

**MUNI  
MED**

Department  
of Histology  
and Embryology

# BLOOD AND HEMATOPOIESIS 2024

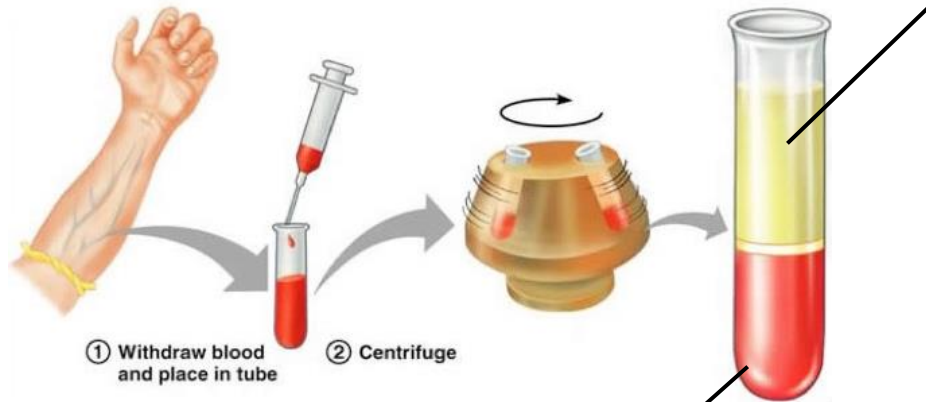
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Department of Histology and Embryology  
LF MU

# BLOOD

## Blood is body fluid

- transport medium (O<sub>2</sub>, CO<sub>2</sub>, metabolites, hormones, nutrients...)
- homeostasis of inner body environment (thermoregulation, acidobasic equilibrium, oncotic pressure)
- integrity of cardiovascular system (clotting cascade)
- immune reactions



## plasma

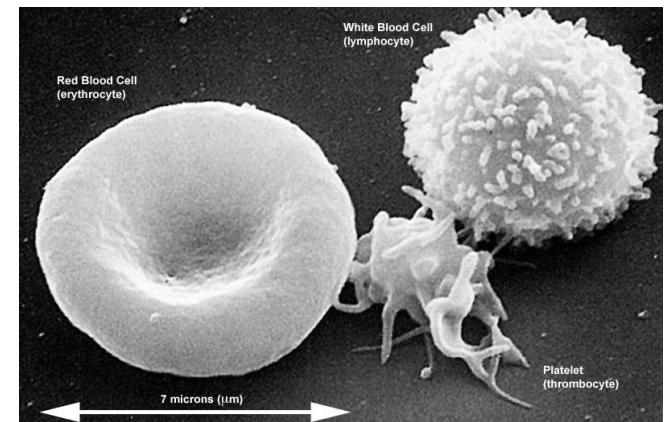
- ions, proteins, low mass organic compounds
- fluid ECM



**Blood can be considered as a specialized connective tissue**

## formed blood elements

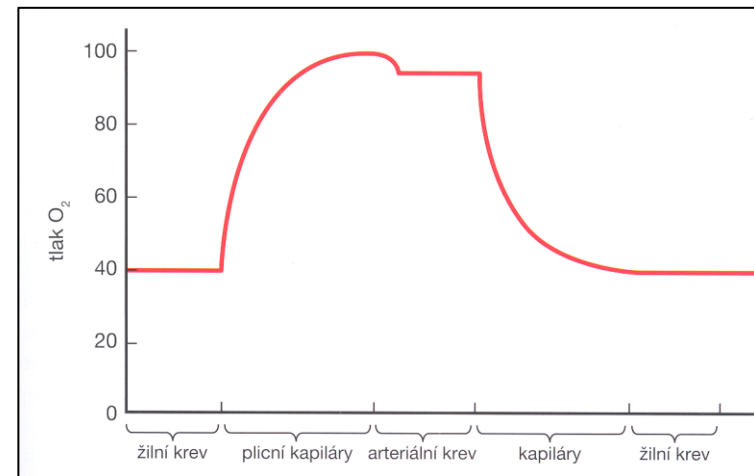
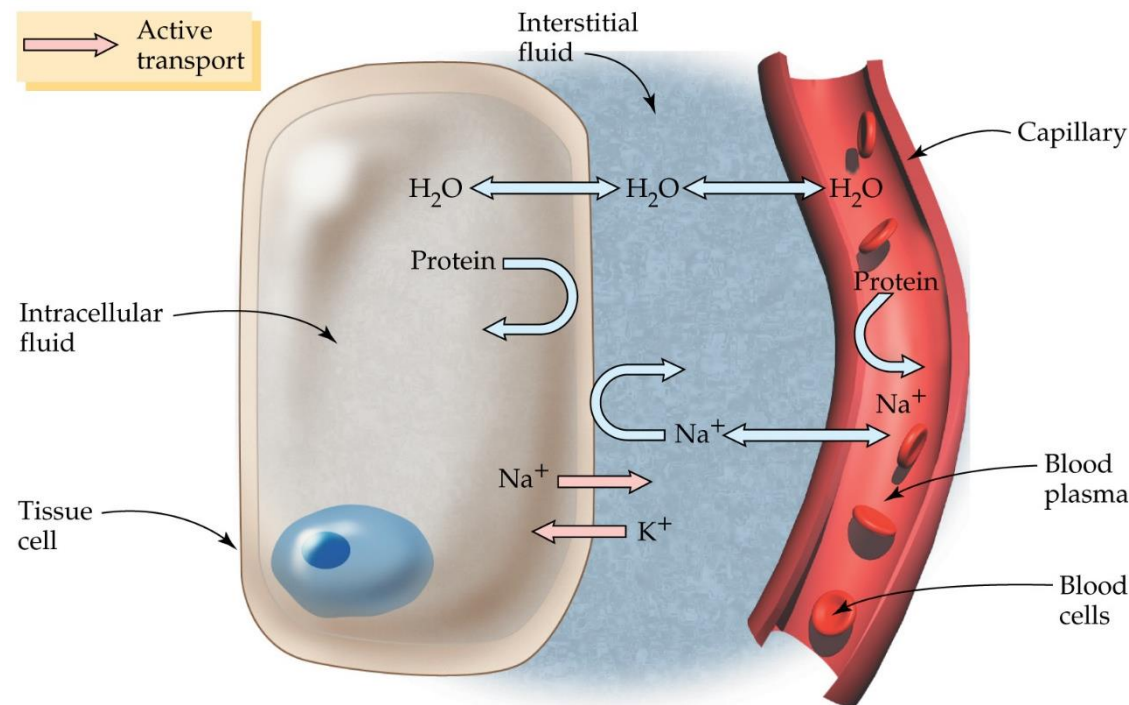
- erythrocytes
- leukocytes
- thrombocytes



# BLOOD PLASMA AND TISSUE FLUID

## plasma

- 2,8-3,5 l
- pH 7.4 ( $\pm 0.05$ )
- ~ 92% **water**
- ~ 1% **ions** ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ), **low mass organic compounds** (glucose, aminoacids, cholesterol, lipids, waste products of metabolism), **respiration gases**
- ~ 7% **proteins** (albumins, globulins, fibrinogen)



Venous blood

Lung capillaries

Arterial blood

Capillaries

Venous blood

# IONS AND LOW MASS MOLECULES OF BLOOD PLASMA (~1%)

- ~ 1% **ions** ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ), **low mass organic compounds** (glucose, aminoacids, cholesterol, lipids, waste products of metabolism), **respiration gases**

	Sodium	136–148 mmol/l	Osmotic pressure, volume, pH
	Potassium	3,7–5,0 mmol/l	Membrane potential of cells (nerve, muscle)
Cations	Calcium	2,15–2,61 mmol/l	Permeability of membranes, blood clotting, neuromuscular junctions
	Magnesium	0,66–0,94 mmol/l	Cofactor of enzymes, neuronal conduction
	Iron ♂	12–27 $\mu\text{mol/l}$	Cofactor of enzymes, in hem of hemoglobin
	Iron ♀	10–24 $\mu\text{mol/l}$	
	Copper	12–22 $\mu\text{mol/l}$	Cofactor of enzymes
	Chlorides	95–110 mmol/l	Osmotic pressure, volume, pH
Anions	Bicarbonates $[\text{HCO}_3]^-$	22–26 mmol/l	Transport of $\text{CO}_2$ , buffer - pH
	$\text{P}_i$	0,6–1,4 mmol/l	Buffer - pH
	Iodide	276–630 $\mu\text{mol/l}$	Hormones of thyroid gland

Memorizing of this table is not necessary for completing our course 😊



# IONS AND LOW MASS MOLECULES OF BLOOD PLASMA (~1%)

- ~ 1% **ions** ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^+$ ,  $\text{Mg}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ), **low mass organic compounds** (glucose, aminoacids, cholesterol, lipids, waste products of metabolism), **respiration gases**

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Glucose	3,3–6,1 mmol/l
Aminoacids	2,3–3,9 mmol/l
Urea	3,0–7,6 mmol/l
Lipids	4–9 g/l
Triacylglycerols	0,5–1,8 mmol/l
Phospholipids	1,8–2,5 g/l
Creatinine	55–110 $\mu\text{mol/l}$
Cholesterol (total)	3,5–5,2 mmol/l
Bilirubin	3,3–18,0 $\mu\text{mol/l}$
Lactate	0,55–2,22 mmol/l

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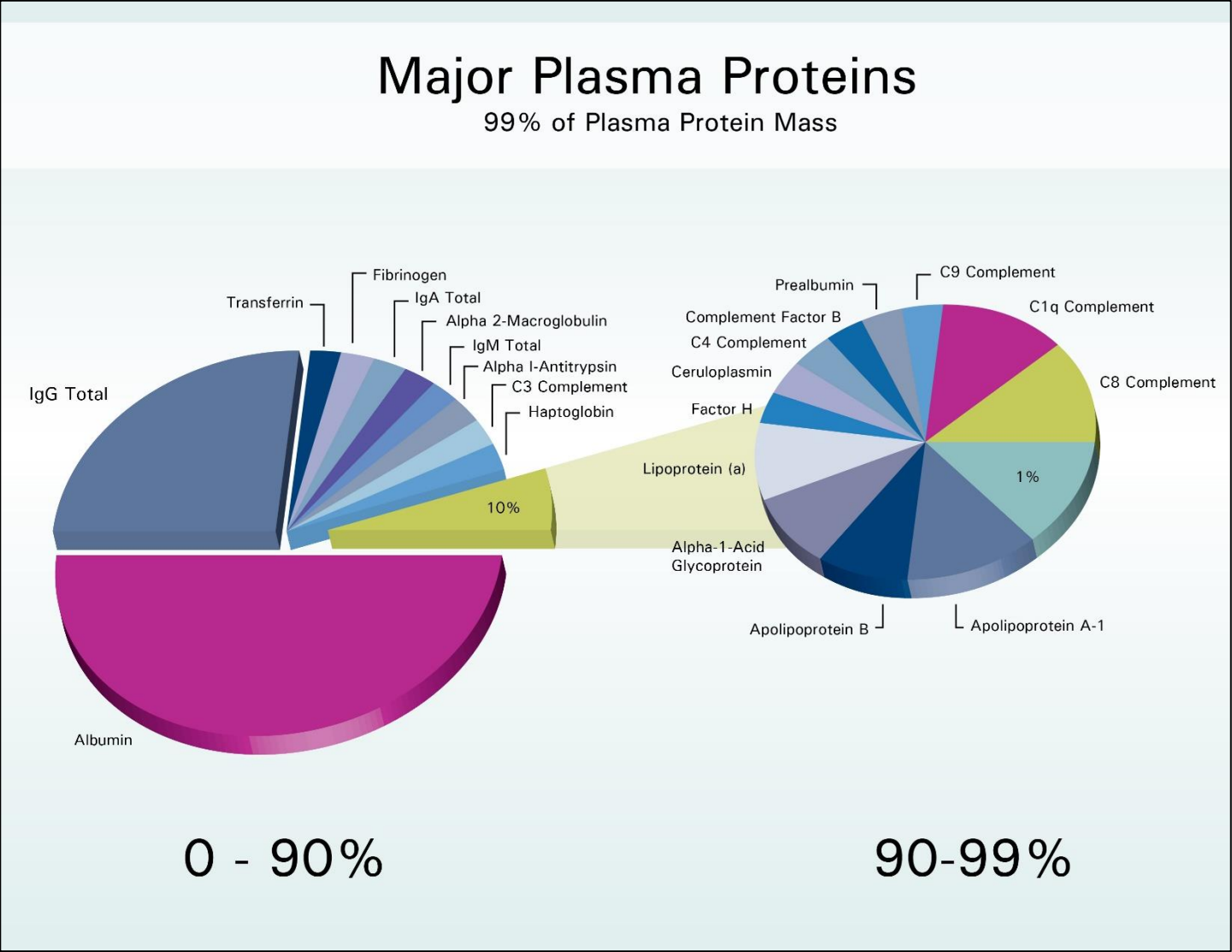
But what is important to know is that:



**COMPOSITION OF BLOOD PLASMA IS CONSTANT**  
and it is regulated in narrow range → essential for **clinical medicine**

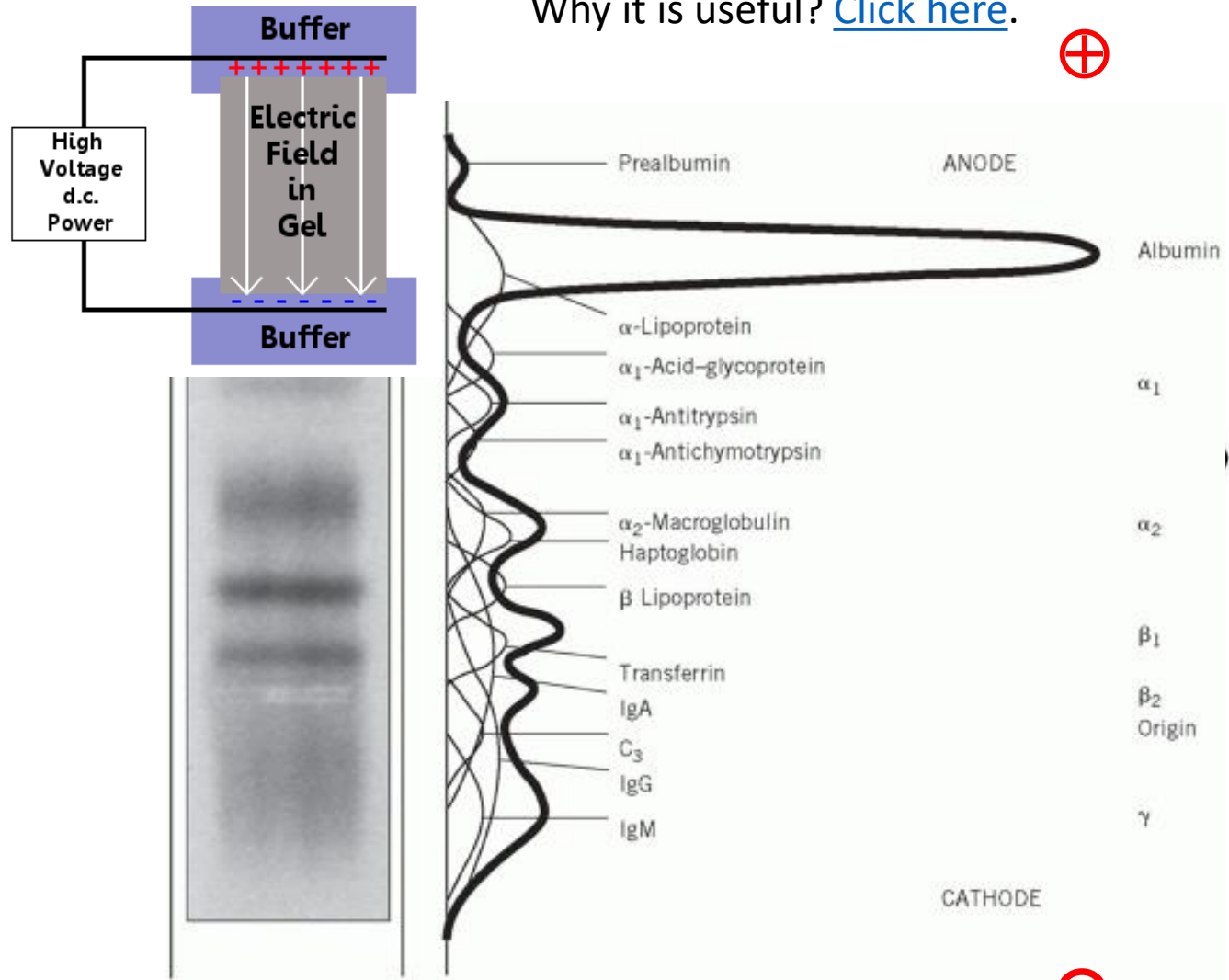
# PROTEINS OF BLOOD PLASMA (7%)

- oncotic blood pressure
- transport
- coagulation
- immune response
- regulatory proteins



# PROTEINS OF BLOOD PLASMA (7%)

- **prealbumin**
- transport
- **albumin**
- 68kDa
- transport
- osmotic pressure
- **α1 region**
- α1 lipoprotein (HDL)
- α1 acid glycoprotein
- α1 antitrypsin
- (α1 fetoprotein)
- **α2 region**
- α2 macroglobulin
- haptoglobin
- **β1 region**
- transferrin
- hemopexin
- β lipoprotein (LDL)
- C4 (complement)
- **β2 region**
- CRP
- fibrinogen
- β2 microglobulin
- C3 (complement)
- **γ region**
- IgA, IgG, IgM



Why it is useful? [Click here.](#)

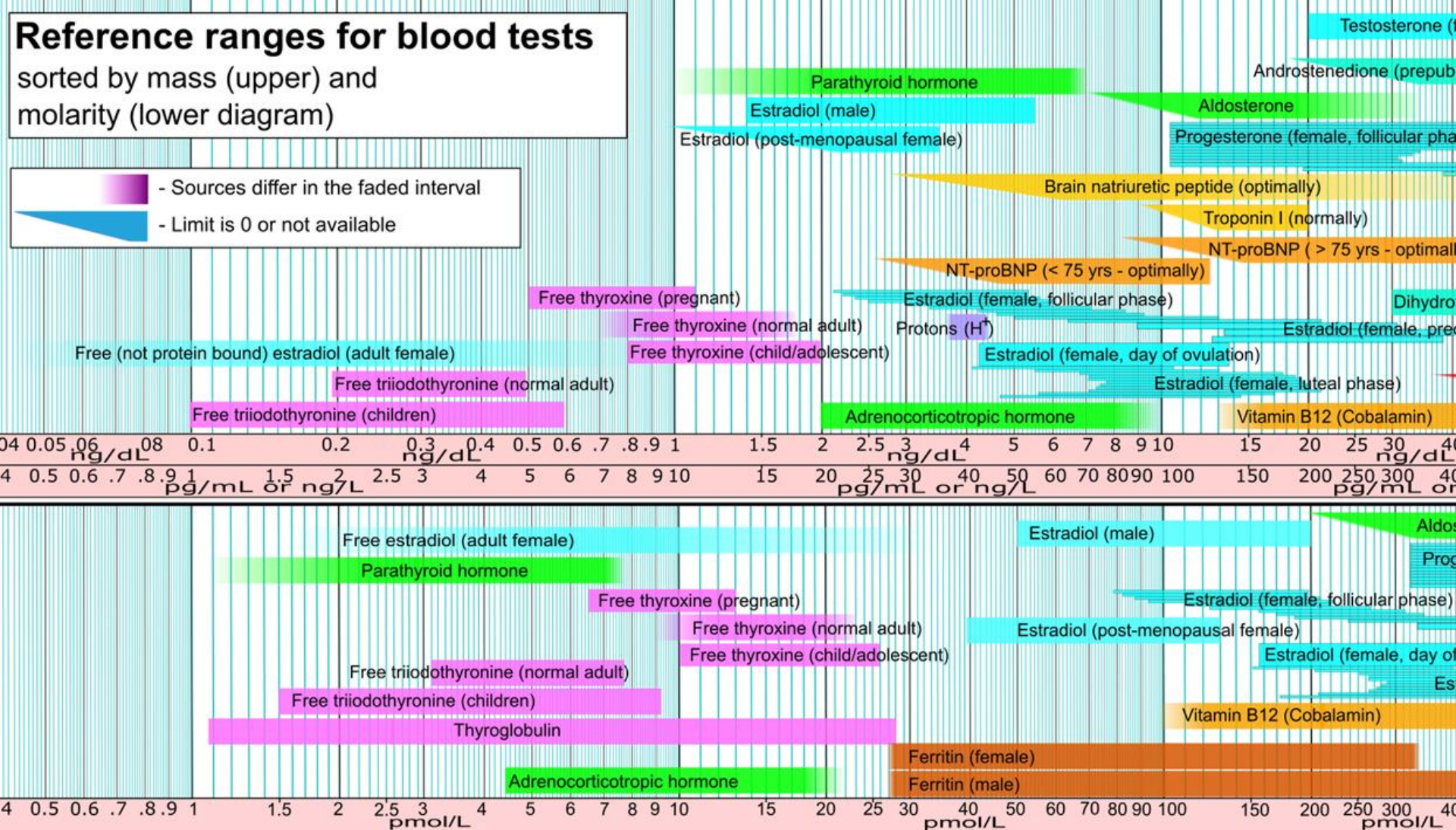


. Electrophoretic separation of serum proteins  
**A.** Electrophoretogram of normal serum on cellulose acetate strip  
**B.** Densitometric scanning from cellulose acetate strip converts bands to characteristic peaks of albumin, α<sub>1</sub>-globulin, α<sub>2</sub>-globulin, β-globulin and γ-globulin

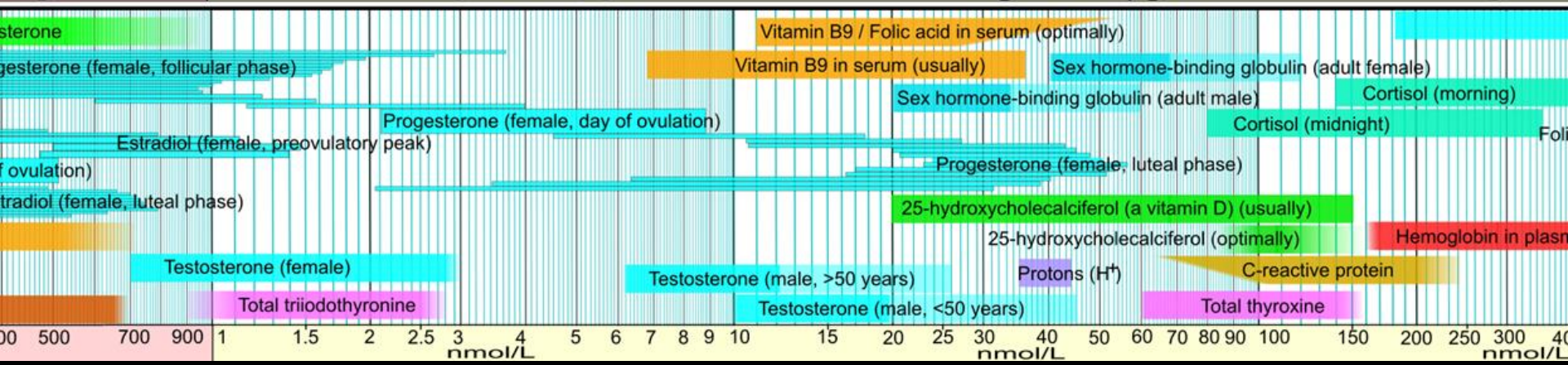
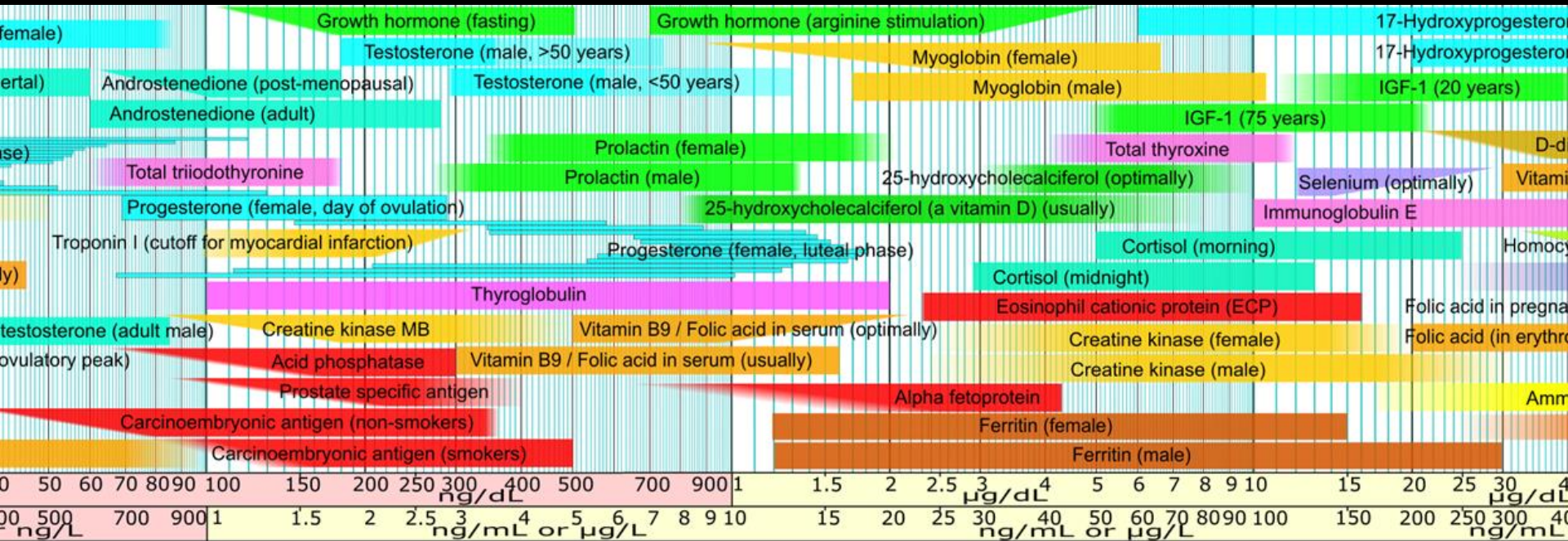
# Reference ranges for blood tests

sorted by mass (upper) and molarity (lower diagram)

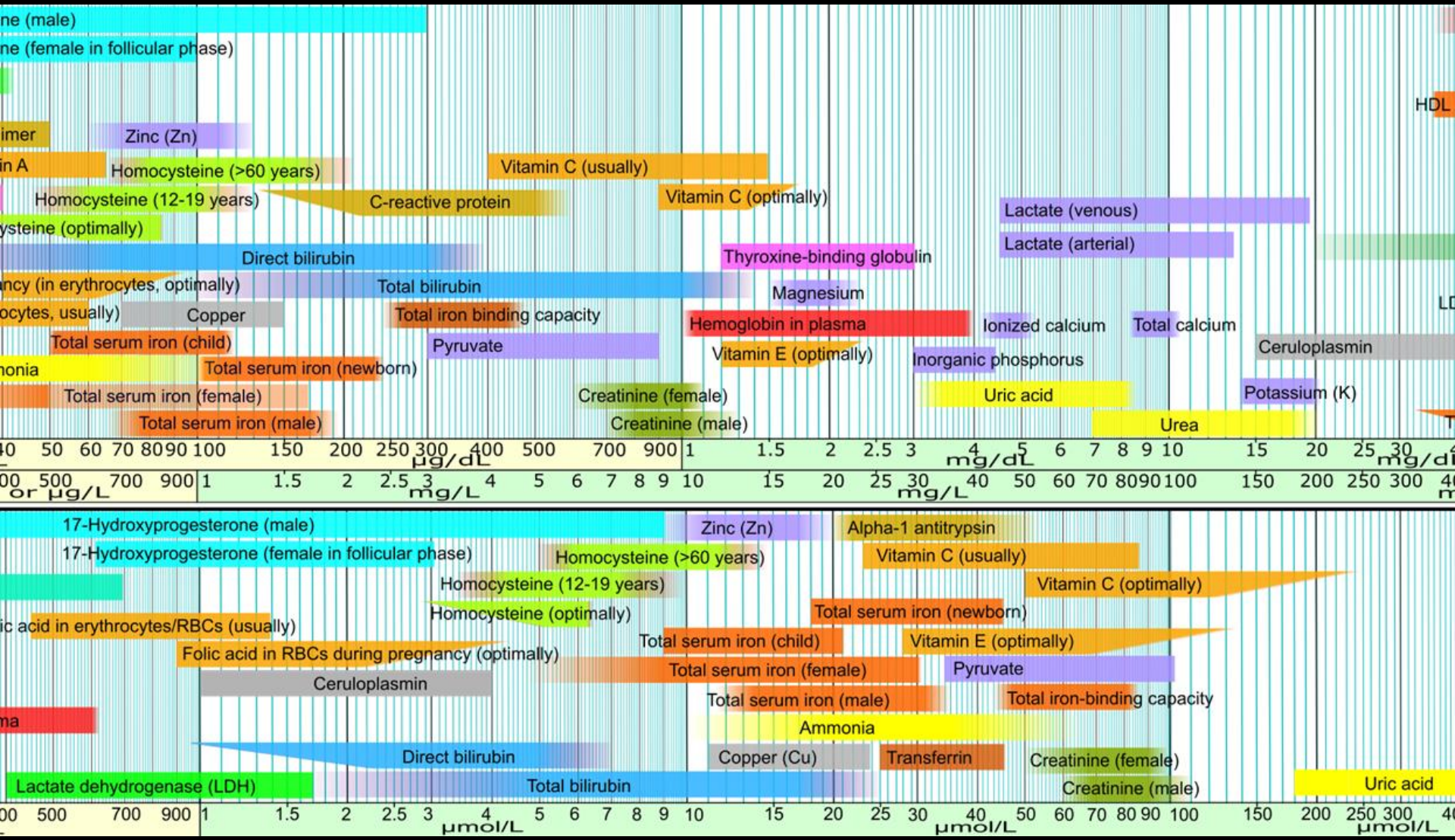
- Sources differ in the faded interval
- Limit is 0 or not available

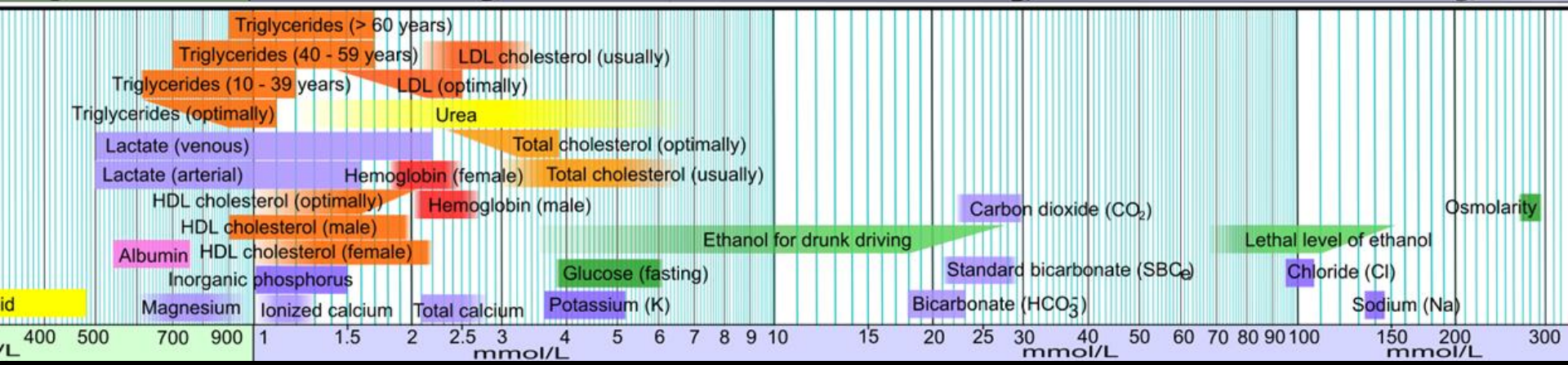
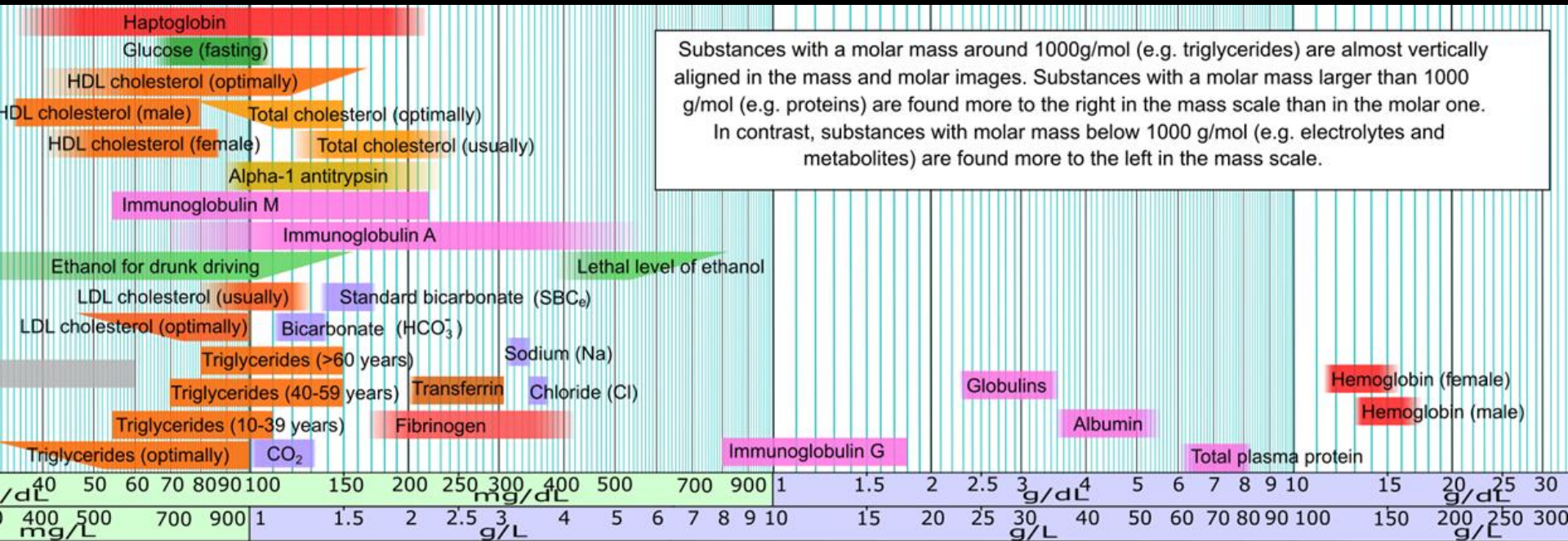








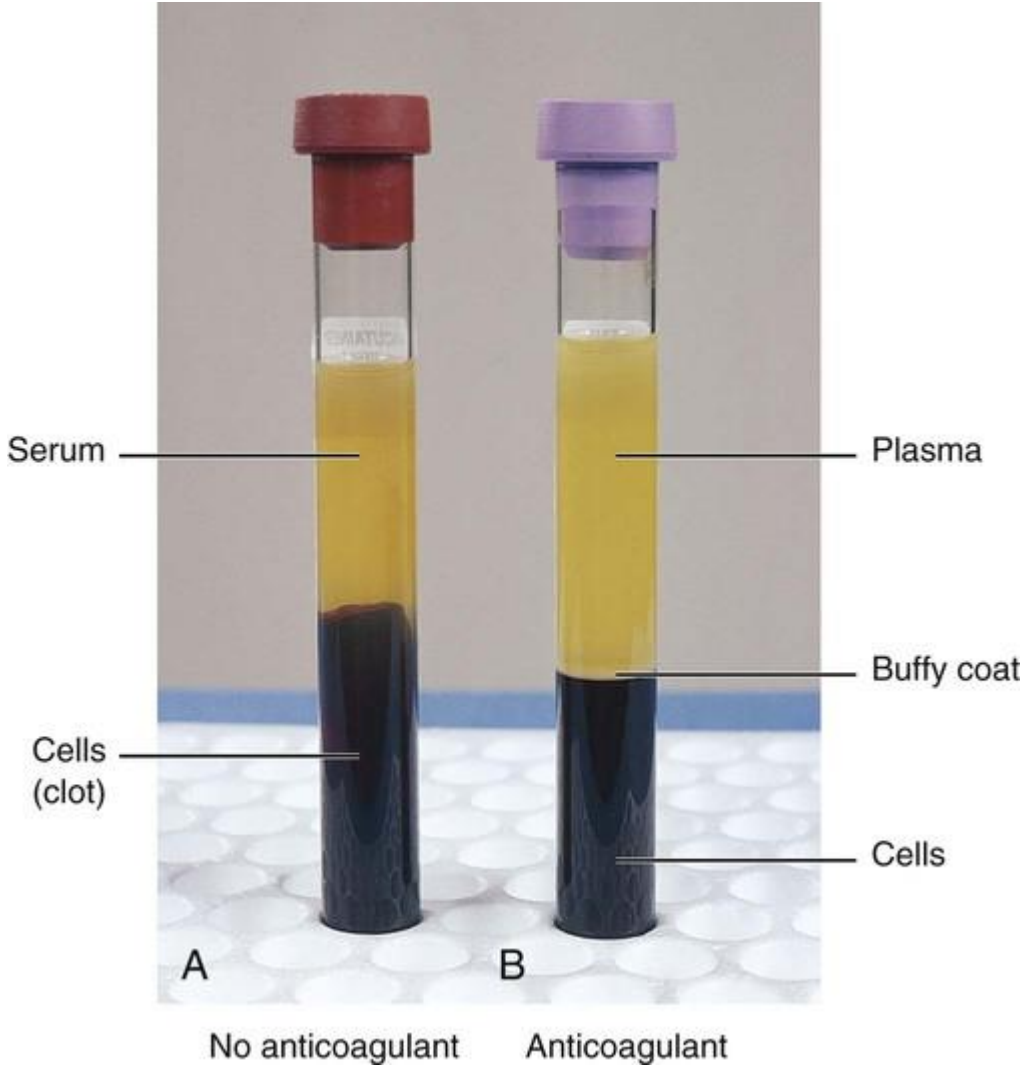






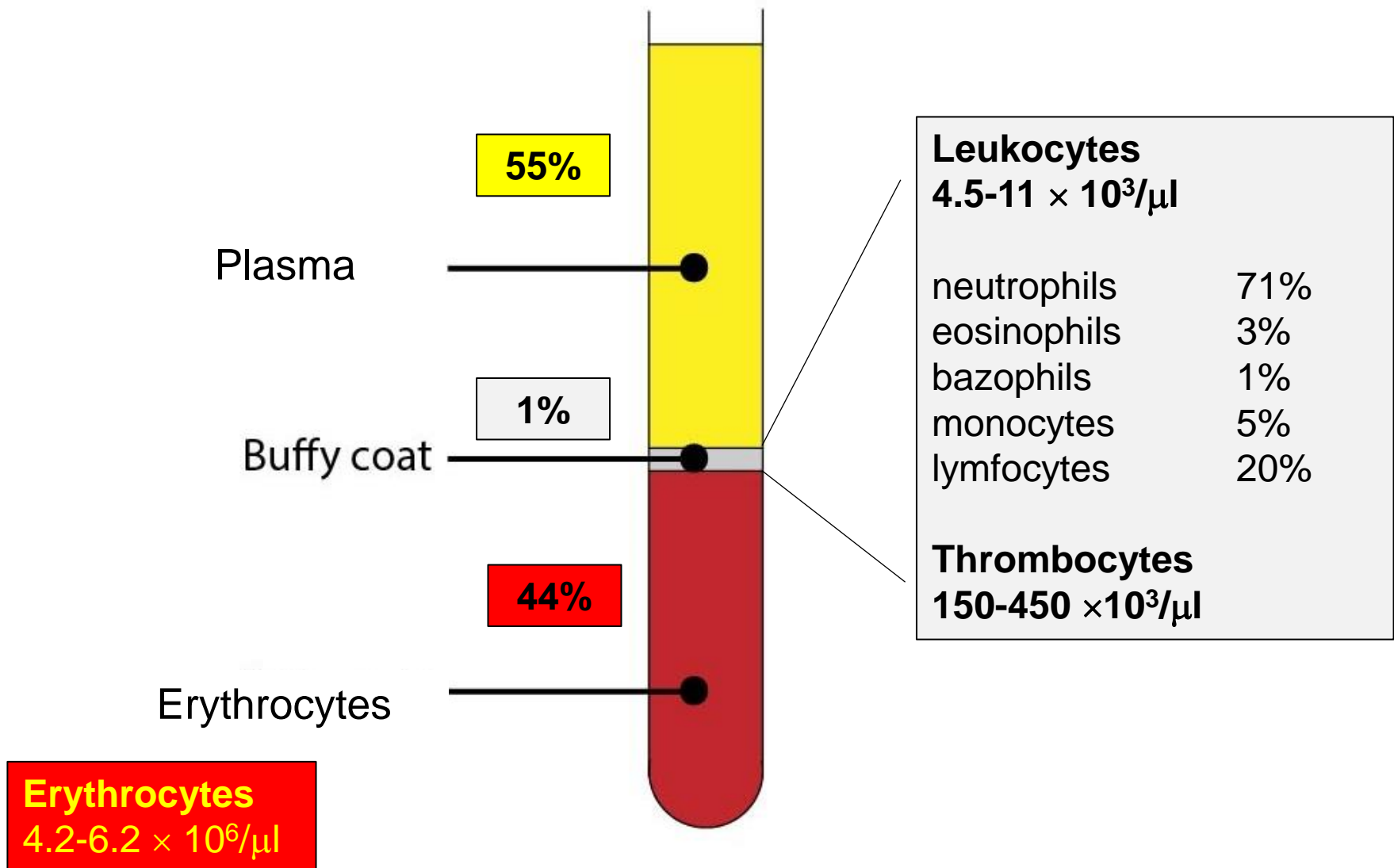
# BLOOD PLASMA AND SERUM

- serum ≠ plasma





# FORMED BLOOD ELEMENTS



# HEMATOCRIT

Ratio of erythrocyte mass volume to volume of full blood

Erythrocytes  
 $4.2-6.2 \times 10^6/\mu\text{l}$

## HEMATOCRIT



$47 \pm 5\%$

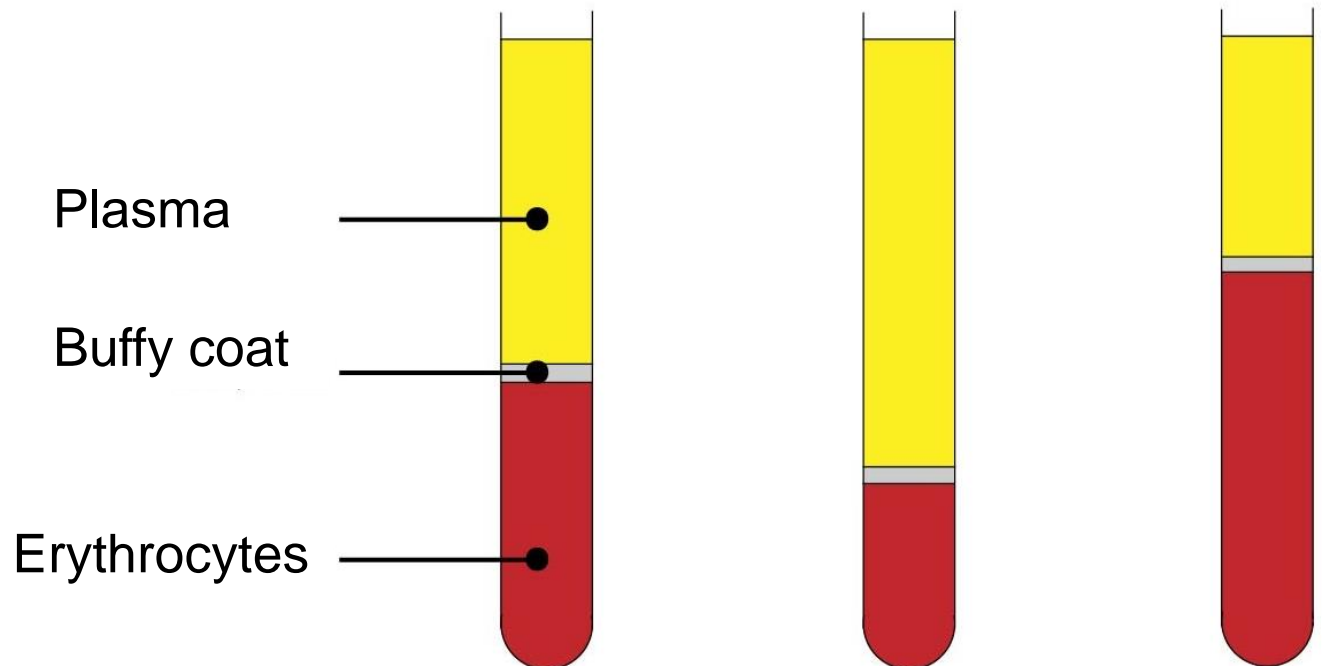


$42 \pm 4\%$

Normal

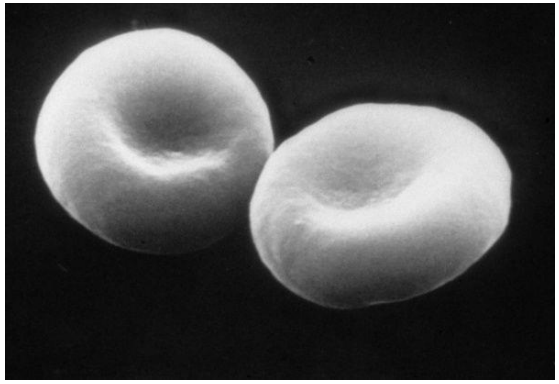
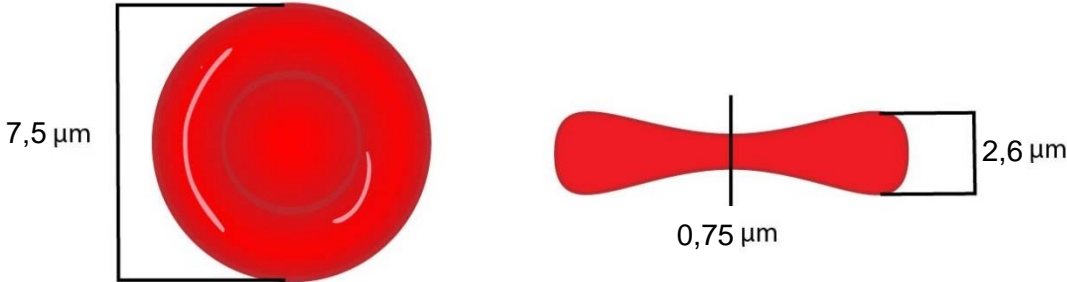
Erythropenia

Polycythemia



# ERYTHROCYTES

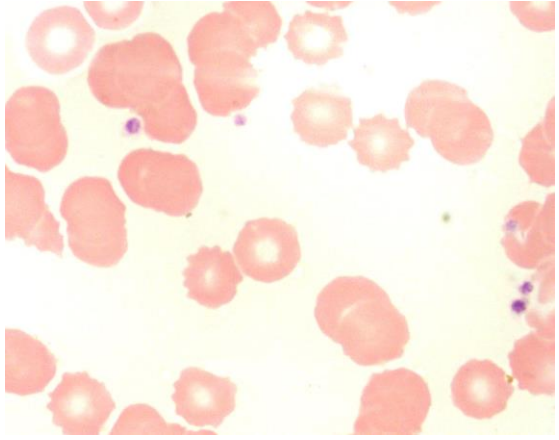
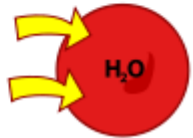
Size depends on **osmotic pressure of environment**



Hypertonic

Isotonic

Hypotonic

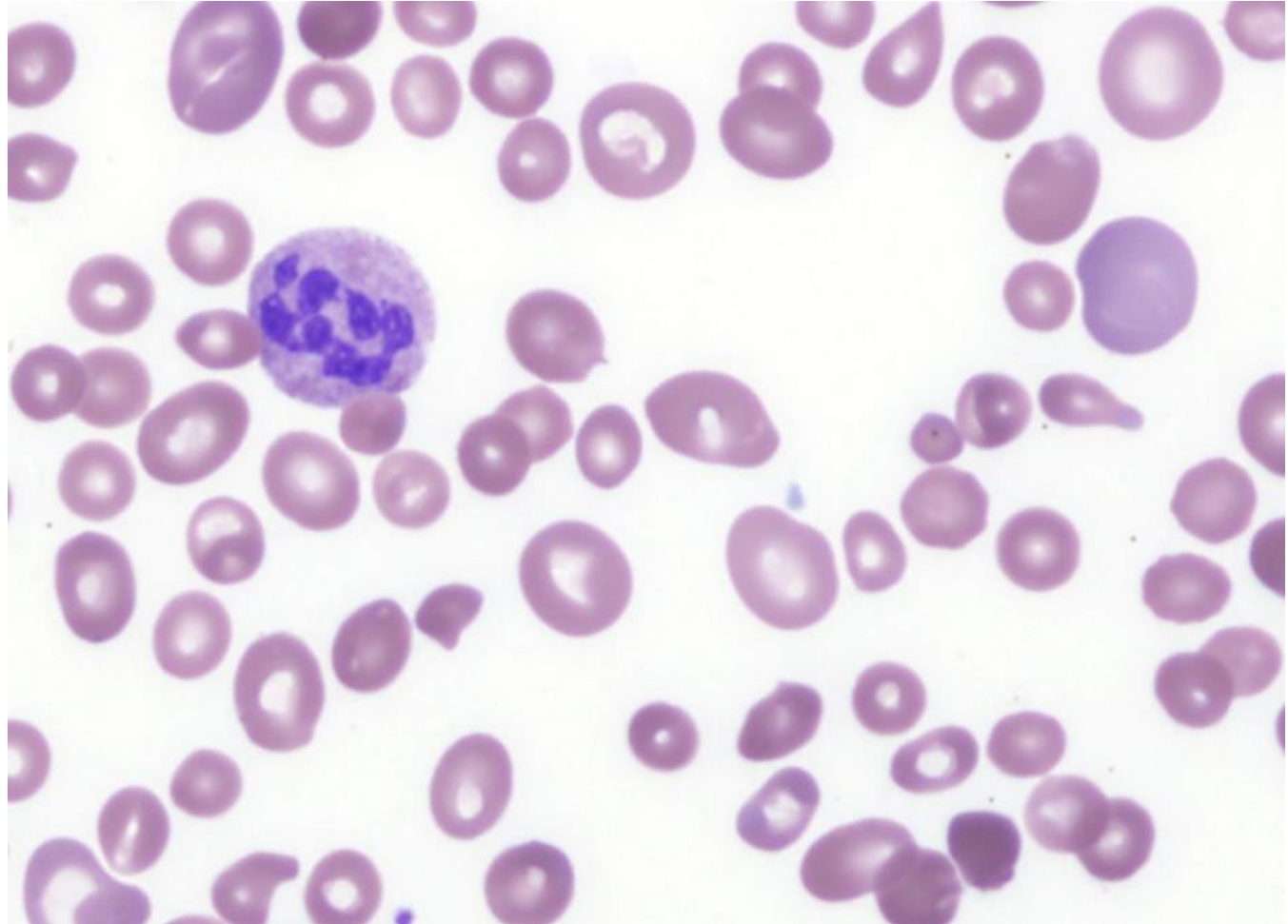


# ERYTHROCYTES

## Deviations from normal size

- **anisocytosis**

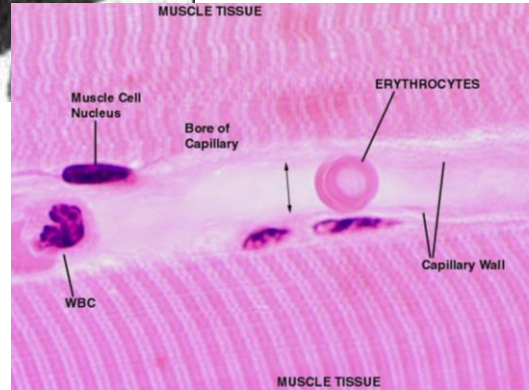
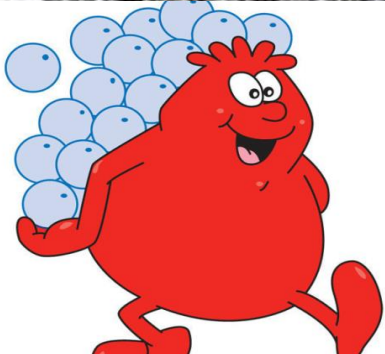
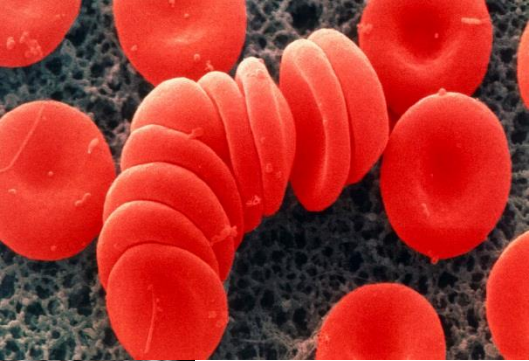
- macrocytes ( $>9\ \mu\text{m}$ )
- microcytes ( $<6\ \mu\text{m}$ )





# ERYTHROCYTES

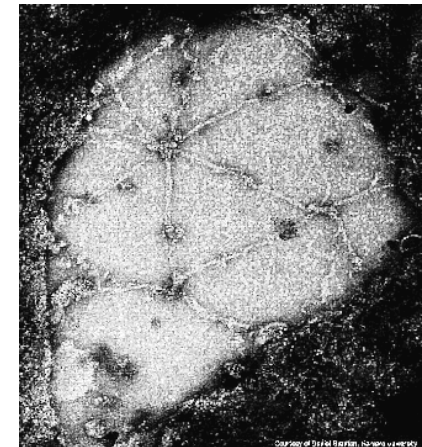
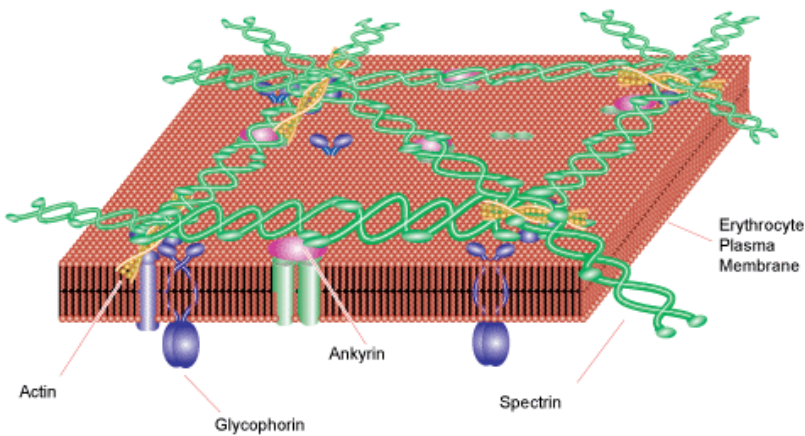
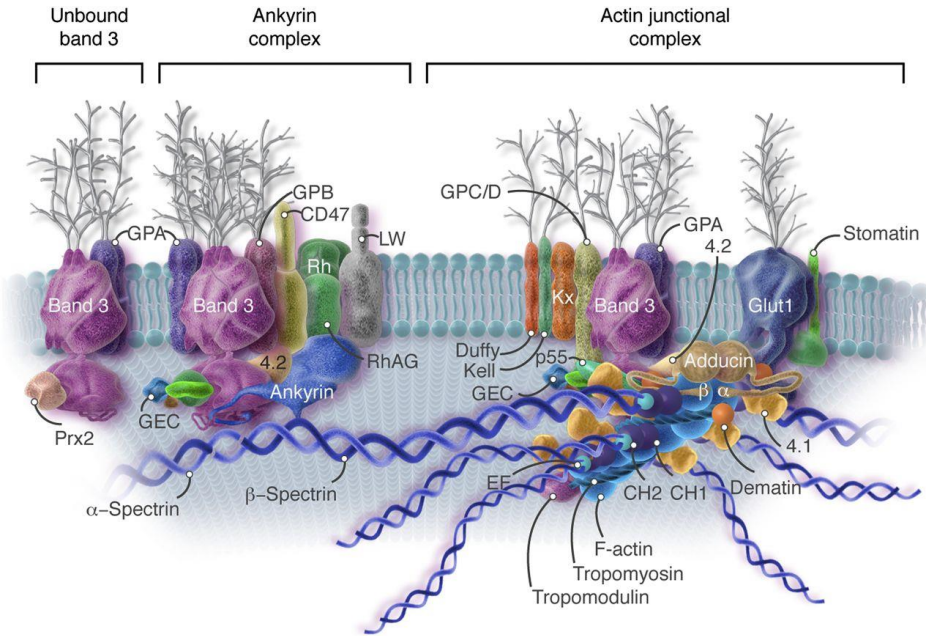
Erythrocyte is amazingly flexible cell



# ERYTHROCYTES

## Shape of erythrocytes

- **integral proteins**
  - band 3, glycoprotein A (ion transporters)
- **spectrin**
- **ankyrin**
- **actin and actin associated proteins**
  - tropomodulin, tropomyosin
- **hemoglobin**

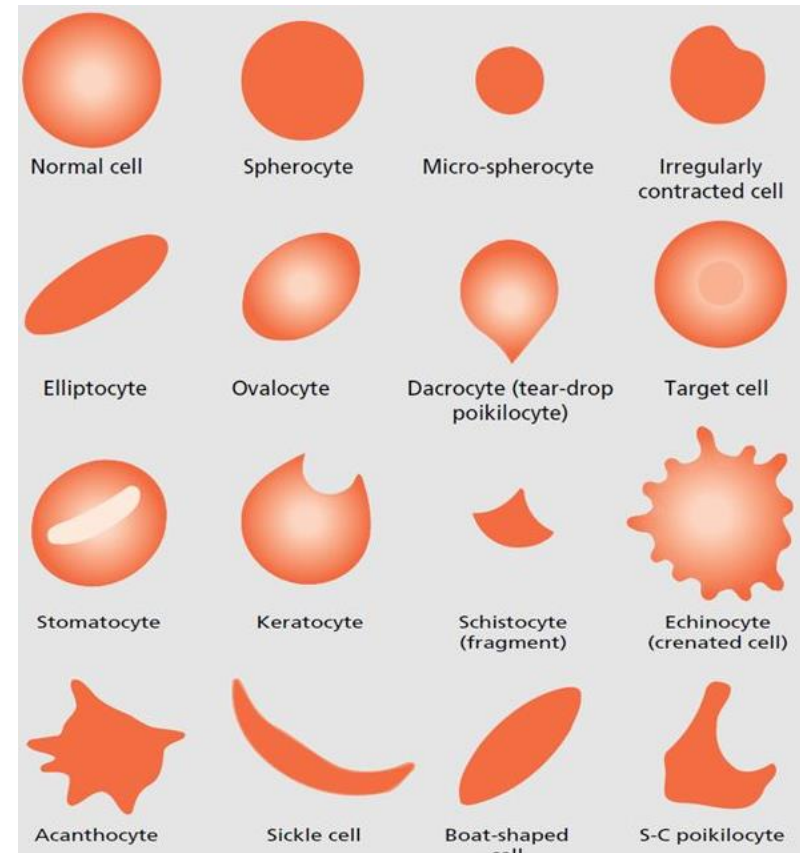
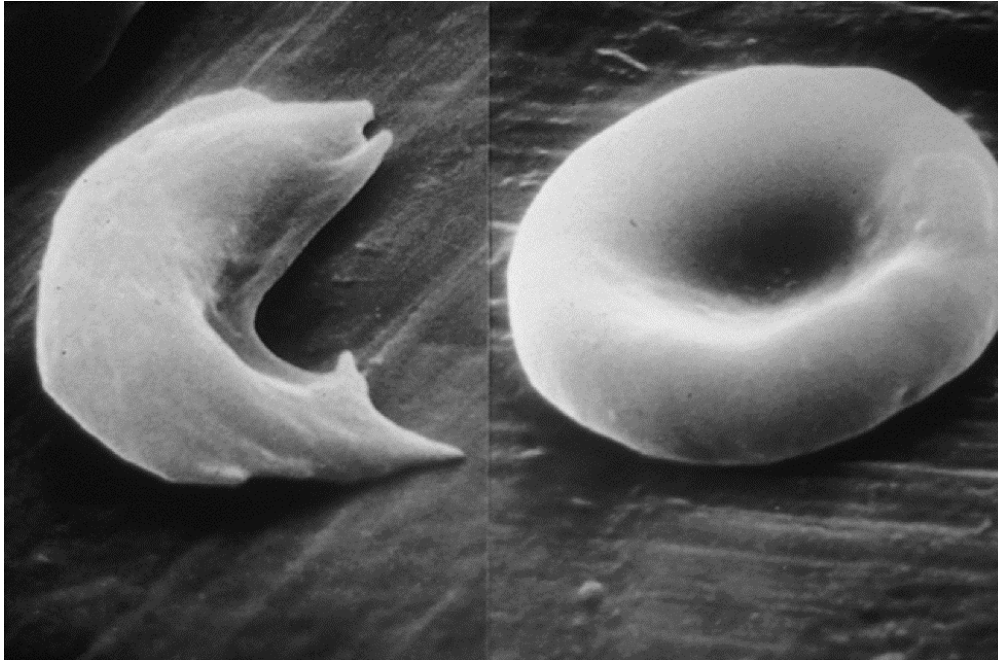




# ERYTHROCYTES

## Deviations from biconcave shape

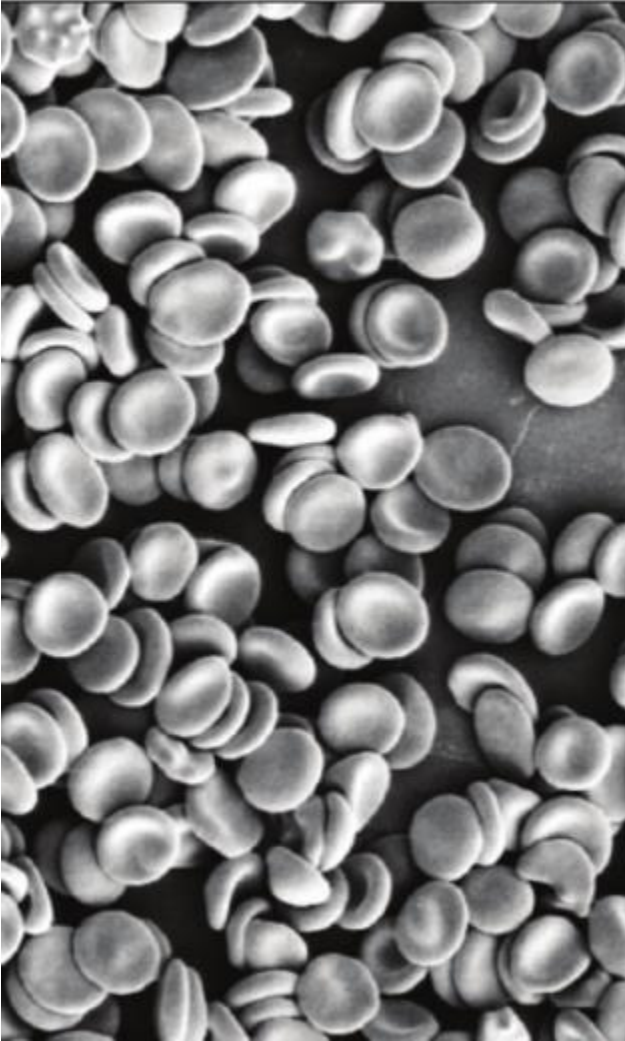
- **poikilocytosis**
  - **acanthocytes** (irregular spikes)
  - **codocytes** („tyre “)
  - **echinocytes** (spiked membrane)
  - **eliptocytes** (elliptic)
  - **spherocytes** (spheroidal)
  - **stomatocytes** (some parts missing or other irregularities)
  - **drepanocytes** (sickle)
  - **dacrocytes** (tear drop)



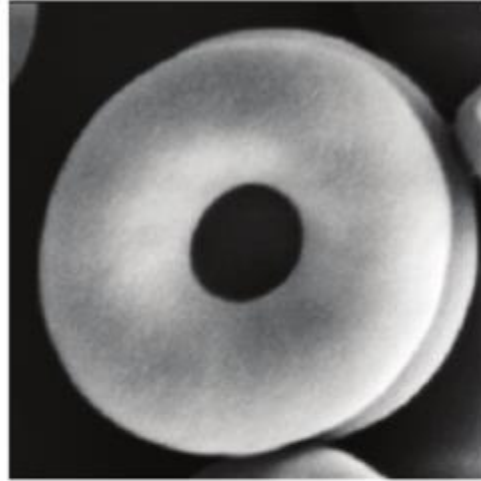
# ERYTHROCYTES

## Deviations from biconcave shape

Normal

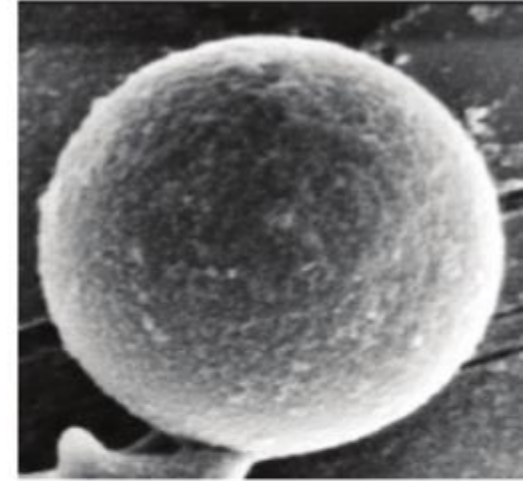


Codocyte

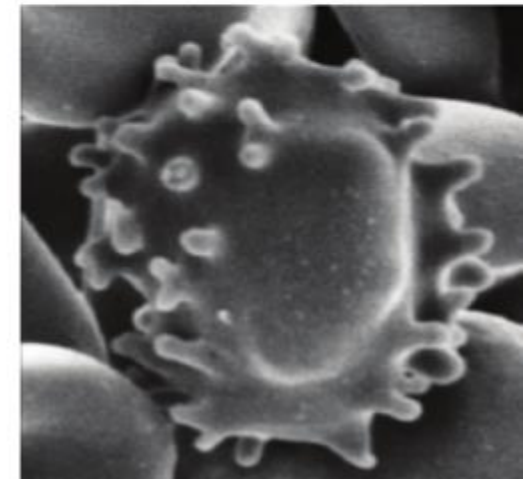
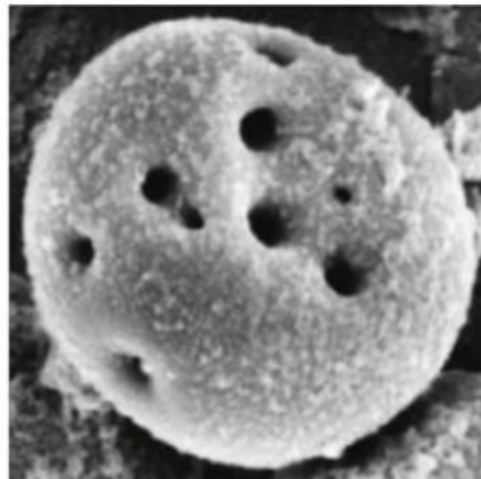


(b)

Spherocyte



(d)

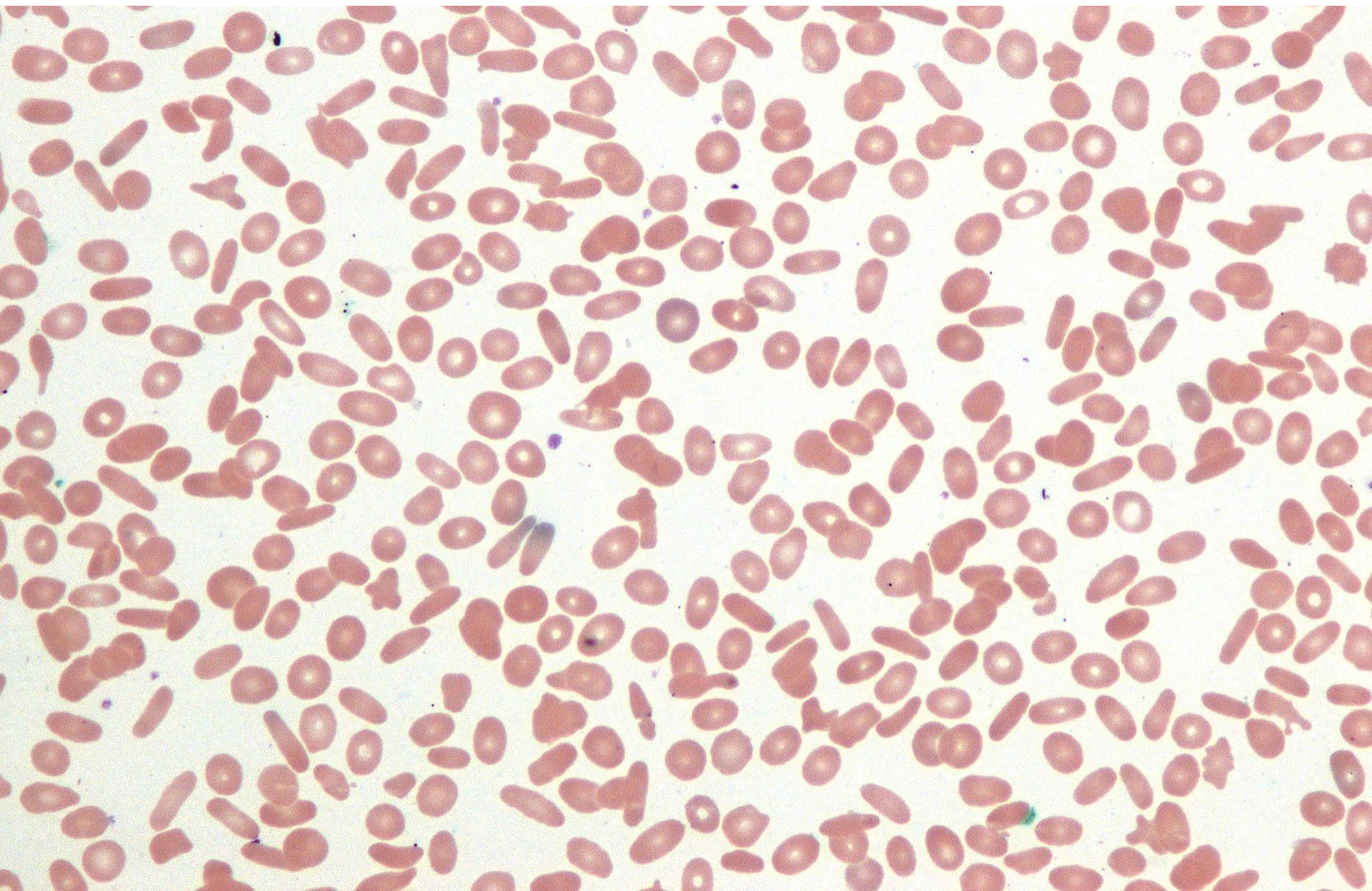


Echinocyte



# ERYTHROCYTES

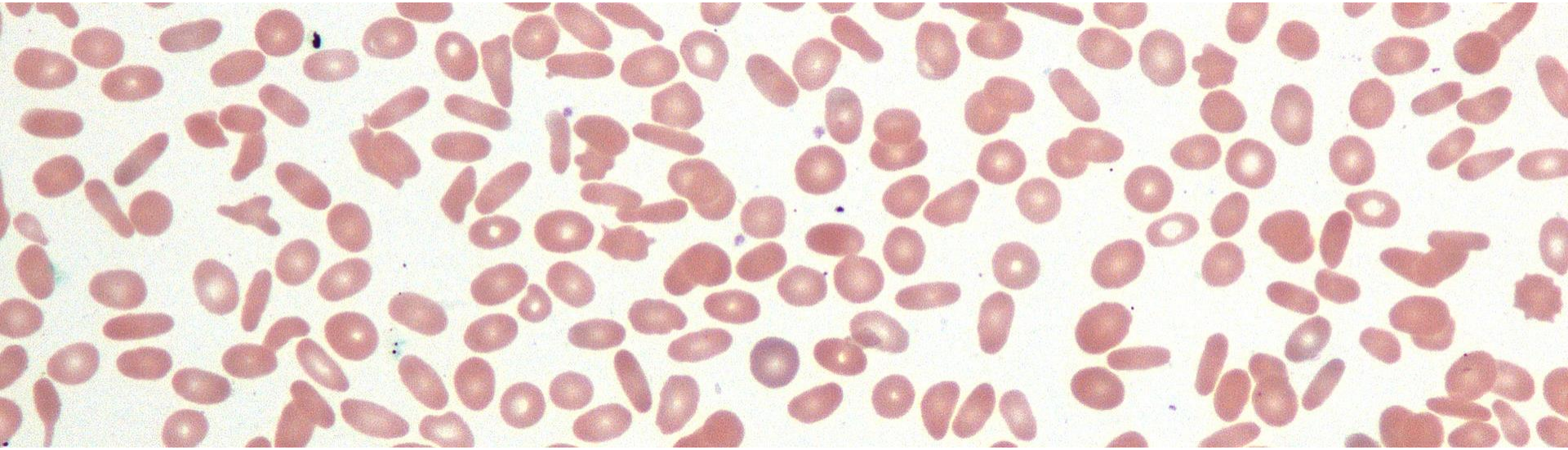
## Hereditary elliptocytosis



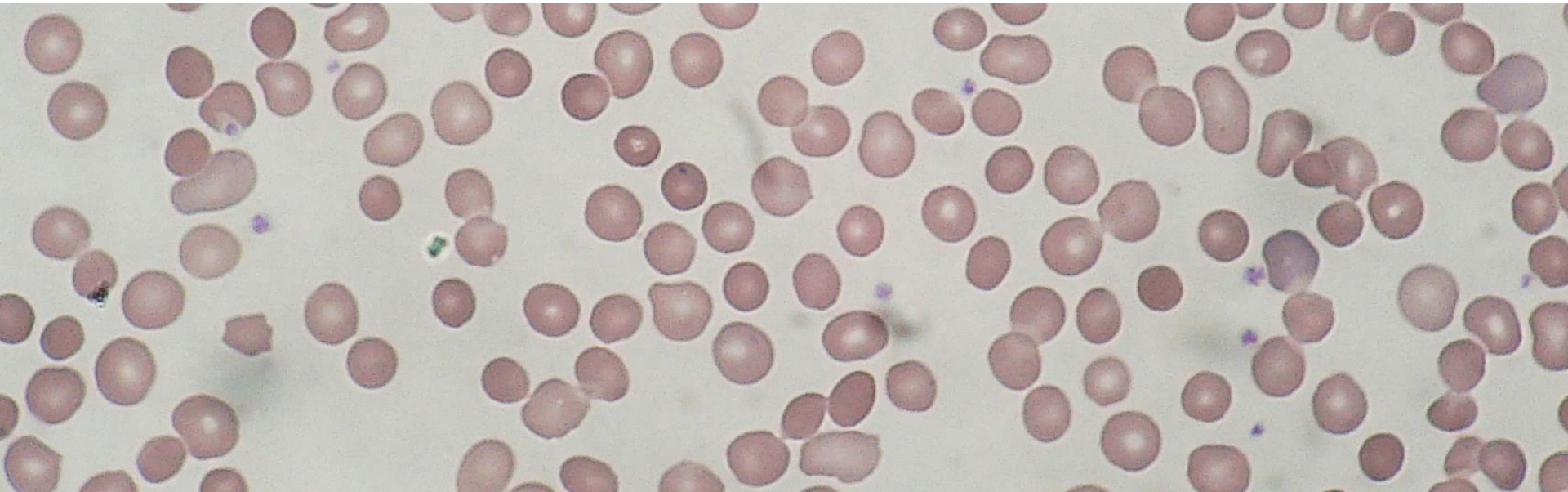


# ERYTHROCYTES

**Hereditary elliptocytosis**



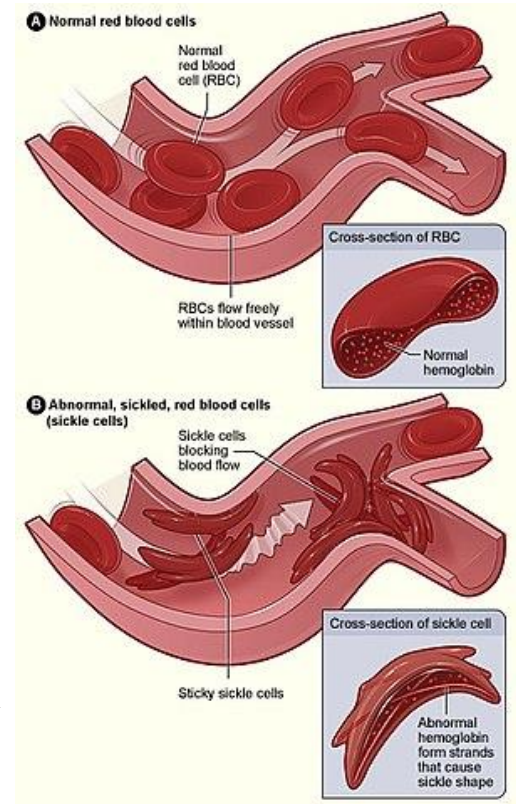
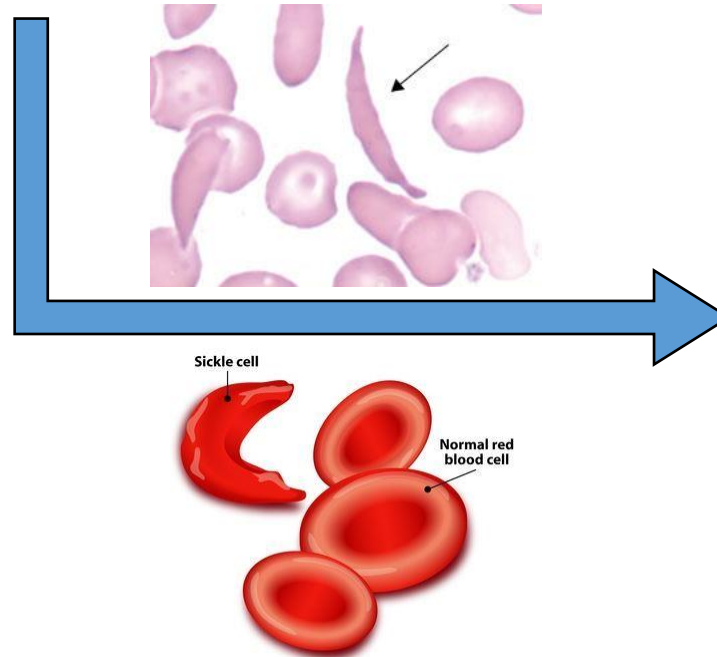
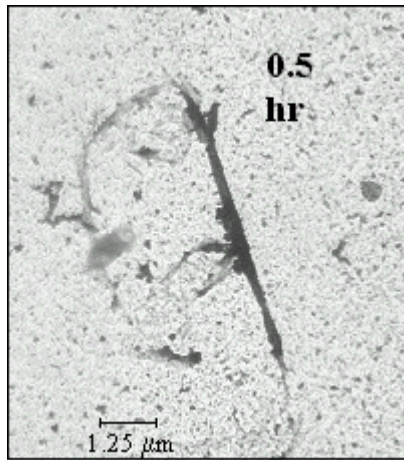
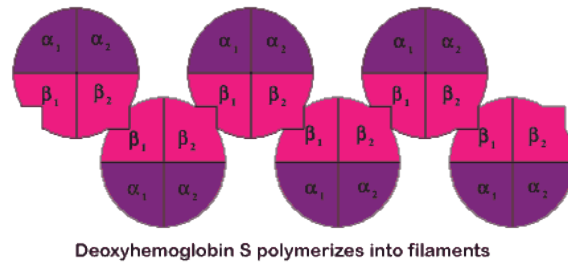
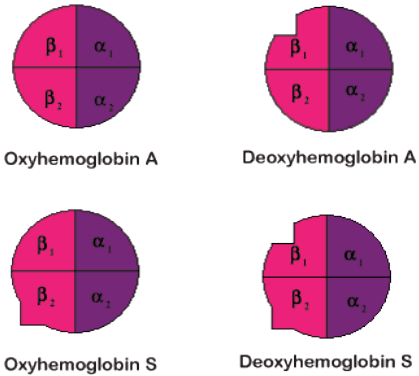
**Hereditary spherocytosis**



# ERYTHROCYTES

## Sickle cell anemia

- Abnormal hemoglobin (hemoglobin S)

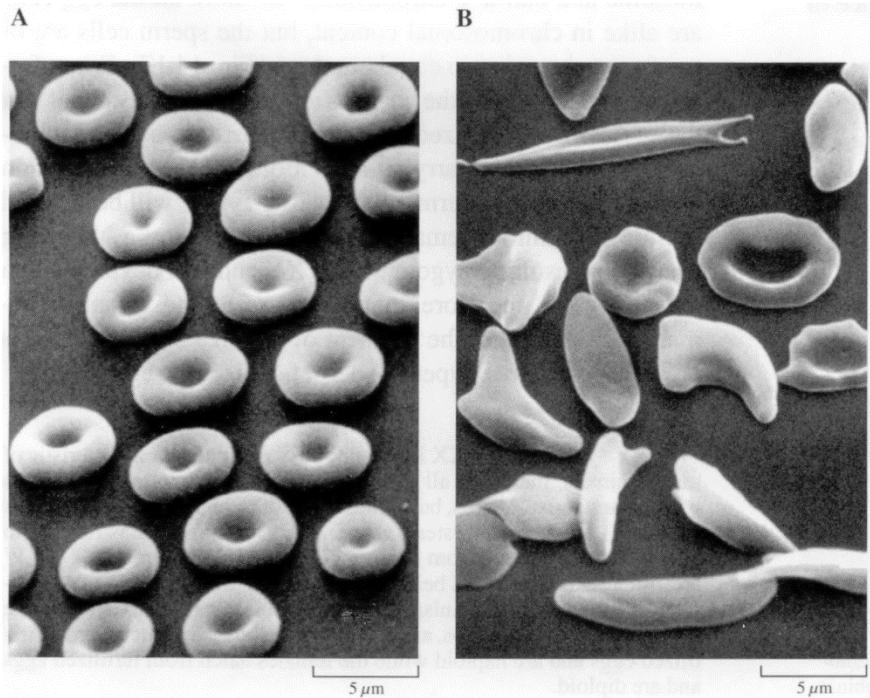




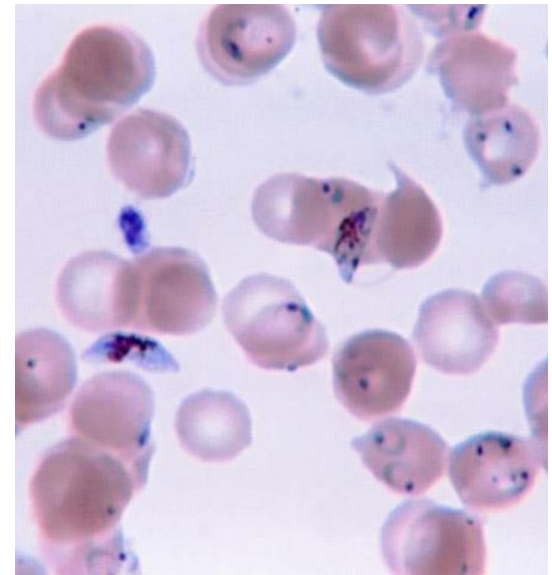
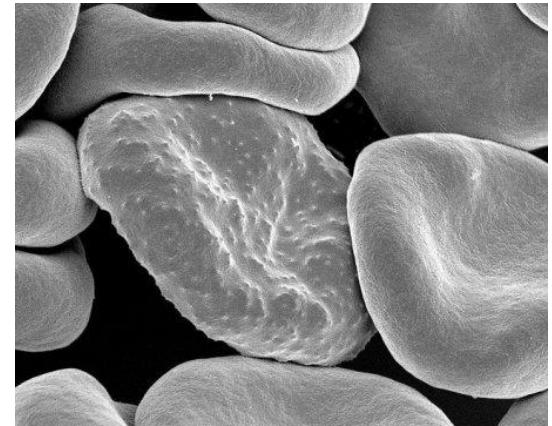
# ERYTHROCYTES

## Sickle cell anemia

- pathological genotype (heterozygote HbS/HbA) is beneficial



## Malaria

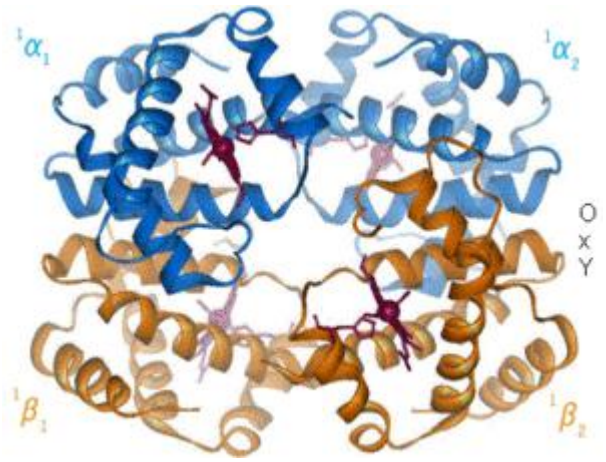
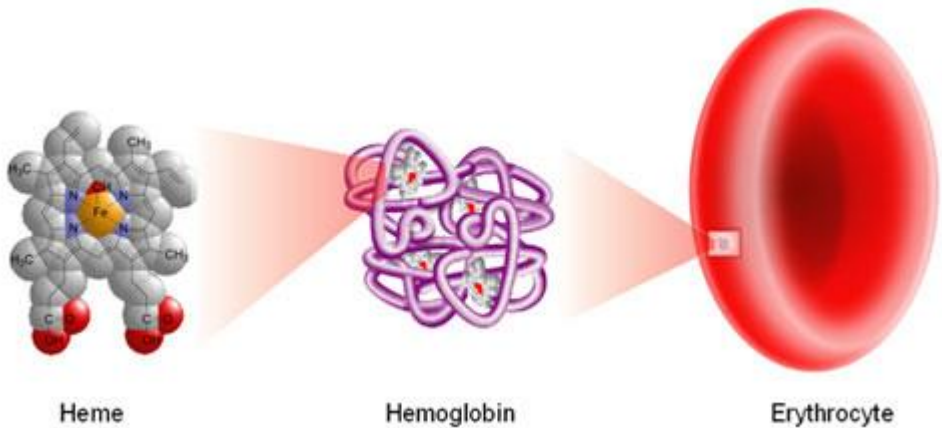
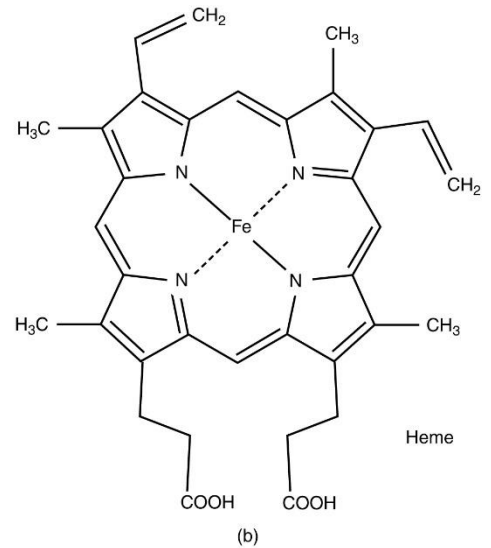
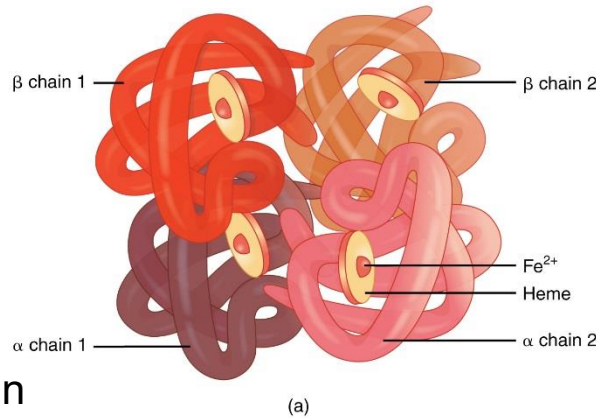


# ERYTHROCYTES

- Erythrocytes **lack nucleus and organelles**
- Anaerobic glycolysis

- **Hemoglobin**

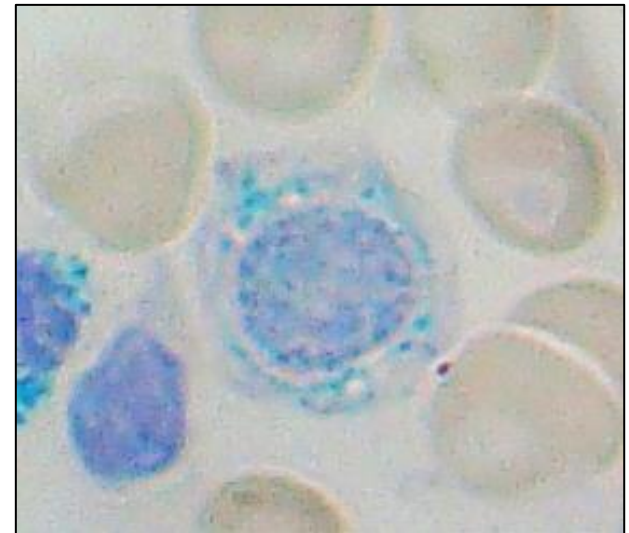
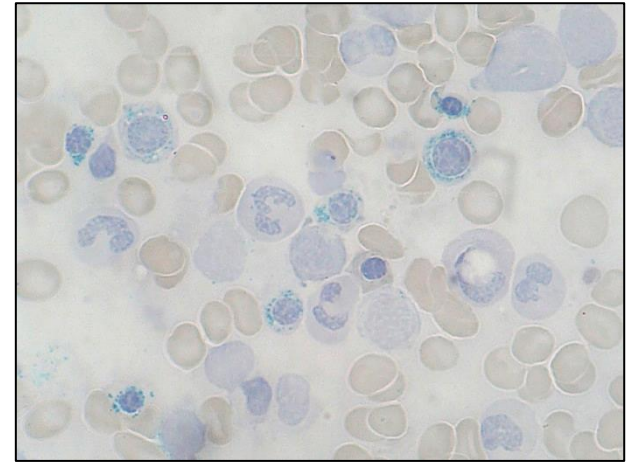
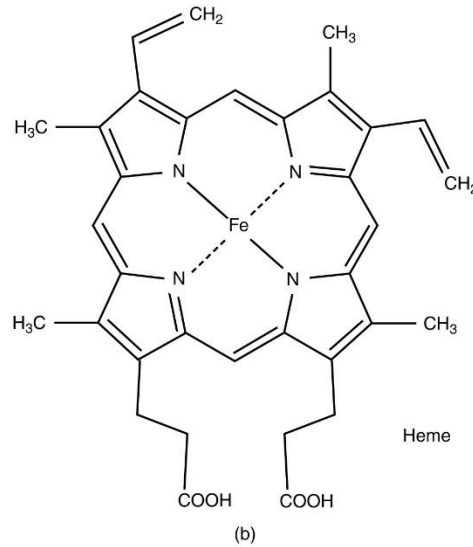
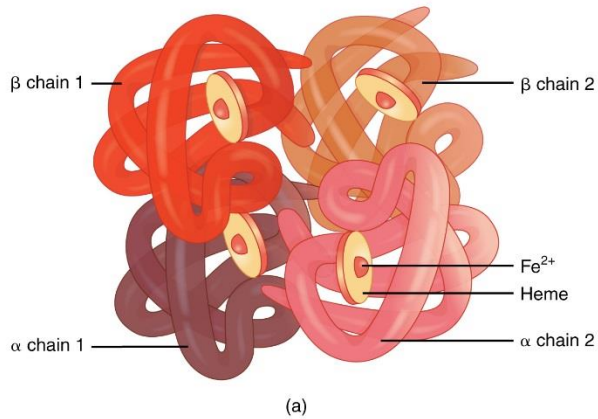
- Hem (haem, porphyrin)
- 4 globular subunits
- iron: cycle between  $Fe^{2+}/Fe^{3+}$
- Bohr effect
- oxyhemoglobin, deoxyhemoglobin
- methemoglobin, carboxyhemoglobin



# ERYTHROCYTES

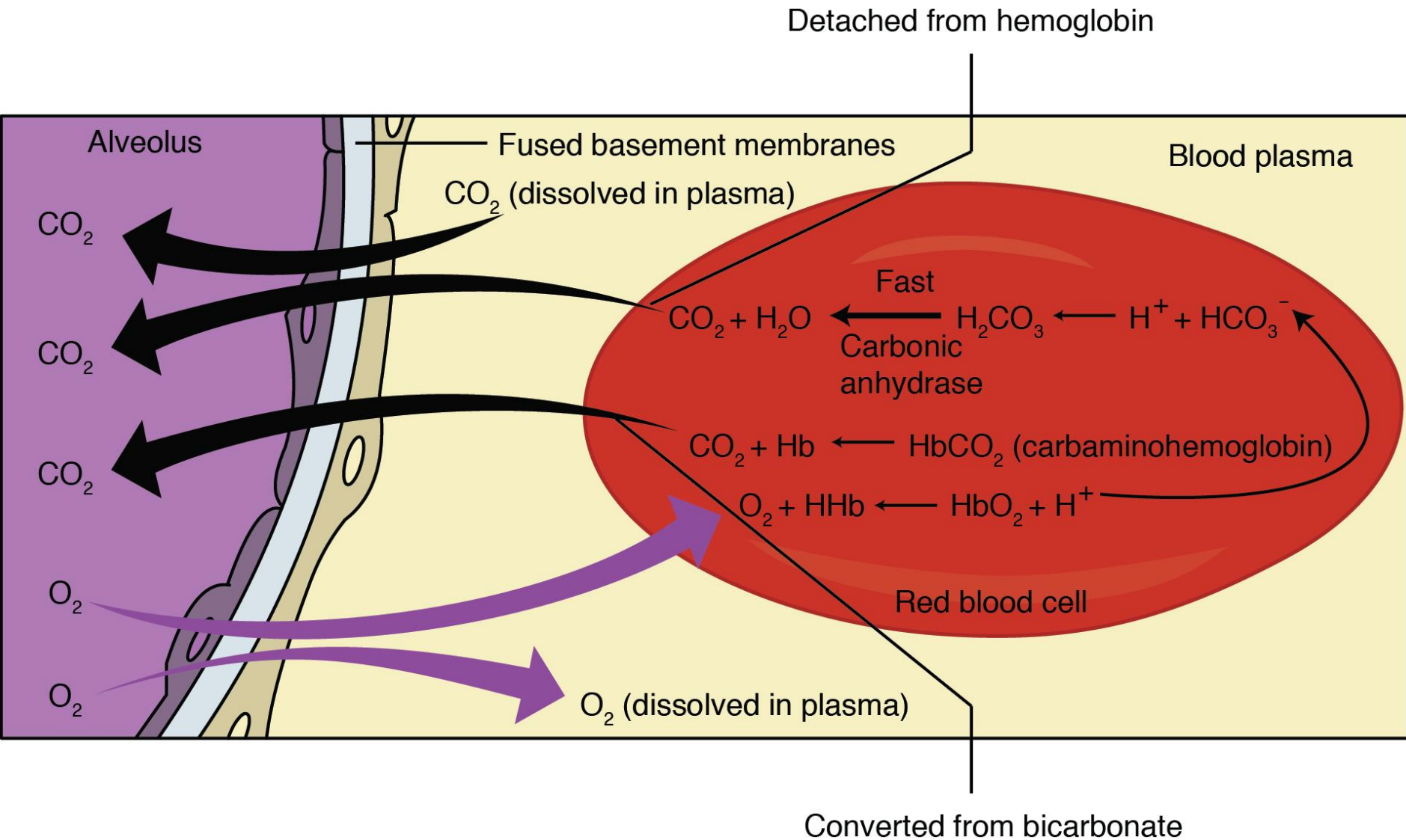
## Sideroblastic anemia

- Mitochondria accumulate iron deposits
- Failure to synthesize hem molecule
- Compromised maturation of erythrocytes
- Congenital (through ALAS2 mutation) or acquired



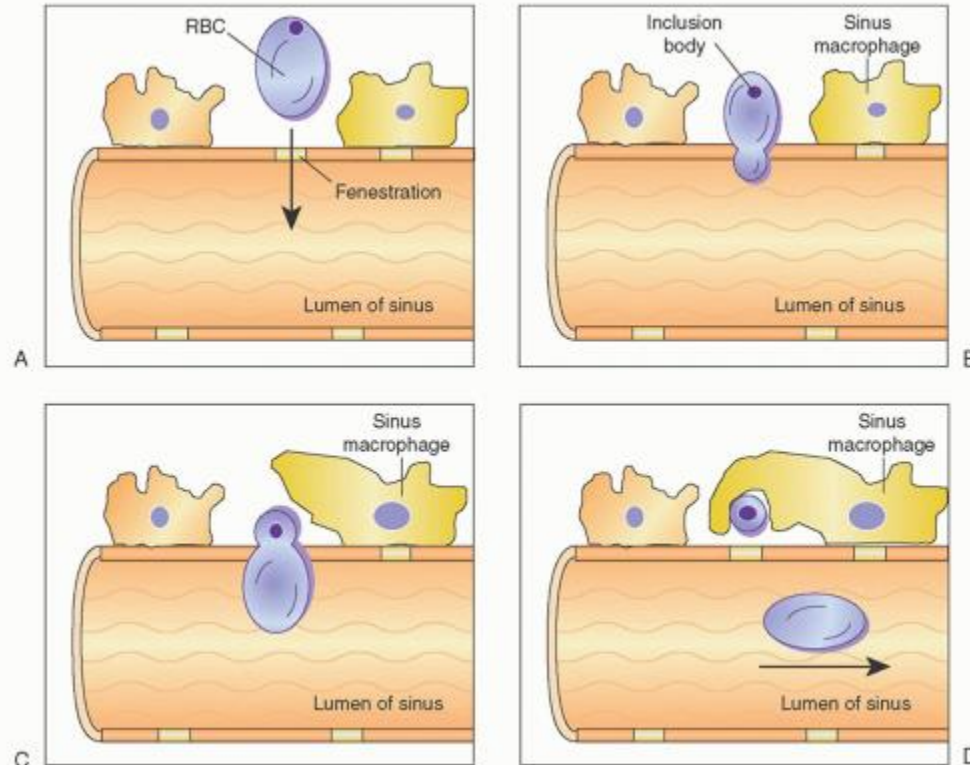
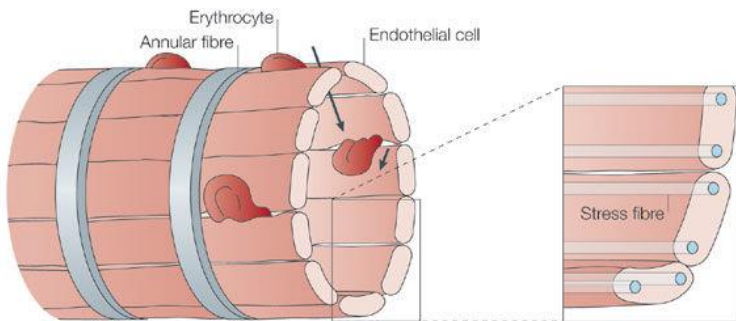
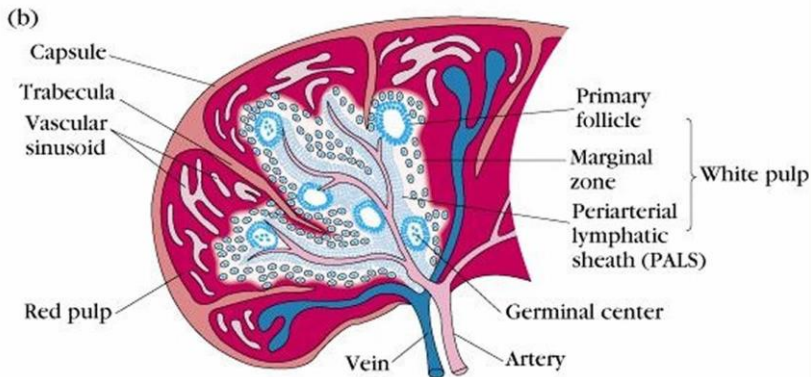
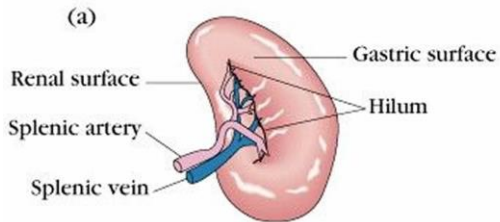
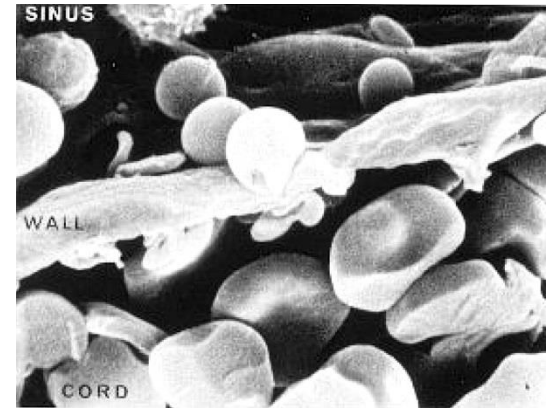


# ERYTHROCYTES



# ERYTHROCYTES

- Life span 120 days
- Constant abrasion
- No regeneration
- Removal of aged or damaged erythrocytes in bone marrow and spleen

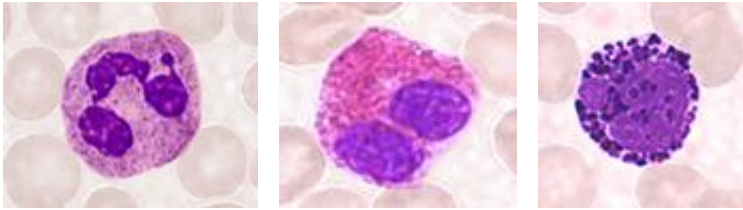


# LEUKOCYTES

- immune response
- morphological classification – **cytoplasmic granules**  
(does not follow hematopoiesis)

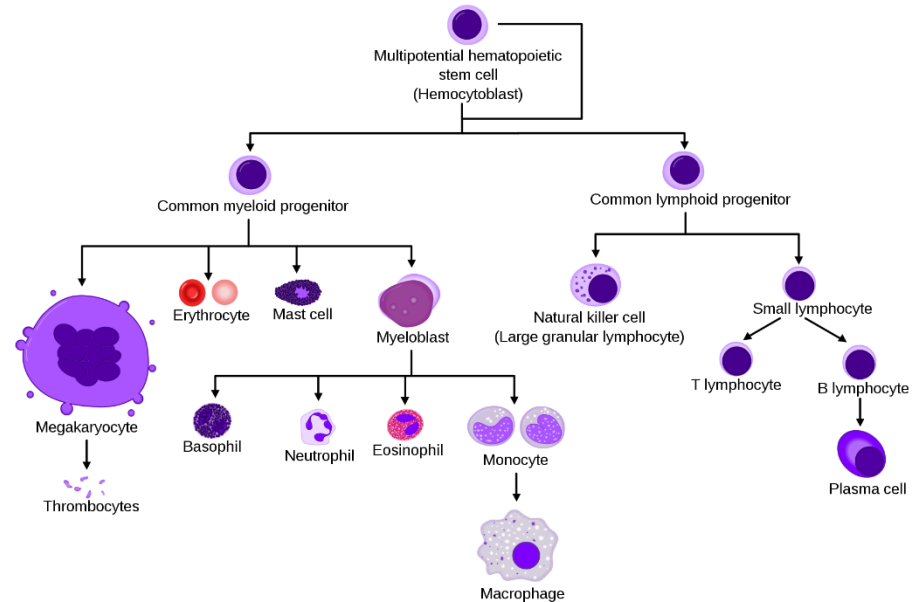
## Granulocytes

Neutrophils    Eosinophils    Basophils



## Agranulocytes

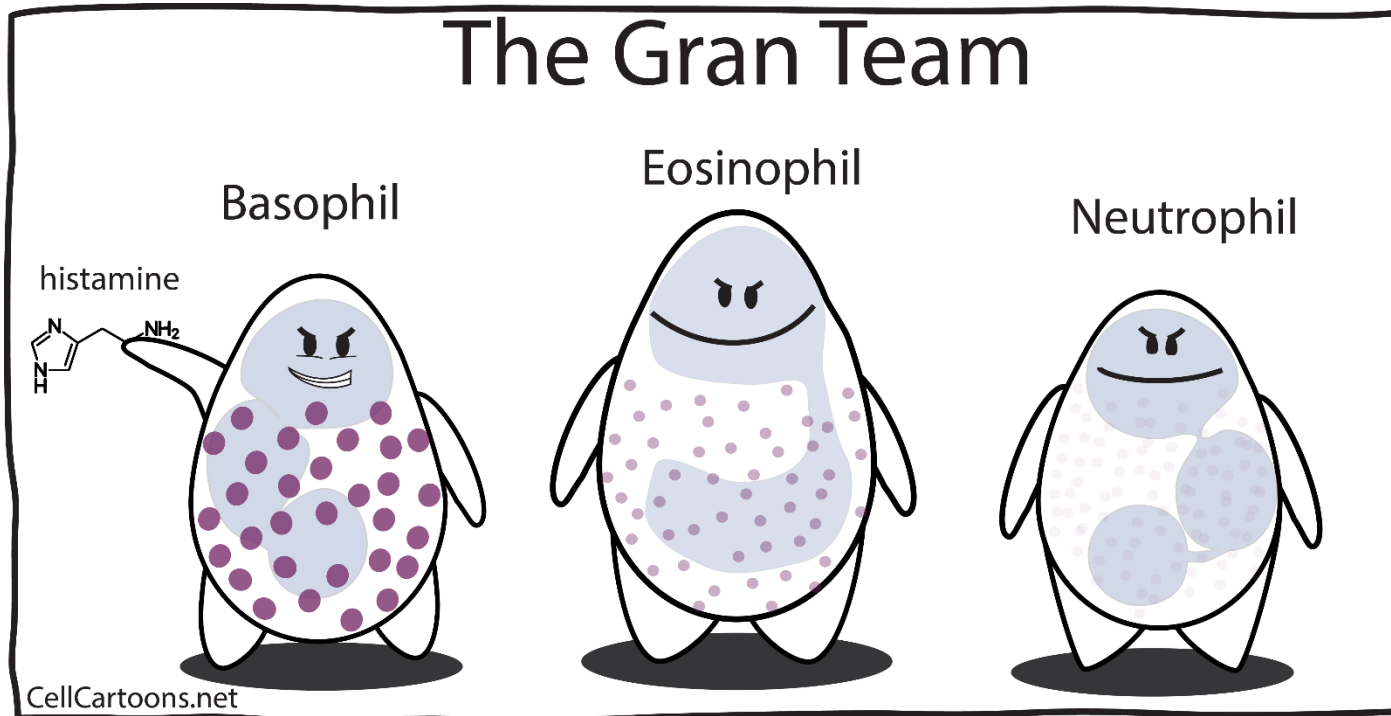
Monocytes    Lymphocytes





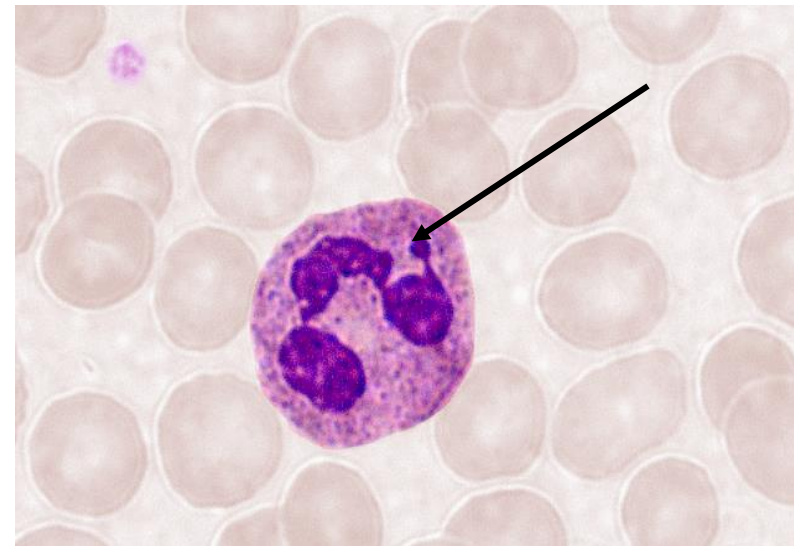
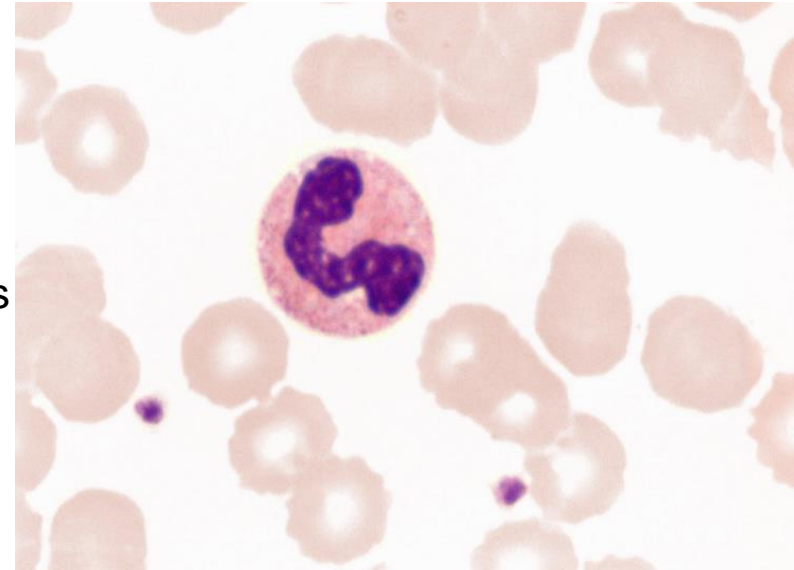
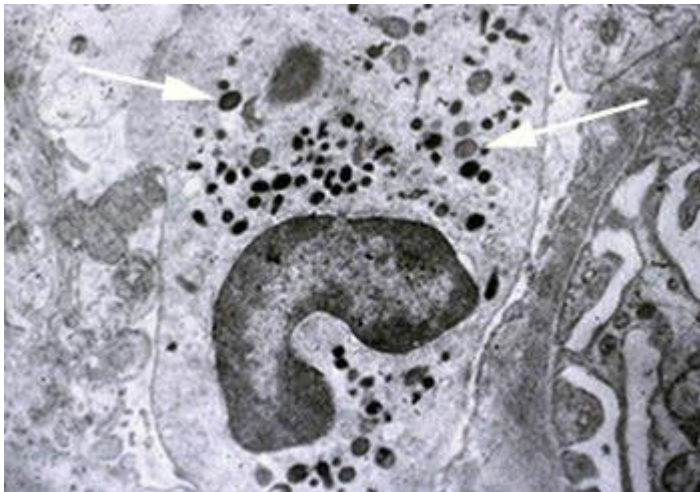
# GRANULOCYTES

- **Primary (azurophilic) granules** derived from lysosomes (= nonspecific granules)
- **Specific (secondary) granules**
- **Polymorphic nucleus**
- Terminally differentiated
- Short lifespan (hours)
- Reduced ER, GA, mitochondria (anaerobic glycolysis)
- Apoptosis



# NEUTROPHILIC GRANULOCYTES

- **Neutrophils**
  - 50-70% of leukocytes in circulation
  - $\varnothing > 12 \mu\text{m}$
  - Segmented nucleus
  - Barr's body in females
  - **Azurophilic (primary) granules**
    - myeloperoxidase, lysozyme, proteases, defensins
  - **Neutrophilic (secondary) granules**
    - collagenase, bactericidal enzymes
  - Chemotaxis of other leukocytes
  - Microphages
- **Neutrophilic band**
- **Neutrophilic segment**

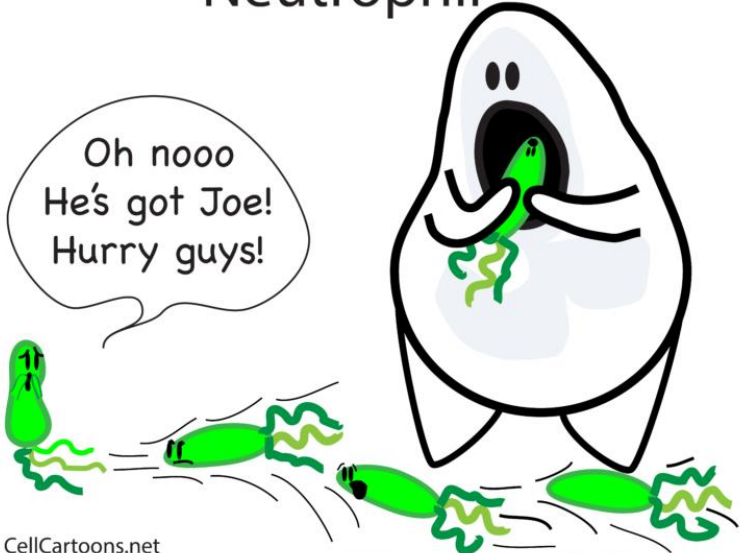


# NEUTROPHILIC GRANULOCYTES



Neutrophil

Oh nooo  
He's got Joe!  
Hurry guys!

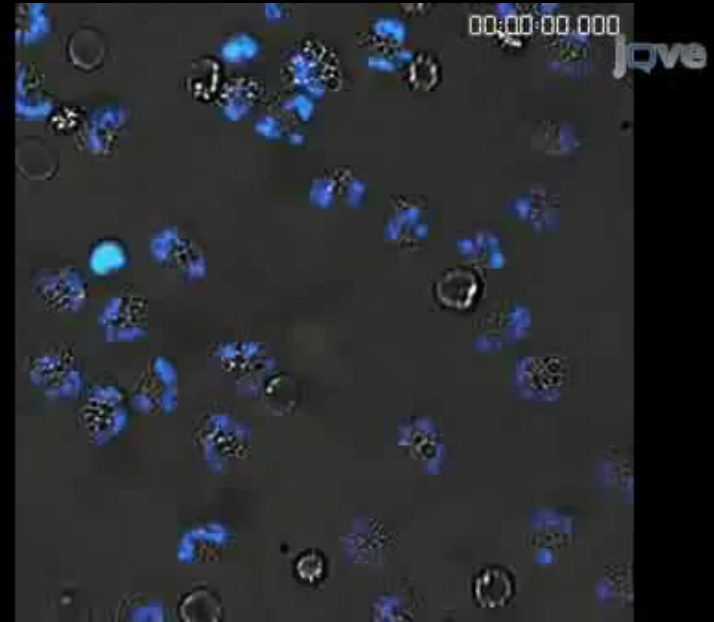
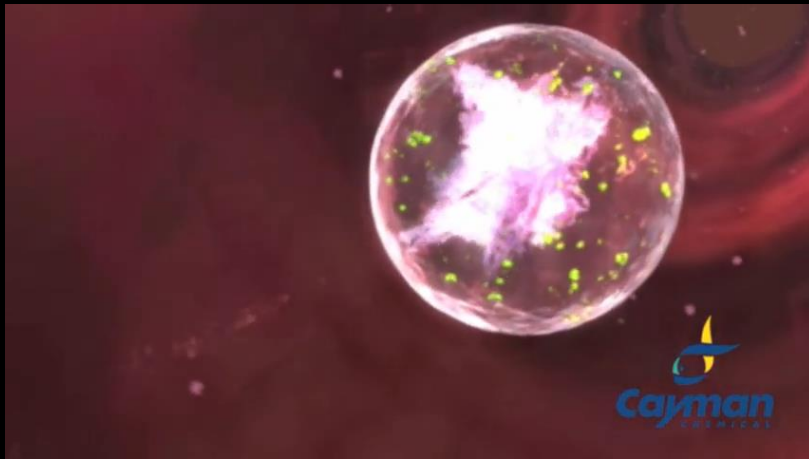




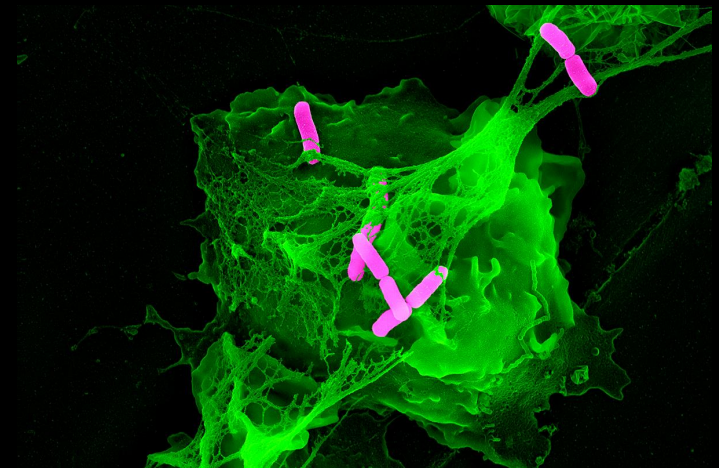
# NEUTROPHILIC GRANULOCYTES

## Hunters

NETs (neutrophil extracellulat traps)

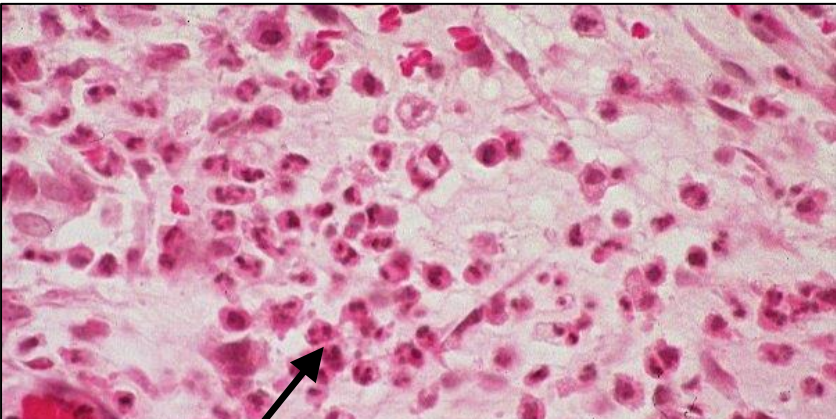
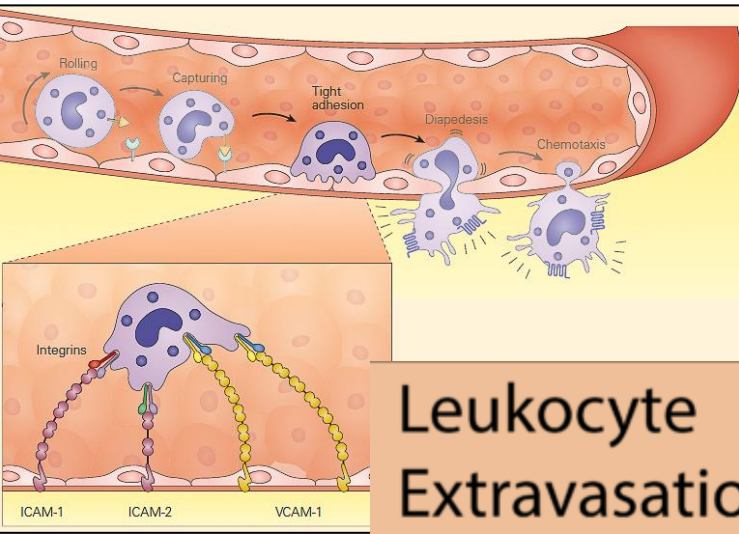


Special form of cell death – „netosis“



# NEUTROPHILIC GRANULOCYTES

- Extravasation (diapedesis)



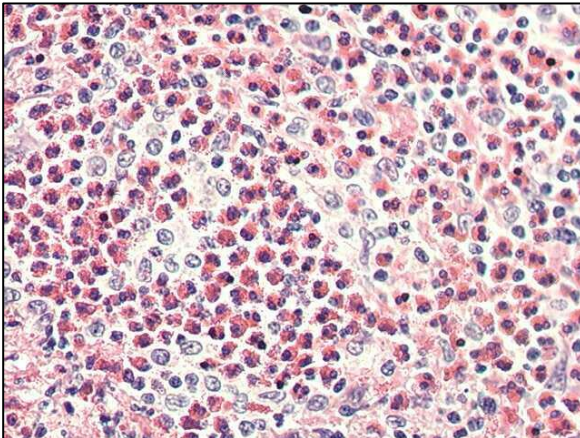
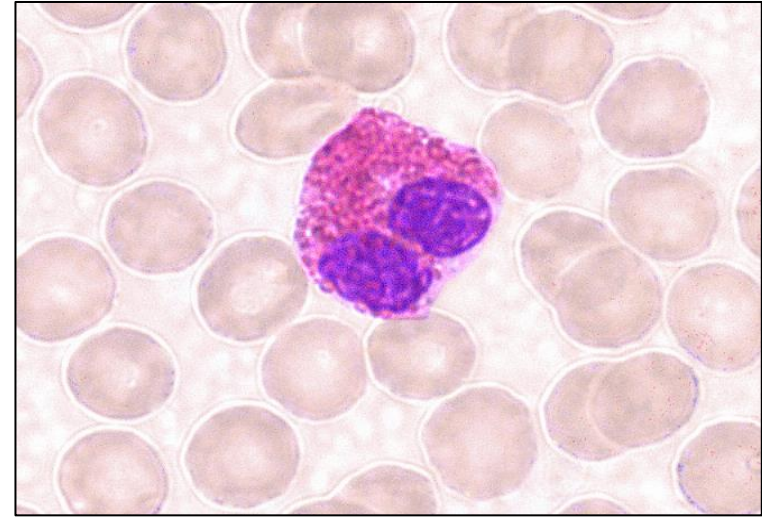
Leukocyte Extravasation

A cartoon illustration showing leukocytes and endothelial cells. One leukocyte is on top of a row of endothelial cells, looking confused. Another leukocyte is below, following a path. A third leukocyte is on the right, looking down. Speech bubbles contain the text: "HOW DID YOU DO THAT???", "JUST FOLLOW THE CHEMOKINES", and "Endothelial Cells".



# EOSINOPHILIC GRANULOCYTES

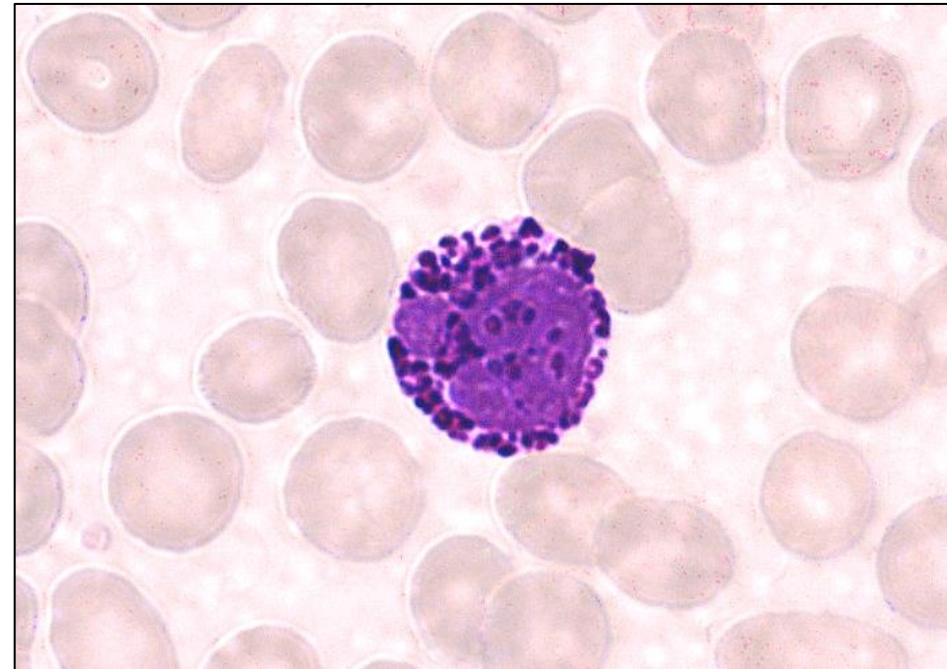
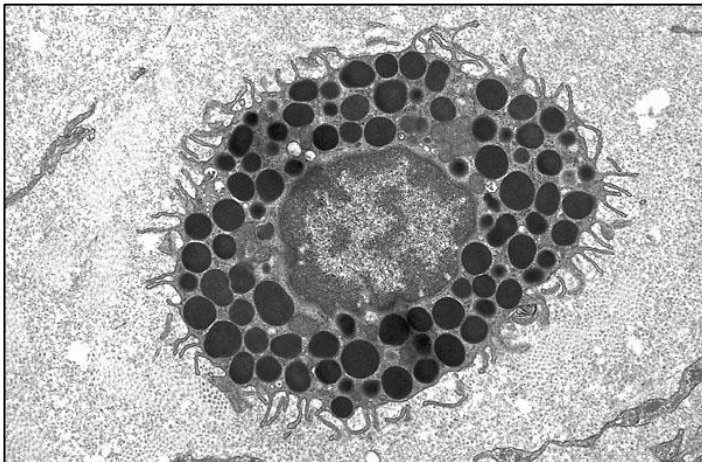
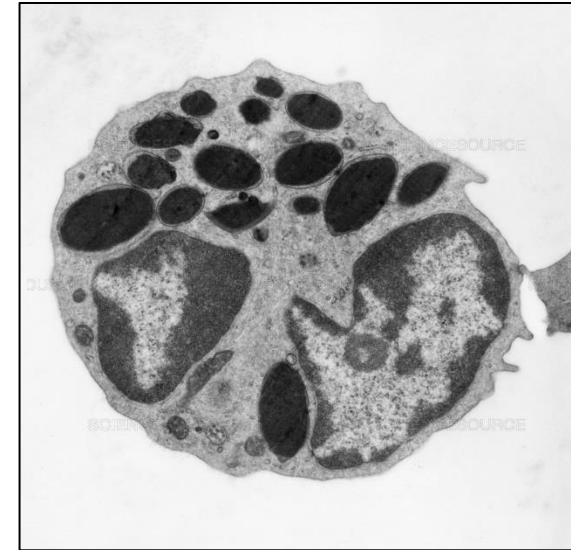
- **Eosinophils**
  - 1-4% of leukocytes in circulation
  - $\varnothing$  12-15  $\mu\text{m}$
  - Irregular, characteristic bi-segmented nucleus
  - **Azurophilic (primary) granules**
    - myeloperoxidase, lysozyme, proteases, defensins
  - **Eosinophilic (secondary) granules**
    - bright red (eosinophilic)
    - major acidic protein
    - peroxidase
    - cytokines, chemokines
- Chemotaxis of other leukocytes
- Phagocytosis of antibody-antigen complexes
- Parasitic infections, allergic reaction
- Chronic inflammation





# BASOPHILIC GRANULOCYTES

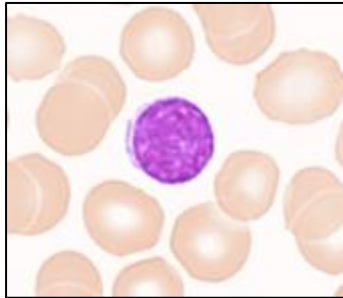
- **Basophils**
  - <1% of leukocytes in circulation
  - $\varnothing$  12  $\mu\text{m}$
  - Irregular, bisegmented nucleus, masked by granules
  - **Azurophilic (primary) granules**
    - myeloperoxidase, lysozyme, proteases, defensins
  - **Basophilic (secondary) granules**
    - 0.5  $\mu\text{m}$
    - large, dark (basophilic)
    - heparin, histamin - vasodilatation
    - phospholipase A
  - Analogs of mast cells
  - Receptors for IgE
  - Allergy, anaphylaxis, inflammation



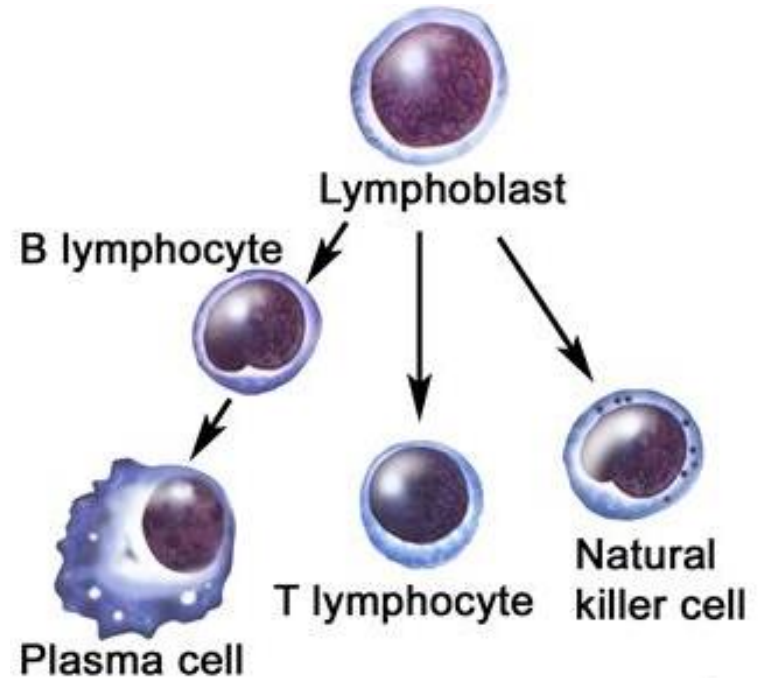
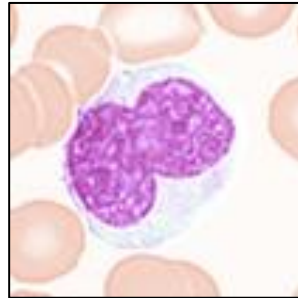
# AGRANULOCYTES

- Only the non-specific, azurophilic granules are present
- **Specific granules absent**
- Non-segmented nucleus

**Lymphocytes**



**Monocytes**

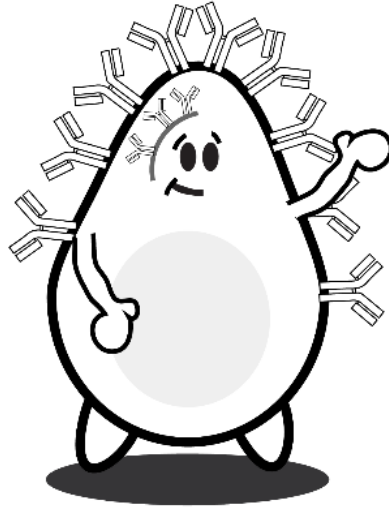


# Lymphocytes

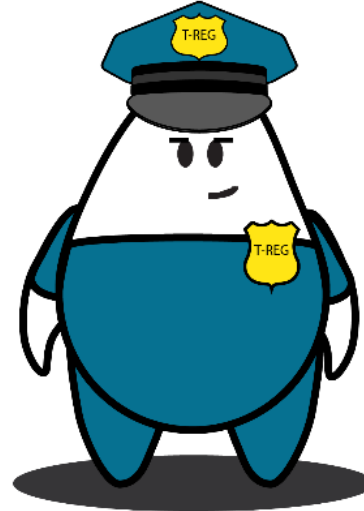
CD8 T Cell



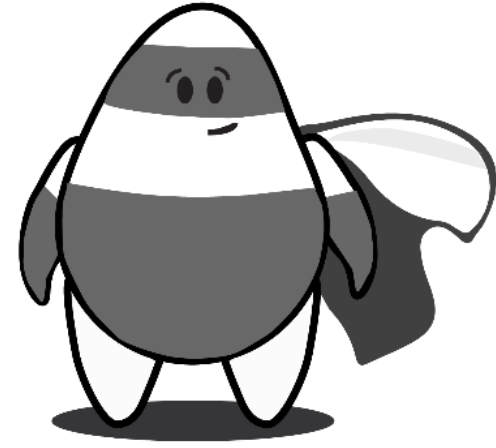
B Cell



Regulatory  
T Cell



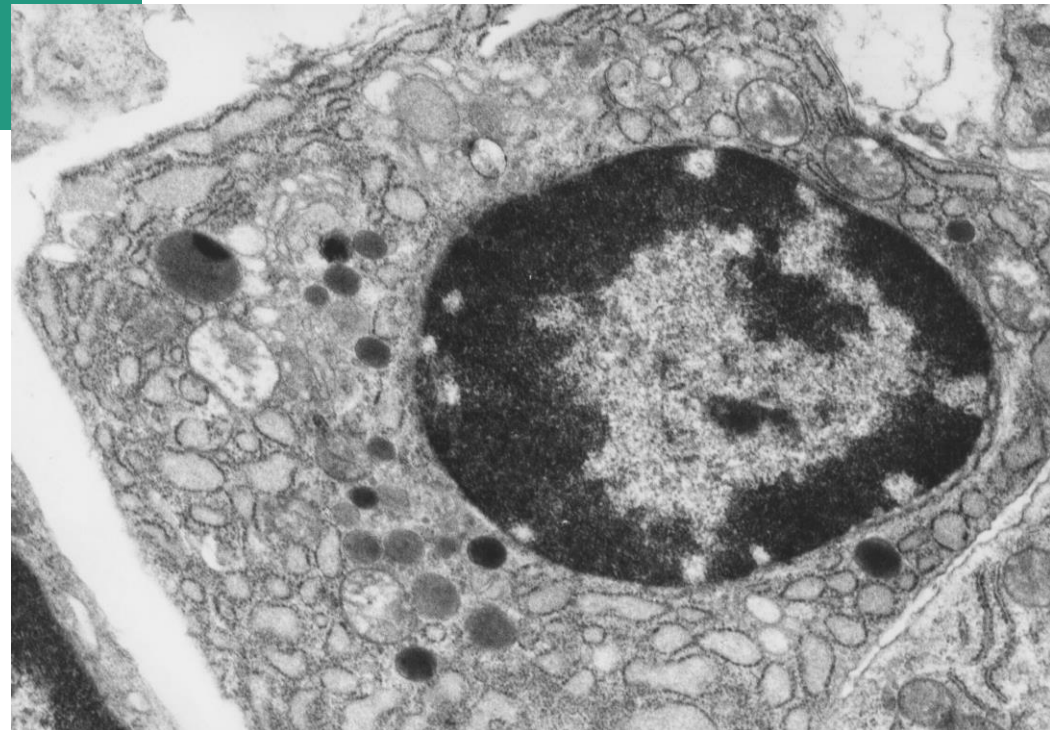
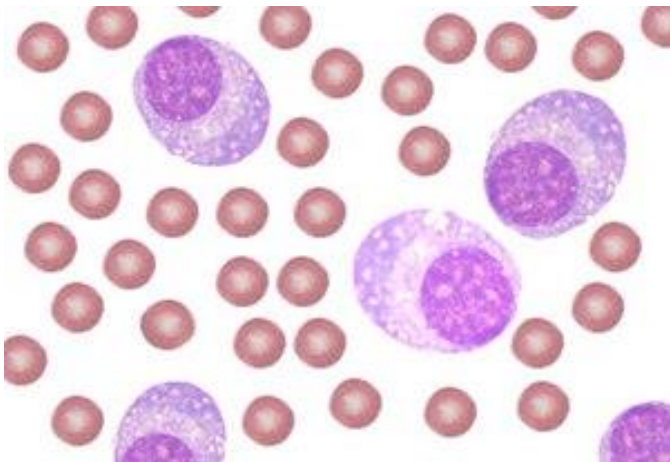
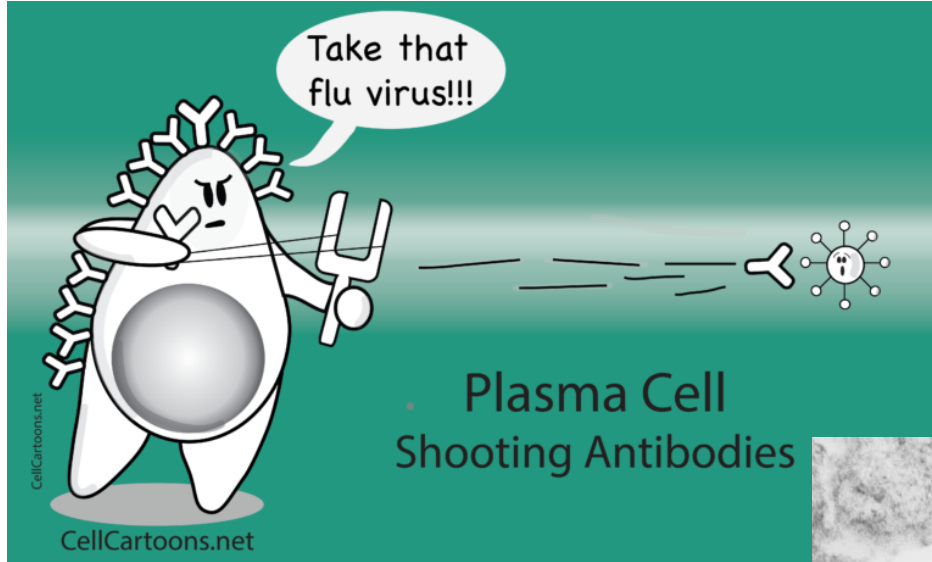
CD4 T Cell





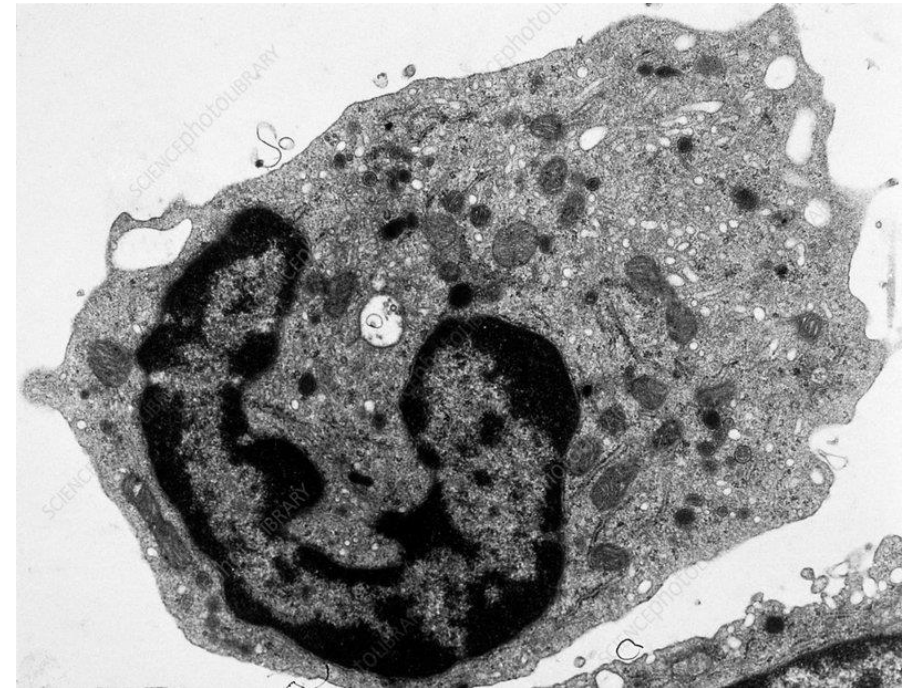
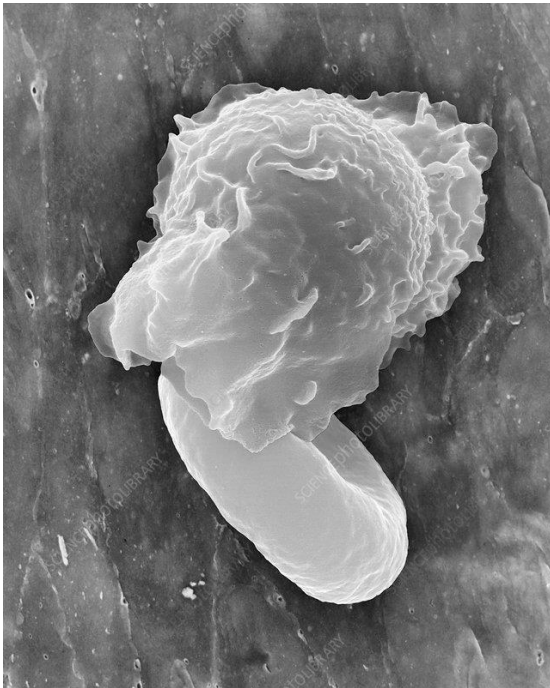
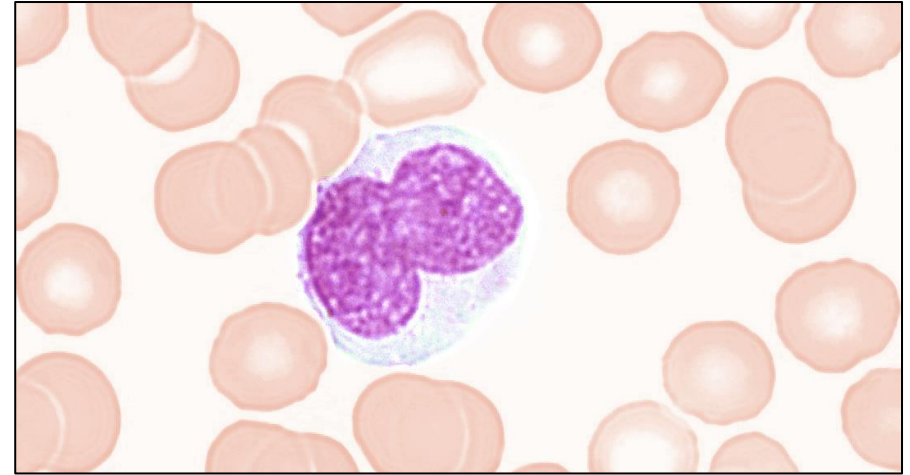
# LYMPHOCYTES

- Plasma cells



# MONOCYTES

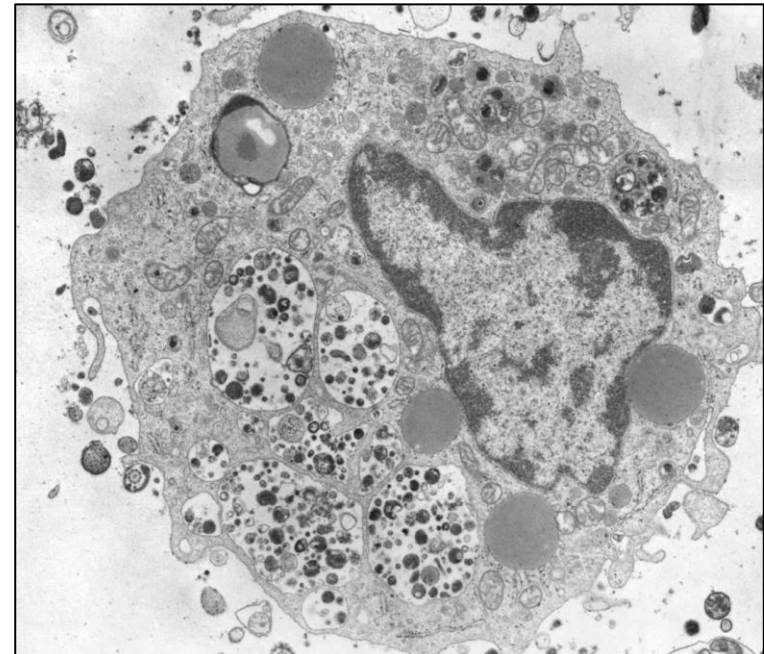
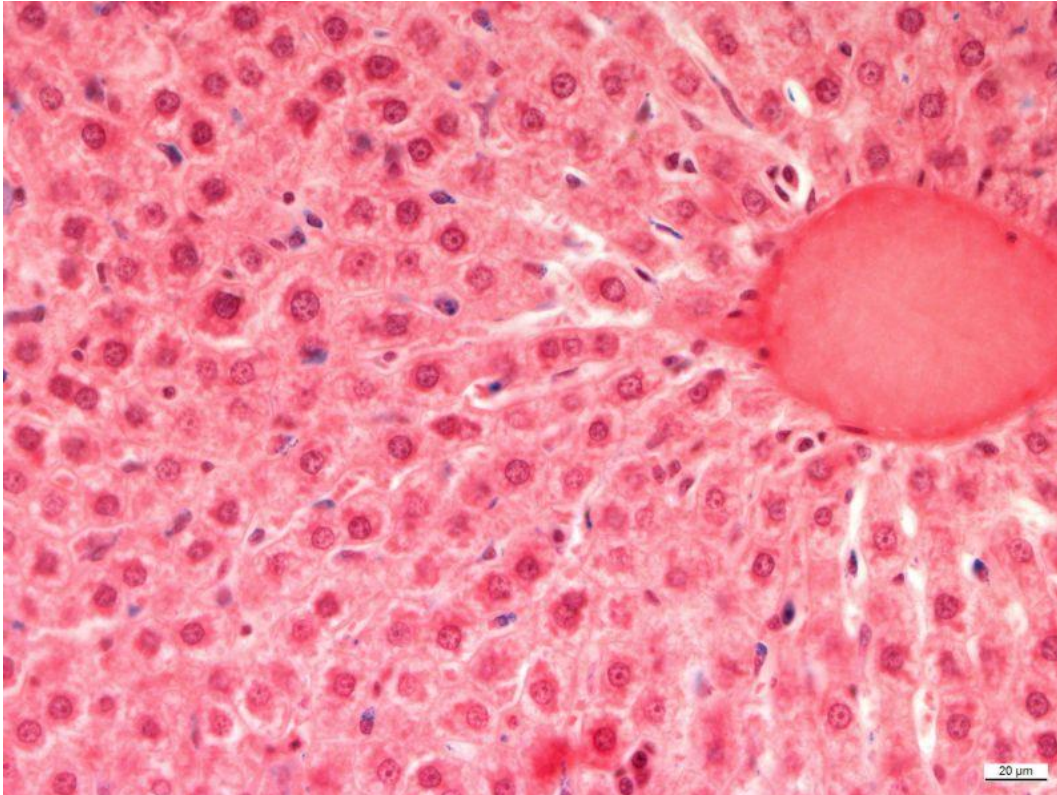
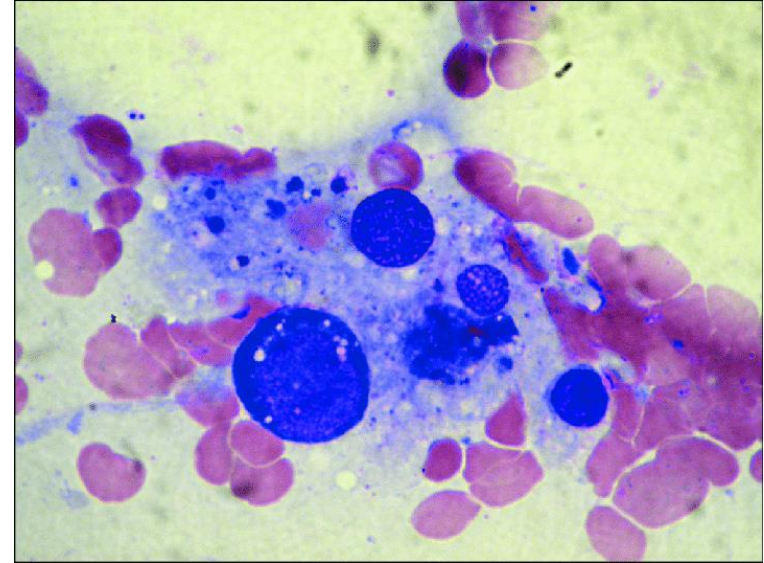
- $\varnothing$  12-15  $\mu\text{m}$
- Circulating precursors of macrophages, osteoclasts, microglia, Kupfer cells and dendritic cells
- Mononuclear phagocytic system
- Large, oval (bean, kidney) nucleus with less condensed chromatin and 2-3 nucleoli
- Basophilic cytoplasm
- Azurophilic granules





# MACROPHAGES

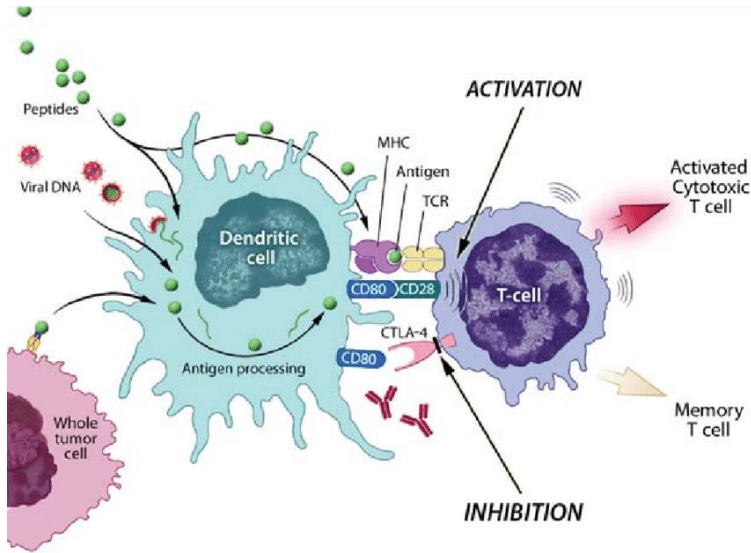
- $\varnothing$  around 21  $\mu\text{m}$
- variable migratory morphology
- phagocytocys
- antigen presentation to T-lymphocytes
- inflammatory response
- tissue regeneration and wound healing
- e.g. histiocytes, Kupffer cells, microglia



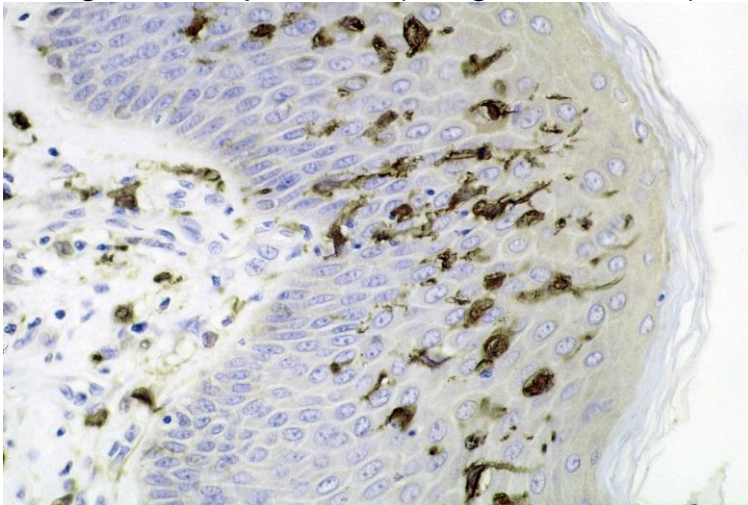


# DENDRITIC CELLS

- „professional“ presentation of antigens to immune cells (MHC II)
- activation or inhibition of lymphocytes
- immune response or immunetolerance



- e.g. DC in epidermis (Langerhans cells)



156 P. Verdijk et al.

Eur. J. Immunol. 2004, 34: 156-164

## Morphological changes during dendritic cell maturation correlate with cofilin activation and translocation to the cell membrane

Pauline Verdijk<sup>1</sup>, Peter A. van Veelen<sup>2</sup>, Arnold H. de Ru<sup>3</sup>, Paul J. Hensbergen<sup>1</sup>, Kensaku Mizuno<sup>4</sup>, Henk K. Koelen<sup>1</sup>, Frits Koning<sup>1</sup>, Cornelis P. Tensen<sup>1</sup> and A. Mieke Mommaas<sup>1</sup>

<sup>1</sup> Department of Dermatology, LUMC, Leiden, The Netherlands  
<sup>2</sup> Center for Electron Microscopy, LUMC, Leiden, The Netherlands  
<sup>3</sup> Department of Immunohaematology and Bloodtransfusion, LUMC, Leiden, The Netherlands  
<sup>4</sup> Department of Biomolecular Sciences, Graduate School of Life Sciences, Tohoku University, Aoba Sendai, Japan

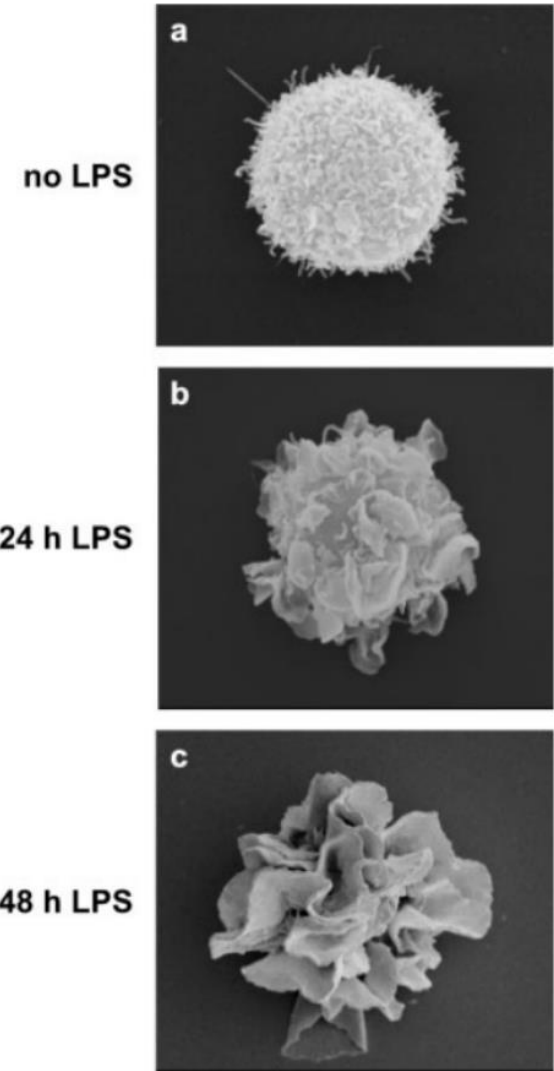
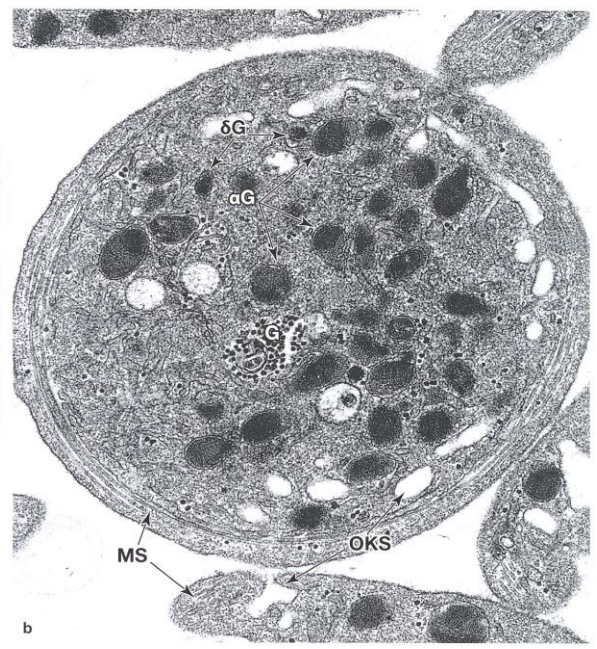
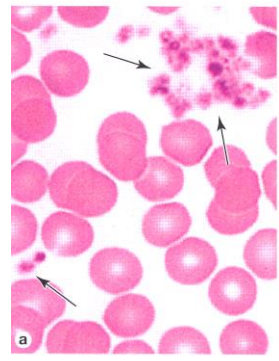
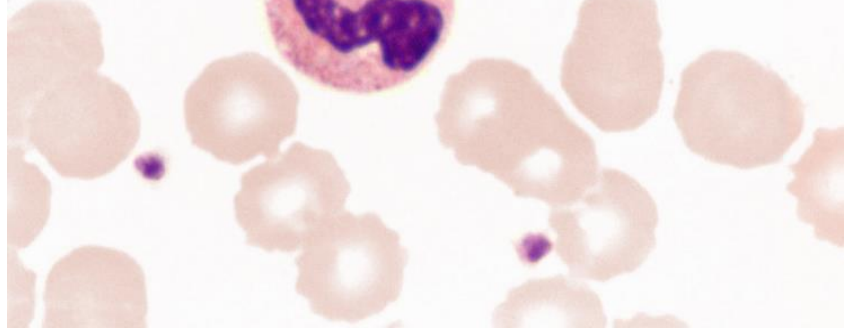
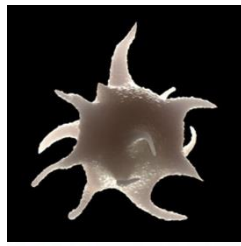


Fig. 1. Immature versus mature DC. Scanning electron micrograph of immature and mature DC. Monocyte-derived DC were cultured without (a) or with LPS for 24 h (b) or 48 h (c). Cells were fixed and allowed to adhere to poly-L-lysine-coated coverslips before preparation for scanning electron microscopy.

# THROMBOCYTES

- Cell fragments without nucleus
- $\varnothing$  2-3  $\mu\text{m}$ , discoid shape
- hyalomere, granulomere
- $150-400 \times 10^3/\mu\text{l}$
- blood clotting, repair of vessel wall

<b><math>\alpha</math>-granules</b> 300-500 nm	fibrinogen, PDGF
<b><math>\delta</math>-granules</b> 250-300 nm	serotonin, $\text{Ca}^{++}$ pyrophosphate ADP, ATP
<b><math>\lambda</math>-granules</b> 175-200 nm	lysosomal enzymes





# THROMBOCYTES

## 1. Primary aggregation of platelets

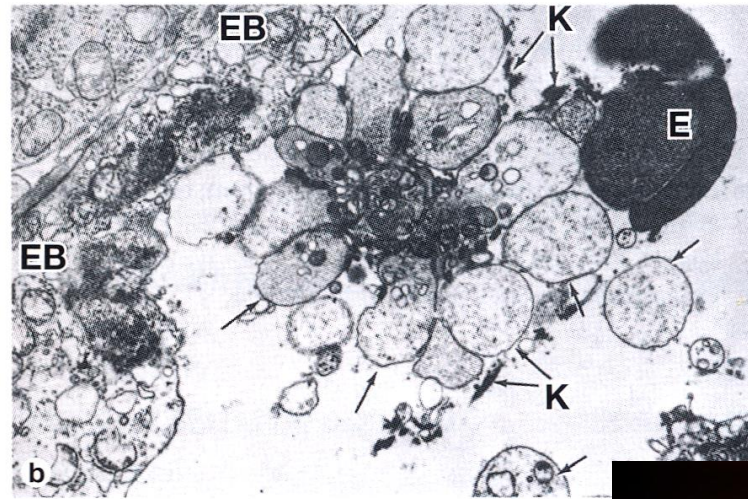
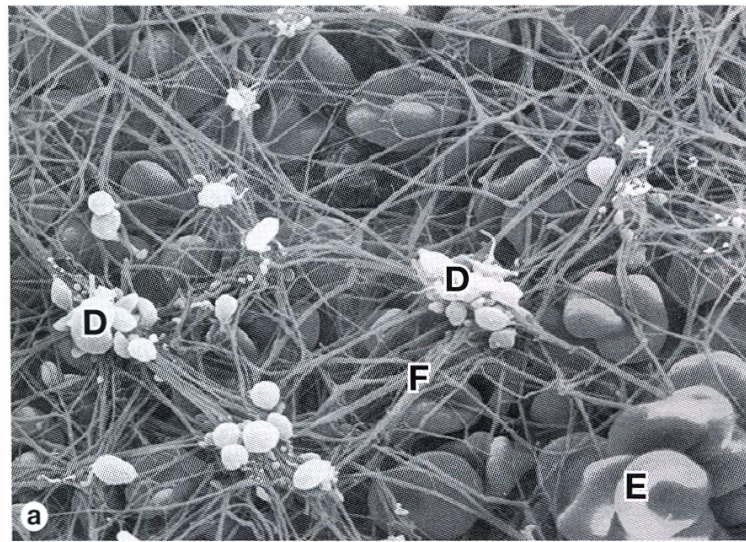
- collagen fibers exposed by endothelial rupture
- platelet clot

## 2. Secondary aggregation of platelets

- clotting factors, ADP from thrombocytes attracts other platelets – *white thrombus*

## 3. Coagulation – blood clotting

- fibrin mesh capturing erythrocytes – *red thrombus*



## 4. Thrombus retraction

- contraction of thrombus (platelet actin and myosin)

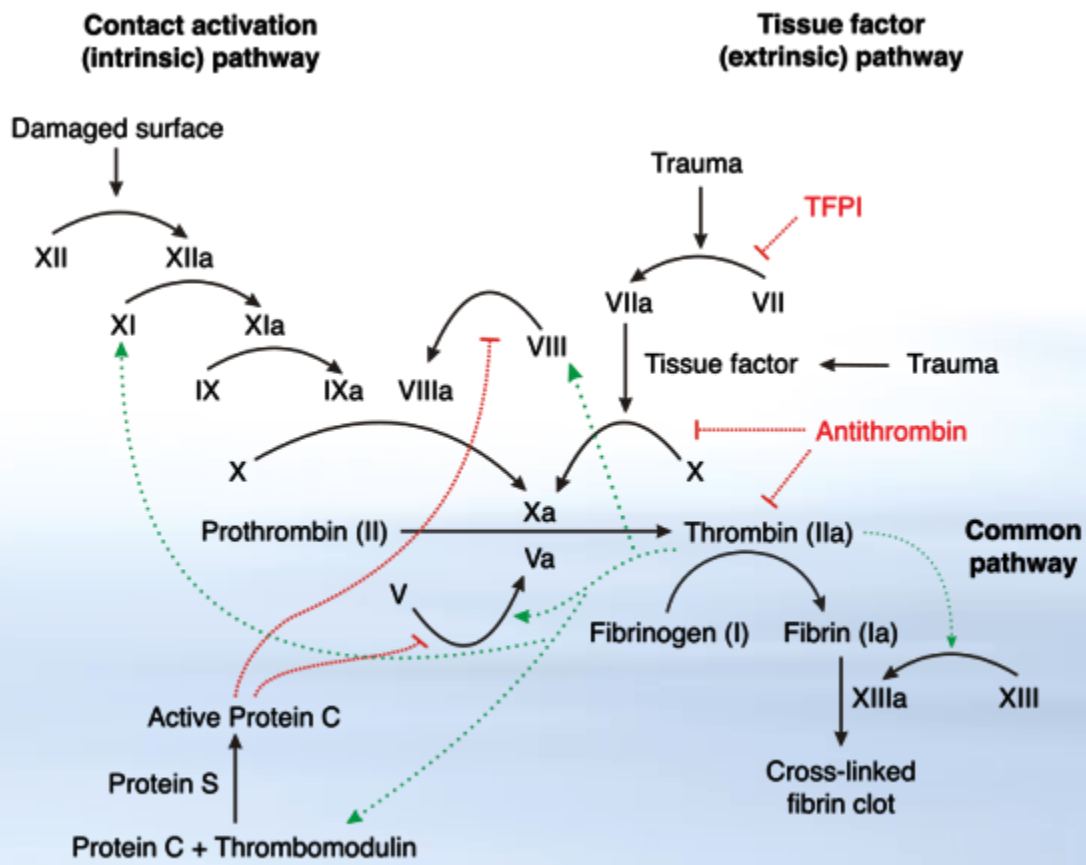
## 5. Thrombolysis

- dissolving of thrombus (plasmin) and tissue regeneration





# THROMBOCYTES



You needn't to know the clotting cascade in full details for our course, leave it for biochemistry



# DIFFERENTIAL WHITE BLOOD CELL COUNT

**THIS SLIDE IS REALLY IMPORTANT**

Neutrophil band 4 %

segment 67 %

**1:17**

**shift to the left**

**shift to the right**

more bands

more segments

Eosinophils 3 %

Basophils 1 %

Lymphocytes 20 %

Monocytes 5 %

$\Sigma = 100 \%$

**Norm**

# DIFFERENTIAL WHITE BLOOD CELL COUNT

## Deviations from the norm:

	↑ Increased	↓ Decreased
Neutrophils	neutrophil granulocytosis	neutrophil granulocytopenia
Eosinophils	eosinophil granulocytosis	eosinophil granulocytopenia
Basophils	basophil granulocytosis	basophil granulocytopenia
Lymphocytes	lymphocytosis	lymphocytopenia
Monocytes	monocytosis	monocytopenia



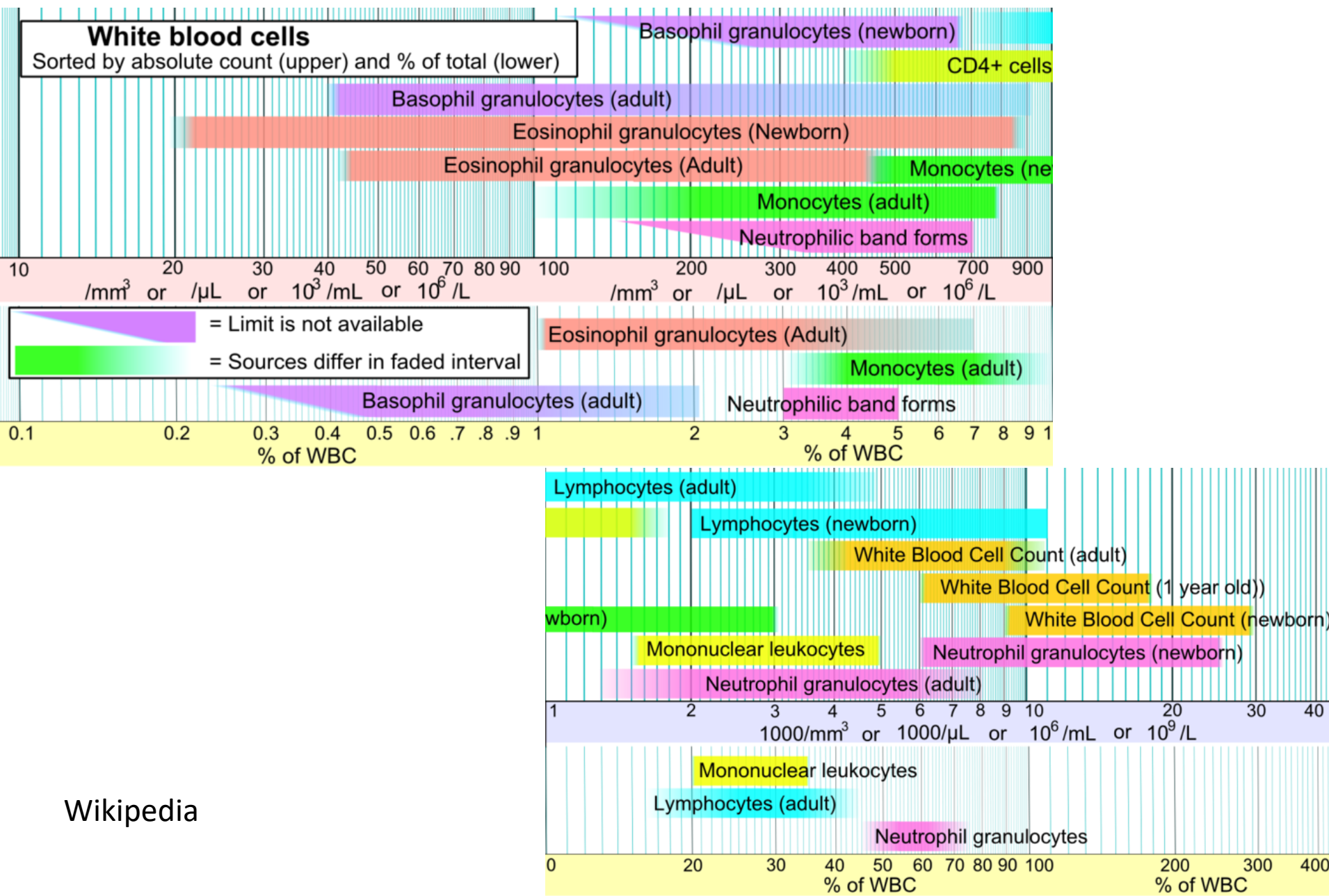
# DIFFERENTIAL WHITE BLOOD CELL COUNT

## Example of population variability

<b>Neutrophils</b>	<b>bands</b>	<b>0-5 %</b>
	<b>segments</b>	<b>35-85 %</b>
<b>Eosinopils</b>		<b>0-4 %</b>
<b>Basophils</b>		<b>0-1 %</b>
<b>Lymphocytes</b>		<b>20-50 %</b>
<b>Monocytes</b>		<b>2-6 %</b>

According to: Haferlach et al. Kapesní atlas hematologie. Grada 2014

# DIFFERENTIAL WHITE BLOOD CELL COUNT



Wikipedia

# DIFFERENTIAL WHITE BLOOD CELL COUNT

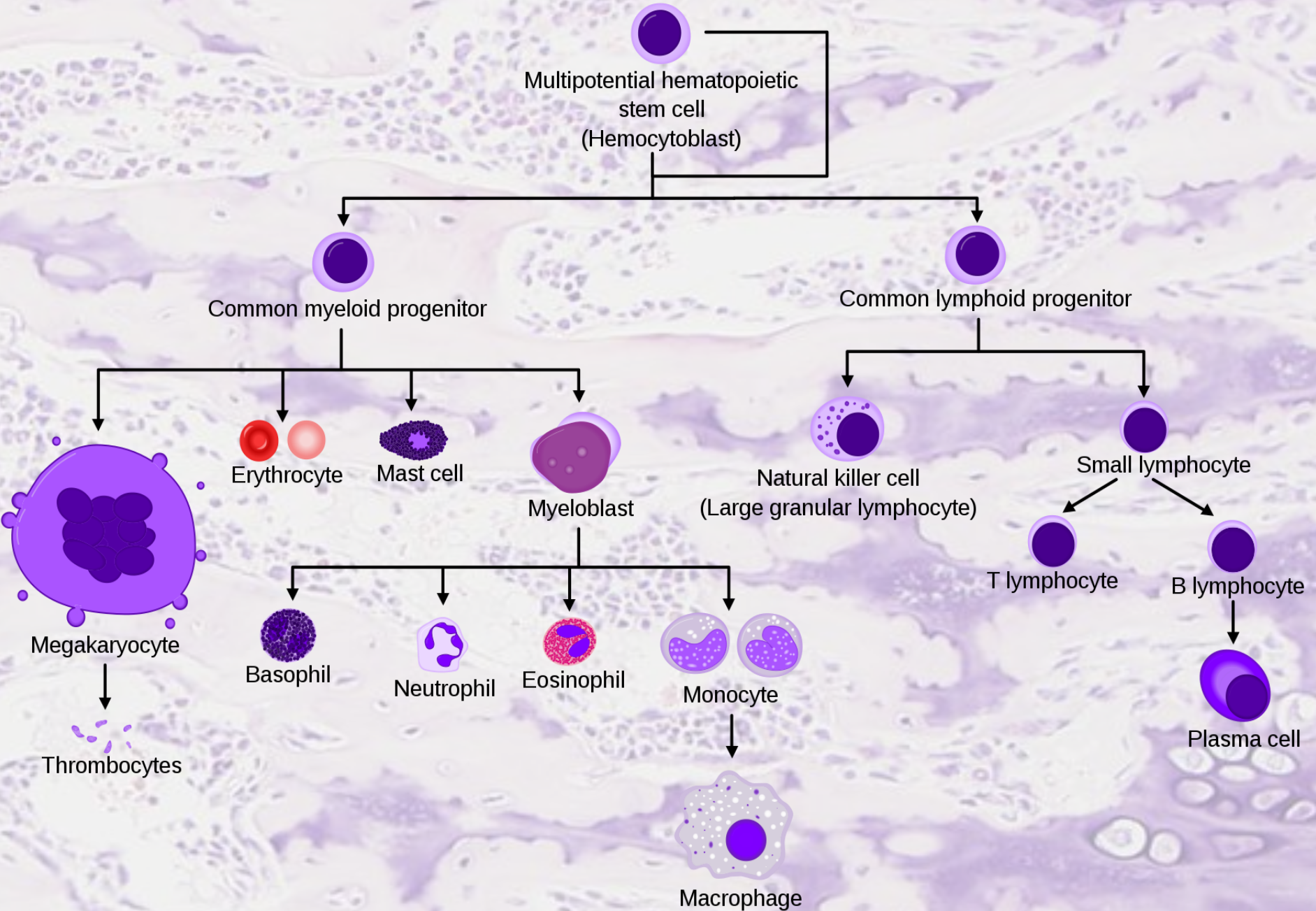
## Age dependence

<b>Age</b>	<b>Leukocytes (<math>\times 10^3</math>)</b>	<b>Neutrophils (%)</b>	<b>Lymphocytes (%)</b>	<b>Monocytes (%)</b>	<b>Eosinophils (%)</b>
Birth	18	61	31	6	2
1 week	12.2	45	41	9	4
1 mo	10.8	35	56	7	3
6 mo	11.9	32	61	5	3
1 yr	11.4	31	61	5	3
4 yr	9.1	42	50	5	3
10 yr	8.1	54	38	4	2
16 yr	7.8	57	35	4	3

WBC, White blood cell.

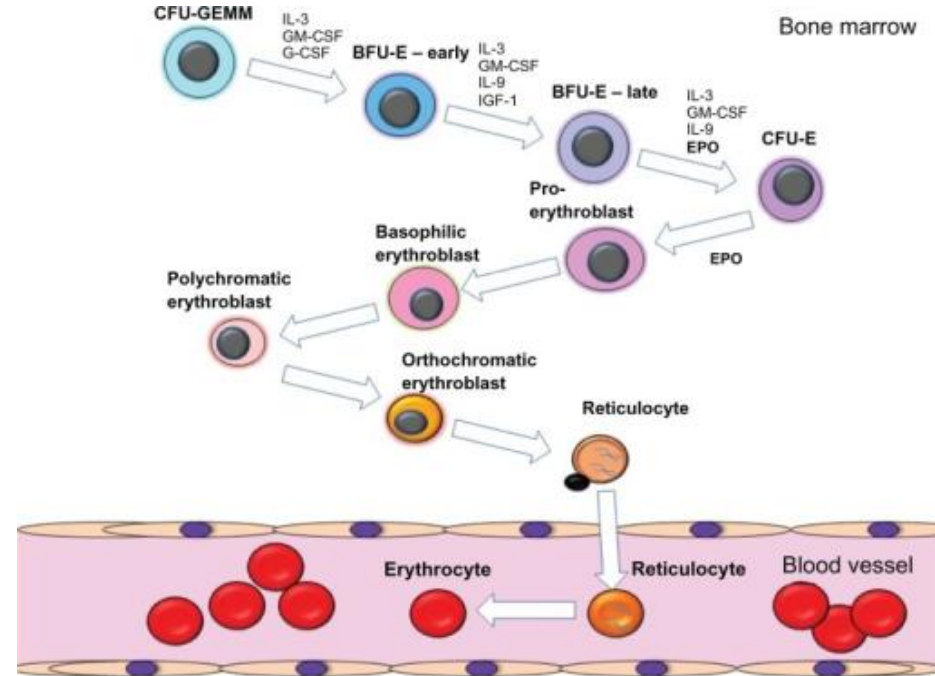


# HEMATOPOIESIS



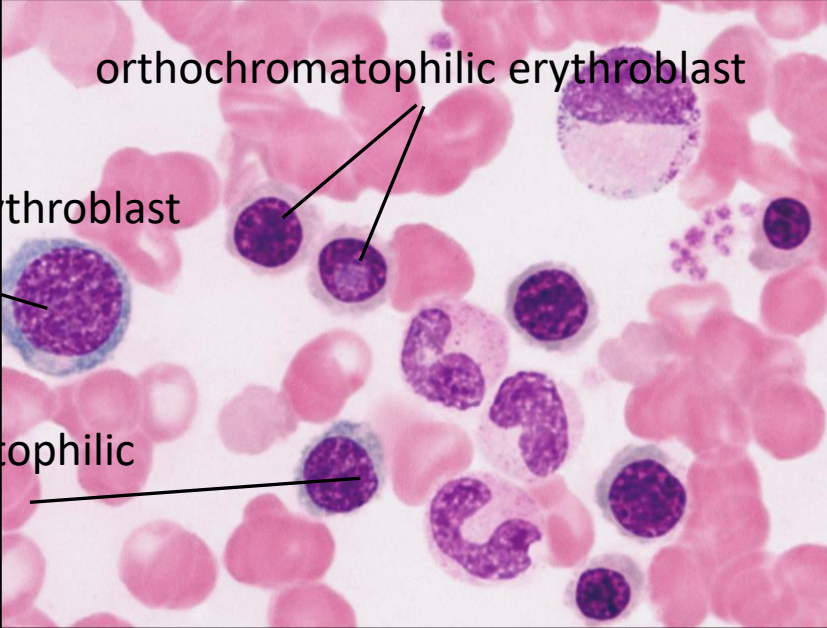
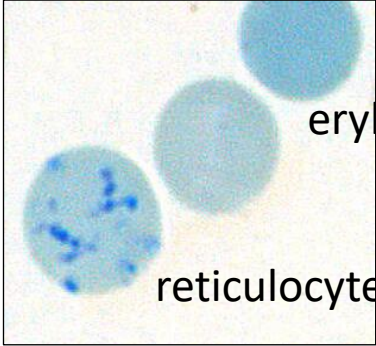
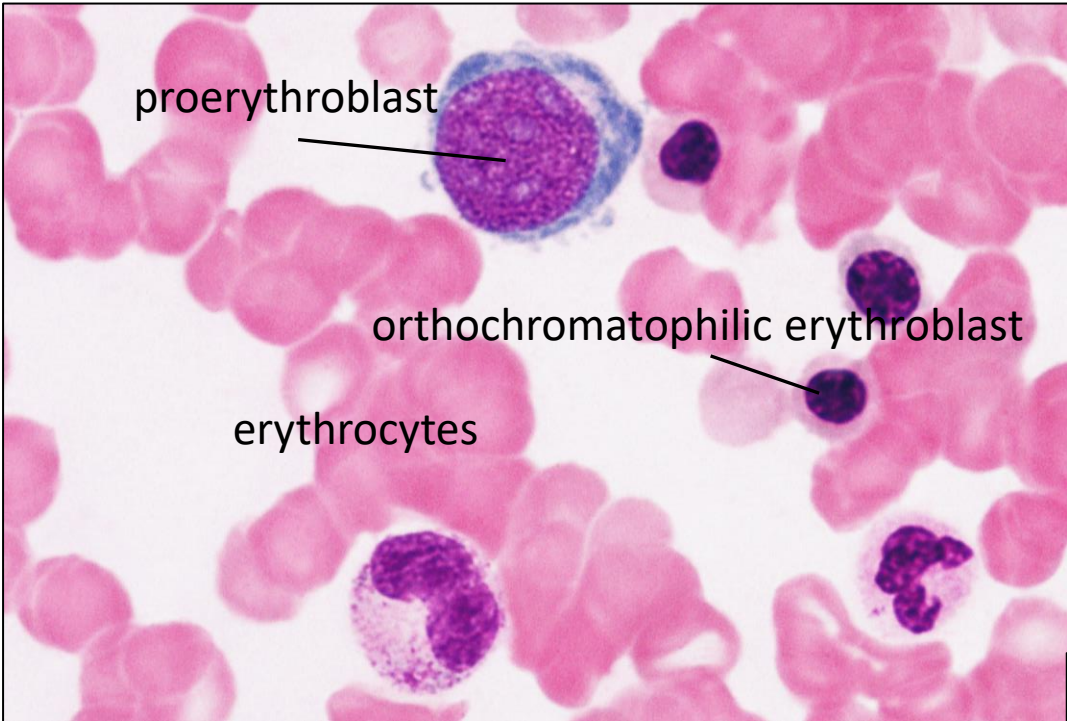
# ERYTHROPOIESIS

- $2 \times 10^{11}$  of new erythrocytes daily
- **proerythroblast** (~14-19  $\mu\text{m}$ )
  - mitotically active
  - dominant, round nucleus with 1-2 nucleoli
  - mildly basophilic cytoplasm
- **basophilic erythroblast** (~13-16  $\mu\text{m}$ )
  - mitotically active
  - heterochromatic nucleus with inconspicuous nucleoli
  - basophilic cytoplasm (sometimes more than in proerythroblast)
- **polychromatophilic erythroblast** (~13-16  $\mu\text{m}$ )
  - mitotically active
  - **production of hemoglobin**
  - blue-gray cytoplasm due to combined basophilic (polyribosomes) and acidophilic aspects (hemoglobin)
  - heterochromatic nucleus (checkerboard appearance)
- **orthochromatophilic erythroblast** (~8-10  $\mu\text{m}$ )
  - mitotically inactive
  - small, compact, eccentric, pyknotic nucleus  $\rightarrow$  **extrusion**
  - mildly acidophilic cytoplasm with basophilic residues
- **reticulocyte** (polychromatophilic erythrocyte, ~ 7-8  $\mu\text{m}$ )
  - **lacks nucleus, still spheroid shape**
  - acidophilic cytoplasm
  - *substantia reticulofilamentosa* visible by supravital staining (brilliant cresyl blue)
- **erythrocyte** (~7-8  $\mu\text{m}$ )
  - anucleate, biconcave disc
  - acidophilic cytoplasm





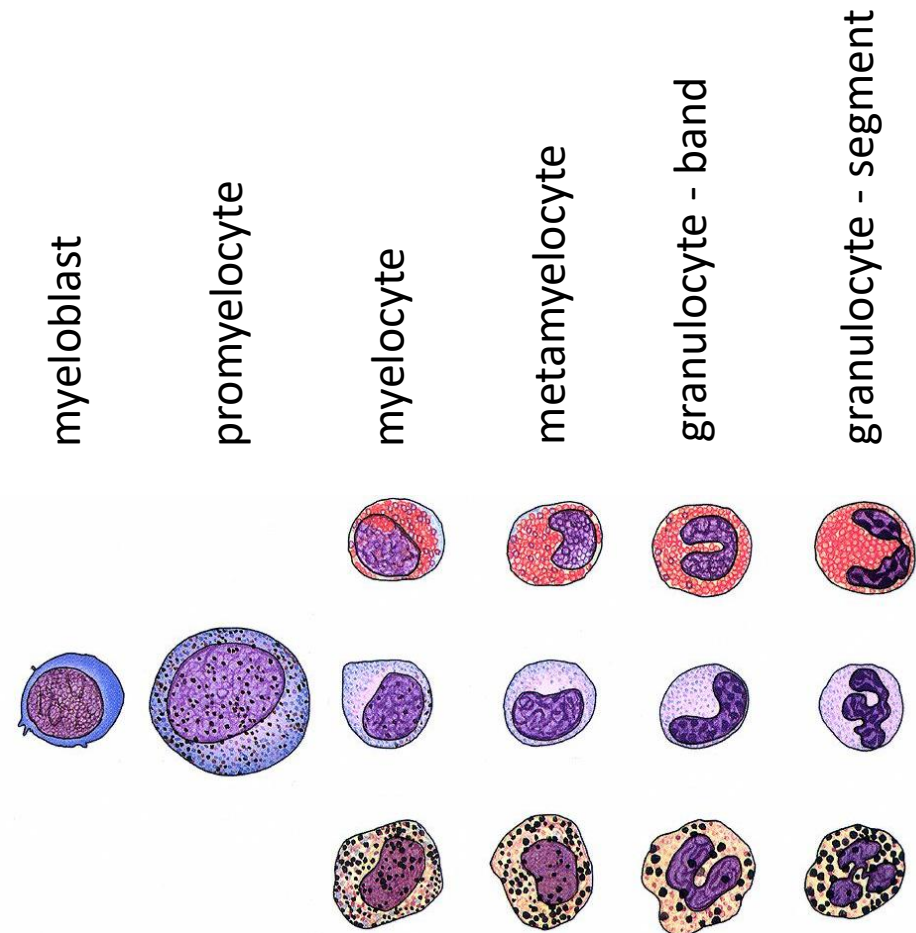
# ERYTHROPOIESIS





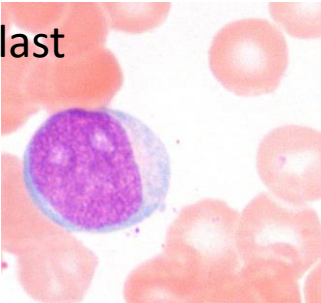
# GRANULOPOIESIS

- **myeloblast** (~15  $\mu\text{m}$ )
  - mitotically active
  - round-oval, euchromatic nucleus
  - 2-6 apparent nucleoli
  - weakly basophilic cytoplasm without granules
- **promyelocyte** (~15-24  $\mu\text{m}$ )
  - mitotically active
  - round-oval nucleus with partly condensed chromatin
  - basophilic cytoplasm with azurophilic granules
- neutrophilic, eosinophilic or basophilic **myelocyte** (~10-16  $\mu\text{m}$ )
  - mitotically active
  - oval or bean-shaped nucleus with condensed chromatin
  - increasing number of specific granules in cytoplasm
- neutrophilic, eosinophilic or basophilic **metamyelocyte** (~10-12  $\mu\text{m}$ )
  - mitotically inactive
  - horseshoe-like nucleus with condensed chromatin
- neutrophilic, eosinophilic or basophilic **granulocyte** (~10-12  $\mu\text{m}$ )
  - segmentation of nucleus
  - cytoplasm rich in specific and azurophilic granules

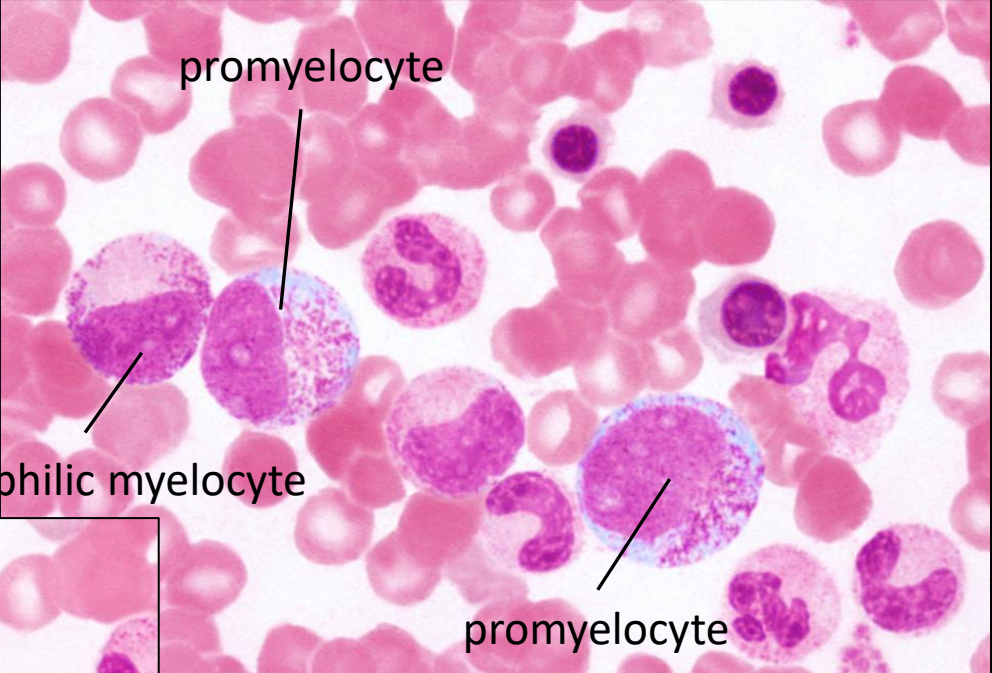


# GRANULOPOIESIS

myeloblast



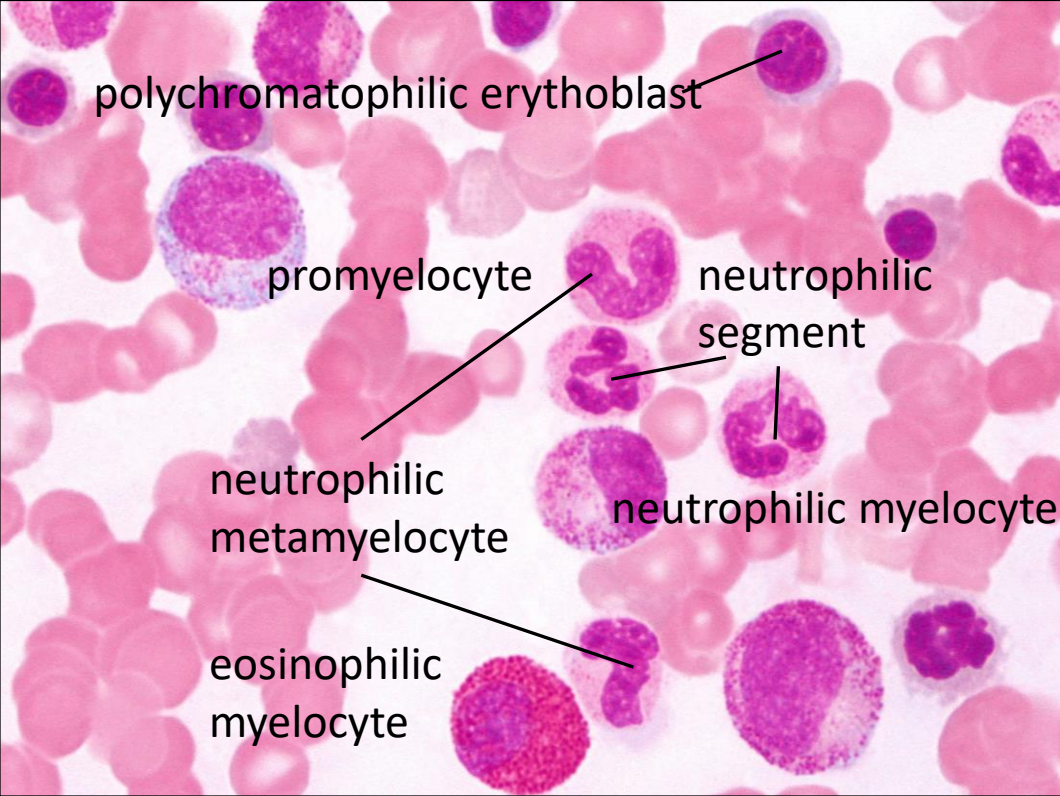
promyelocyte



neutrophilic myelocyte

promyelocyte

polychromatophilic erythroblast



promyelocyte

neutrophilic segment

neutrophilic metamyelocyte

neutrophilic myelocyte

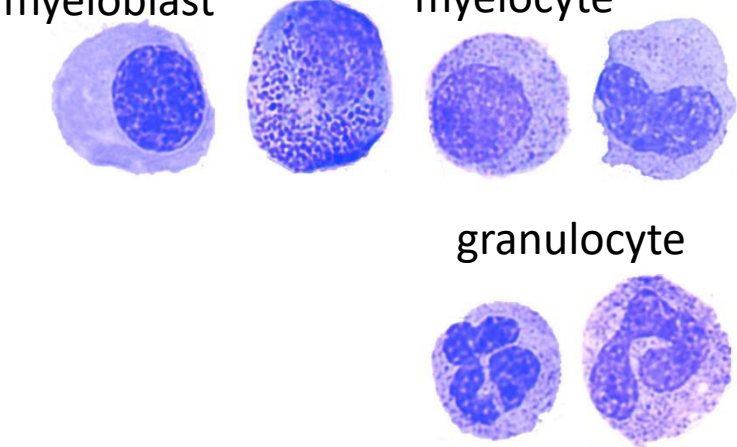
eosinophilic myelocyte

promyelocyte

metamyelocyte

myeloblast

myelocyte

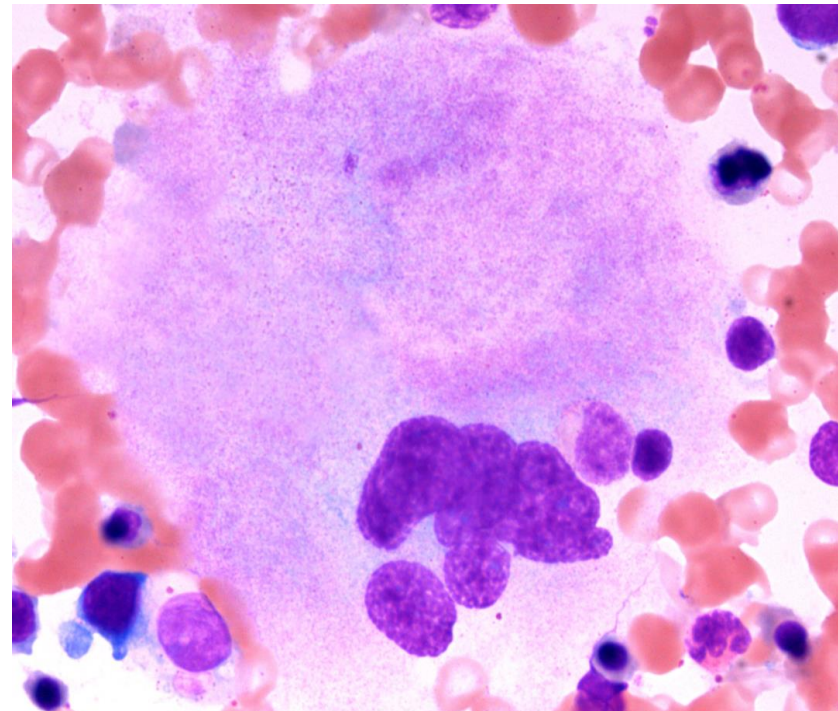
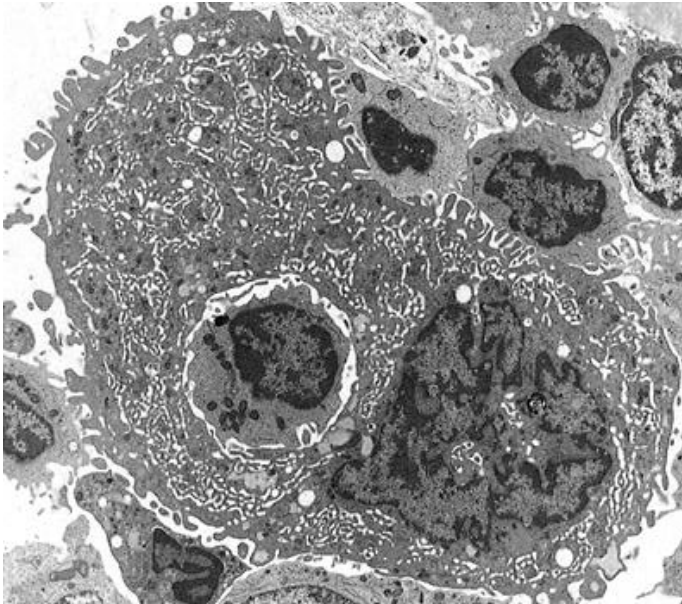
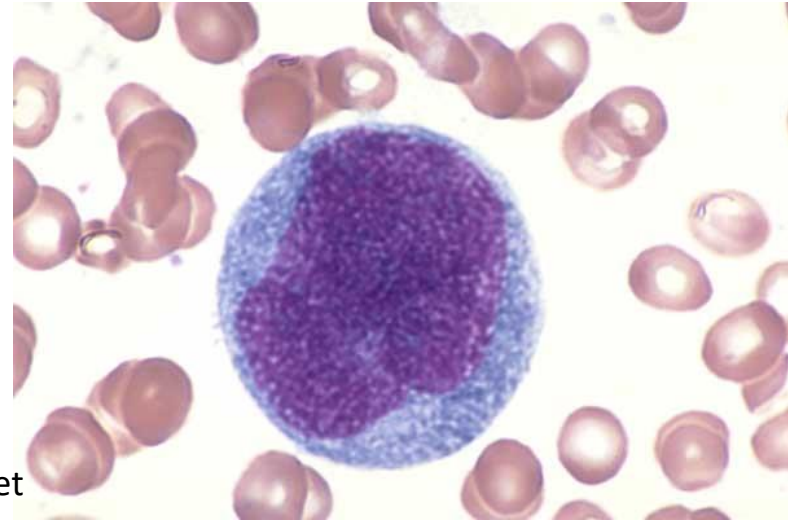


granulocyte



# THROMBOPOIESIS

- **megakaryoblast** (up to 30  $\mu\text{m}$ )
  - large oval, nonlobed nucleus with prominent nucleoli
  - basophilic cytoplasm
  - successive endomitoses without karyokinesis and cytokinesis
- **promegakaryocyte** (up to 100  $\mu\text{m}$ )
  - large cell with polyploid nucleus (8n-64n)
- **megakaryocyte** (80-150  $\mu\text{m}$ )
  - polyploid, multilobed nucleus (8n-64n)
  - azurophilic and platelet granules
  - multiple centrioles, ER and Golgi apparatus
  - numerous peripheral invaginations of plasma membrane – platelet demarcation channels defining individual thrombocytes
  - release of **thrombocytes** into bone marrow sinusoids





# MONOCYTOPOIESIS AND LYMPHOPOIESIS

## MONOCYTOPOIESIS

- **monoblast** (~16  $\mu\text{m}$ )
  - round, bean shaped nucleus with 2-6 nucleoli
  - mildly basophilic cytoplasm
- **promonocyte** (~16-20  $\mu\text{m}$ )
  - mitotically active (1-2 divisions)
  - large nucleus with mild indentation, unapparent nucleoli
  - basophilic cytoplasm
  - azurophilic granules
- **monocyte**
  - short-time in circulation, then extravasation and differentiation to tissue macrophages

## LYMPHOPOIESIS

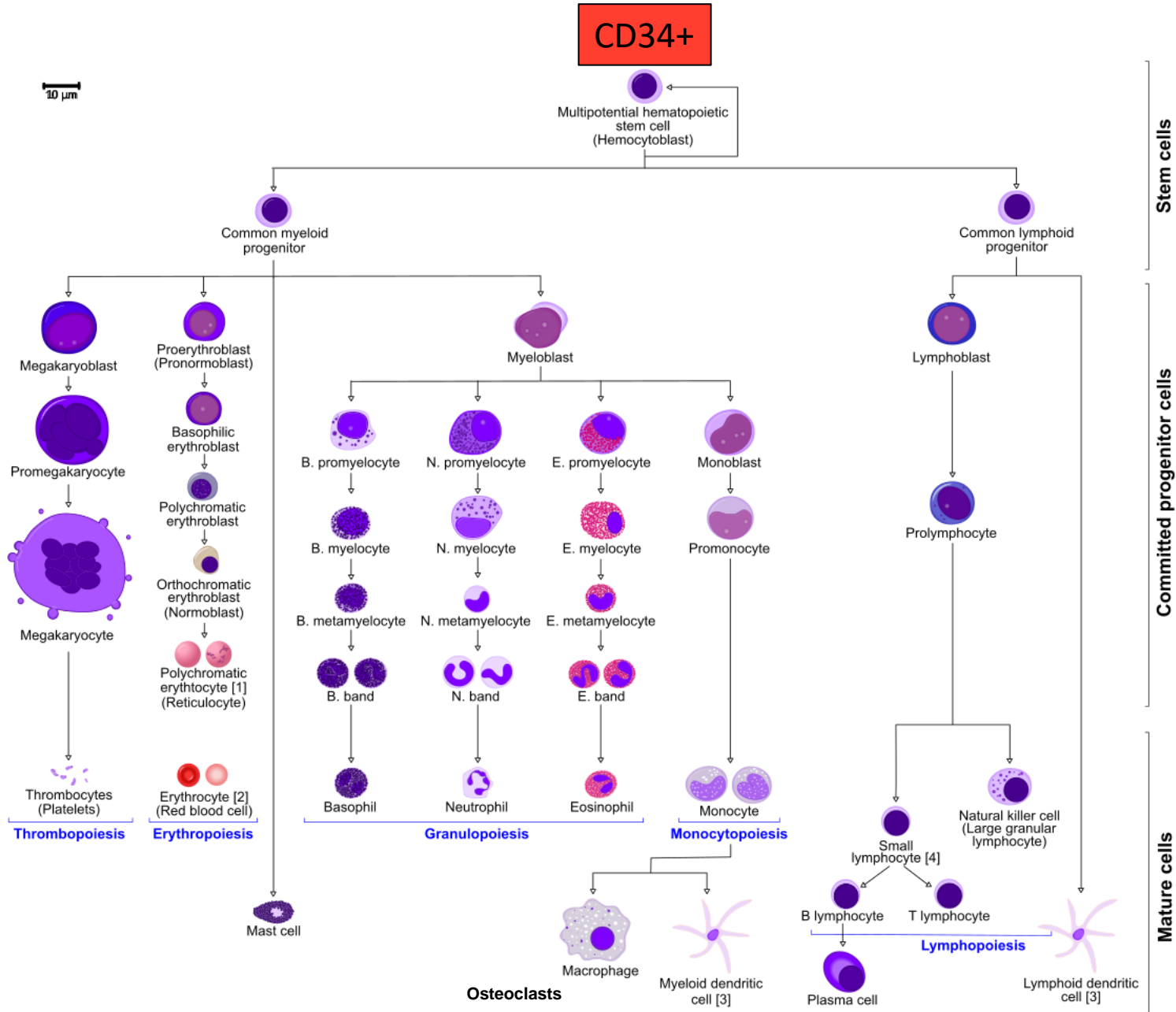
- **lymphoblast** (~18-20  $\mu\text{m}$ )
  - round-oval nucleus with several nucleoli
  - mildly-basophilic cytoplasm without azurophilic granules
- **prolymphocyte** (~12-15  $\mu\text{m}$ )
  - morphological transition and maturation to lymphocytes
- **lymphocyte**
  - further maturation and differentiation outside bone marrow

# OVERVIEW OF ADULT HEMATOPOIESIS

Bone marrow

Blood

Tissue



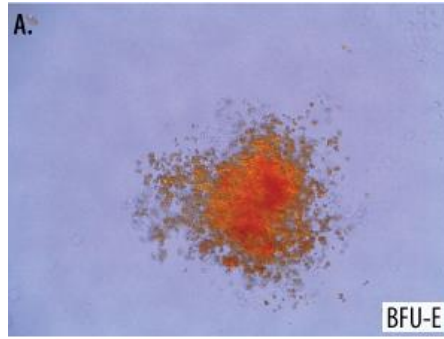
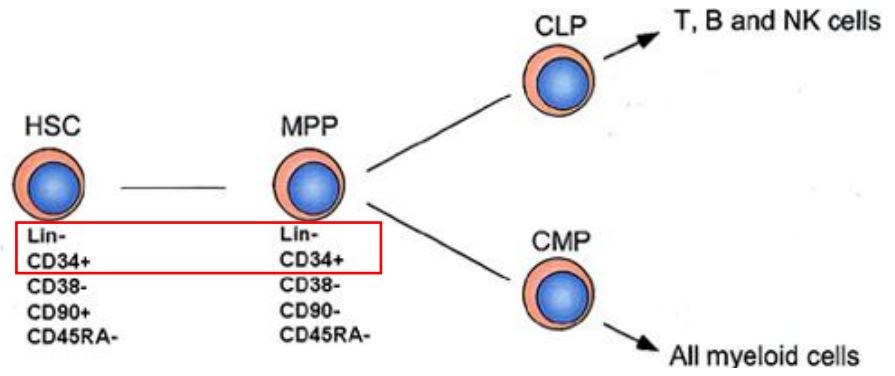
# HEMATOPOIETIC STEM CELLS AND PROGENITORS

- **Hematopoietic stem cell**

- Quiescent, slow cell cycle
- Bone marrow niche
- Transmembrane phosphoglycoprotein CD34<sup>+</sup> - adhesion within niche
- No expression of lineage surface markers (Lineage negative or Lin<sup>-</sup>)
- Autologous transplantations

- **Colony/Burst – Forming Unit – CFU/BFU**

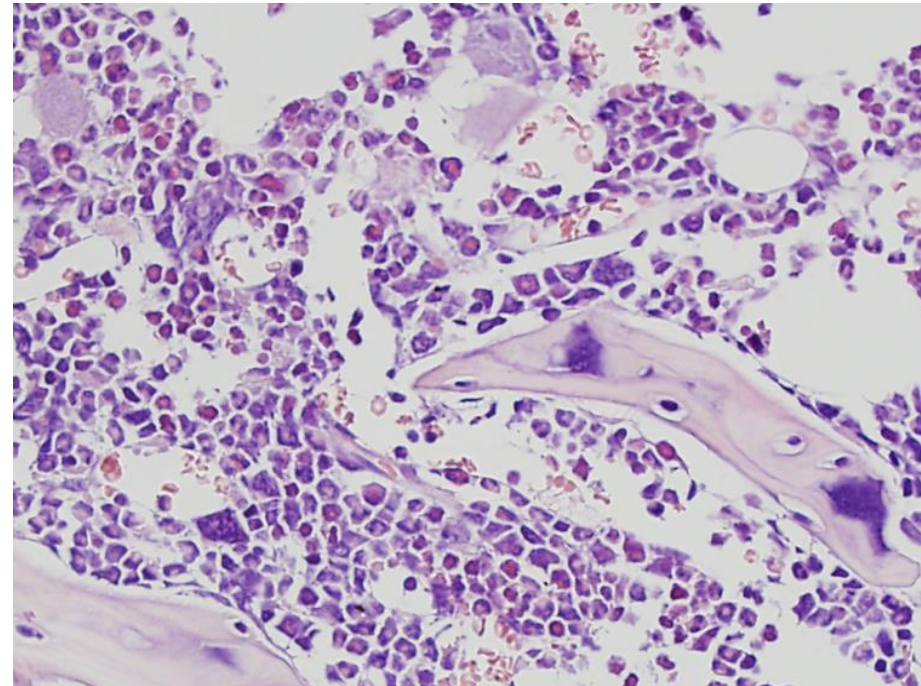
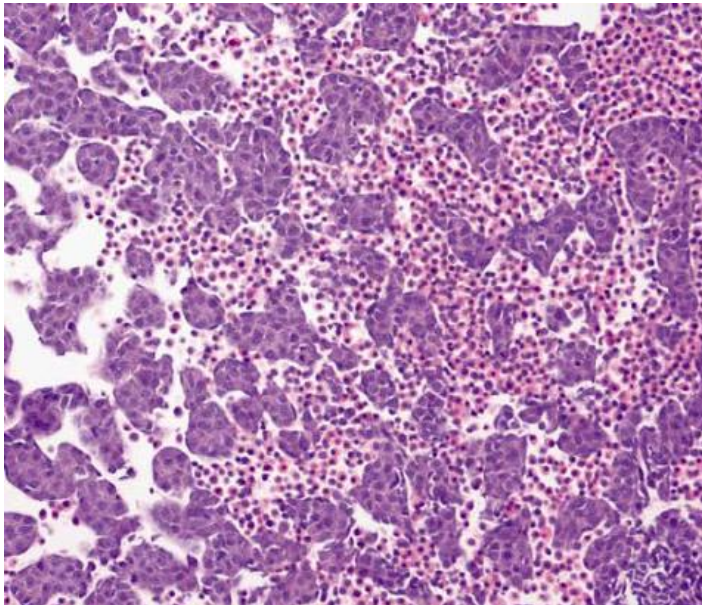
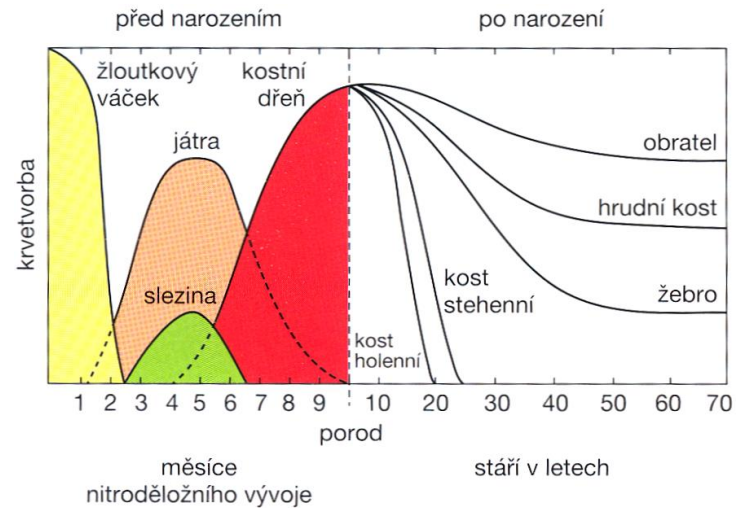
- Progenitors of individual lines characterized in vitro
- Colonies in vitro





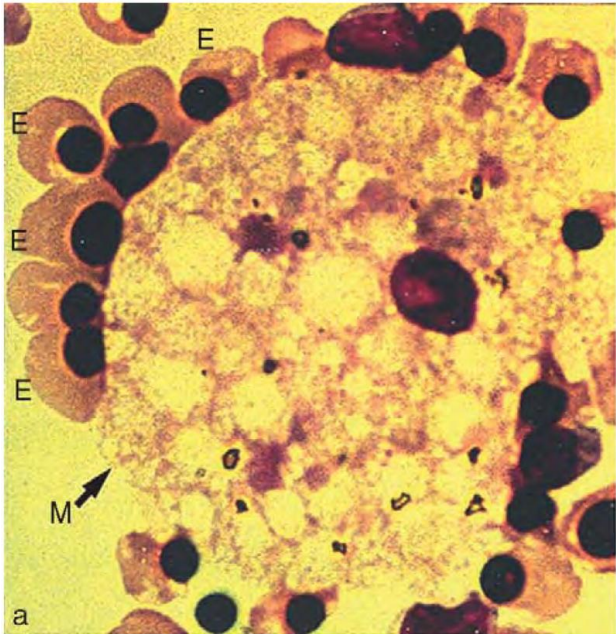
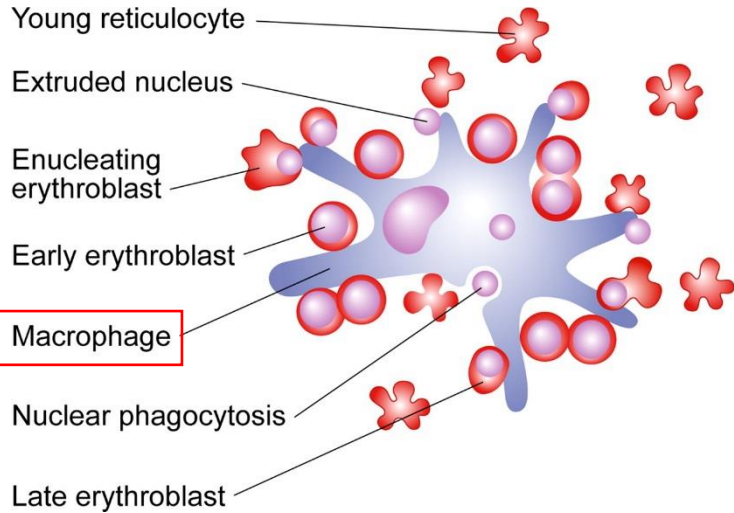
# EMBRYONIC HEMATOPOIESIS

- **Extraembryonic mesoblastic period (day 16-20 – week 8)**
  - yolk sac
  - classical model – hemangioblasts (bipotent cells)
  - large, nucleated erythroid cells
- **aorta-gonad-mesonephros (day 28 – week 4)**
- **hepatolienal period (month 1 – birth)**
  - colonization of fetal liver and spleen
- **medullary period (month 4-6. – rest of life)**
  - bone marrow

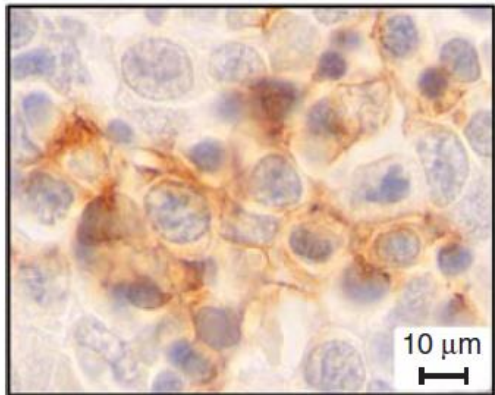


# HEMATOPOIETIC ISLANDS

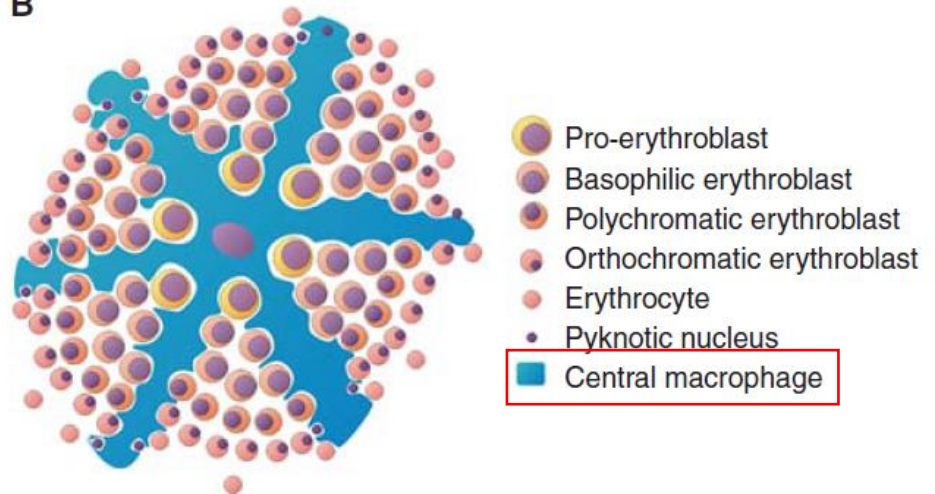
- hepatolienal and bone marrow hematopoiesis
- erythroblast islands



A



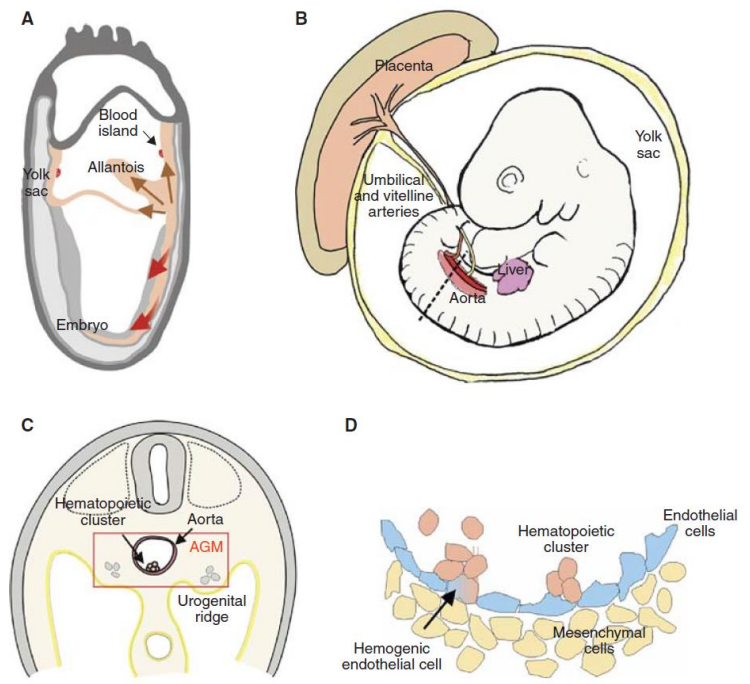
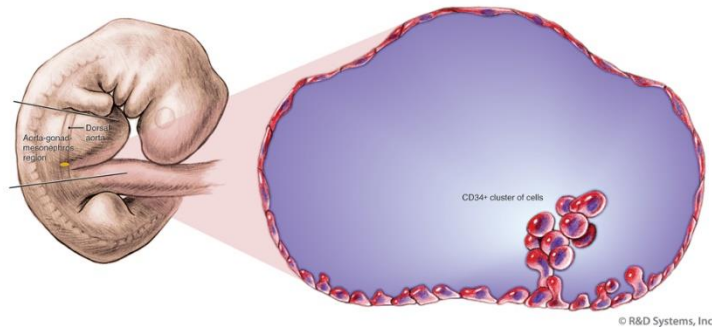
B



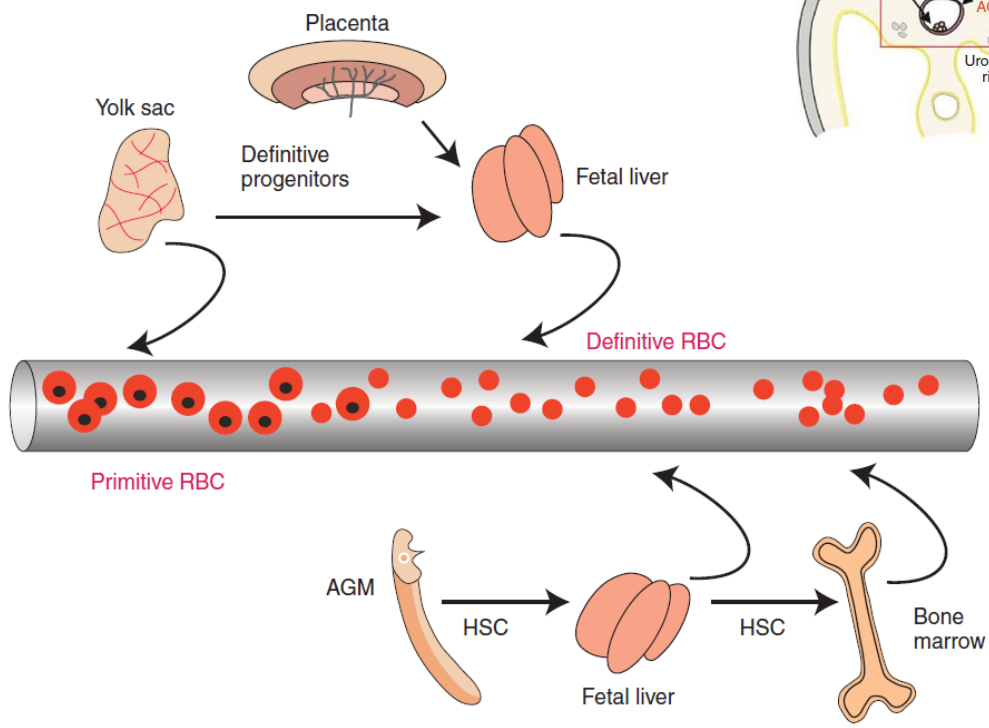


# INTRAEMBRYONIC HEMATOPOIESIS

- **Aorta-gonad-mesonephros (day 28 – week 4)**
- para-aortic clusters in mesoderm of splanchnopleura
- source of embryonic HSCs



- **Placenta**

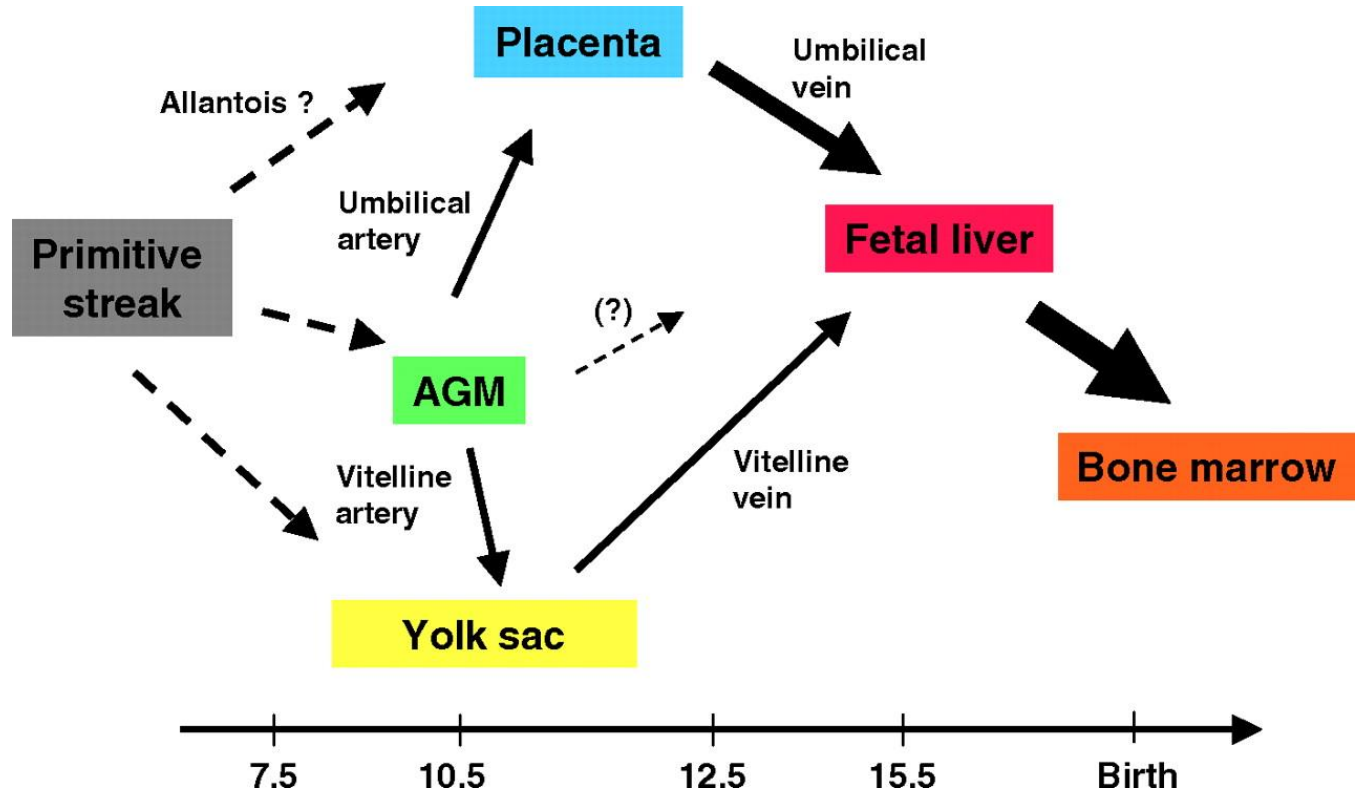




# SUMMARY OF HEMATOPOIESIS

## Embryonic

- yolk sac
- AGM
- liver and spleen
- bone marrow



## Adult

- bone marrow (yellow, red)
- extramedullar hematopoiesis rare (pathology)

# Thank you for attention

