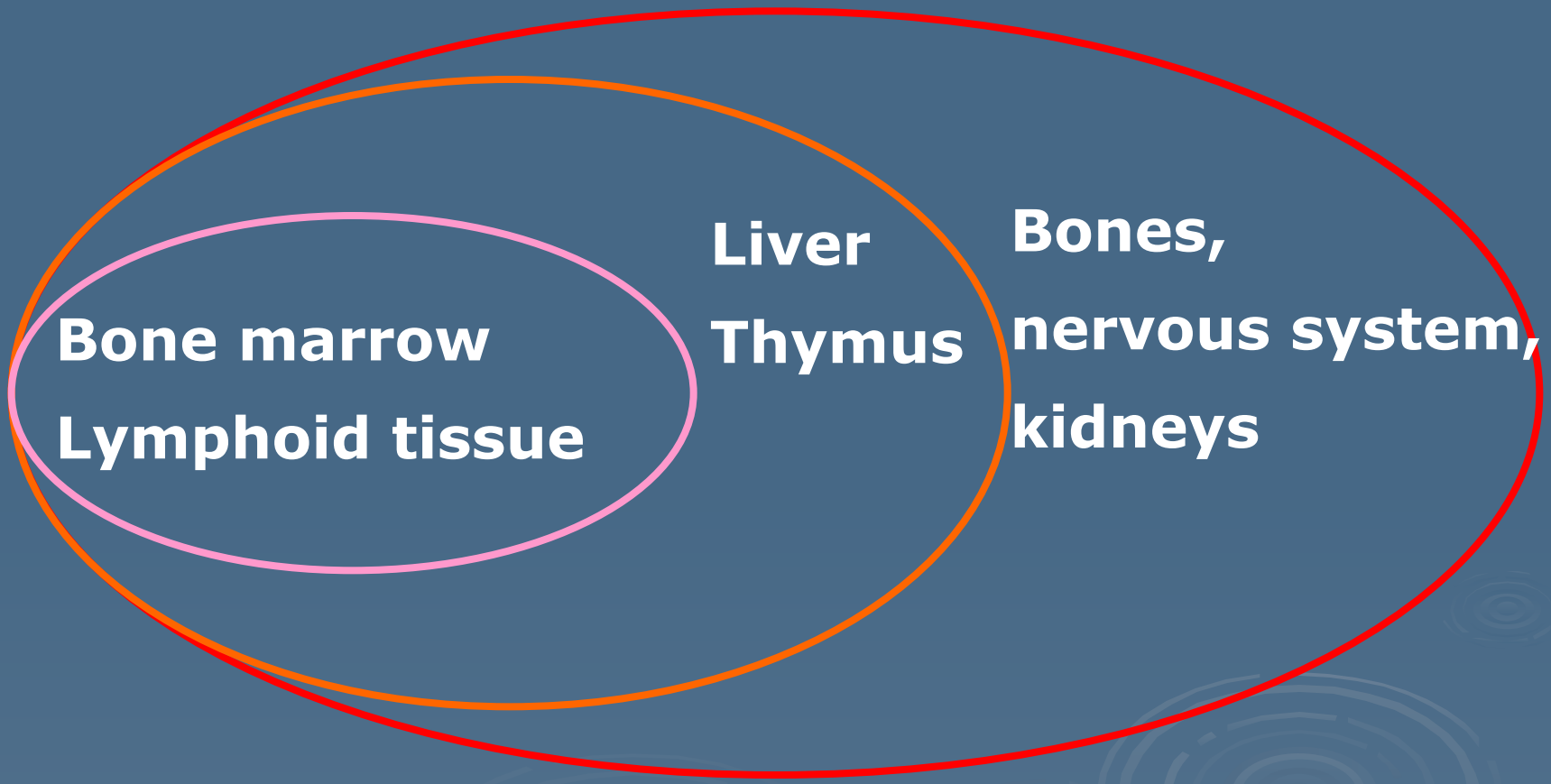
Supression of hemopoiesis:

- metaplastic anemia
- secondary immunodeficiency syndrome
- easy bruising and bleeding

Leukemic infiltration

- splenomegaly, hepatomegaly
- lymphadenopathy
- bone and joint pain

Stages of leukemic infiltration



Leukemia types

Acute leukemia

- growth of immature poorly differentiated cells
- "hiatus leukemicus" - a lack of cell stages of maturation between blasts and mature cells in leukocytic formula
- occur in children and young adults
- rapid progression and spread of the malignant cells to the organs of the body

Chronic leukemia

- growth of abnormal mature cells
- more slowlier rate of tumor progression
- mostly occurs in older people, but can theoretically occur in any age group

Leukemia classification

- **leukopenic form** - WBC count lower than $4*10^9/L$
- **aleukemic form** – WBC count lower than $10*10^9/L$.
- **subleukemic form** – 10-50 $*10^9/L$, a few blasts in peripheral blood.
- **leukemic form** – more than 50 $*10^9/L$, blasts prevalence in peripheral blood.

Leukemia classification (ICD-10)

Acute leukemias:

- **Acute Undifferentiated Leukemia** (pluripotent stem cell is affected) AUL
- **Acute Myeloblastic Leukemia** (AML)
- **Acute Lymphoblastic Leukemia** (ALL)

Chronic Leukemias:

- **Chronic Lymphocytic Leukemia** (CLL)
- **Chronic Myeloid Leukemia** (CML)

Acute myeloblastic leukemia

a cancer of the myeloid line of WBC

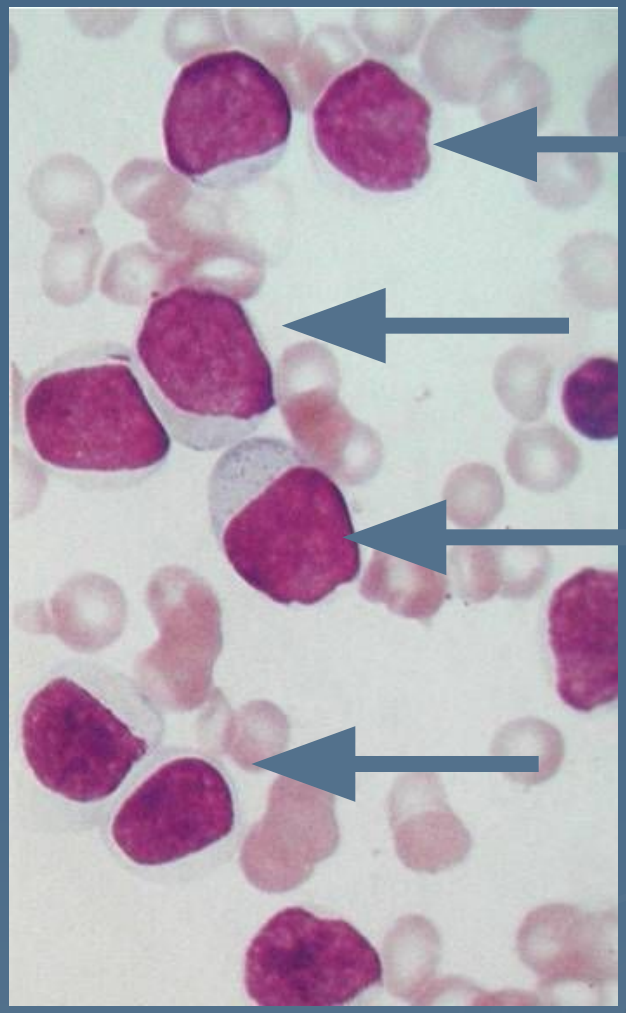
- the most common acute leukemia affecting adults
- increased number of malignant WBC displace normal hemopoiesis
- decreased count of RBC, platelets, and normal WBC.

Acute myelogenous leukemia

Common symptoms: fever, weight loss, loss of appetite.

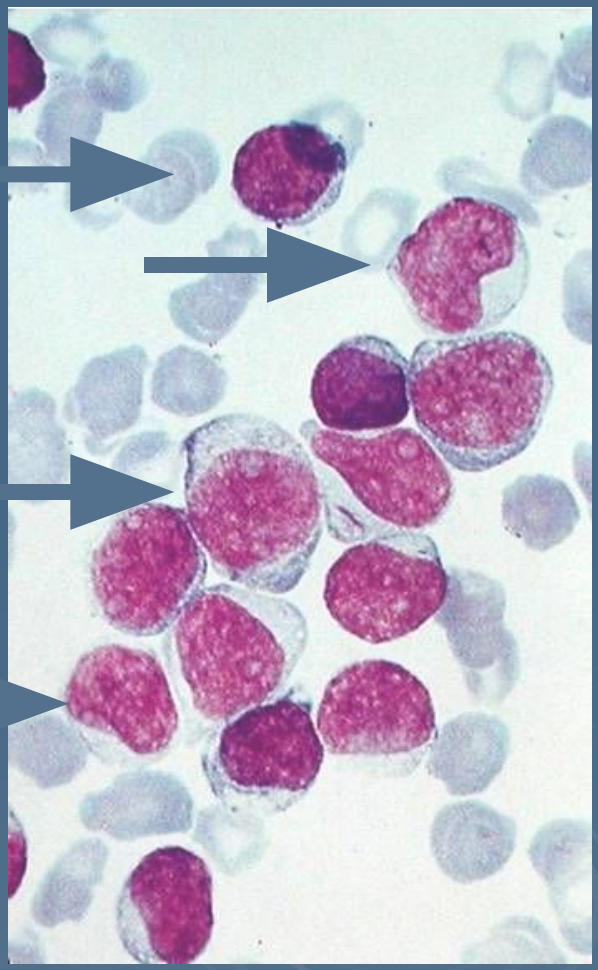
- the patient has persistent or frequent infections
- metaplastic anemia - can cause fatigue, paleness, and shortness of breath with exertion.
- lack of platelets can lead to easy bruising or bleeding with minor trauma.
- bone pain and joint pain and.
- enlargement of the spleen and lymph node swelling is not significant

Acute myelogenous leukemia



Peripheral blood

Myeloblasts



Bone marrow

Acute myelogenous leukemia

- myeloblasts in a peripheral blood and their prevalence in marrow.
- hiatus leukemicus -lack of cell stages of maturation between myeloblasts and mature neutrophils

Eosinophils	Basophils	Neutrophils						Lymphocytes	Monocytes
		myeloblasts	promyelocytes	myelocytes	juvenile	band	segmented		
0	0	62	0	0	0	3	23	11	1

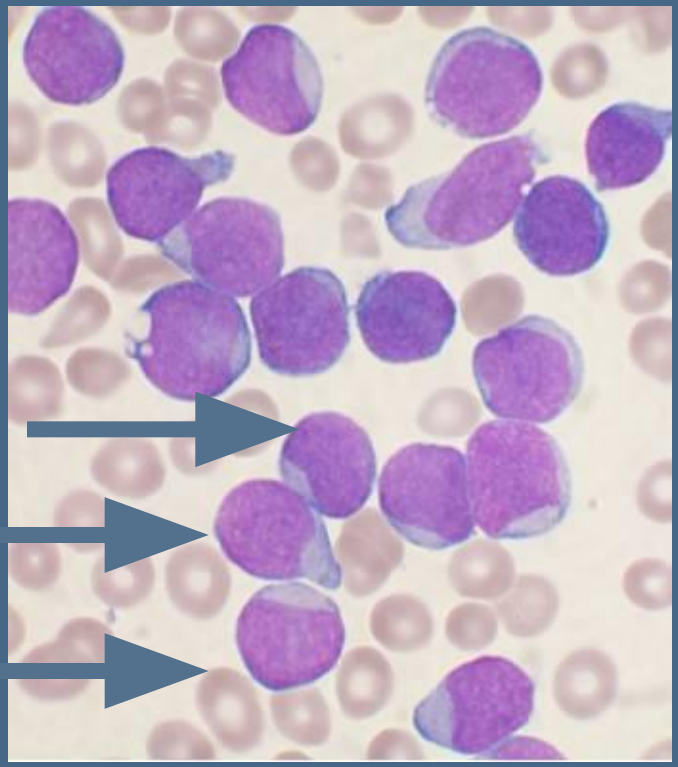
- absence of eosinophils and basophils in the leukocytic formula.
- anemia and thrombocytopenia; they indicate leukemia severity.

Acute lymphoblastic leukemia

- children of 2-4 years old
- affection of lymphatic nodes and spleen.
  - enlarged mediastinal nodes there are dry cough, shortness of breath;
  - enlarged mesoperitoneal nodes can cause stomachaches.
- Pains in bones (more often in shins)
- Other clinical signs: fatigue, pallor, infection, and easy bruising and bleeding

Acute lymphoblastic leukemia

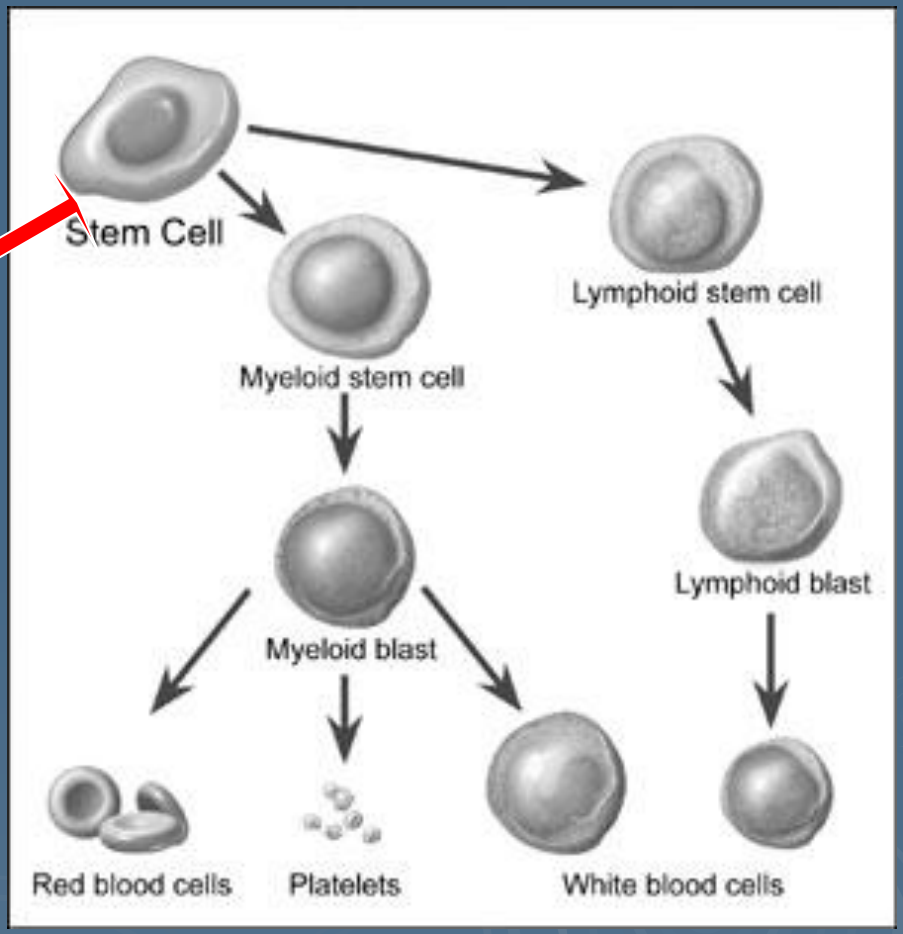
Lymphoblasts in peripheral blood smear



Eosinophils	Basophils	Neutrophils				Lymphocytes					Monocytes
		myelocytes	juvenile	band	segm.	lymphoblasts	prolymphocytes	big lymphocytes	medium L.	small L.	
0	0	0	0	1	16	61	0	0	0	19	3

Undifferentiated leukemia

- Acute undifferentiated leukemia affects pluripotent blood stem cell.
- This is one of the most malignant forms of acute leukemia (fast progress, severe course).



Chronic myelogenous leukemia

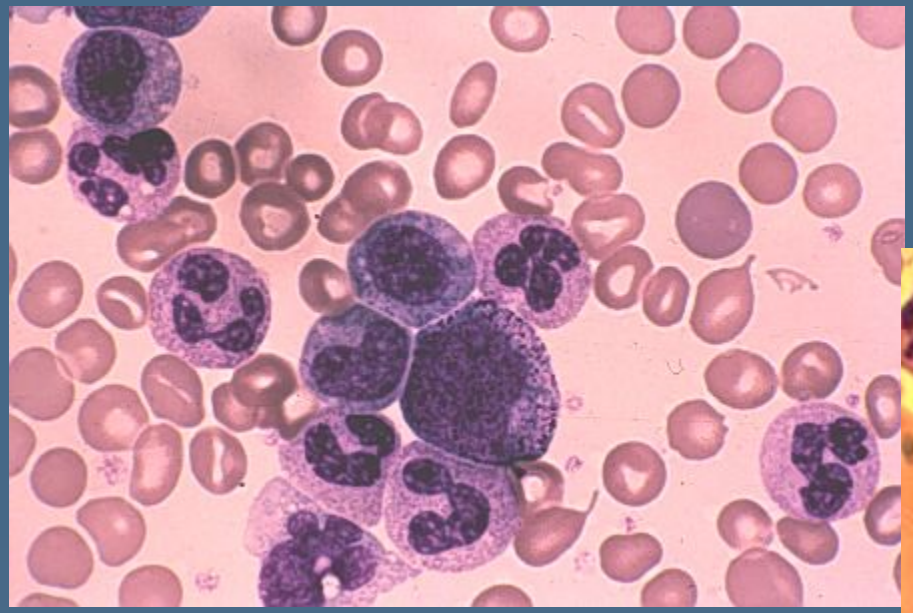
- abnormal proliferation of myeloid cells
- characteristic chromosomal translocation called the Philadelphia chromosome.
- Symptoms: malaise, fever, increased susceptibility to infections, anemia, and thrombocytopenia.
- enlargement of spleen and liver (due to leukemic infiltration)
- fat marrow of long bones is replaced with myeloid tissue.

Chronic myelogenous leukemia

- detecting the Philadelphia chromosome
- absence of hiatus leukemicus
- eosinophil-basophil association

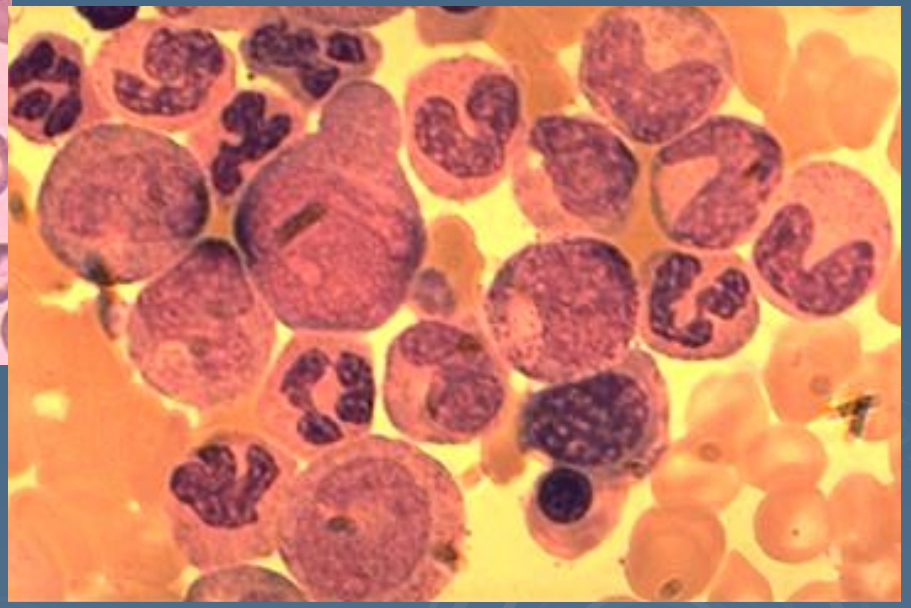
Eosinophils	Basophils	Neutrophils						Lymphocytes	Monocytes
		myeloblasts	promyelocytes	myelocytes	juvenile	band	segmented		
8	4	6	10	16	15	13	12	10	6

Chronic myelogenous leukemia



peripheral blood

bone marrow



Chronic myelogenous leukemia

- **Chronic phase**: mild symptoms of fatigue or abdominal fullness.
- **Accelerated phase:** further increase in granulocytes count, decrease of RBC and platelets, increasing splenomegaly.
- **Blast crisis;** behaves like an acute leukemia, >20% myeloblasts in peripheral blood .

Chronic lymphogenous leukemia

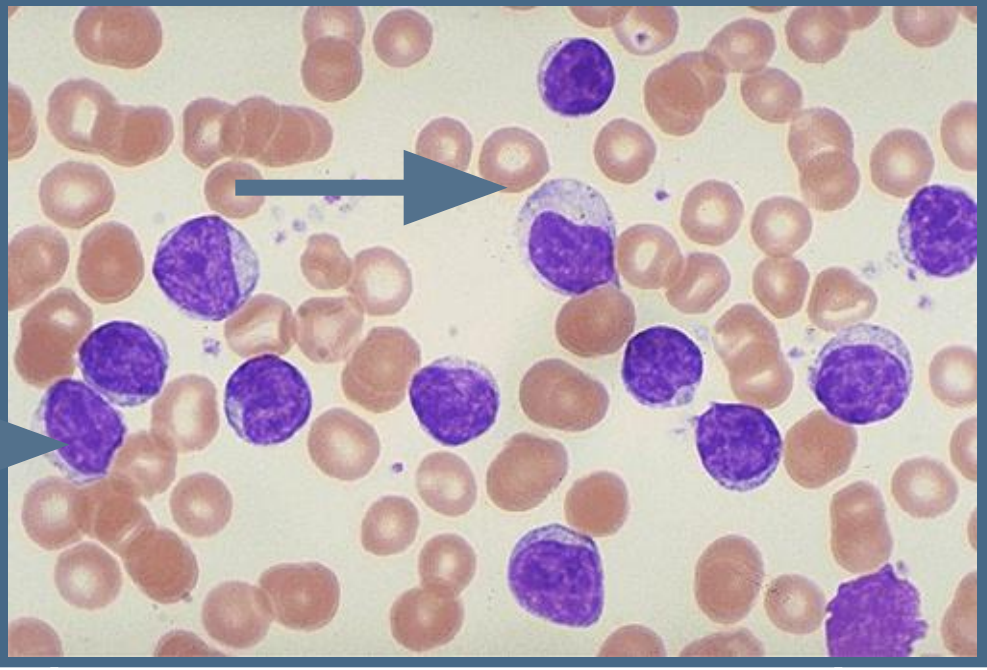
- lymphoid hyperplasia of hemopoetic organs (lymphatic nodes, spleen, marrow)
- accompanied by lymphoid infiltration of other organs and tissues.
- suppression of myelopoesis (anaemia, granulocytopenia and trombocytopenia.
- the bulk of CLL is formed by mature lymphocytes

Chronic lymphogenous leukemia

- CLL is considered to be benign, non-malignant tumour.
- B-population of lymphocytes is mainly affected.
- severe violations of immunity.
- predominance of mature lymphocytes
- presence of all lymphocytes maturation forms
- Gumprekht’s shadows

Chronic lymphogenous leukemia

lymphocytes



Eosinophils	Basophils	Neutrophils				Lymphocytes					Monocytes
		myelocytes	juvenile	band	segm.	lymphoblasts	prolymphocytes	big lymphocytes	medium L.	small L.	
0	0	0	0	2	36	5	9	11	14	19	3