

# BLOOD AND HEMATOPOIESIS

A 3D digital illustration of a blood vessel. The vessel is shown in a cross-section, with a reddish-brown interior. Numerous red blood cells, depicted as biconcave discs, are scattered throughout the vessel. Interspersed among the red cells are several white blood cells, shown as larger, spherical cells with a lighter, yellowish hue. The overall scene is set against a dark, textured background that suggests the inner lining of the vessel.

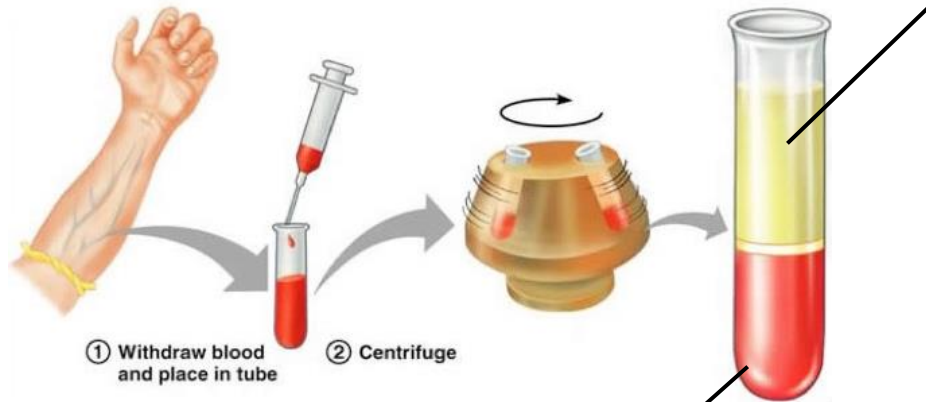
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LF MU

# 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

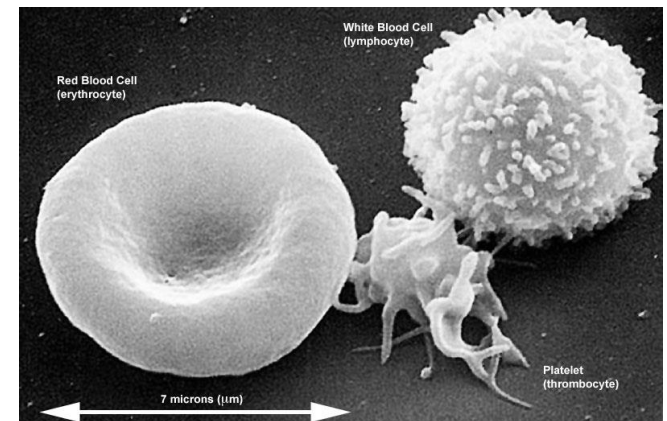
- ions, proteins, low mass organic compounds
- fluid ECM



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

## formed blood elements

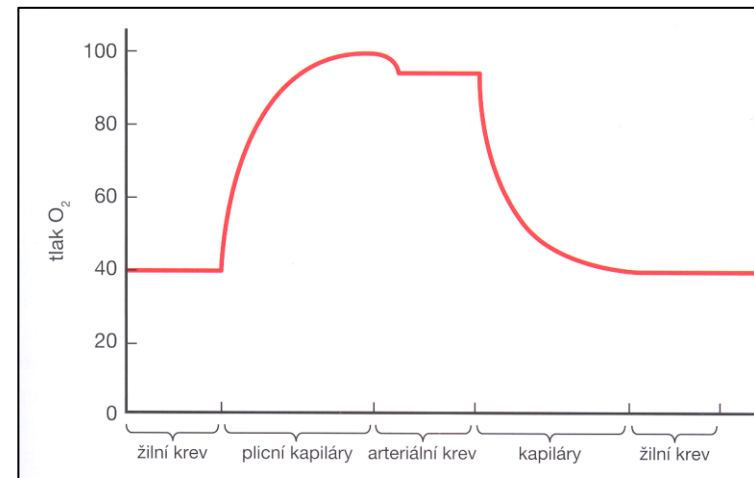
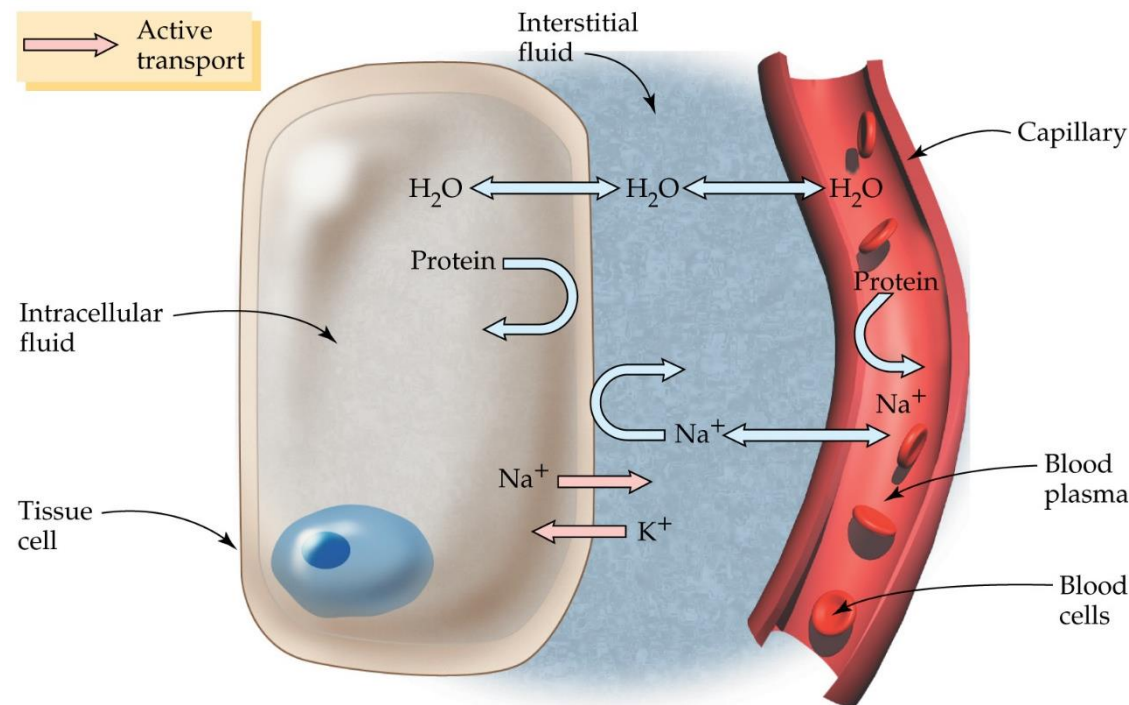
- erythrocytes
- leukocytes
- thrombocytes



# 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** (Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>+</sup>, Mg<sup>+</sup>, Cl<sup>-</sup>, HCO<sub>3</sub><sup>-</sup>), **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 μmol/l	Cofactor of enzymes, in hem of hemoglobin
	Iron ♀	10–24 μmol/l	
	Copper	12–22 μmol/l	Cofactor of enzymes
	Chlorides	95–110 mmol/l	Osmotic pressure, volume, pH
Anions	Bicarbonates [HCO <sub>3</sub> ] <sup>-</sup>	22–26 mmol/l	Transport of CO <sub>2</sub> , buffer - pH
	P <sub>i</sub>	0,6–1,4 mmol/l	Buffer - pH
	Iodide	276–630 μmol/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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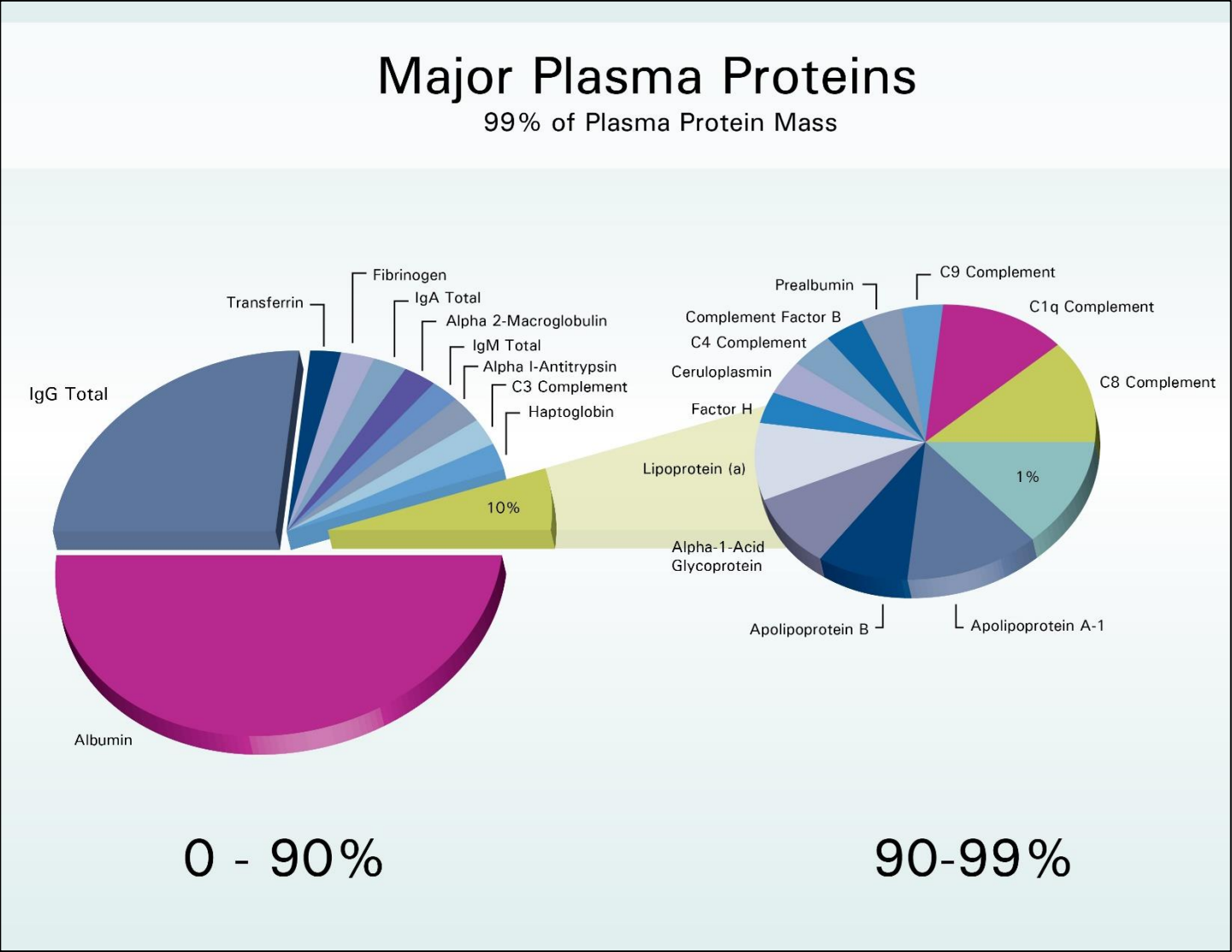
But what is important to know is that:



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

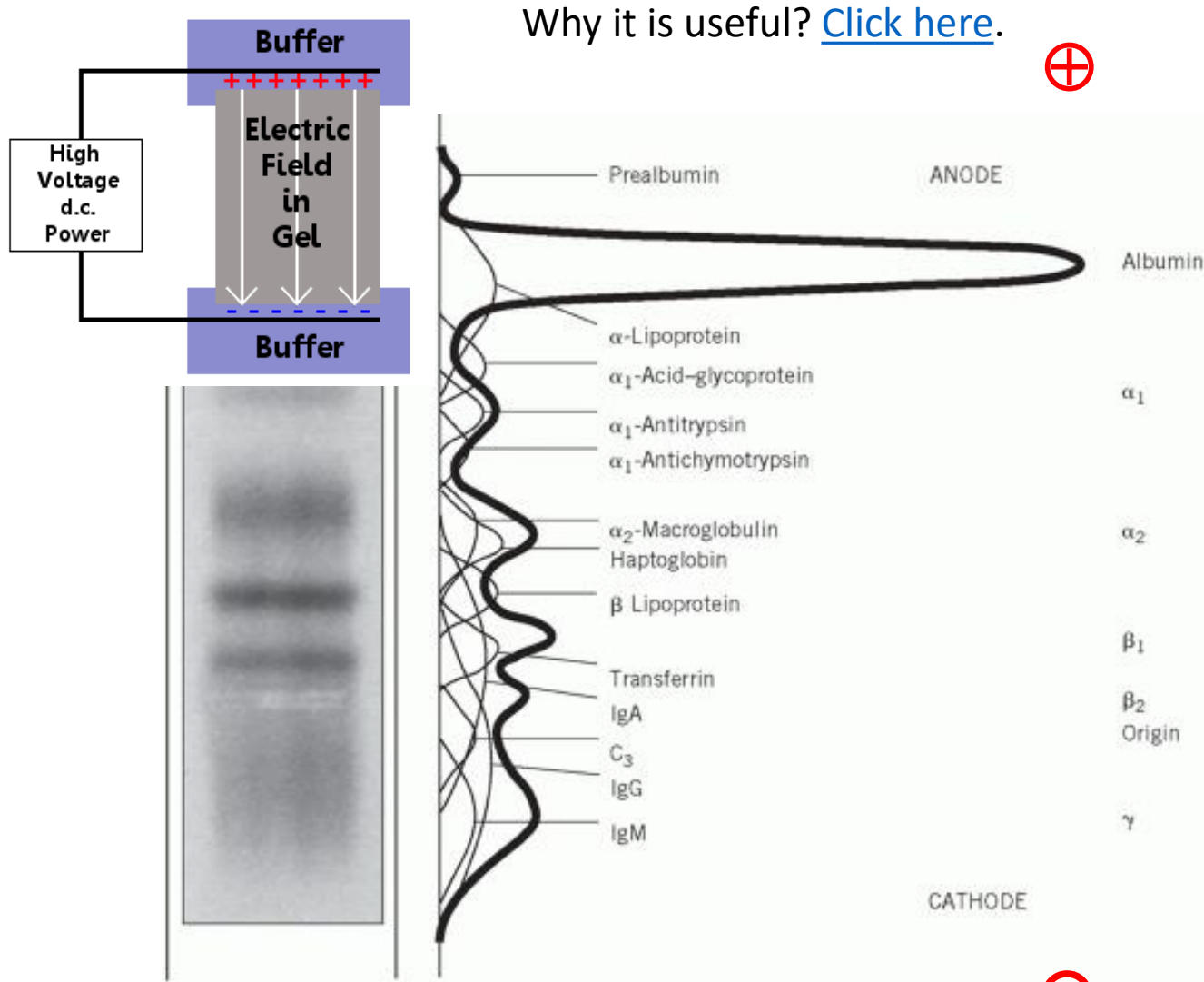
# PROTEINS OF BLOOD PLASMA (7%)

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



# PROTEINS OF BLOOD PLASMA (7%)

- **prealbumin**
- transport
- **albumin**
- 68kDa
- transport
- osmotic pressure
- **$\alpha_1$  region**
- $\alpha_1$  lipoprotein (HDL)
- $\alpha_1$  acid glycoprotein
- $\alpha_1$  antitrypsin
- ( $\alpha_1$  fetoprotein)
- **$\alpha_2$  region**
- $\alpha_2$  macroglobulin
- haptoglobin
- **$\beta_1$  region**
- transferrin
- hemopexin
- $\beta$  lipoprotein (LDL)
- C4 (complement)
- **$\beta_2$  region**
- CRP
- fibrinogen
- $\beta_2$  microglobulin
- C3 (complement)
- **$\gamma$  region**
- IgA, IgG, IgM

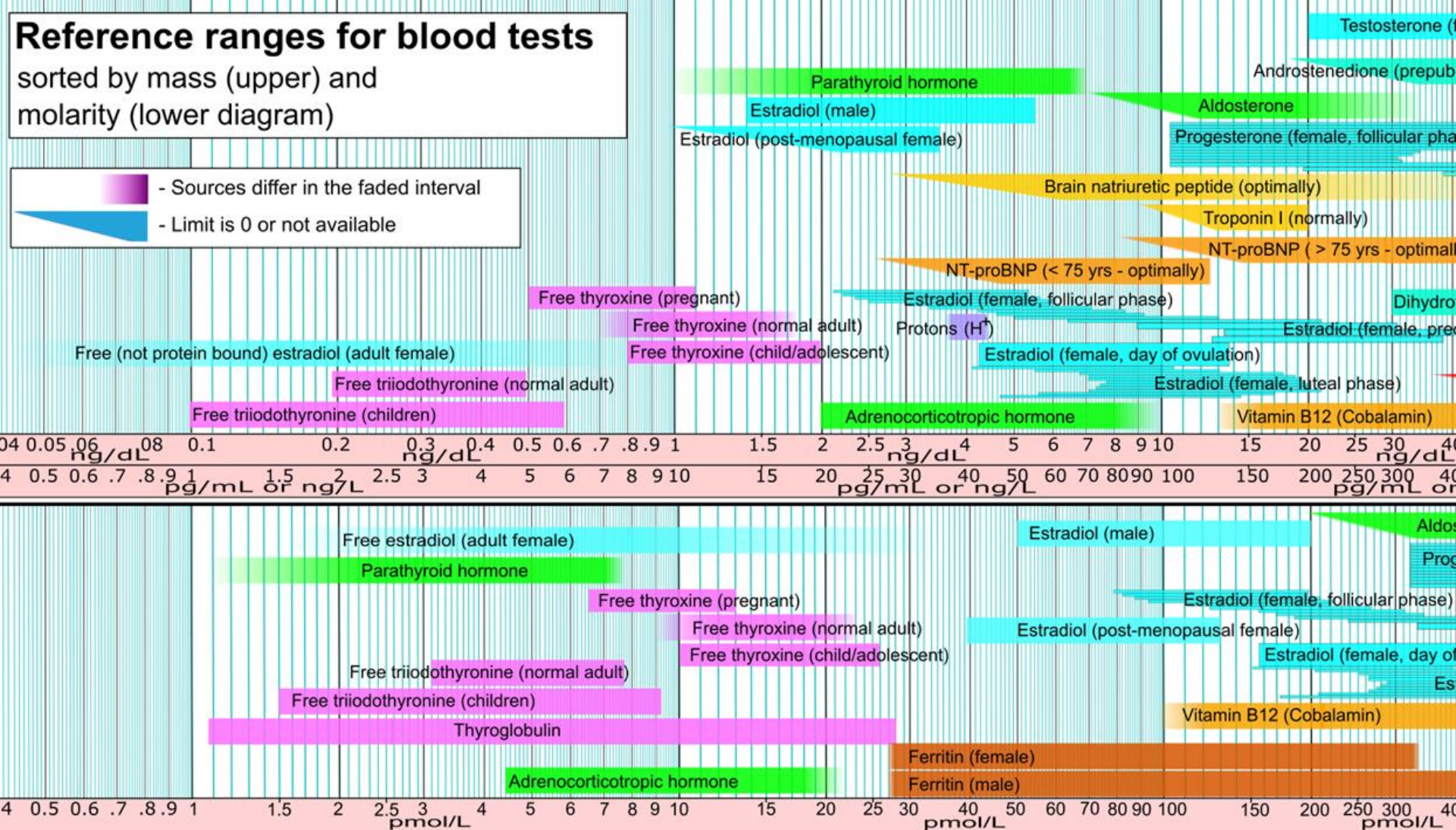


. Electrophoretic separation of serum proteins  
**A.** Electrophoretogram of normal serum on cellulose acetate strip  
**B.** Densitometric scanning from cellulose acetate strip converts bands to characteristic peaks of albumin,  $\alpha_1$ -globulin,  $\alpha_2$ -globulin,  $\beta$ -globulin and  $\gamma$ -globulin

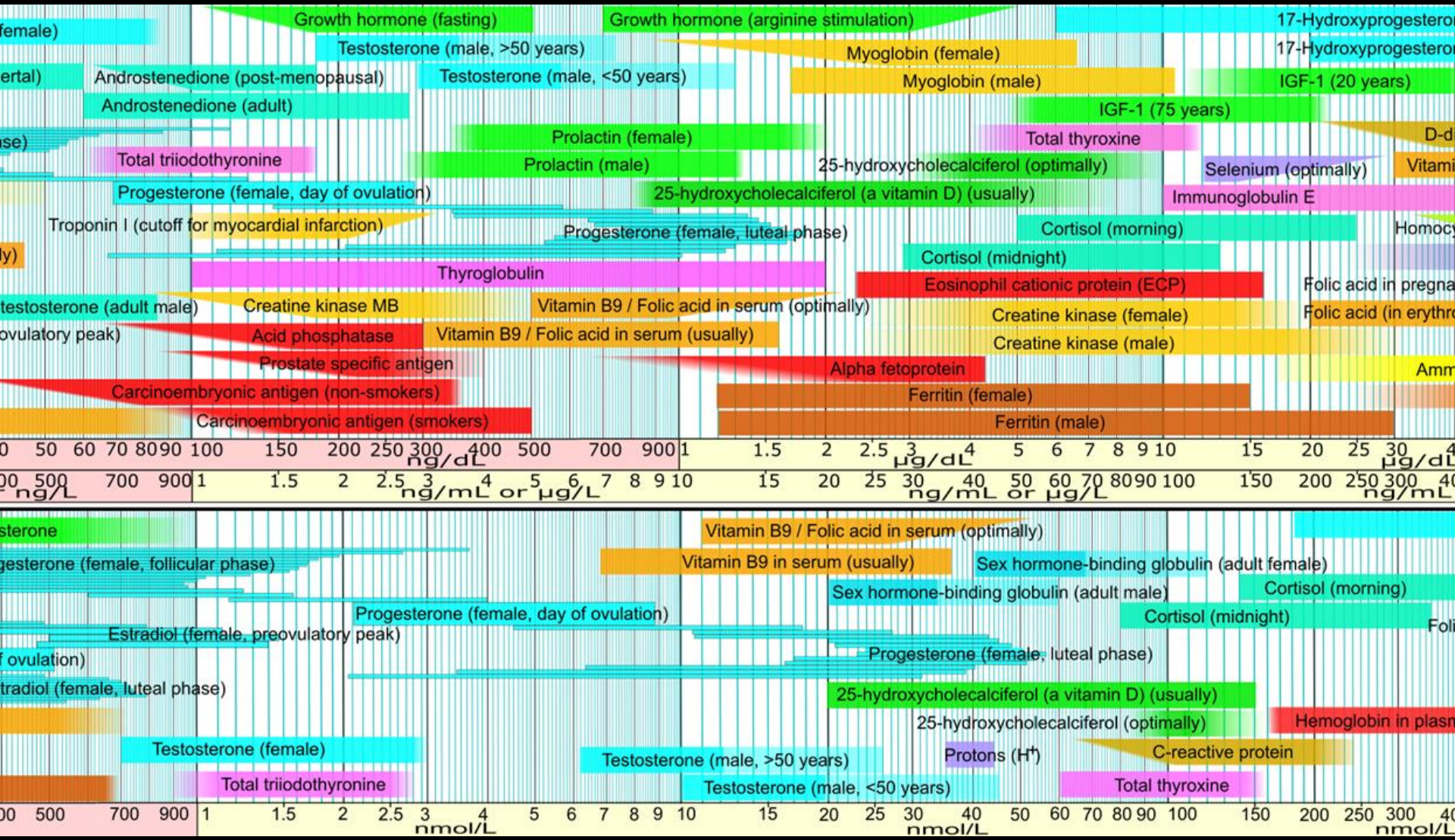
# Reference ranges for blood tests

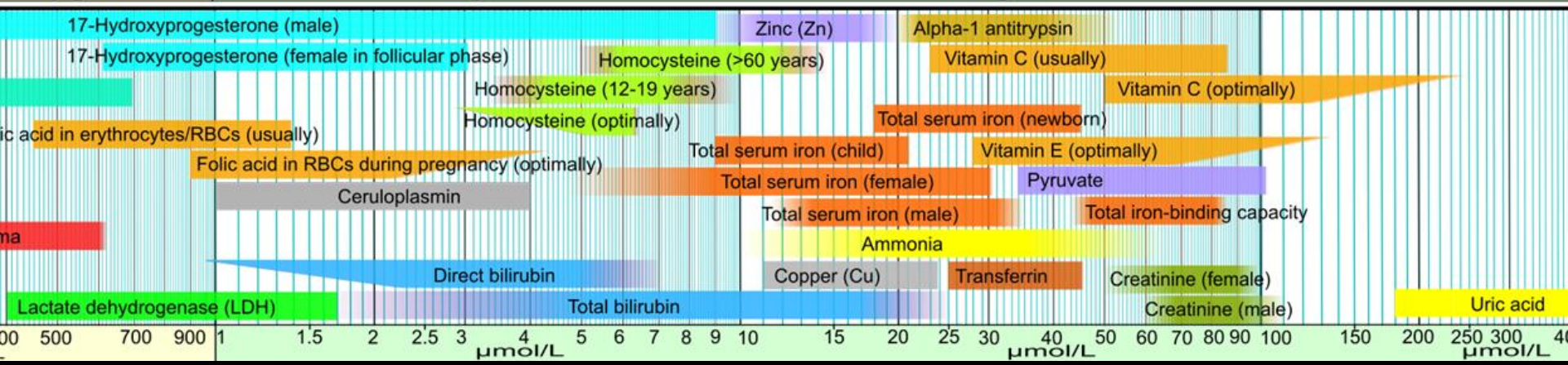
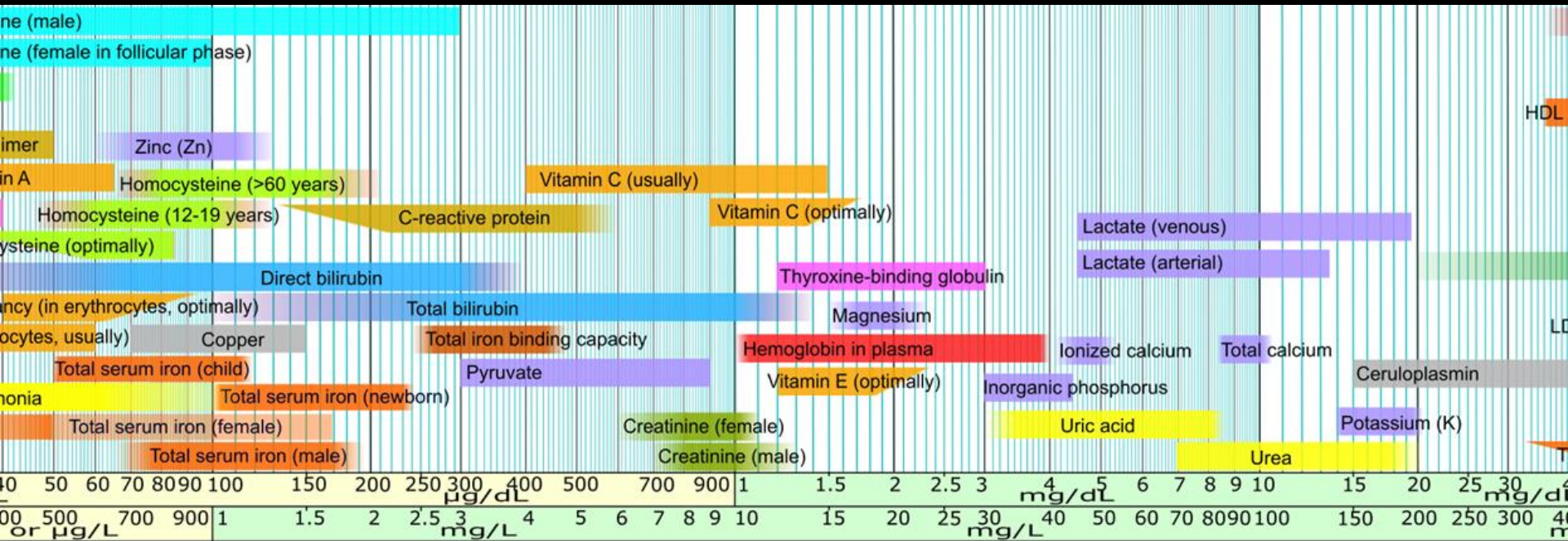
sorted by mass (upper) and molarity (lower diagram)

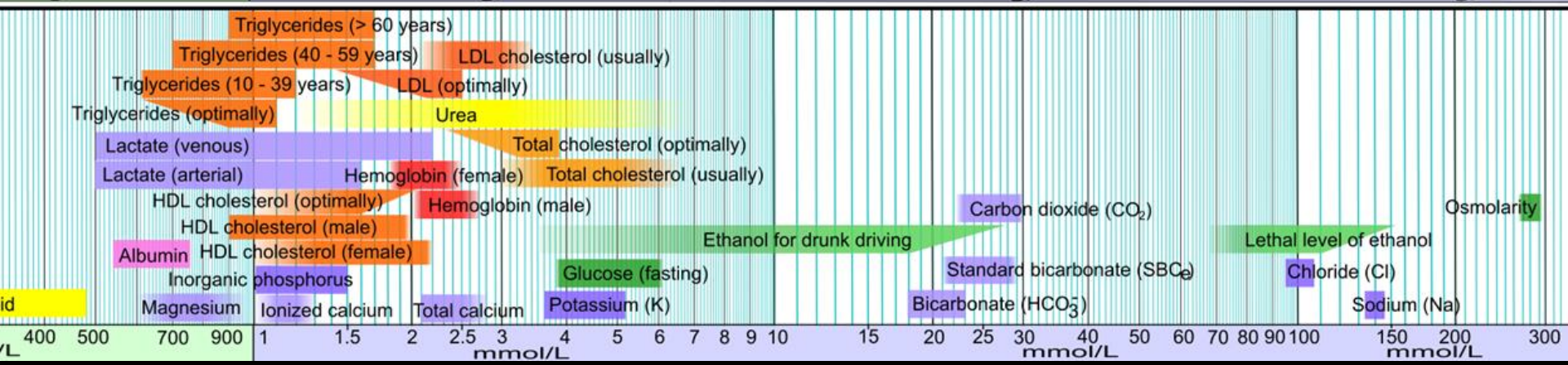
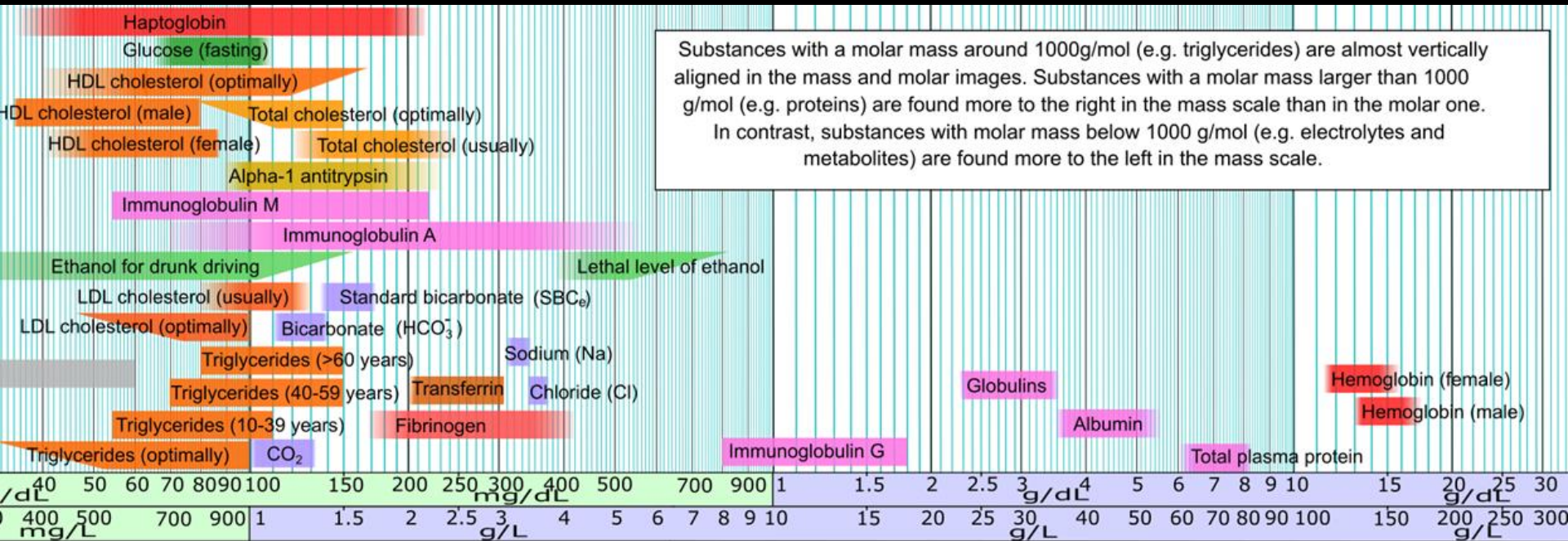
- Sources differ in the faded interval
- Limit is 0 or not available





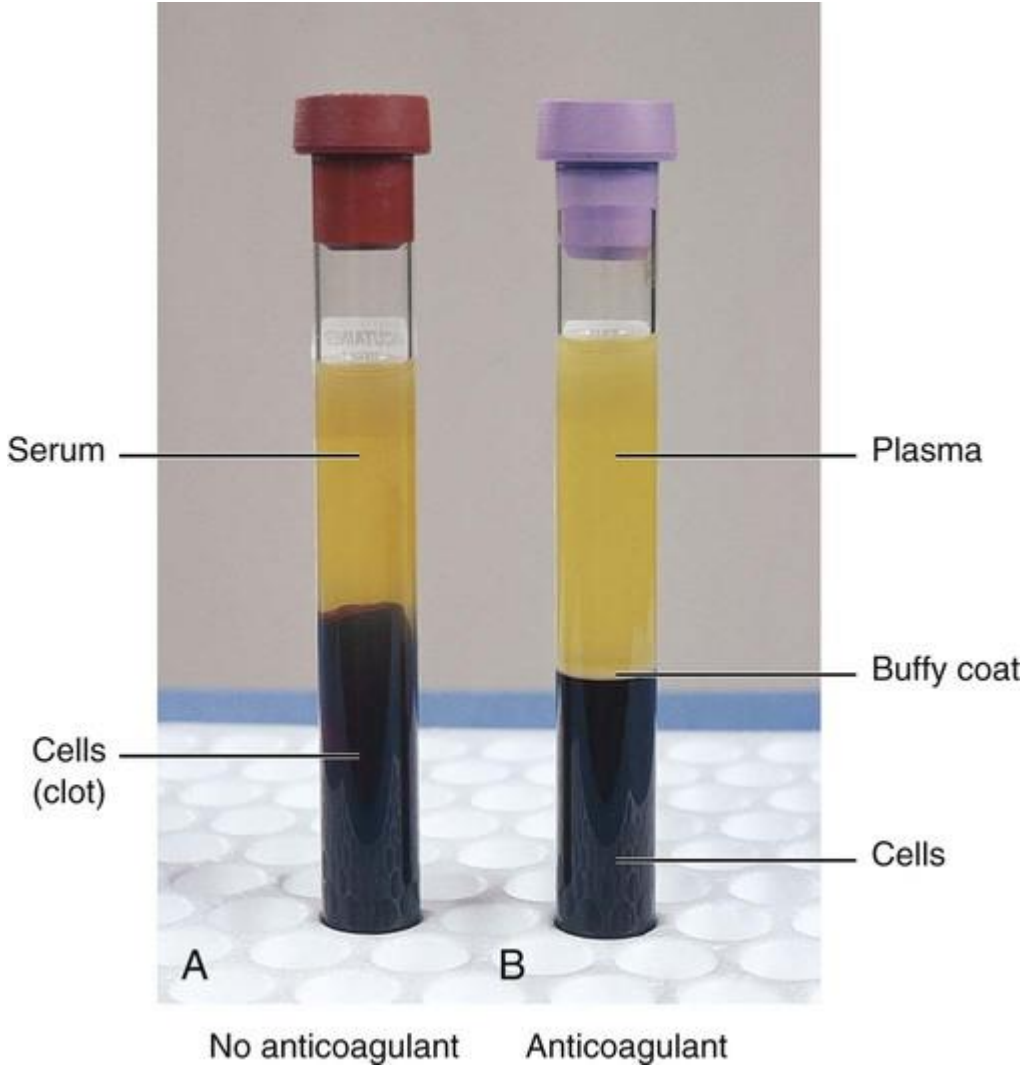




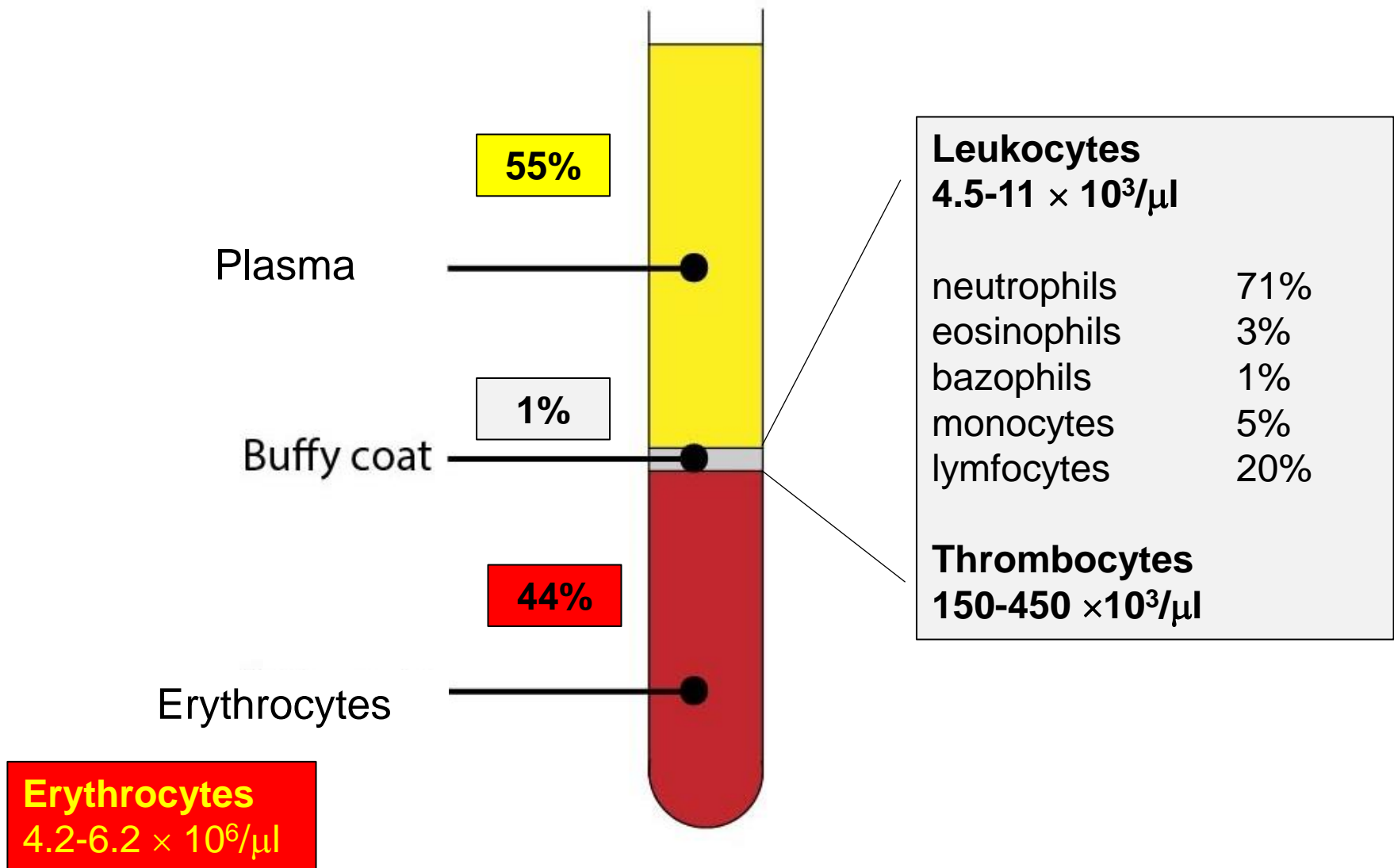


# BLOOD PLASMA AND SERUM

- 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±5%**

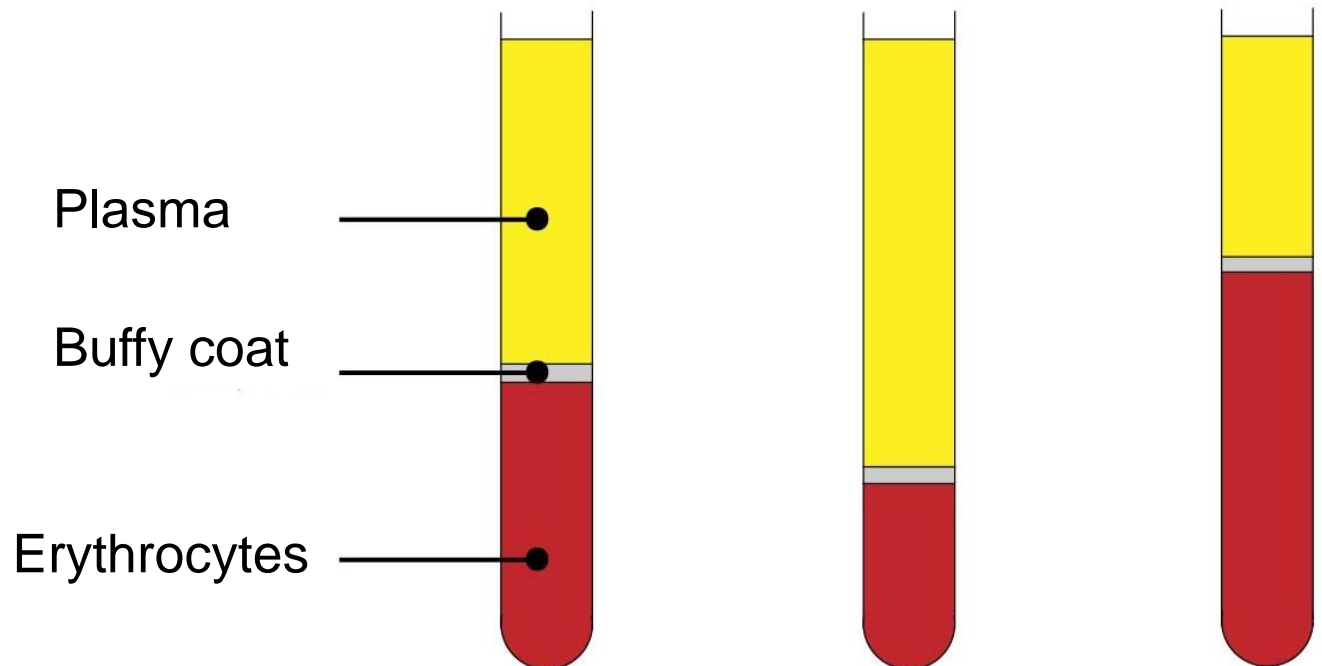


**42±4%**

Normal

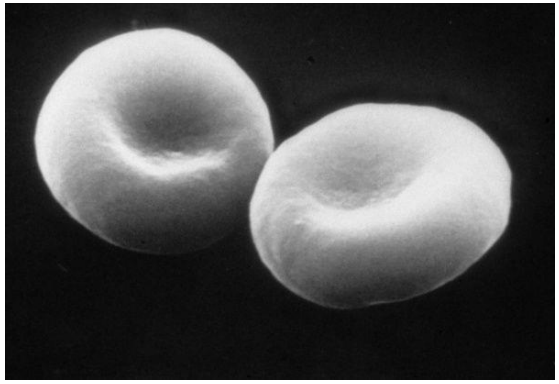
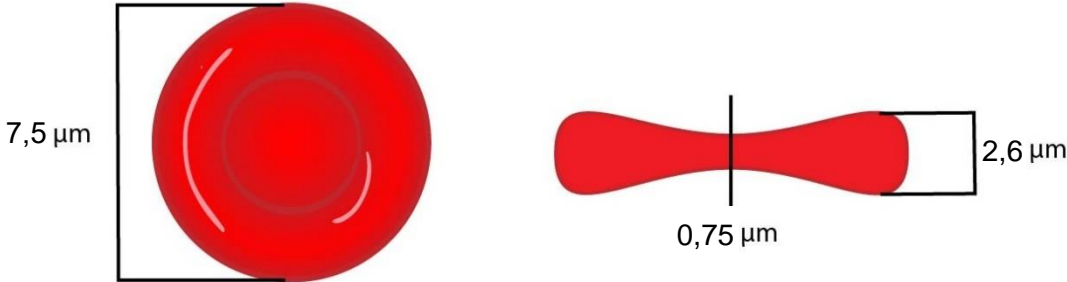
Erythropenia

Polycythemia



# ERYTHROCYTES

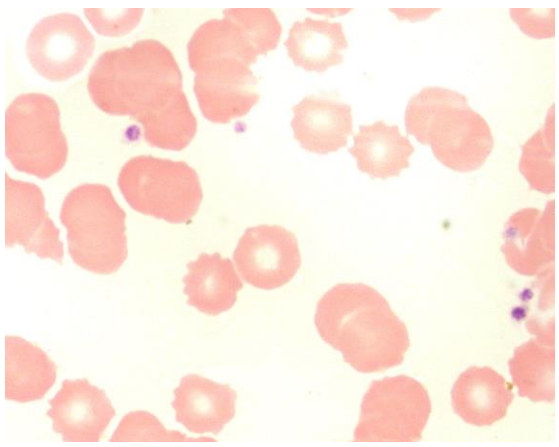
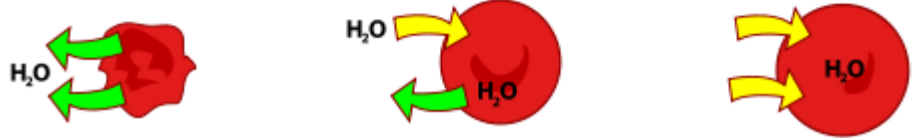
Size depends on **osmotic pressure of environment**



Hypertonic

Isotonic

Hypotonic

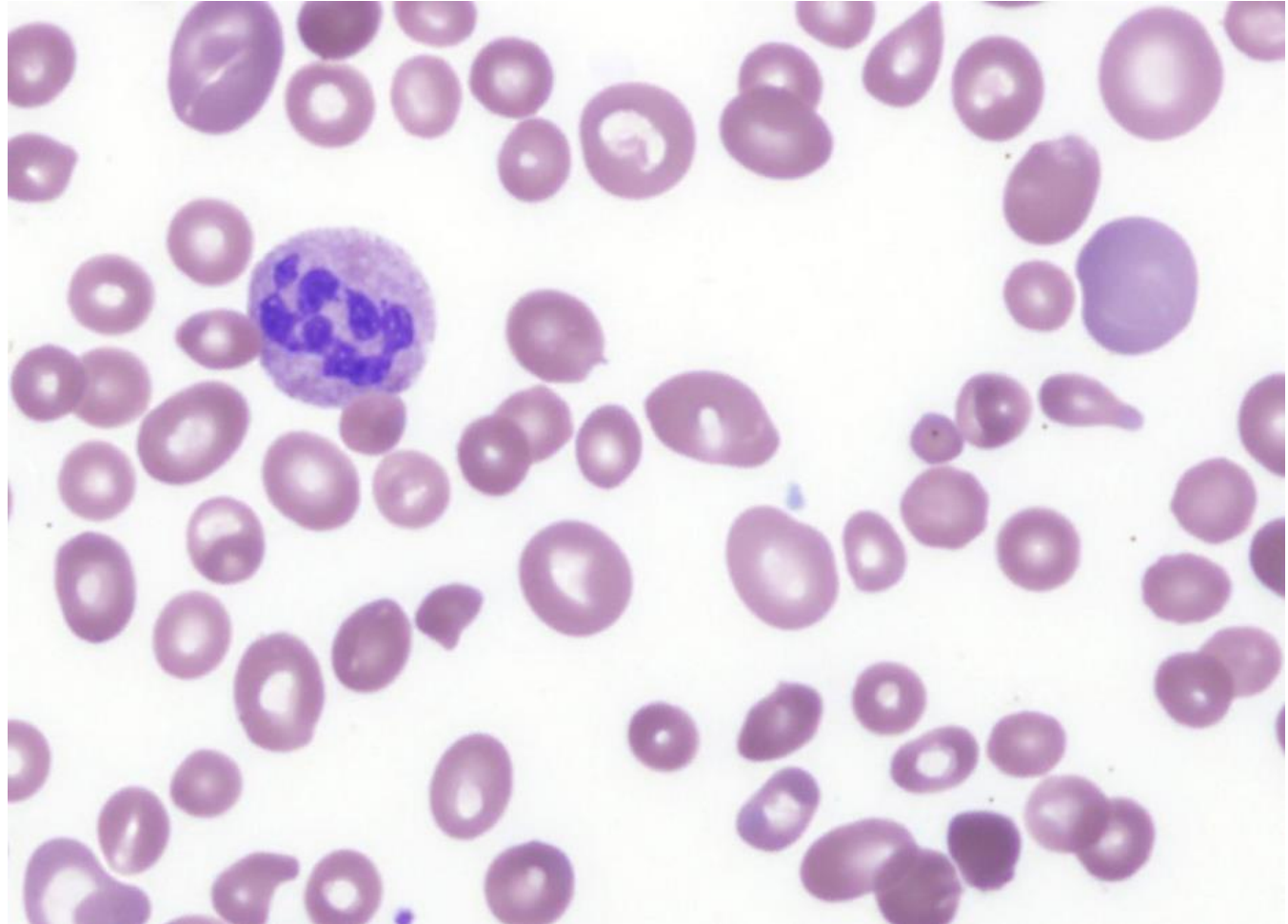


# ERYTHROCYTES

## Deviations from normal size

- **anisocytosis**

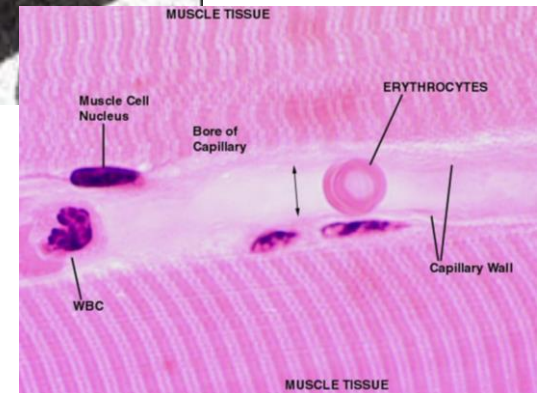
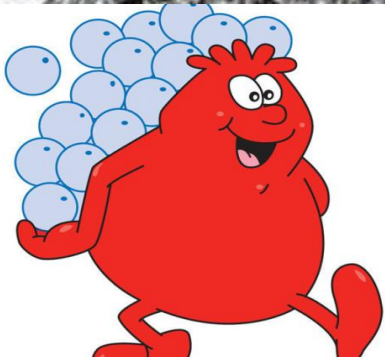
- macrocytes ( $>9\ \mu\text{m}$ )
- microcytes ( $<6\ \mu\text{m}$ )





# ERYTHROCYTES

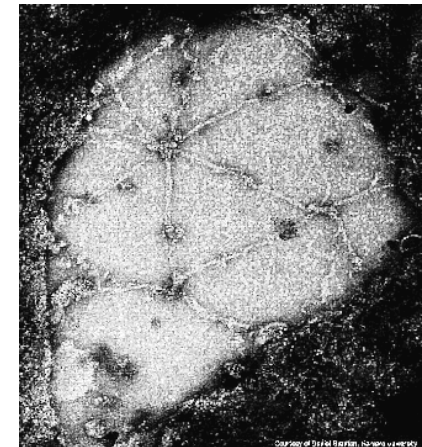
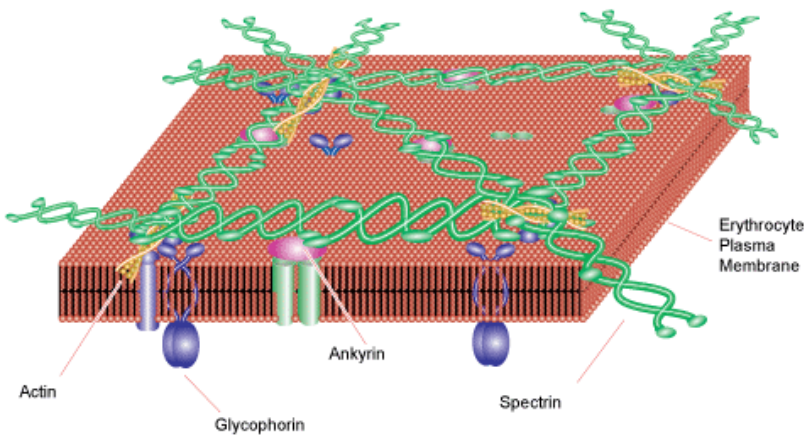
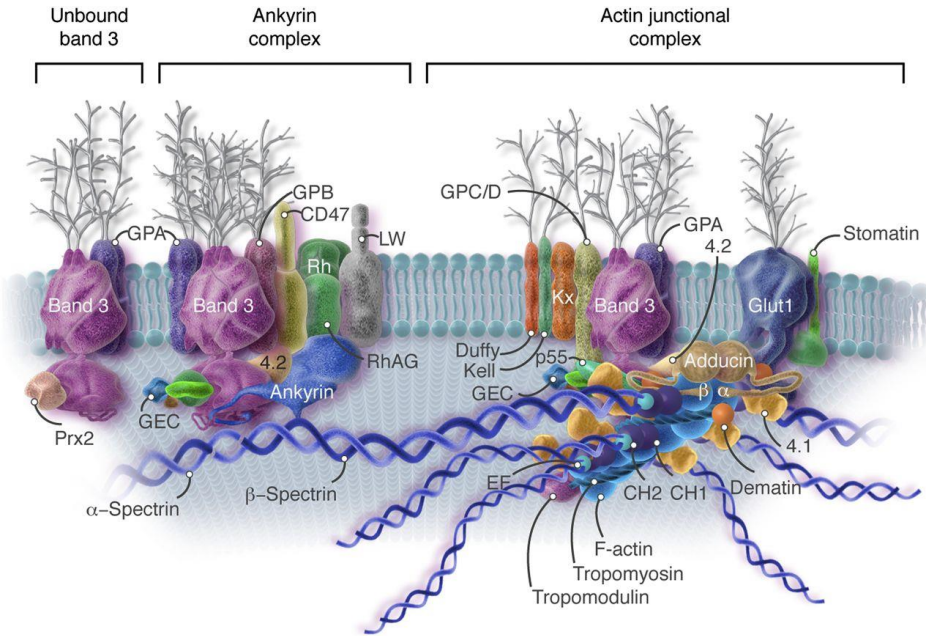
Erythrocyte is amazingly flexible cell



# ERYTHROCYTES

## Shape of erythrocytes

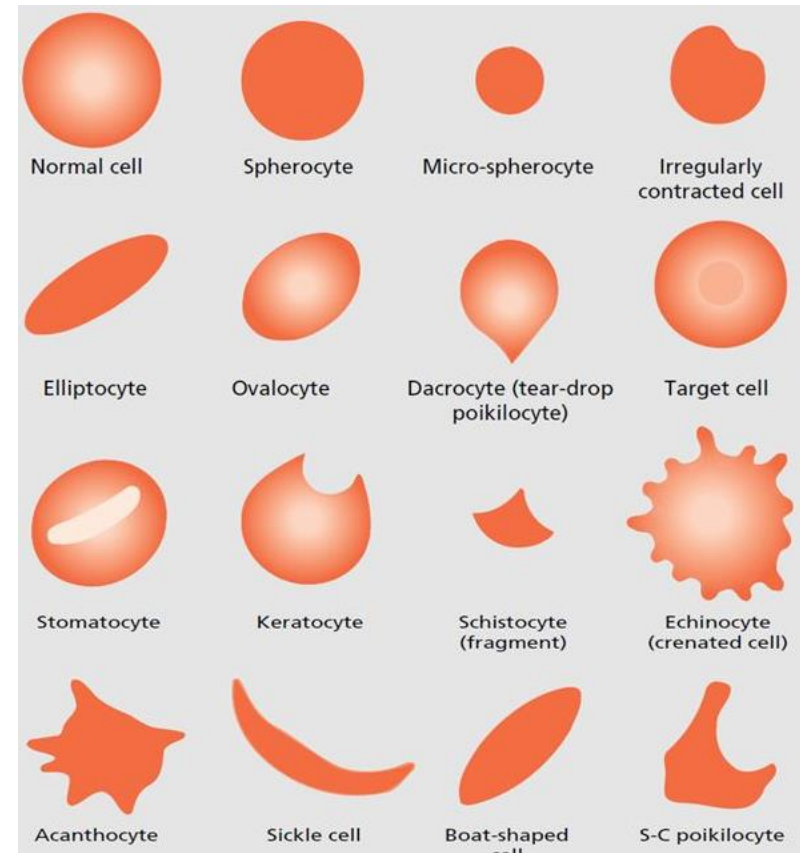
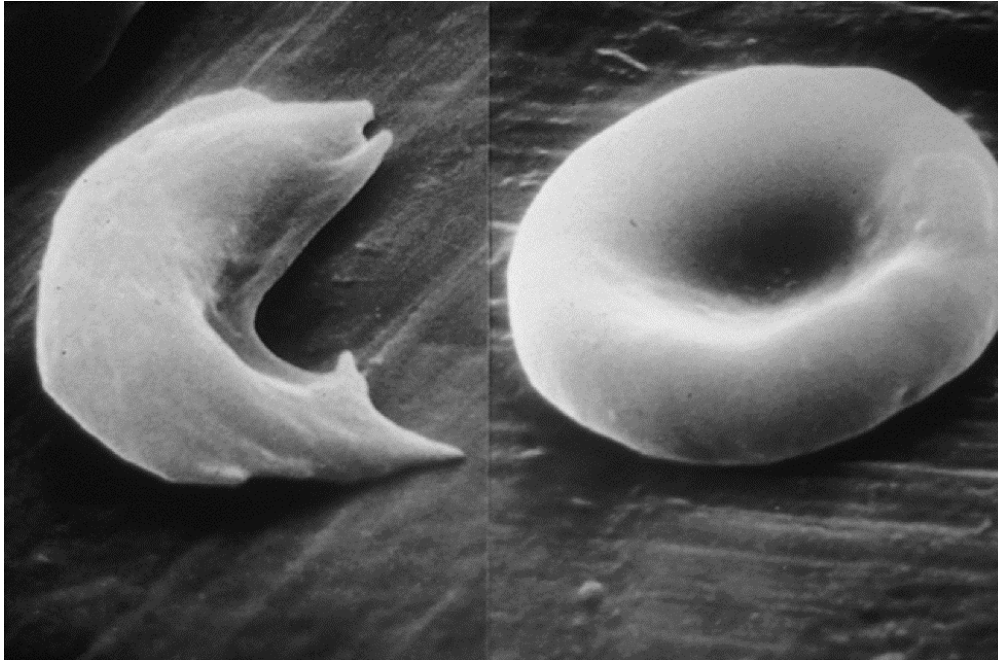
- **integral proteins**
  - band 3, glycoprotein A (ion transporters)
- **spectrin**
- **ankyrin**
- **actin and actin associated proteins**
  - tropomodulin, tropomyosin
- **hemoglobin**



# ERYTHROCYTES

## Deviations from biconcave shape

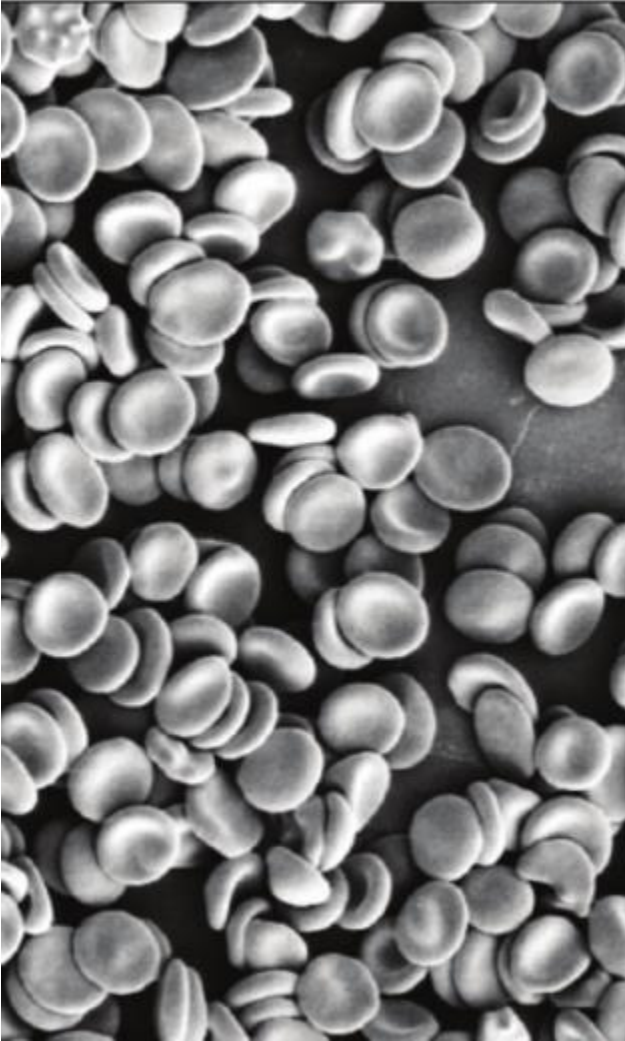
- **poikilocytosis**
  - **acanthocytes** (irregular spikes)
  - **codocytes** („tyre “)
  - **echinocytes** (spiked membrane)
  - **eliptocytes** (elliptic)
  - **spherocytes** (spheroidal)
  - **stomatocytes** (some parts missing or other irregularities)
  - **drepanocytes** (sickle)
  - **dacrocytes**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



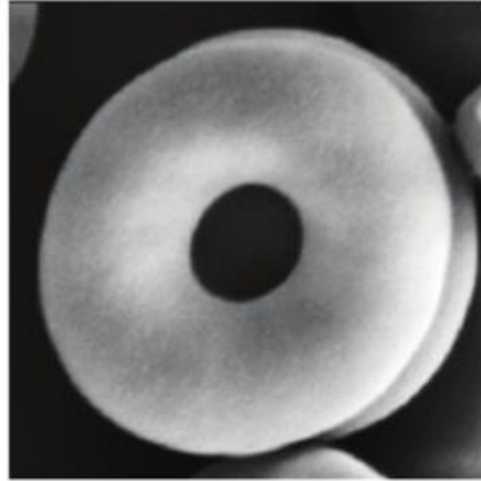
# ERYTHROCYTES

## Deviations from biconcave shape

Normal

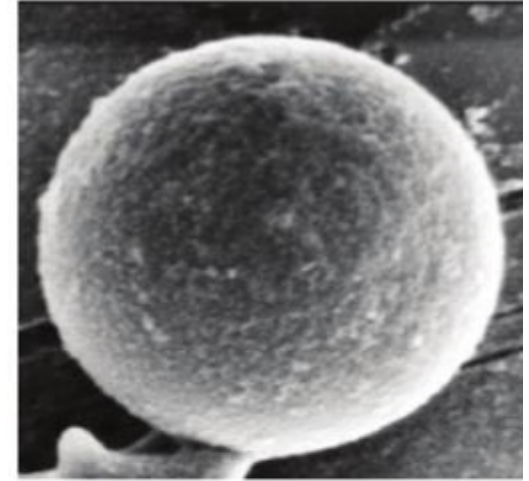


Codocyte

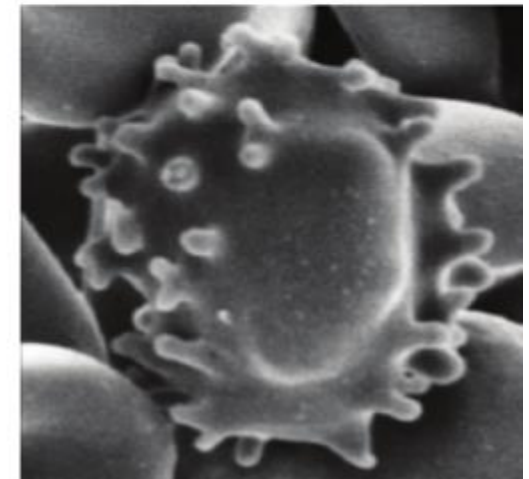
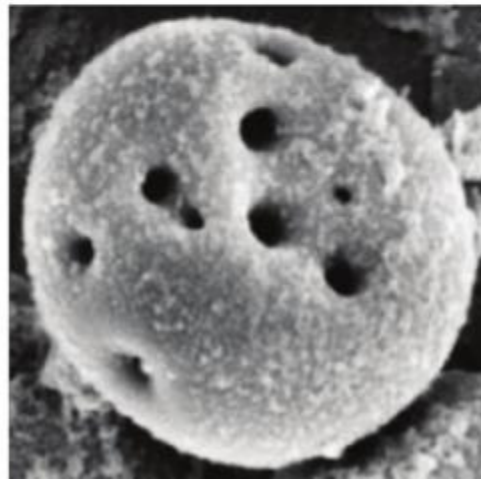


(b)

Spherocyte



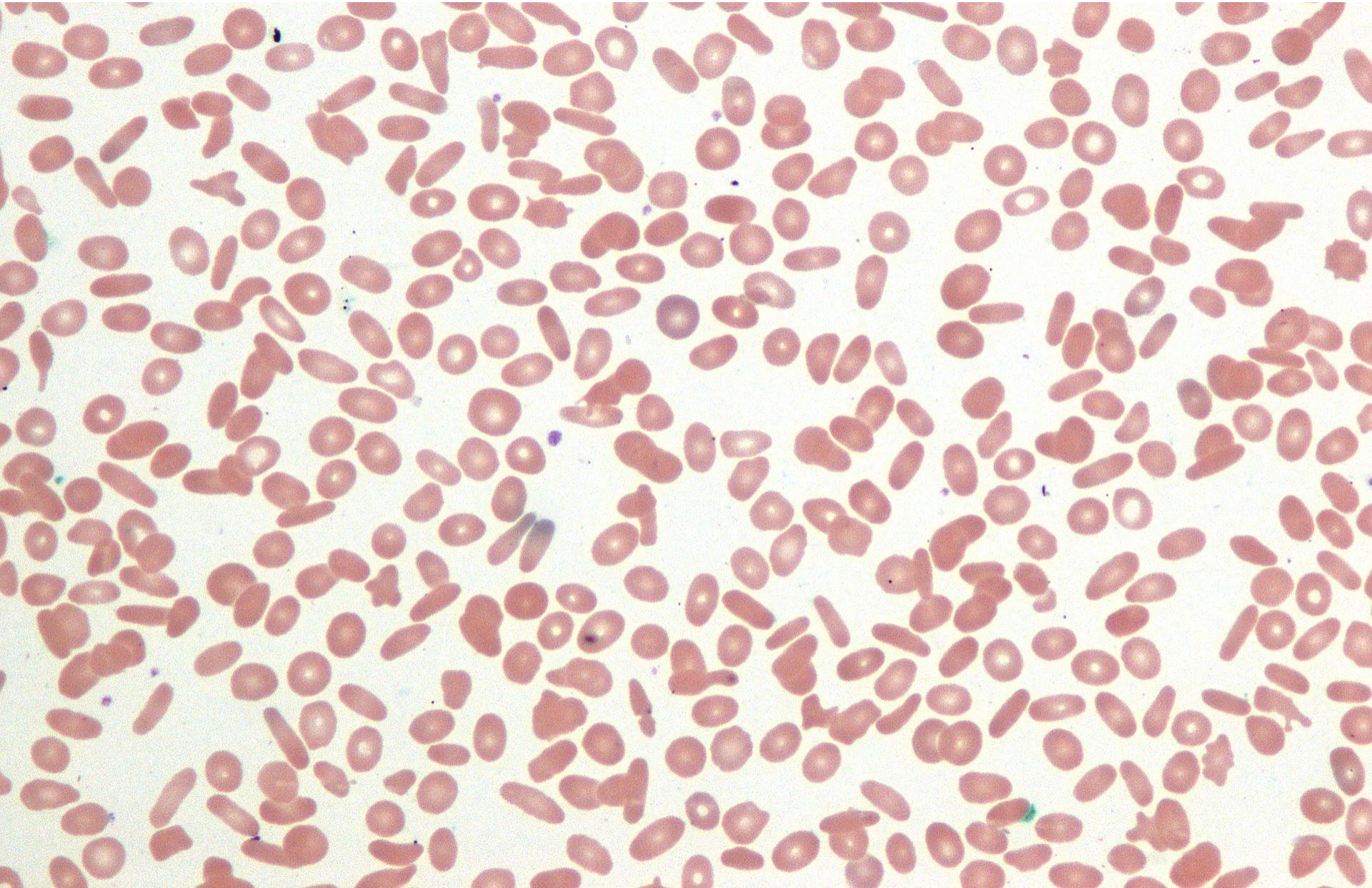
(d)



Echinocyte

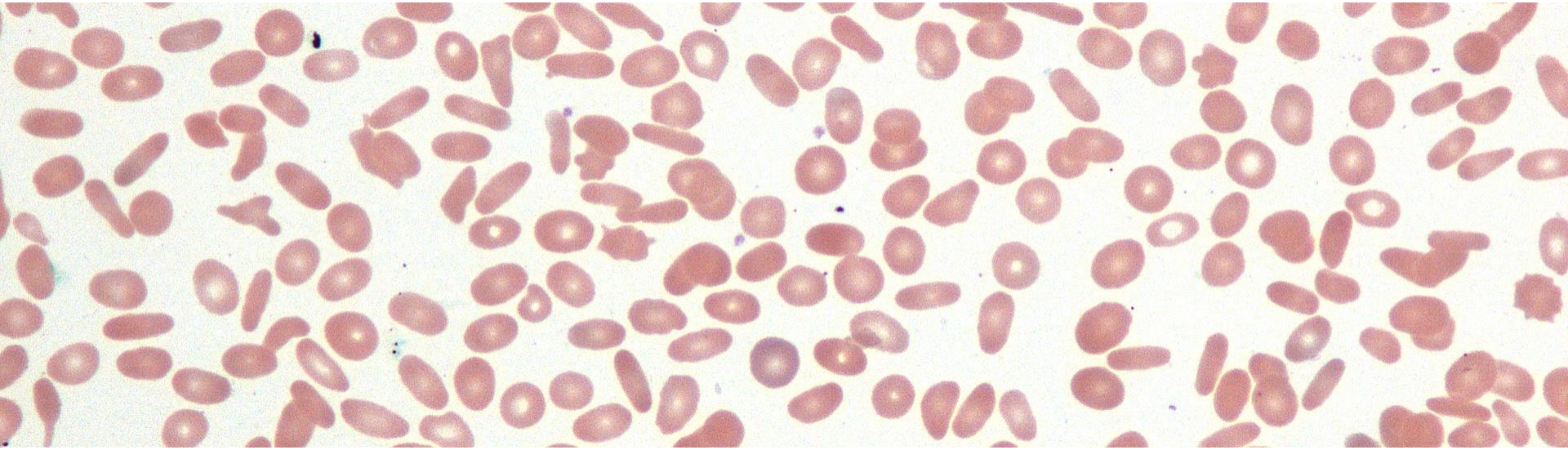
# ERYTHROCYTES

## Hereditary elliptocytosis

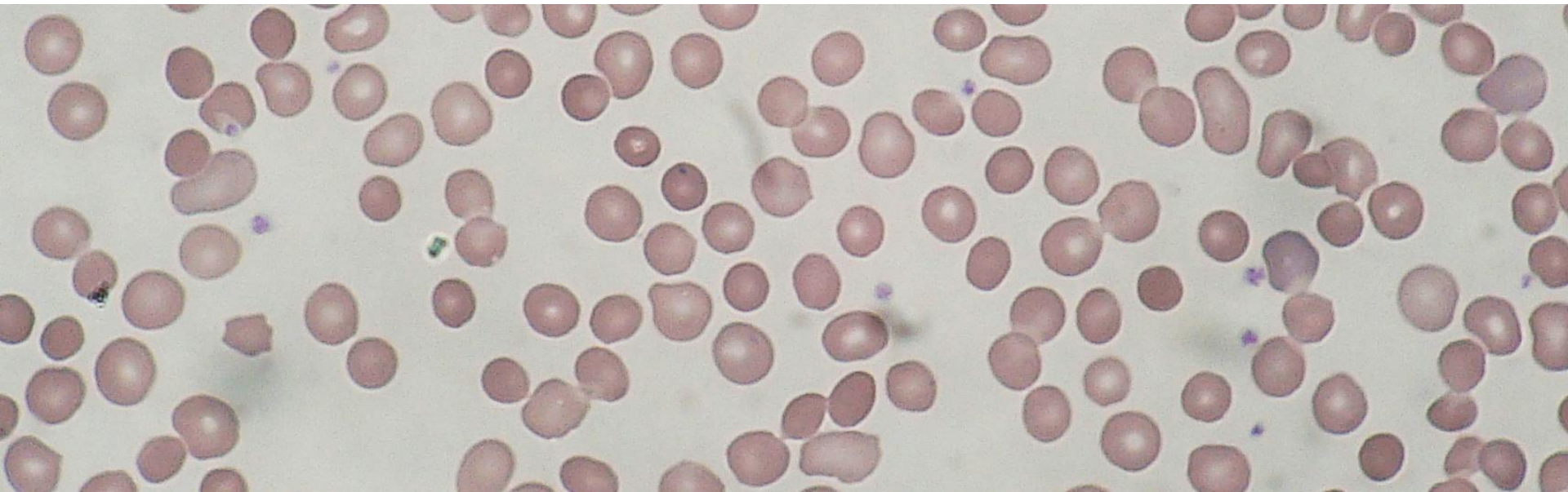


# ERYTHROCYTES

**Hereditary elliptocytosis**



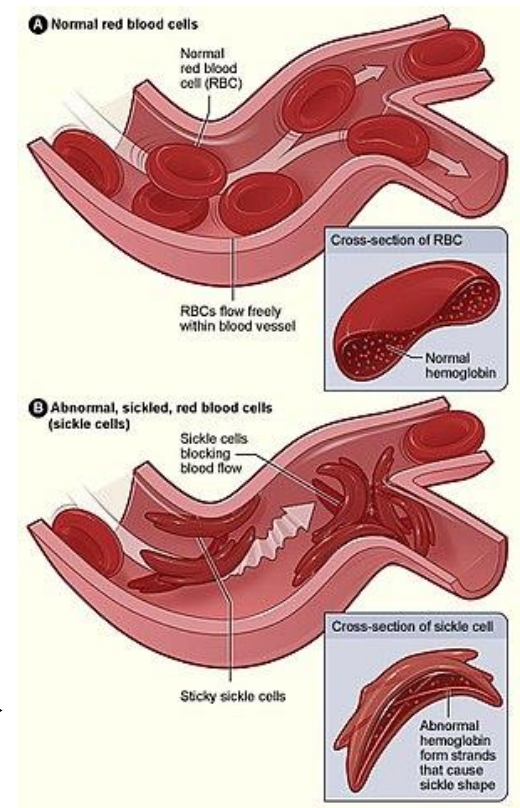
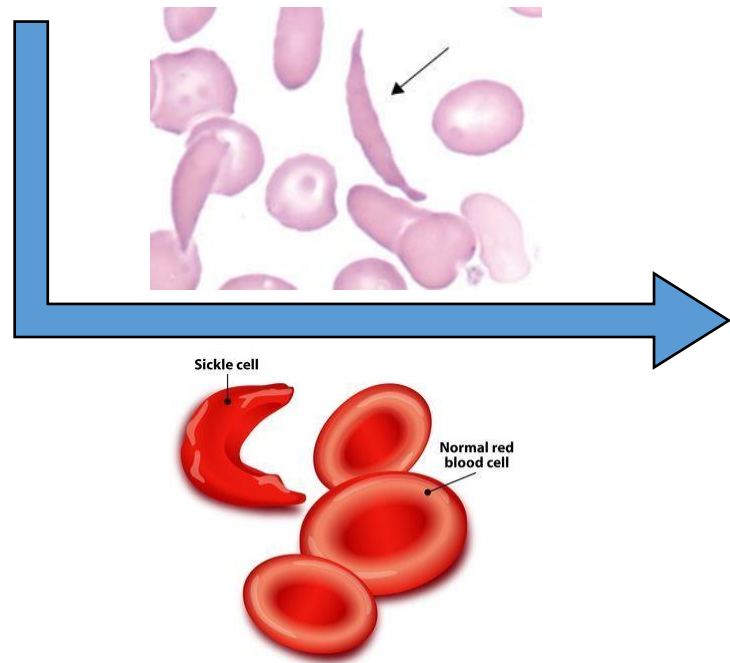
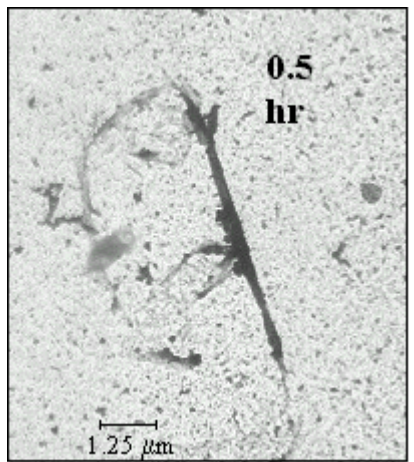
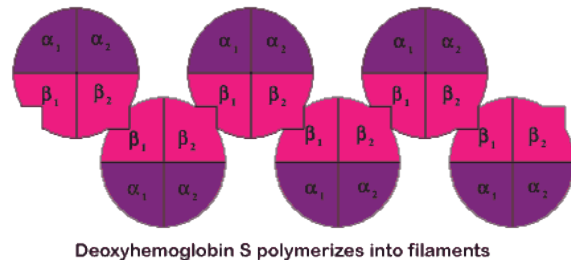
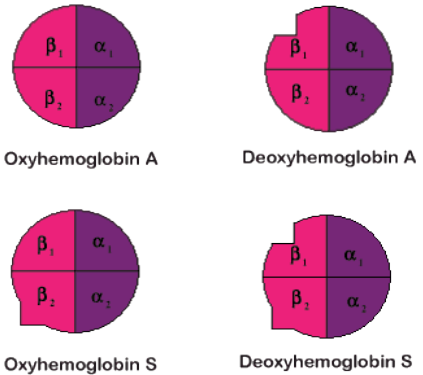
**Hereditary spherocytosis**



# ERYTHROCYTES

## Sickle cell anemia

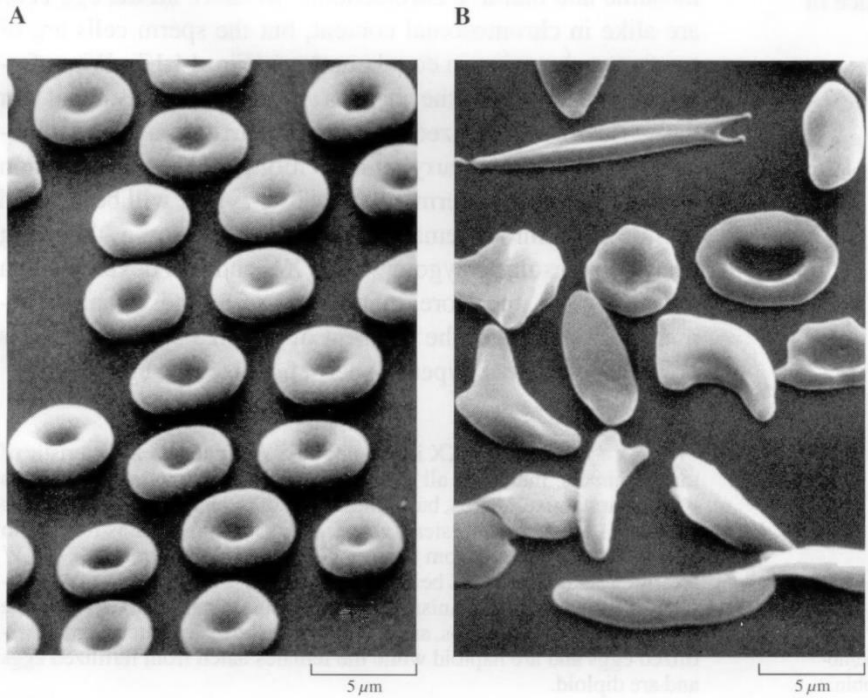
- Abnormal hemoglobin (hemoglobin S)



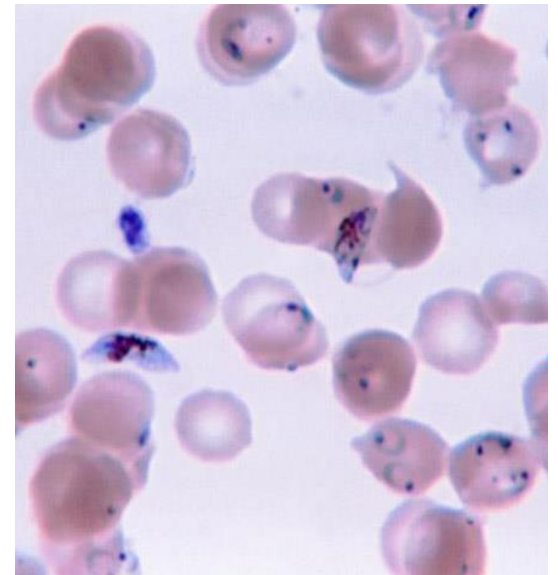
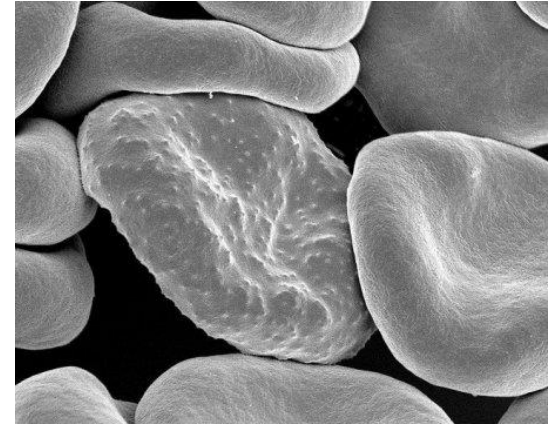
# ERYTHROCYTES

## Sickle cell anemia

- pathological genotype (heterozygote HbS/HbA) is beneficial



## Malaria



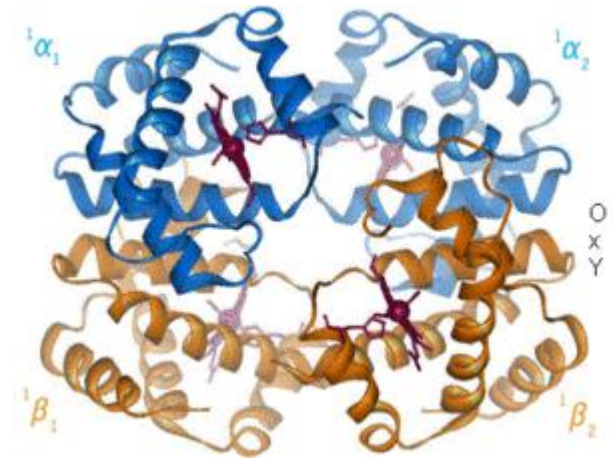
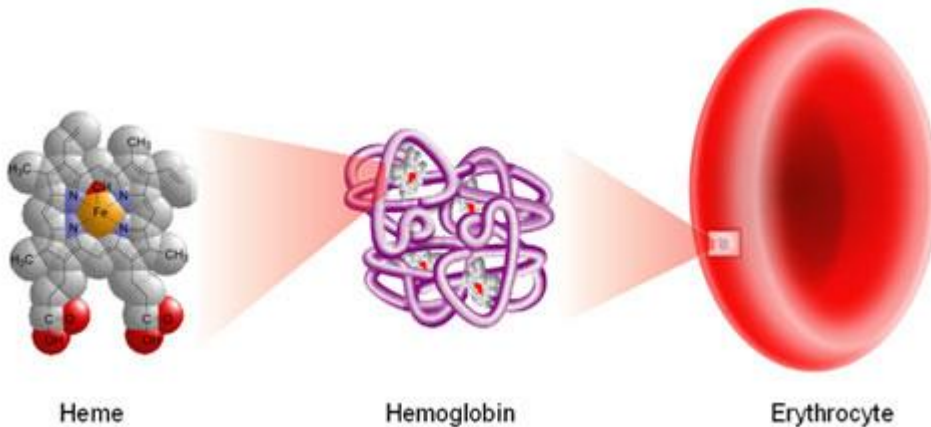
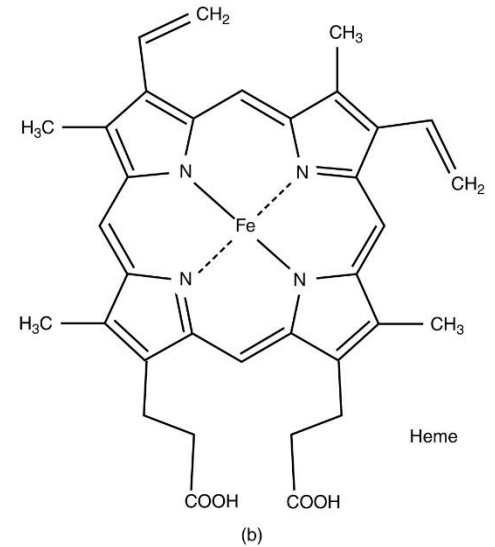
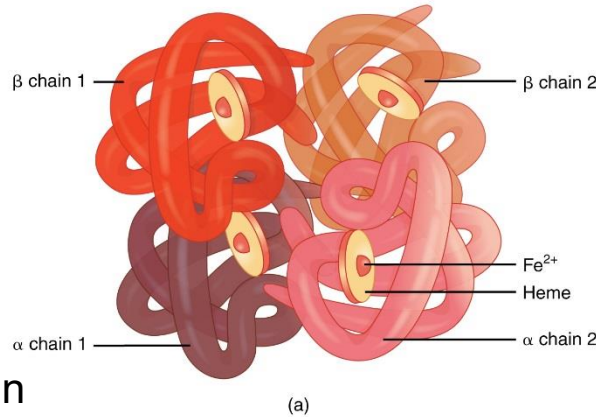


# ERYTHROCYTES

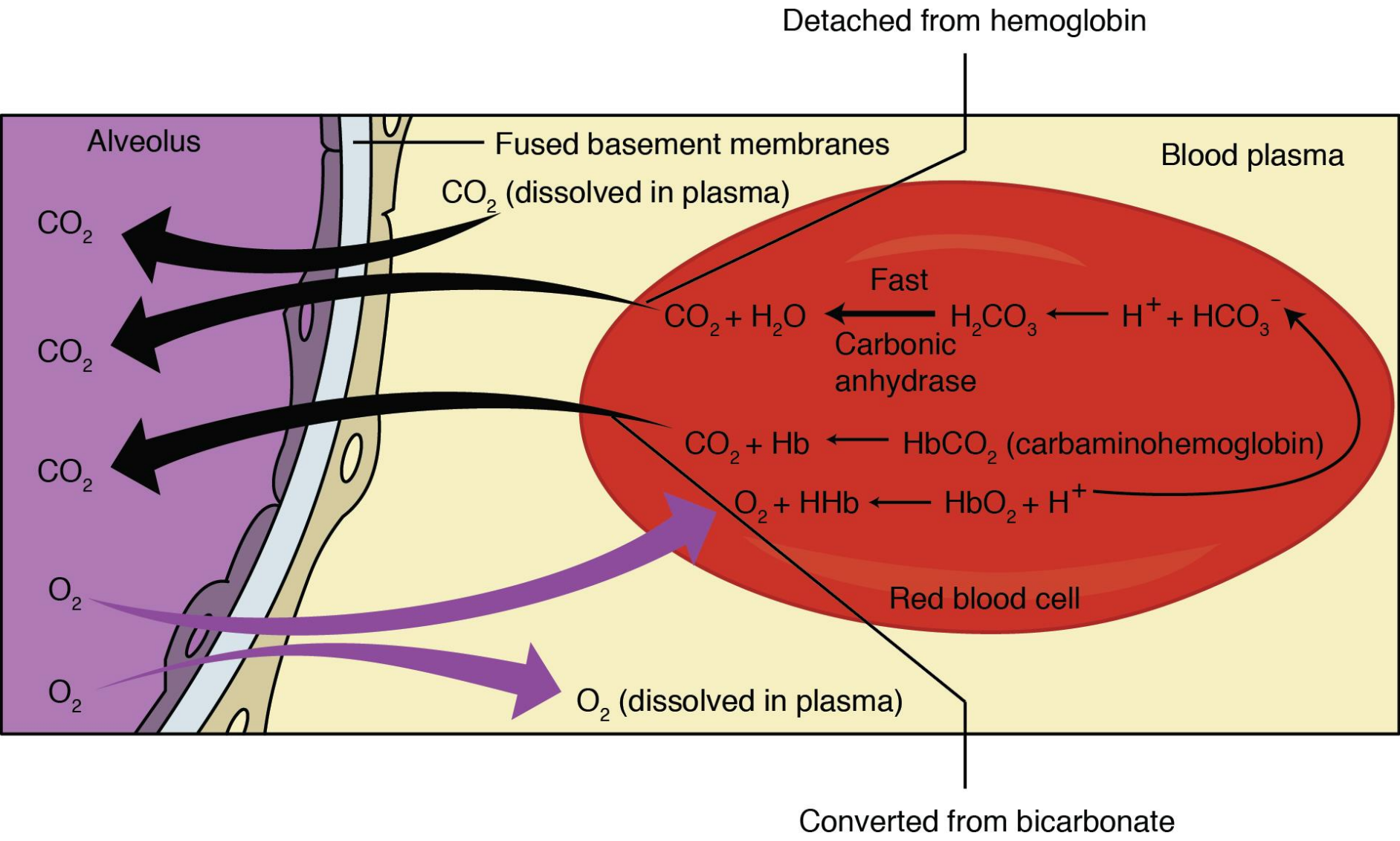
- Erythrocytes **lack nucleus and organelles**
- Anaerobic glykolysis

- **Hemoglobin**

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

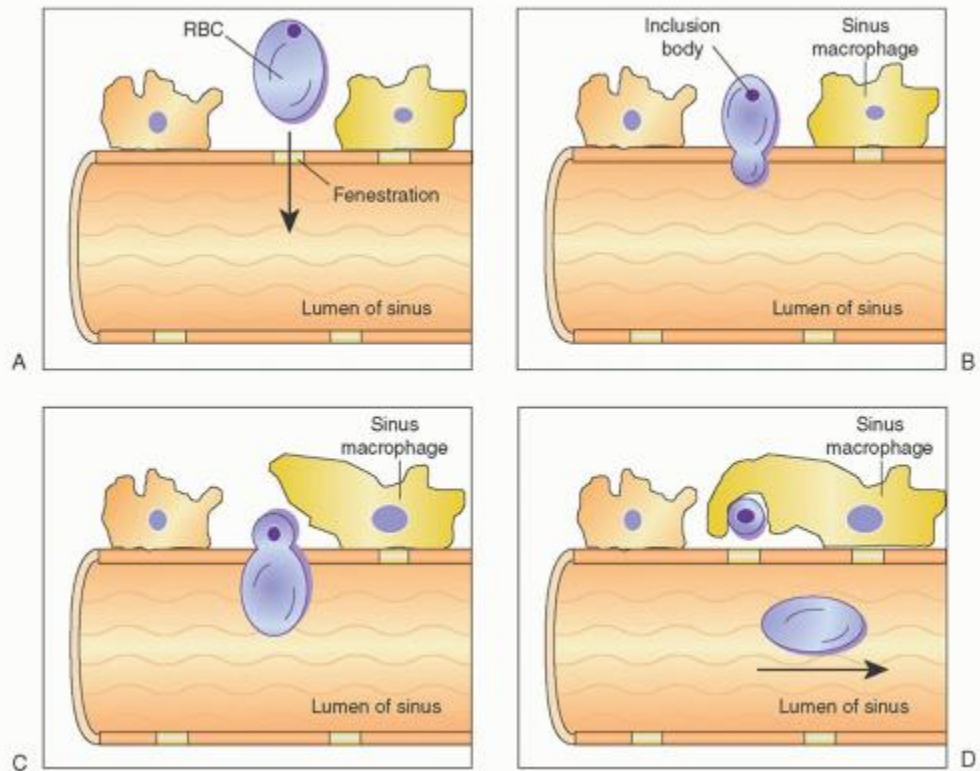
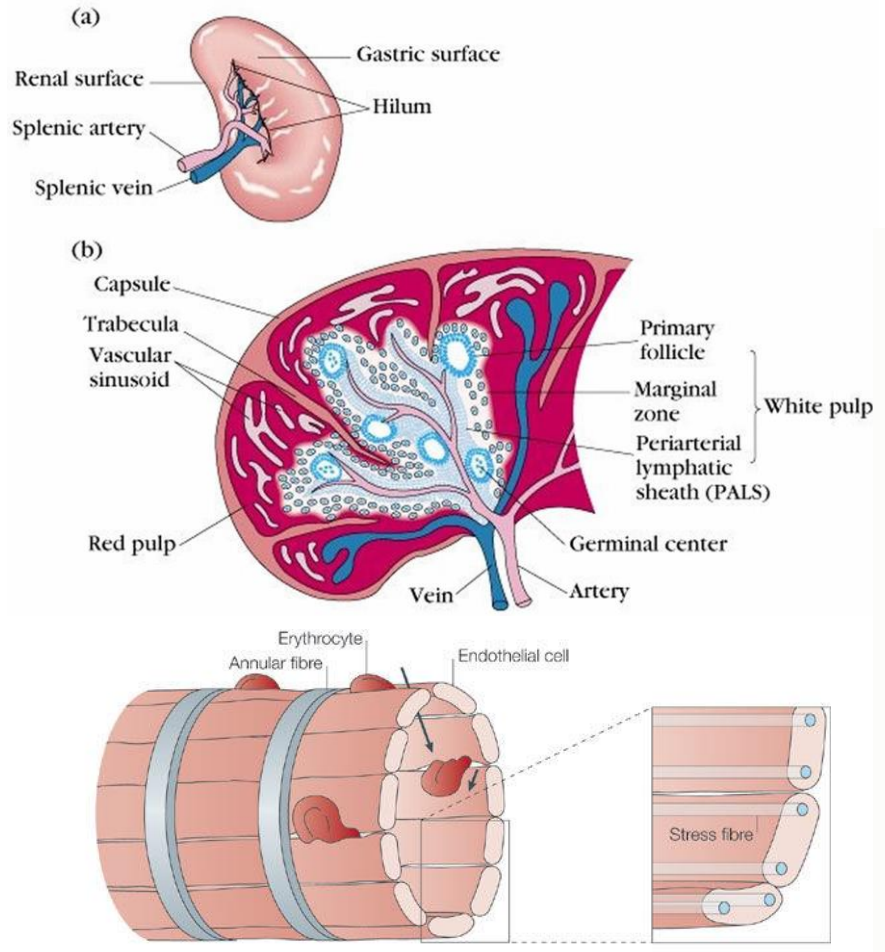
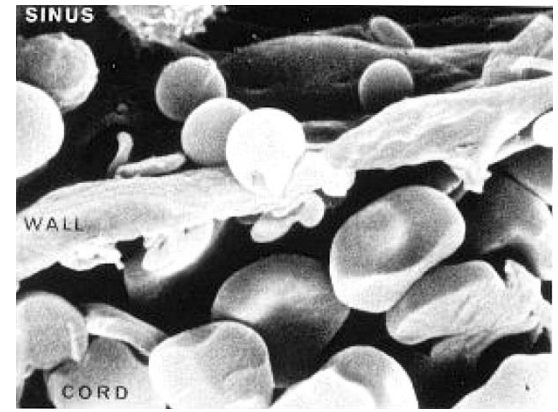


# ERYTHROCYTES



# ERYTHROCYTES

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

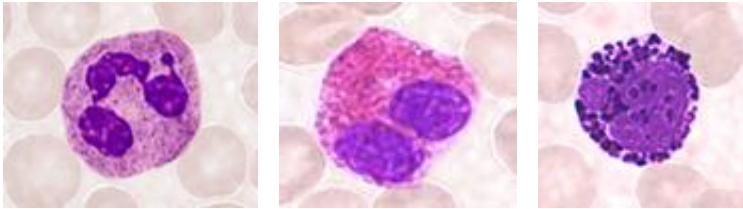


# LEUKOCYTES

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

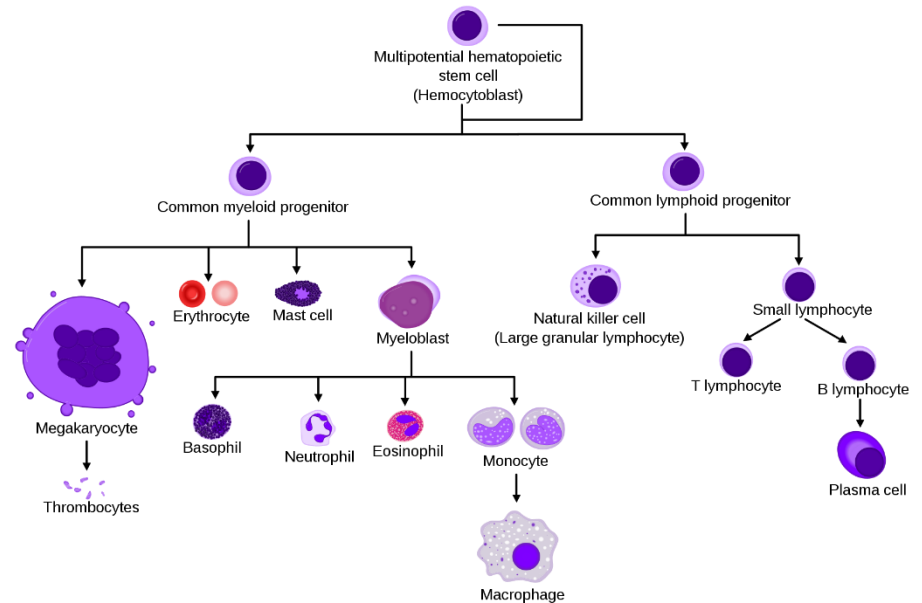
## Granulocytes

Neutrophils    Eosinophils    Basophils



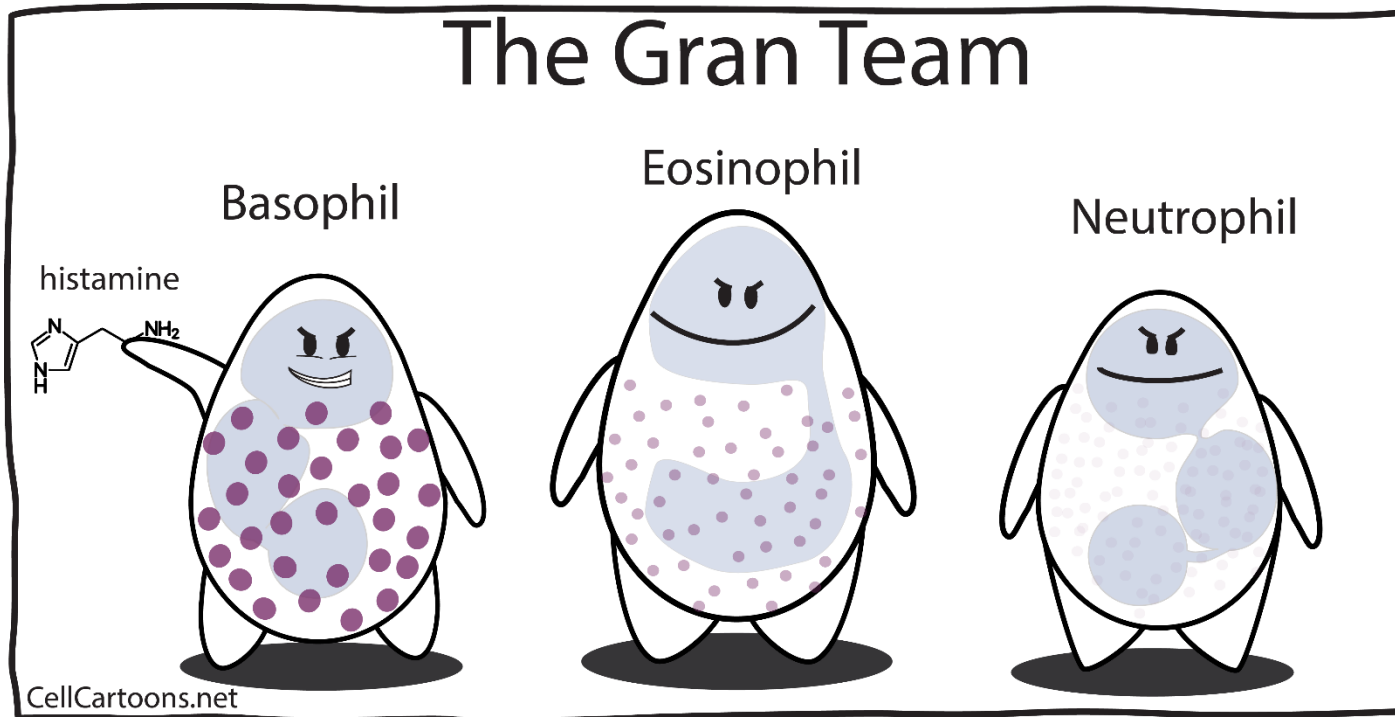
## Agranulocytes

Monocytes    Lymphocytes



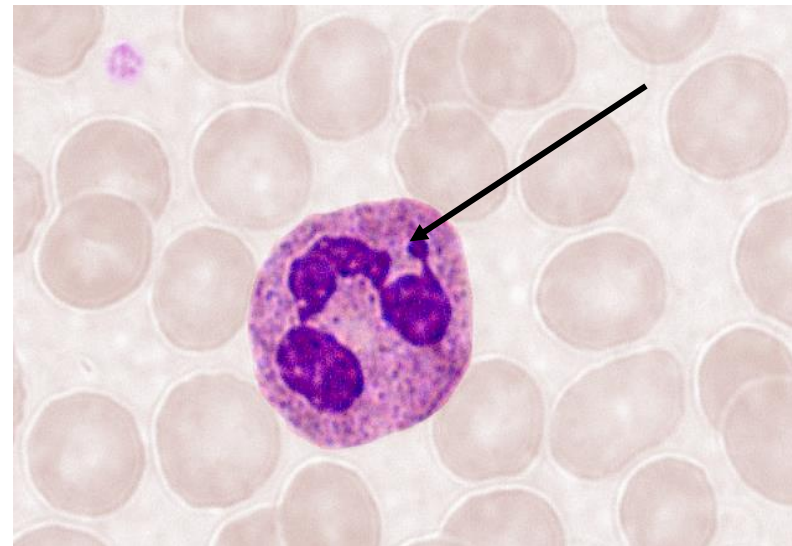
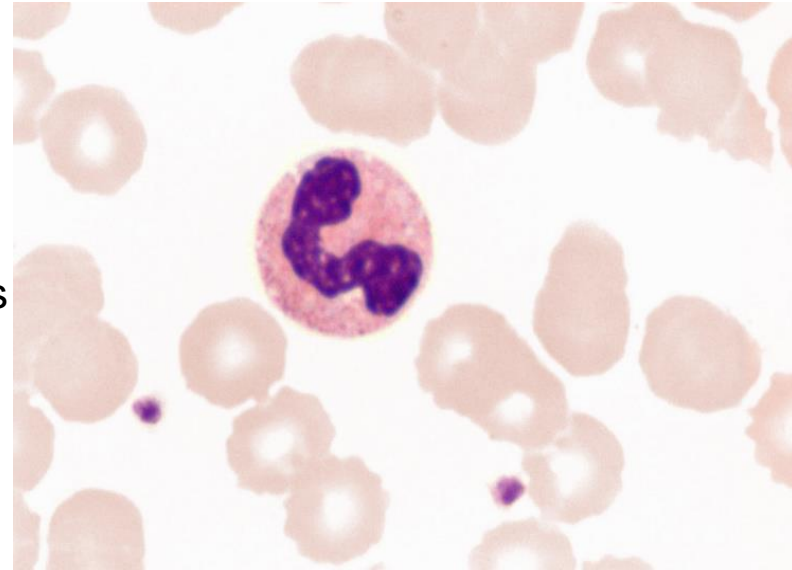
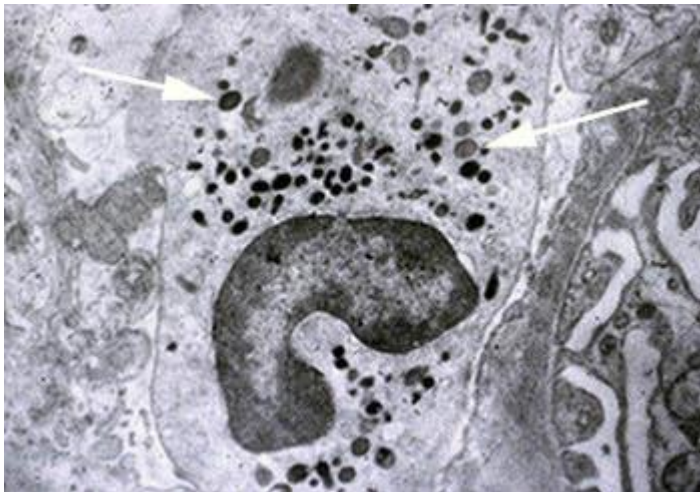
# GRANULOCYTES

- **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**

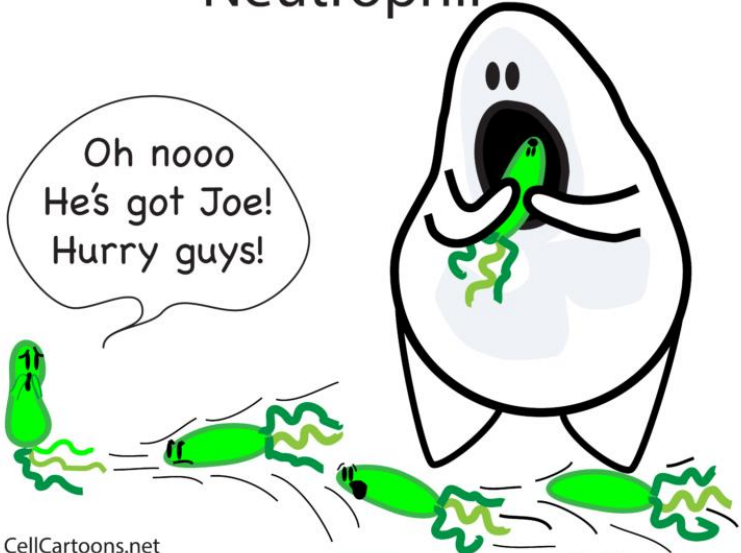


# NEUTROPHILIC GRANULOCYTES



Neutrophil

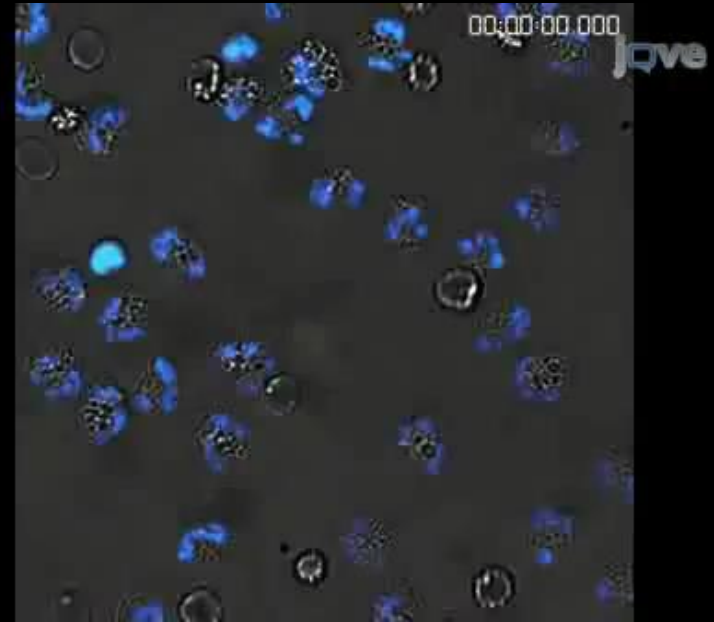
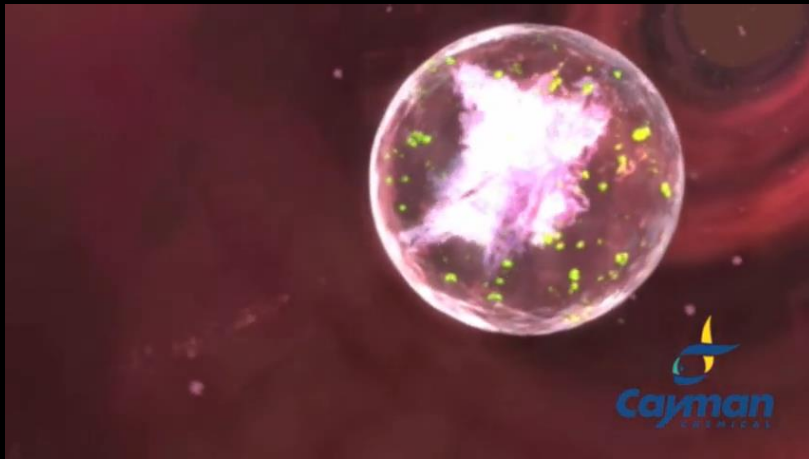
Oh nooo  
He's got Joe!  
Hurry guys!



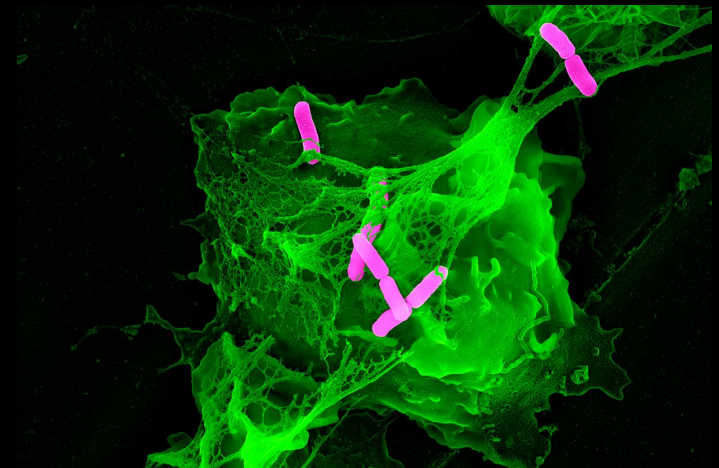
# NEUTROPHILIC GRANULOCYTES

## Hunters

NETs (neutrophil extracellulat traps)



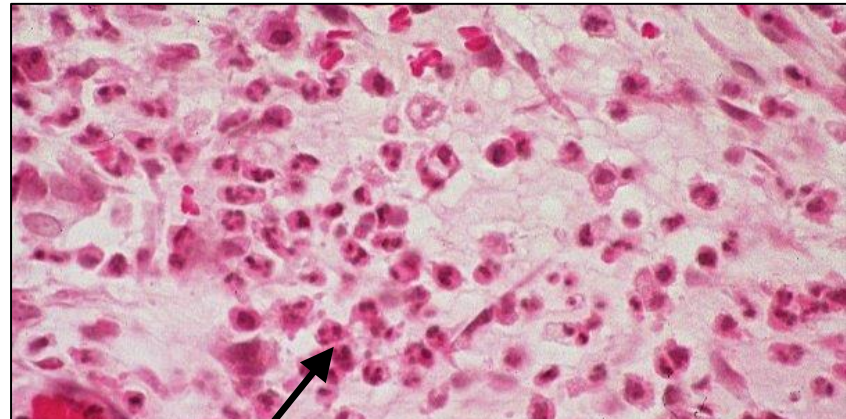
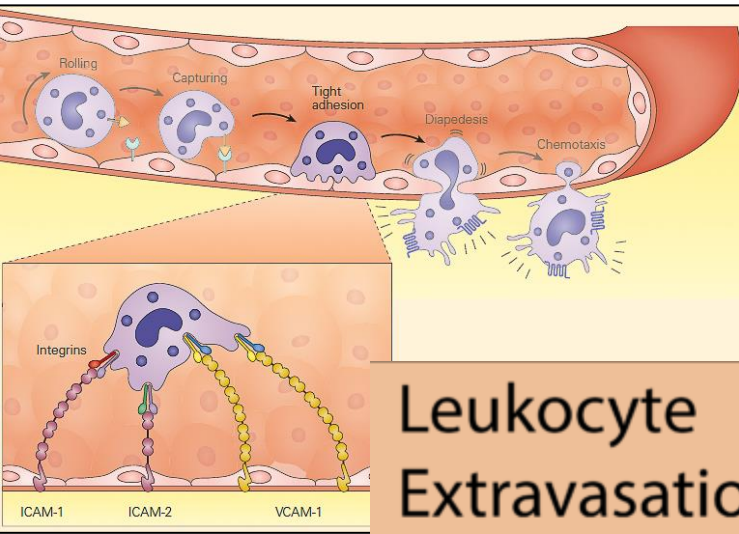
Special form of cell death – „netosis“





# NEUTROPHILIC GRANULOCYTES

- Extravasation (diapedesis)

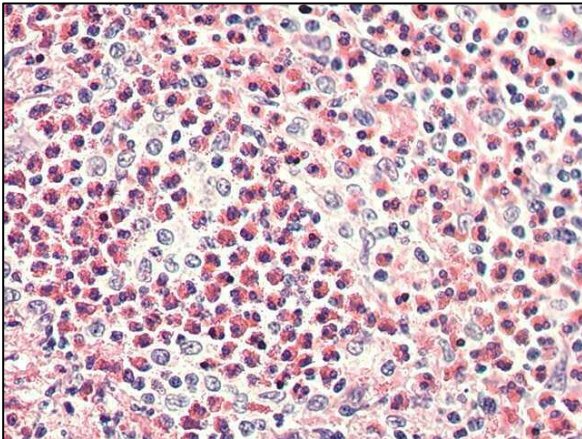
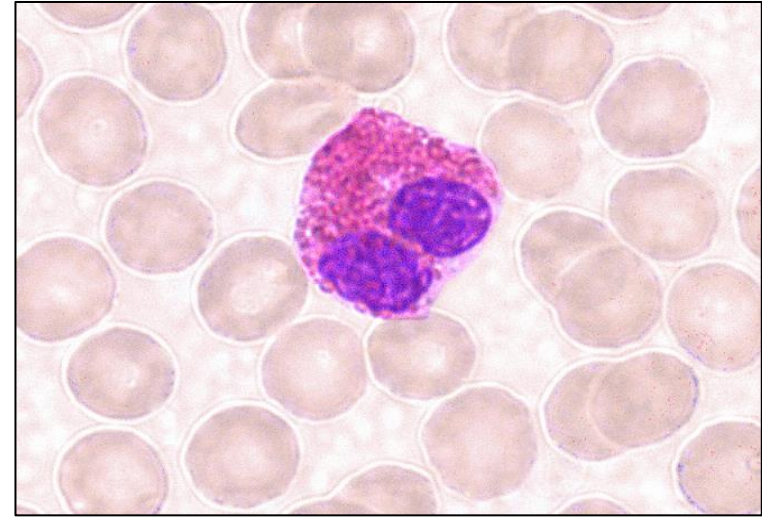


Leukocyte Extravasation

A cartoon illustration depicting a leukocyte (white blood cell) moving through a layer of endothelial cells. The leukocyte is shown in the process of diapedesis, squeezing between the cells. A speech bubble from the leukocyte says "HOW DID YOU DO THAT???", and a speech bubble from the endothelial cells says "JUST FOLLOW THE CHEMOKINES". The endothelial cells are labeled "Endothelial Cells". The website "CellCartoons.net" is visible in the bottom right corner.

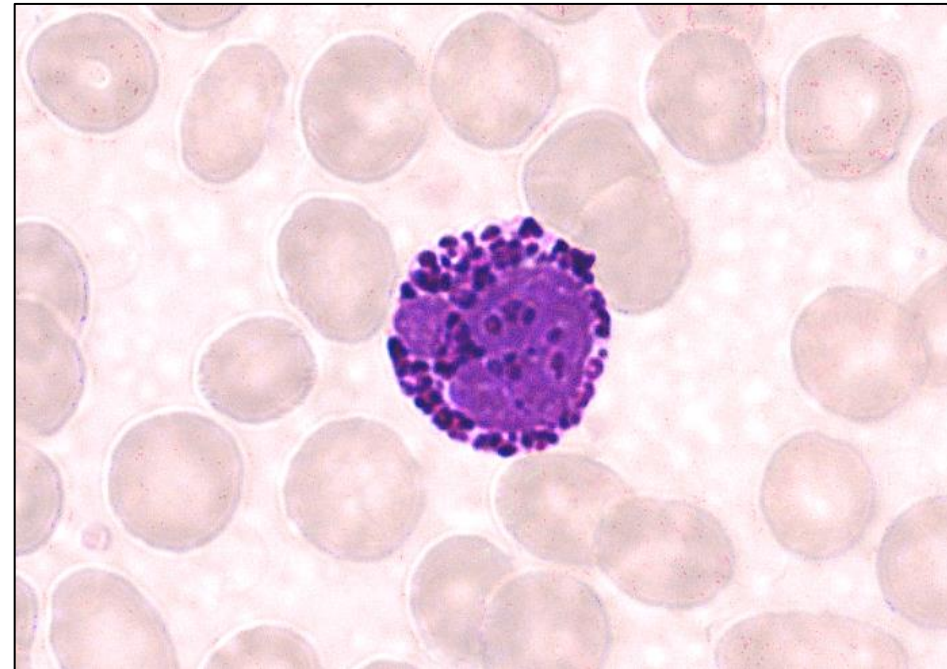
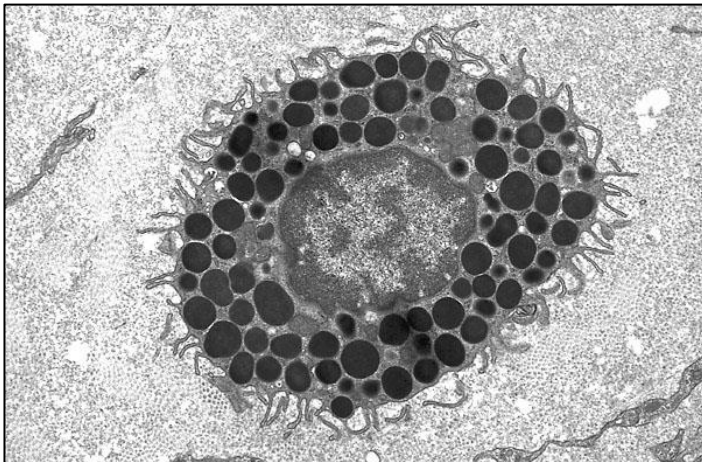
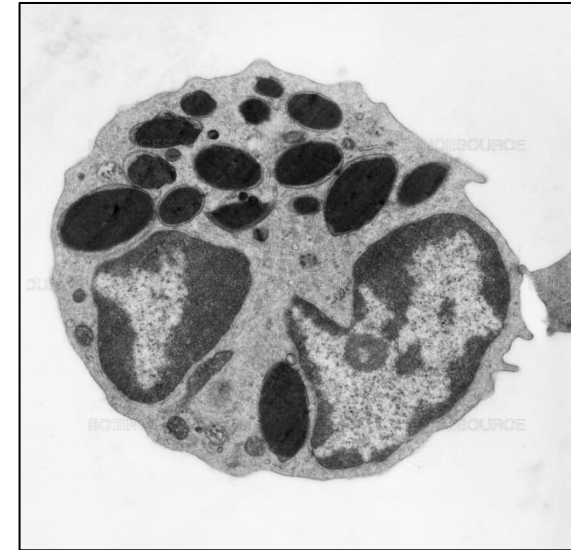
# EOSINOPHILIC GRANULOCYTES

- **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

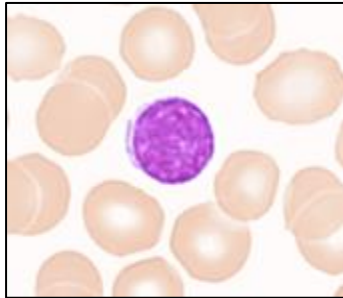
- **Basophils**
  - <1% of leukocytes in circulation
  - $\varnothing$  12  $\mu\text{m}$
  - Irregular, bisegmented nucleus, masked by granules
- **Azurophilic (primary) granules**
  - myeloperoxidase, lysozyme, proteases, defensins
- **Basophilic (secondary) granules**
  - 0.5  $\mu\text{m}$
  - large,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



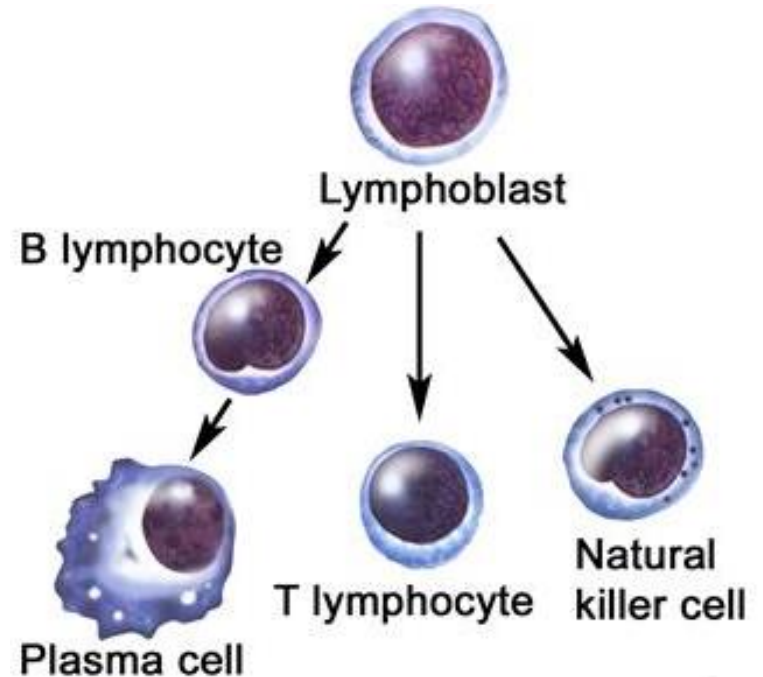
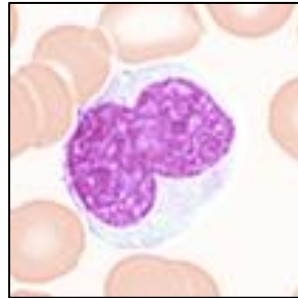
# AGRANULOCYTES

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

**Lymphocytes**



**Monocytes**

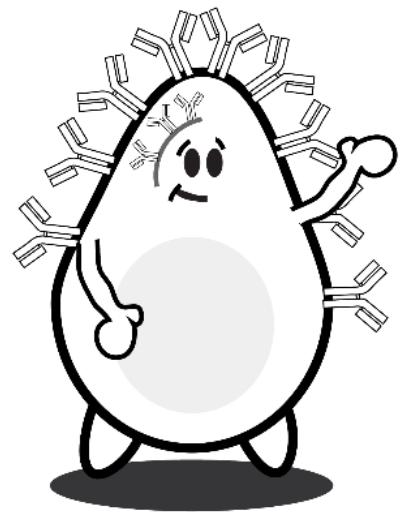


# Lymphocytes

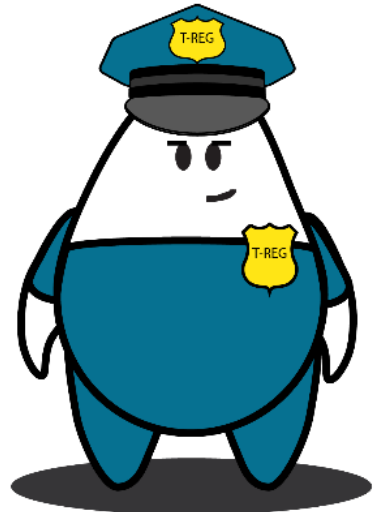
CD8 T Cell



B Cell



Regulatory  
T Cell

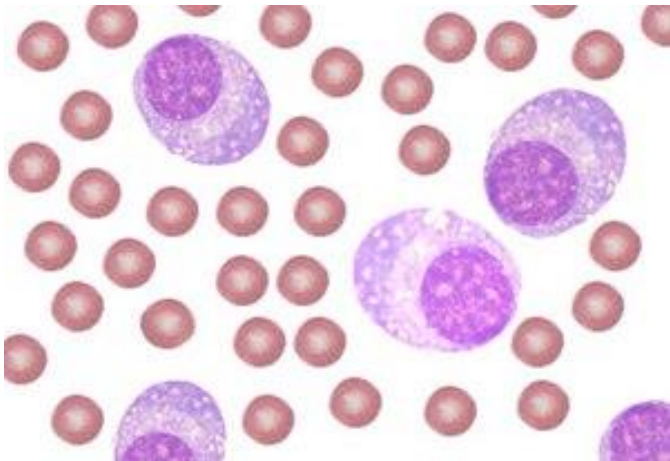
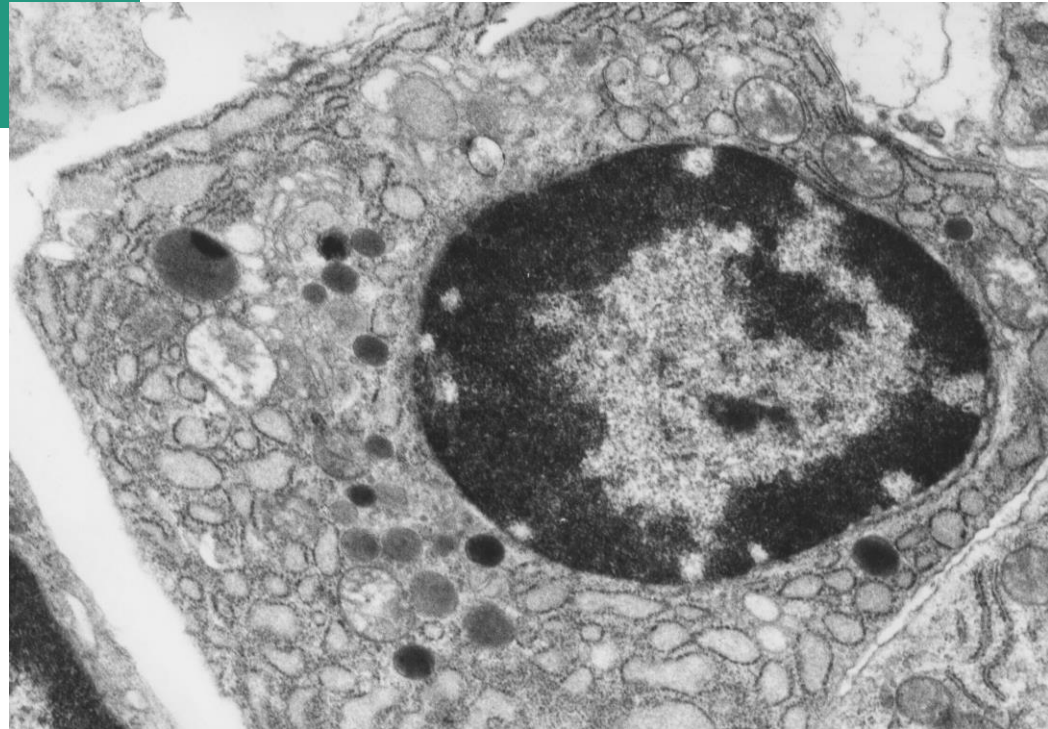
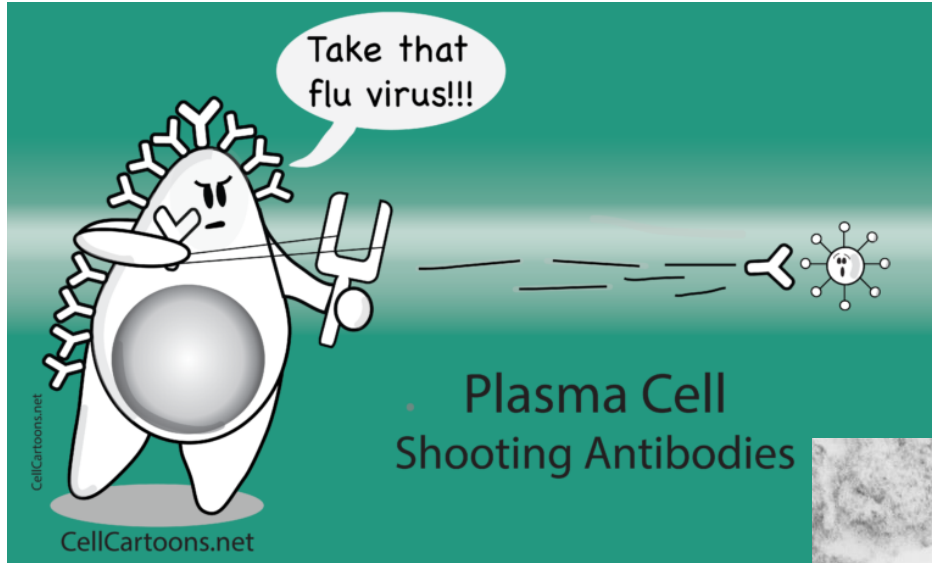


CD4 T Cell



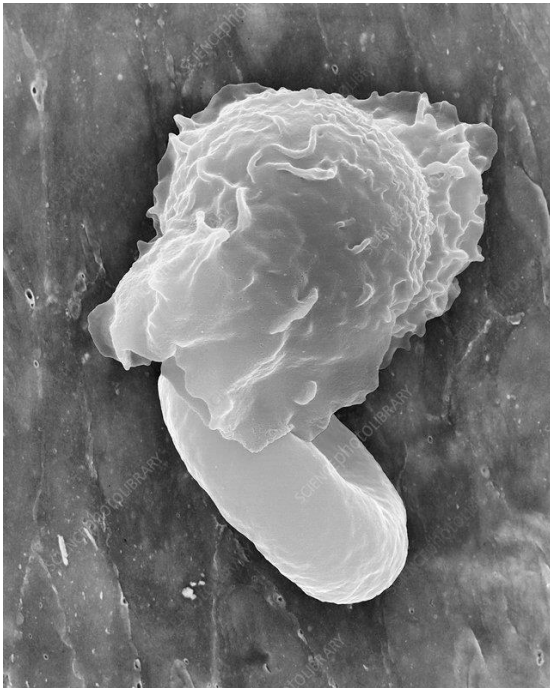
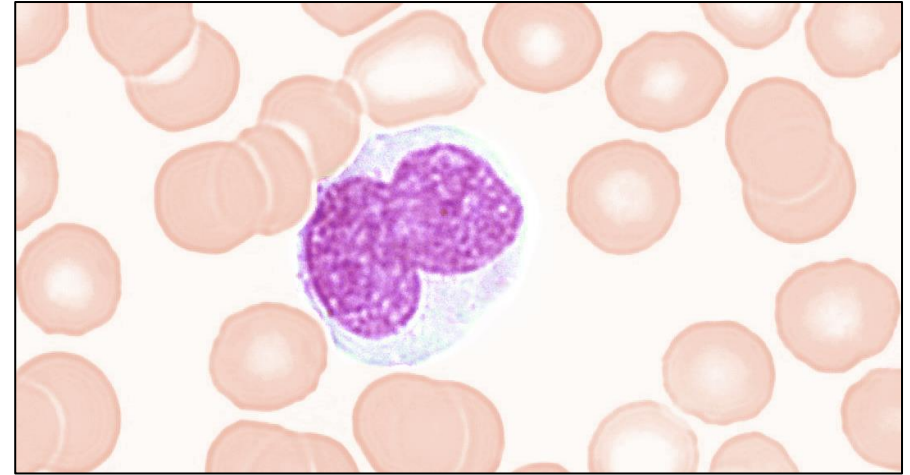
# LYMPHOCYTES

- Plasma cells



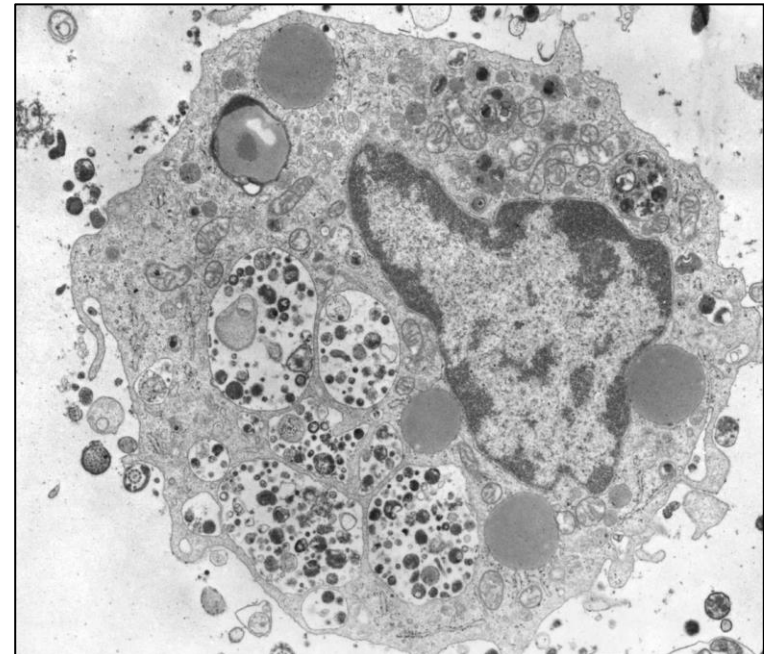
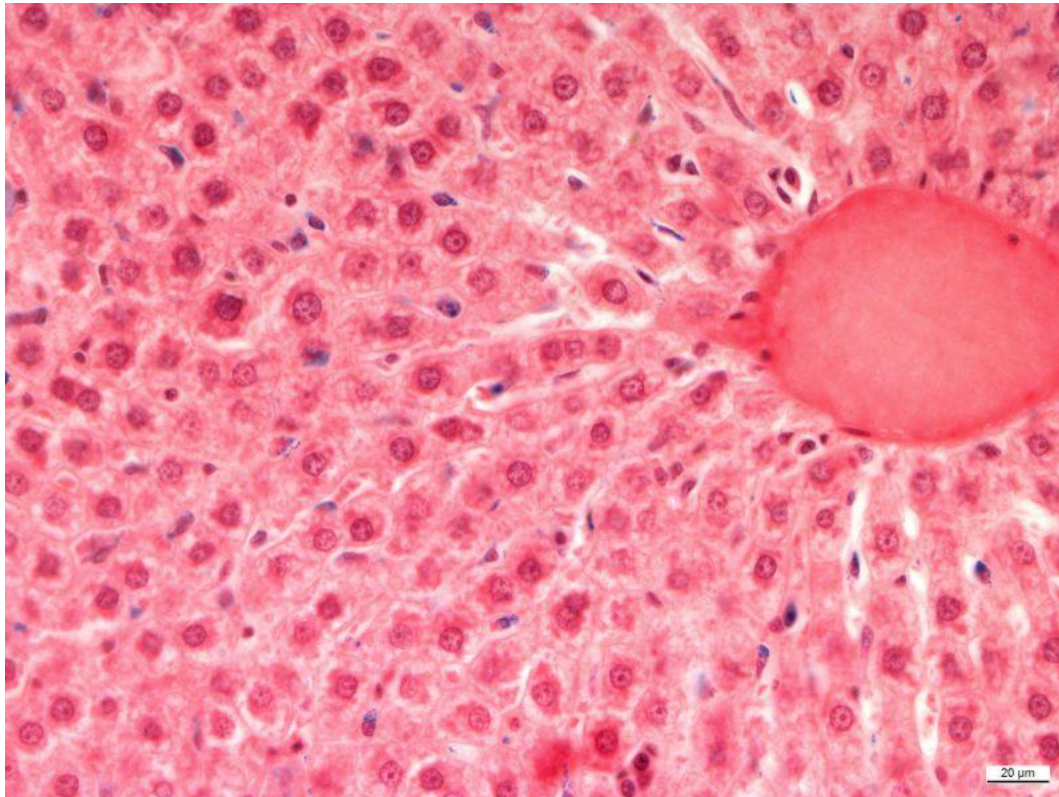
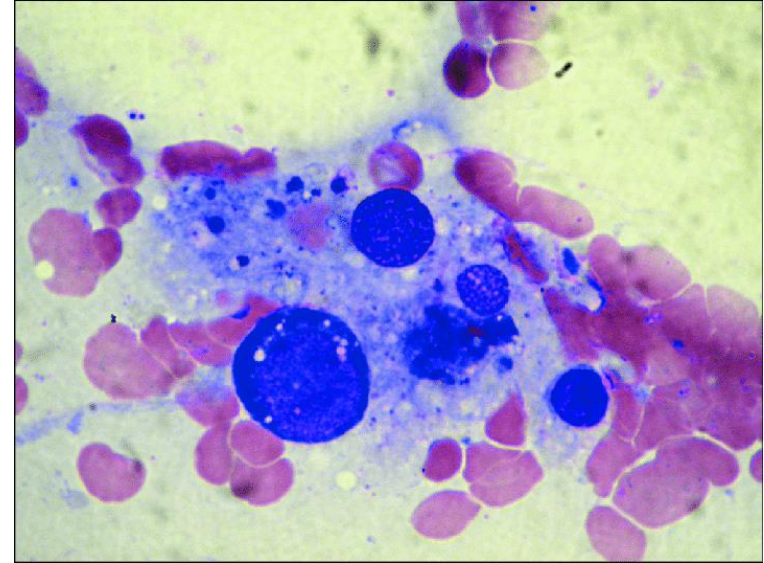
# MONOCYTES

- $\varnothing$  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

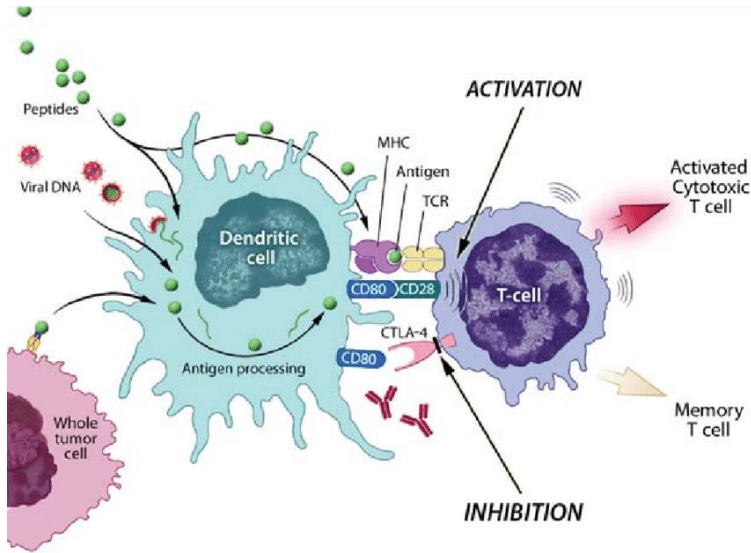
- $\varnothing$  around 21  $\mu\text{m}$
- variable migratory morphology
- phagocytocys
- antigen presentation to T-lymphocytes
- inflammatory response
- tissue regeneration and wound healing
- e.g. histiocytes, Kupffer cells, microglia



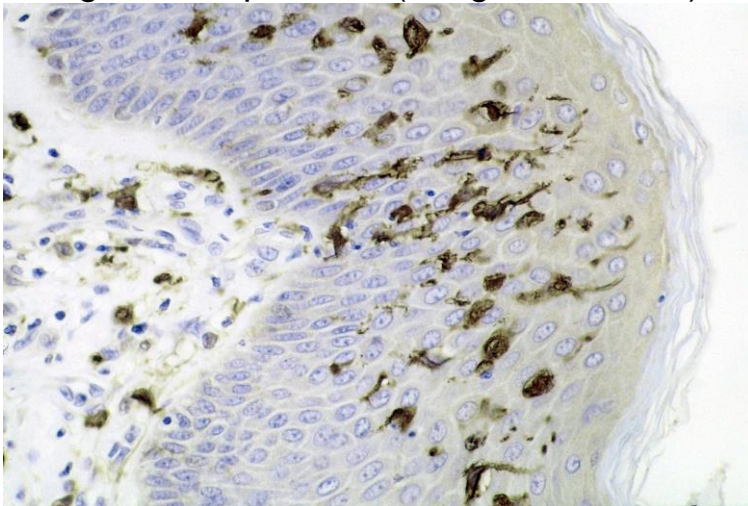


# DENDRITIC CELLS

- „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. Koeren<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

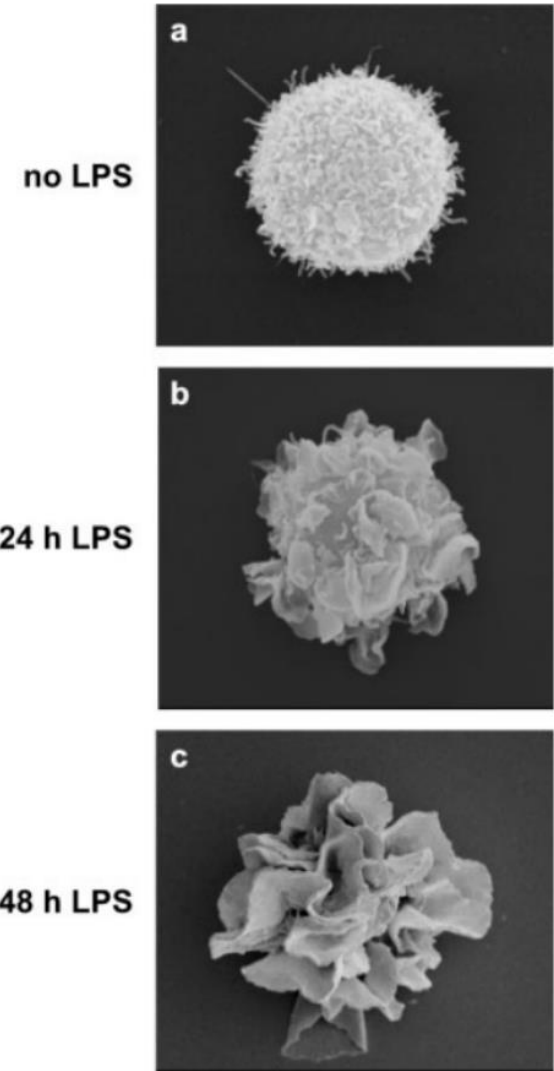
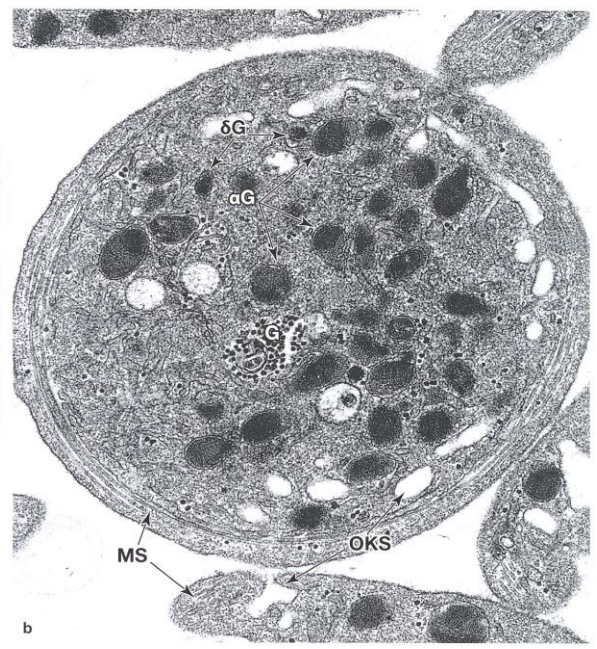
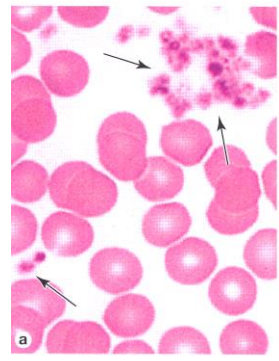
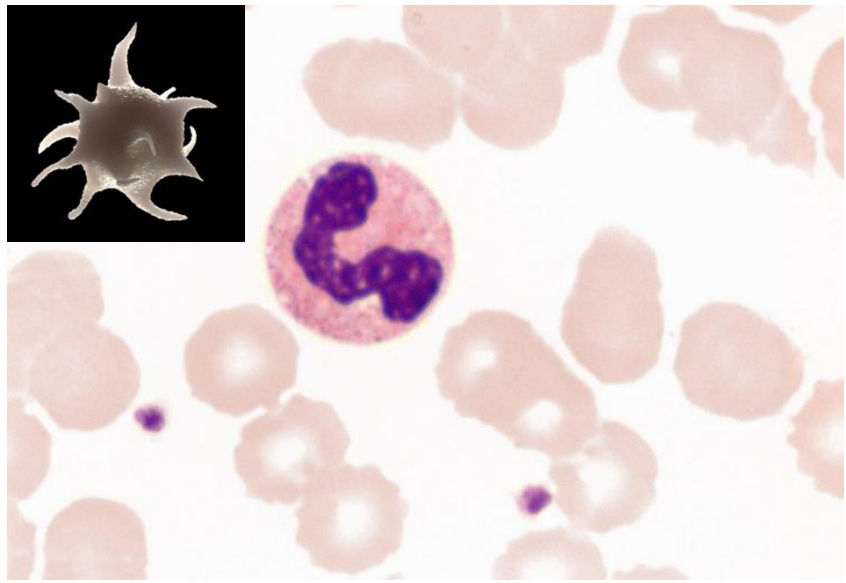
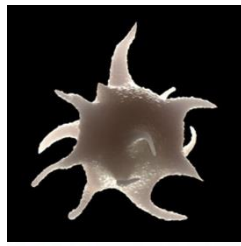


Fig. 1. Immature versus mature DC. Scanning electron micrograph of immature and mature DC. Monocyte-derived DC were cultured without (a) or with LPS for 24 h (b) or 48 h (c). Cells were fixed and allowed to adhere to poly-L-lysine-coated coverslips before preparation for scanning electron microscopy.

# 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

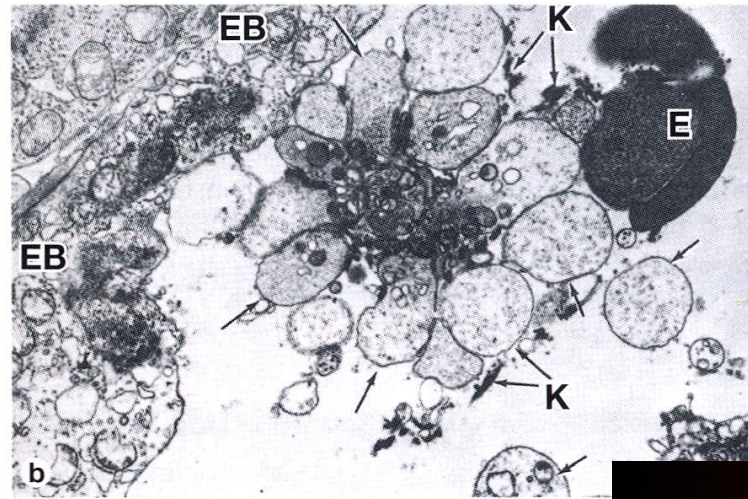
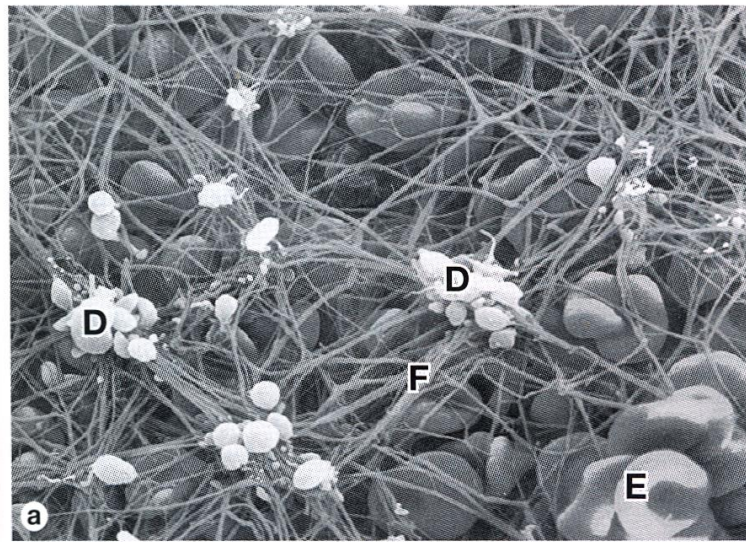
- collagen fibers exposed by endothelial rupture
- platelet clot

## 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

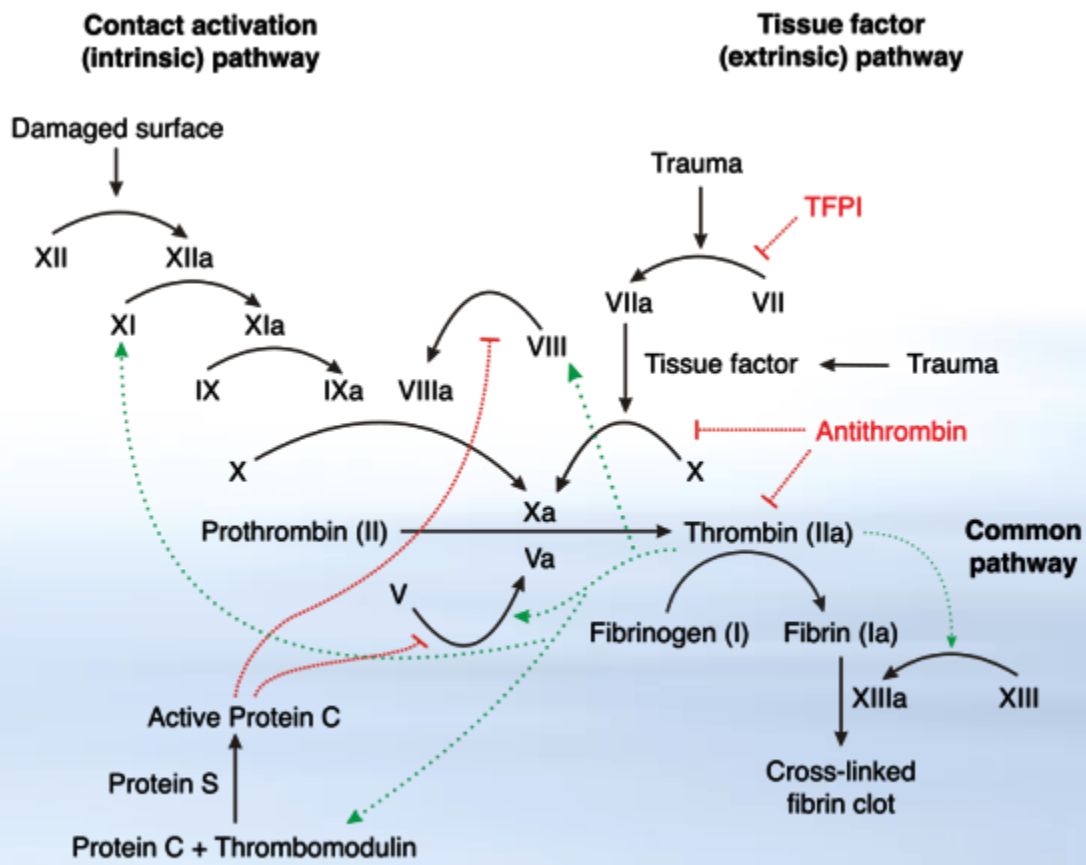
- contraction of thrombus (platelet actin and myosin)

## 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 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

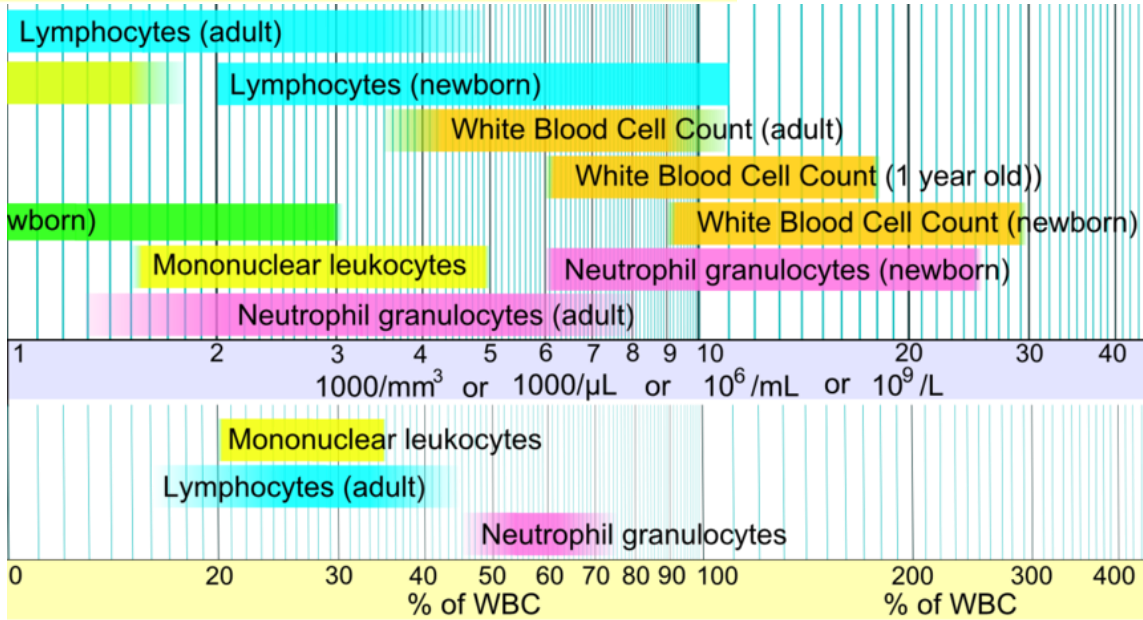
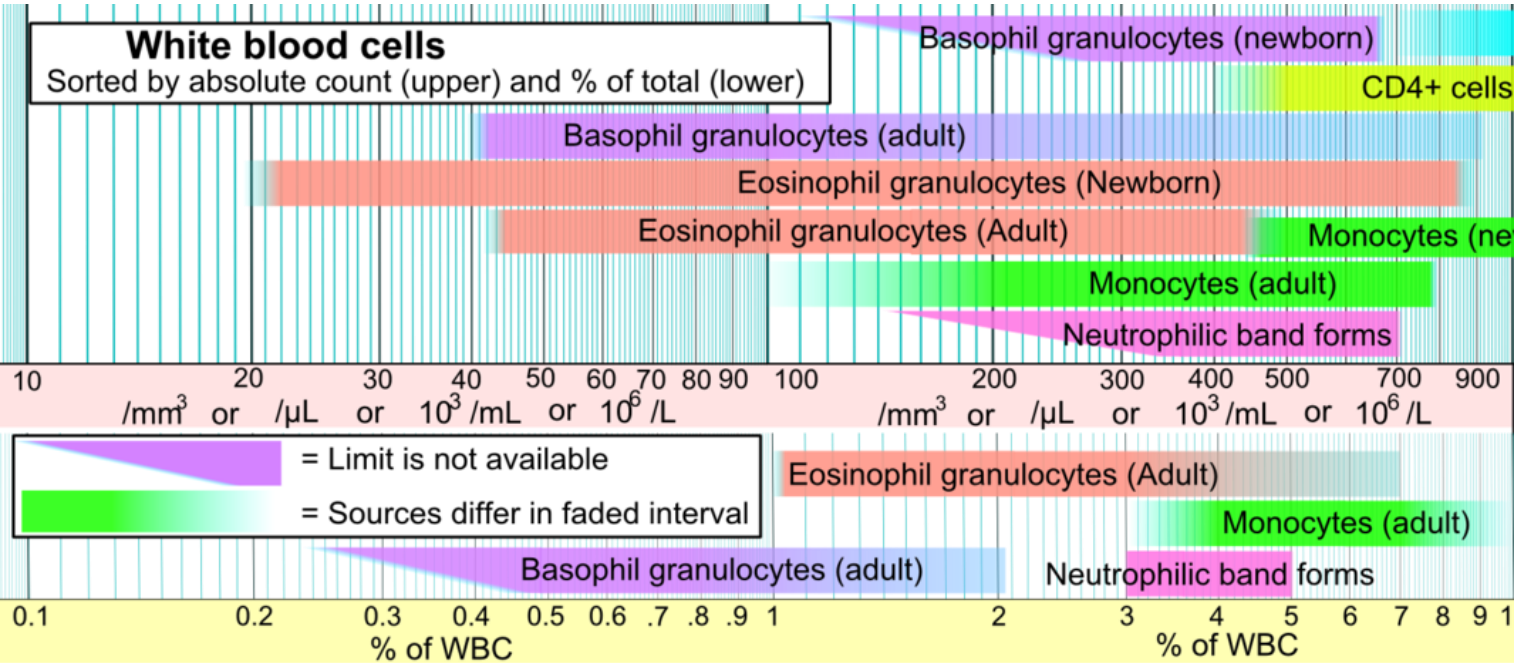
## Example of population variability

<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

**White blood cells**  
Sorted by absolute count (upper) and % of total (lower)



Wikipedia



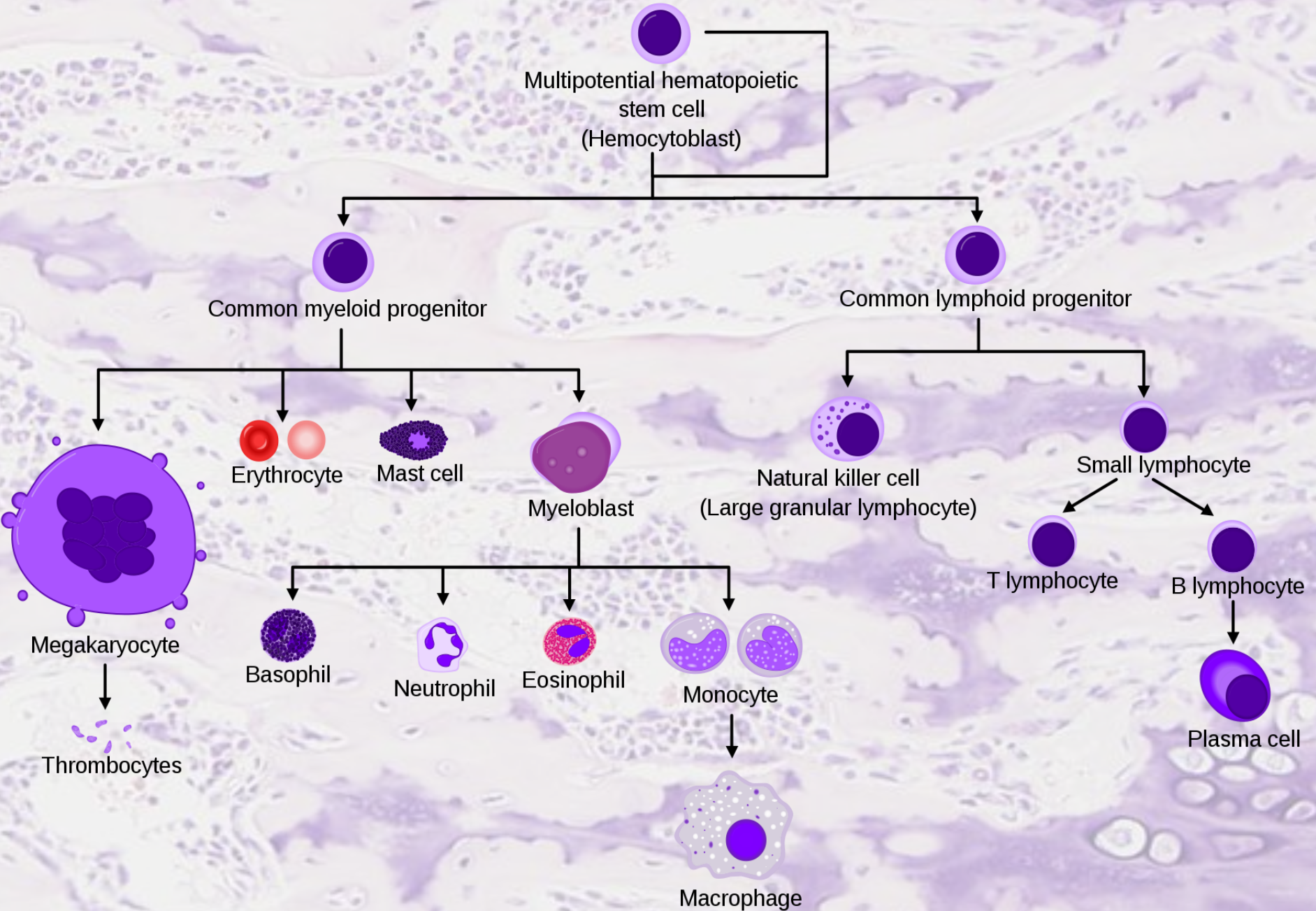
# DIFFERENTIAL WHITE BLOOD CELL COUNT

## 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

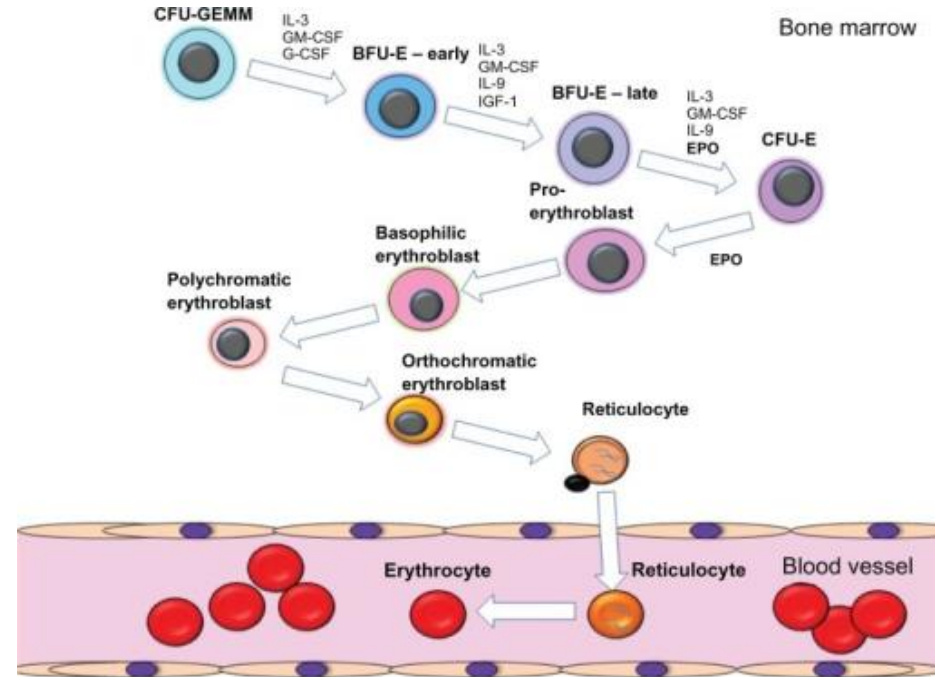
WBC, White blood cell.

# HEMATOPOIESIS

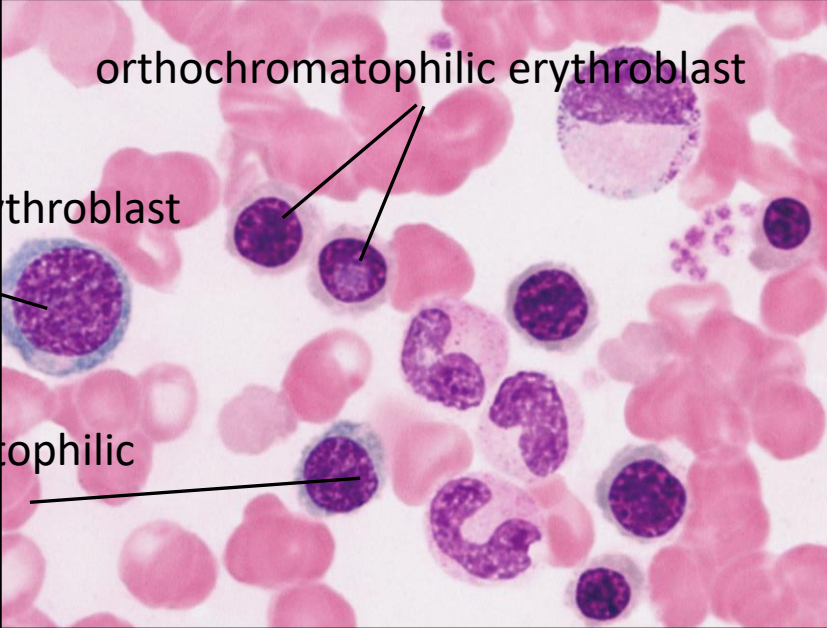
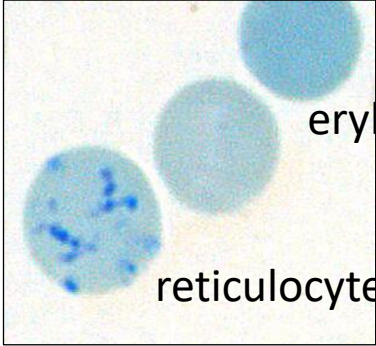
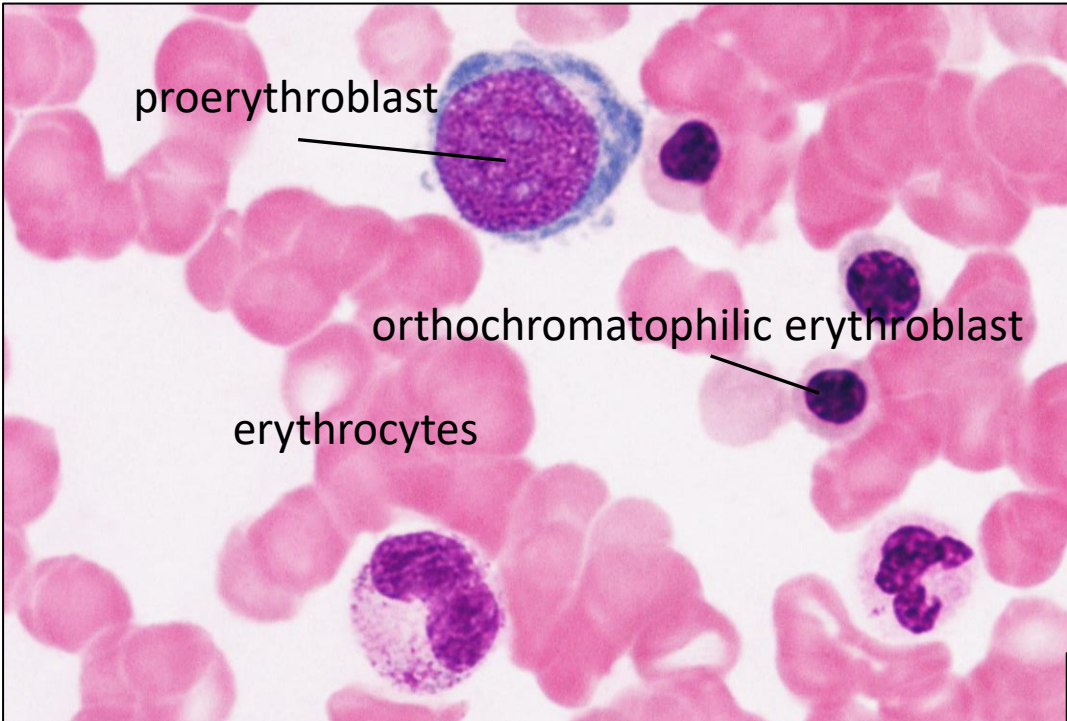


# ERYTHROPOIESIS

- **$2 \times 10^{11}$  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, pycnotic nucleus → **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

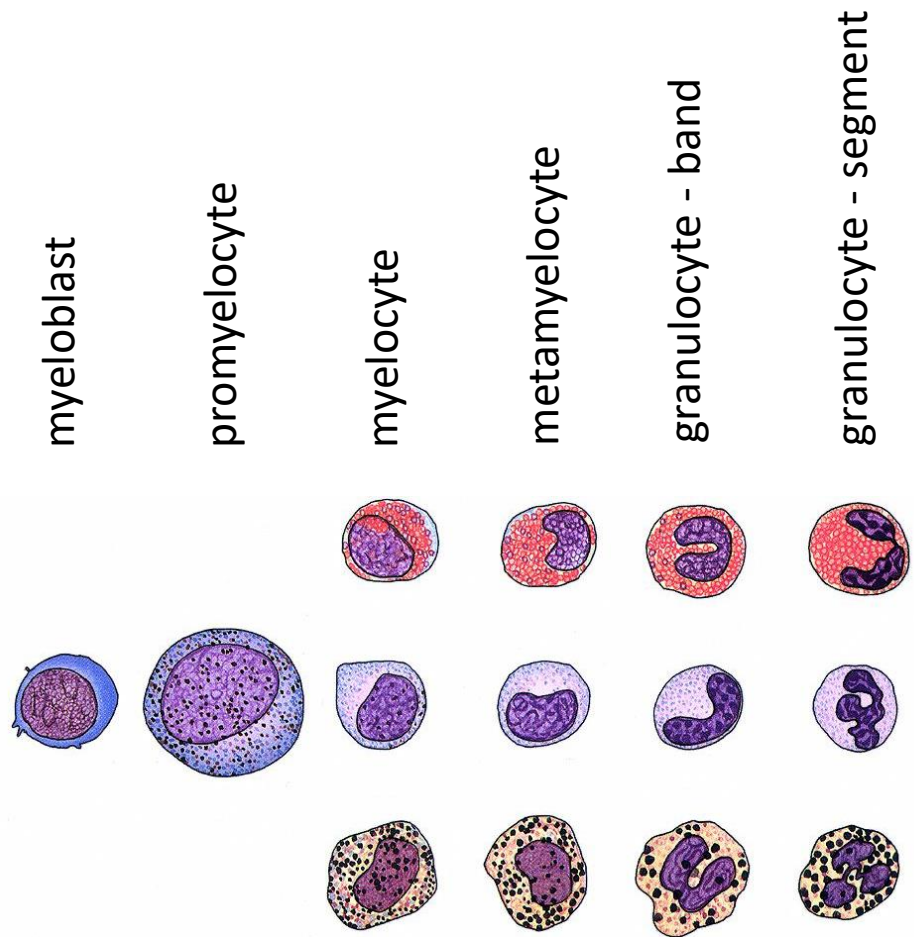


# ERYTHROPOIESIS



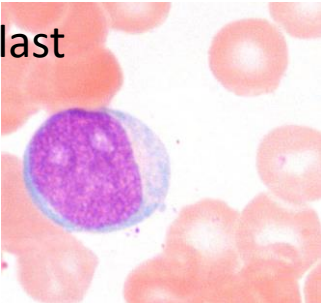
# GRANULOPOIESIS

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

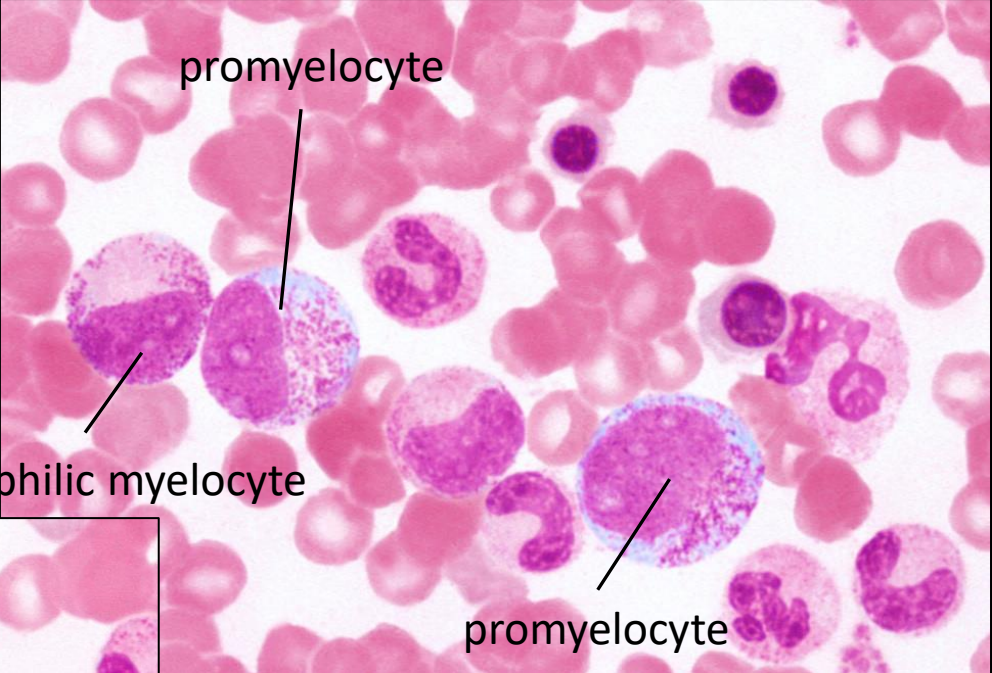


# GRANULOPOIESIS

myeloblast



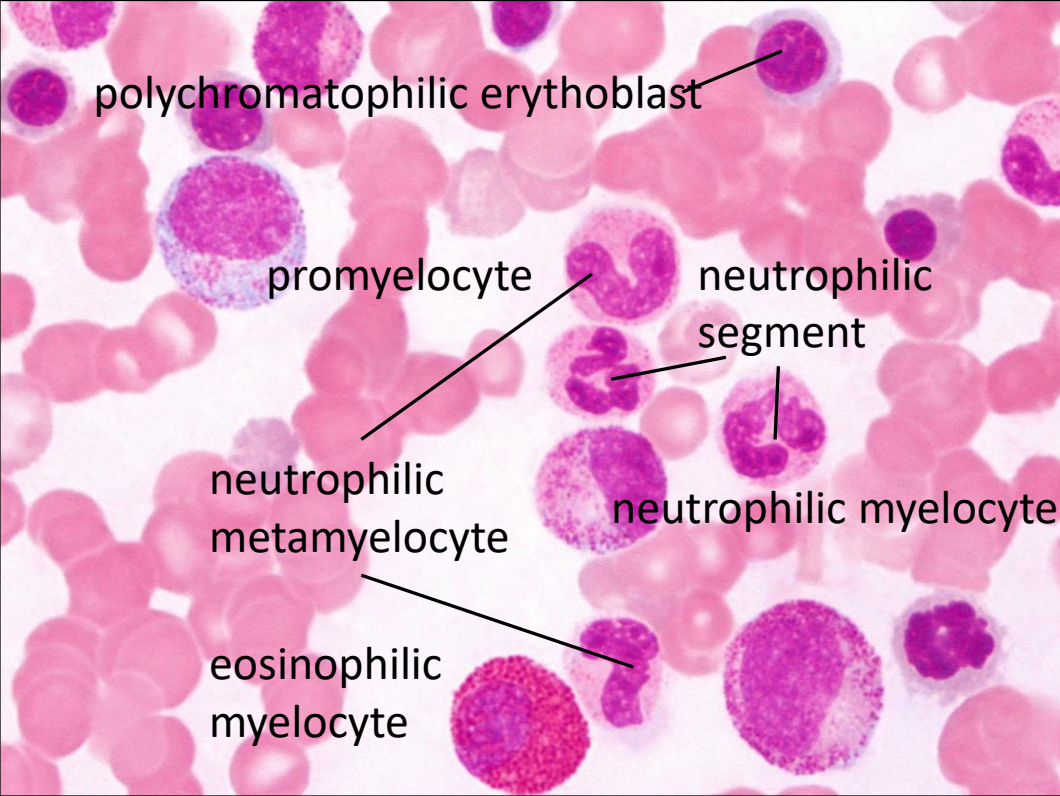
promyelocyte



neutrophilic myelocyte

promyelocyte

polychromatophilic erythroblast



promyelocyte

neutrophilic segment

neutrophilic metamyelocyte

neutrophilic myelocyte

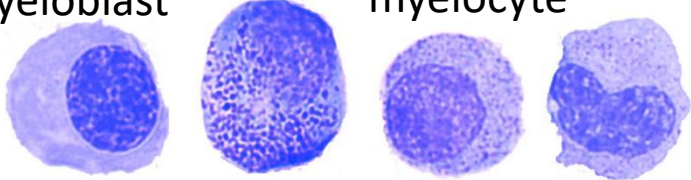
eosinophilic myelocyte

promyelocyte

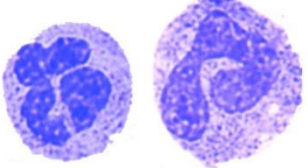
metamyelocyte

myeloblast

myelocyte

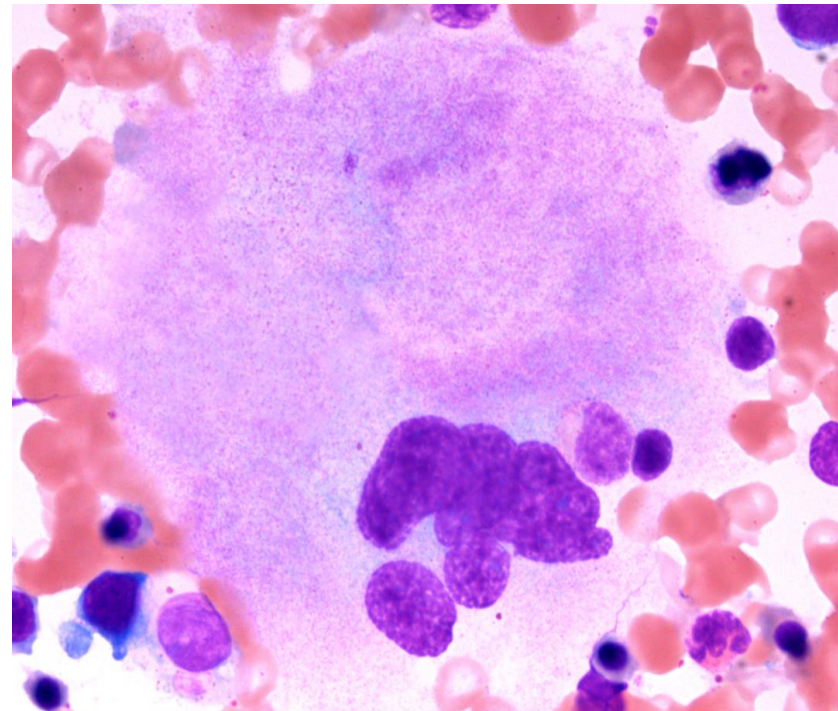
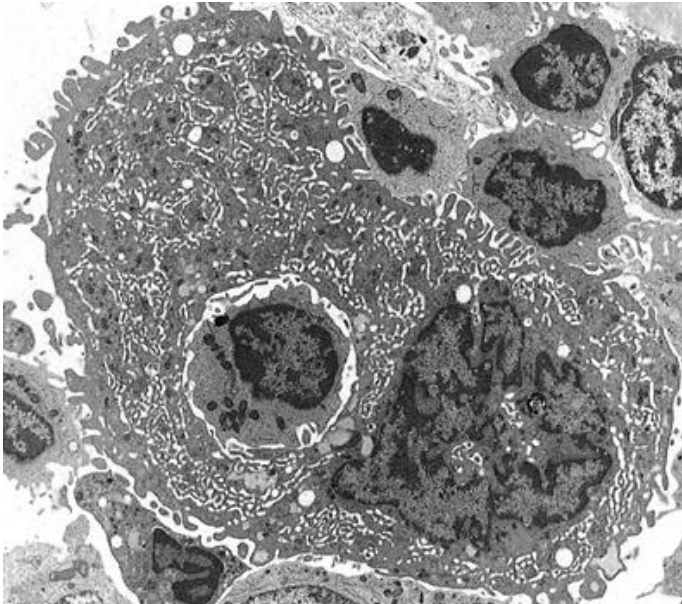
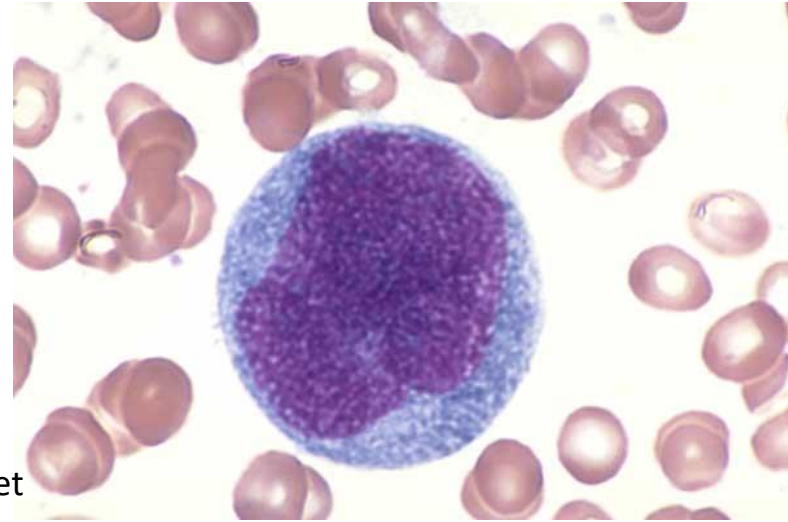


granulocyte



# 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

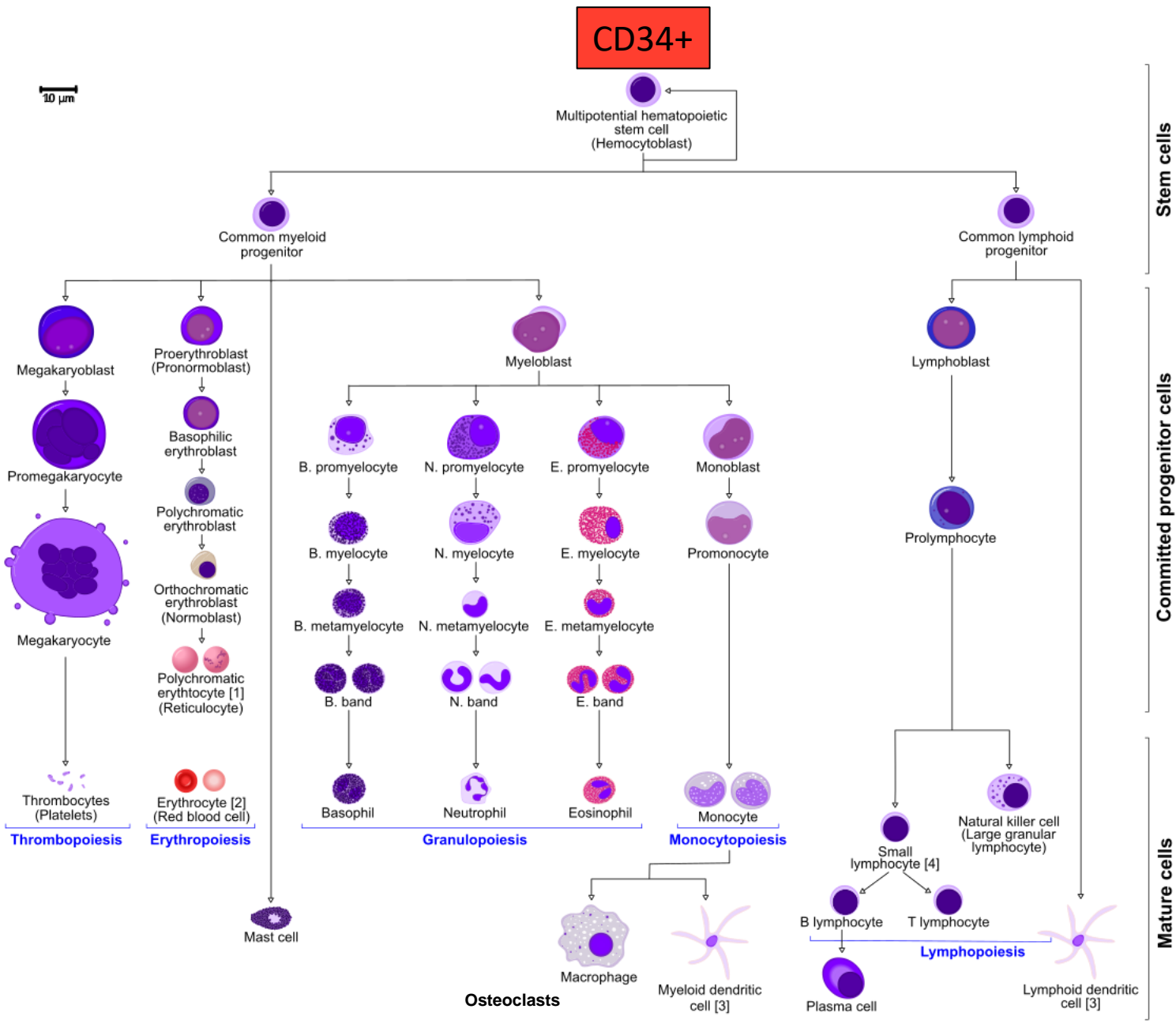
## LYMPHOPOIESIS

- **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



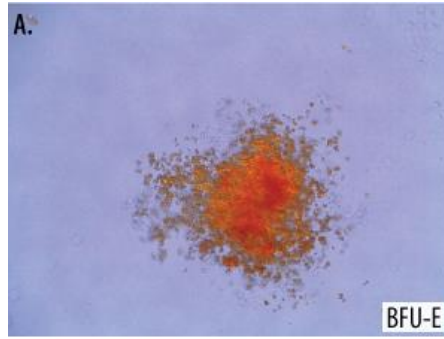
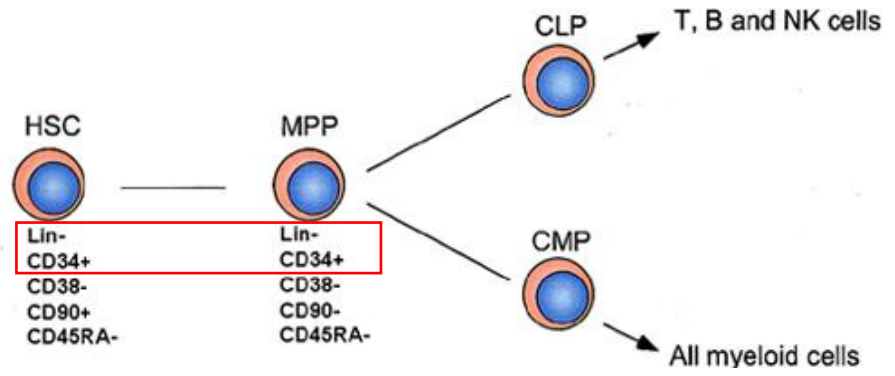
# HEMATOPOIETIC STEM CELLS AND PROGENITORS

## 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

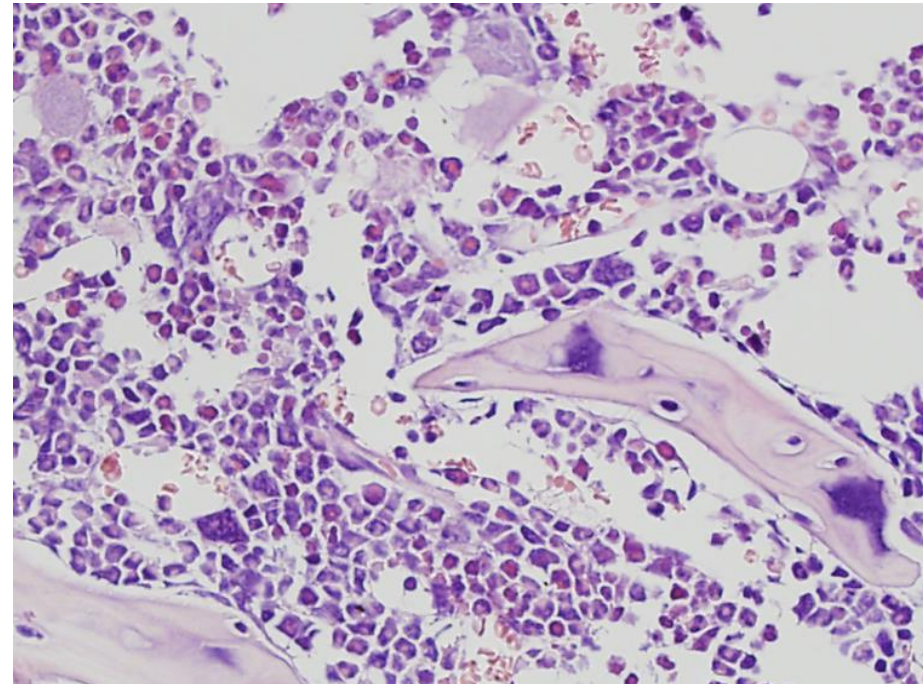
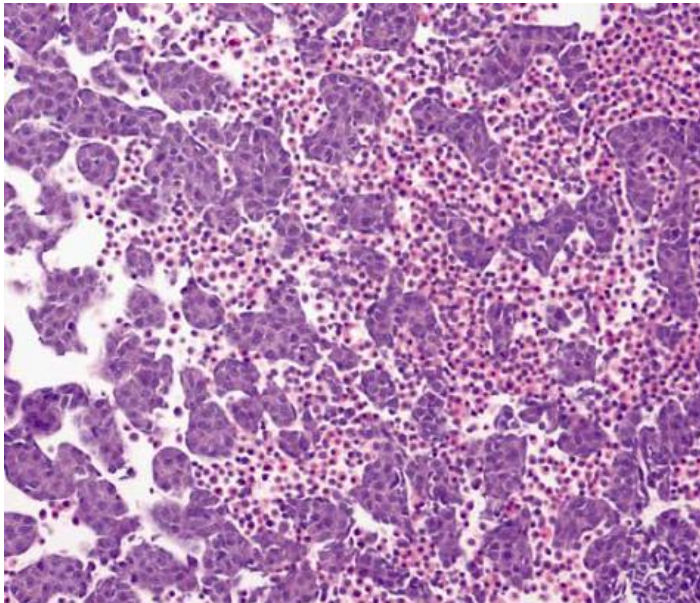
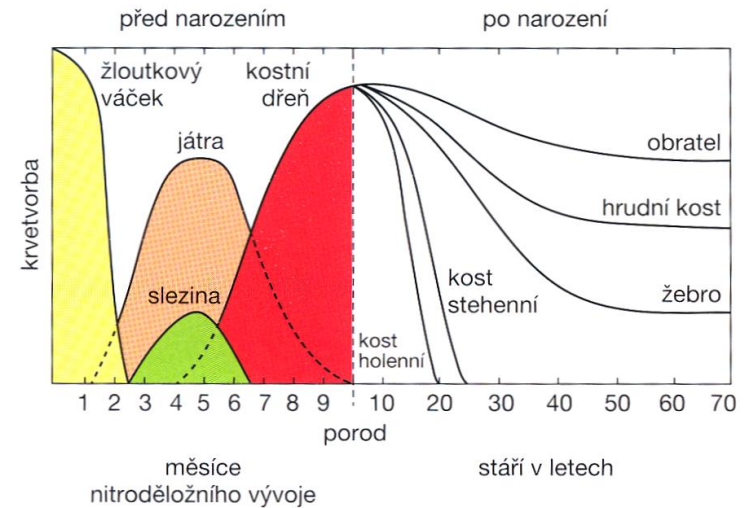
## Colony/Burst – Forming Unit – CFU/BFU

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



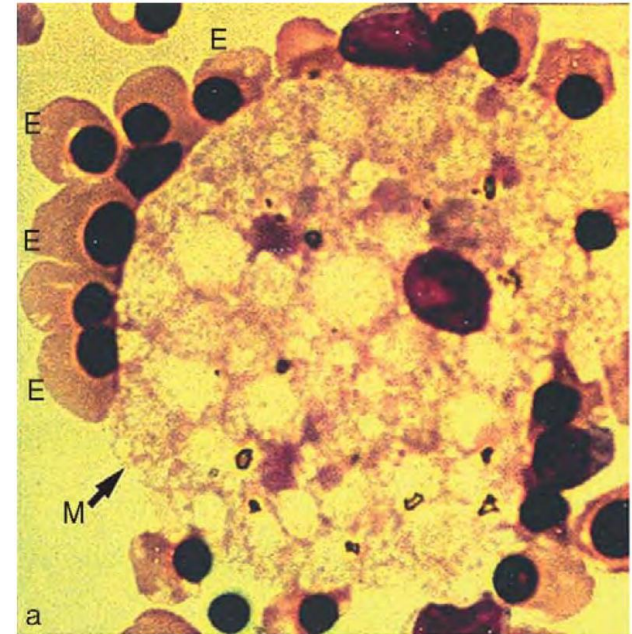
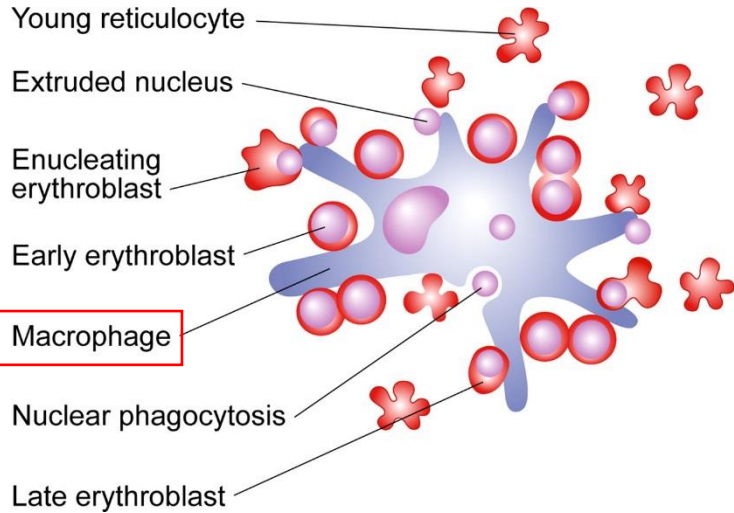
# EMBRYONIC HEMATOPOIESIS

- **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

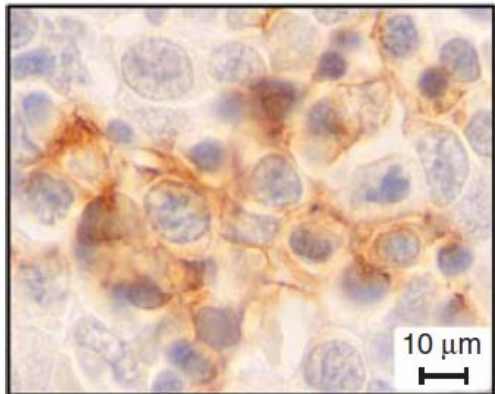


# HEMATOPOIETIC ISLANDS

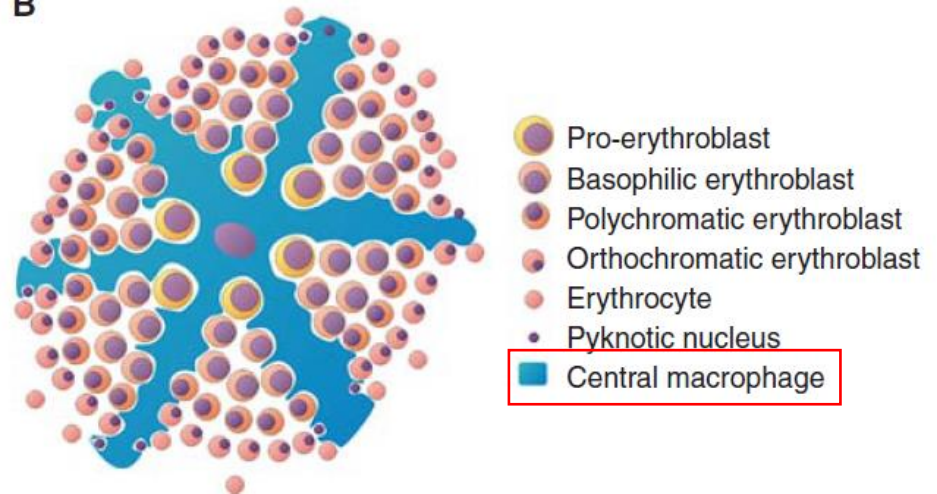
- hepatolienal and bone marrow hematopoiesis
- erythroblast islands



A

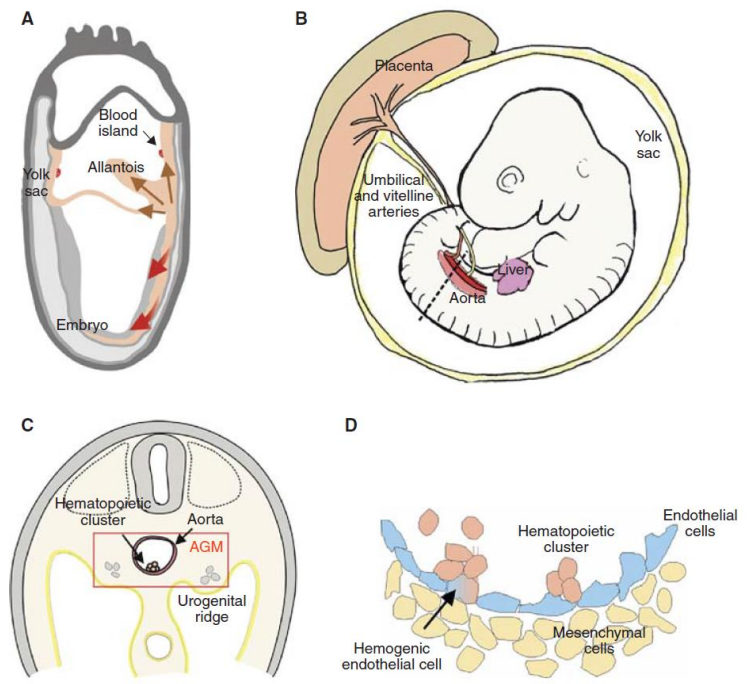
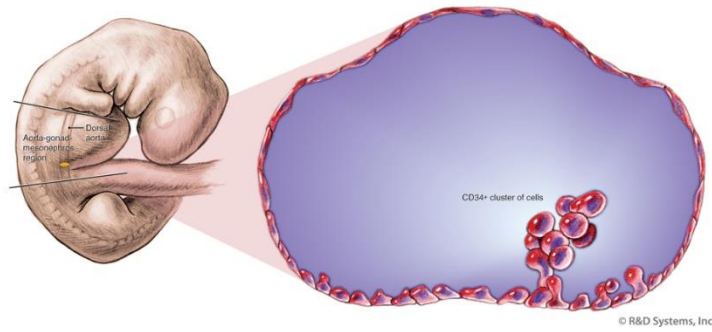


B

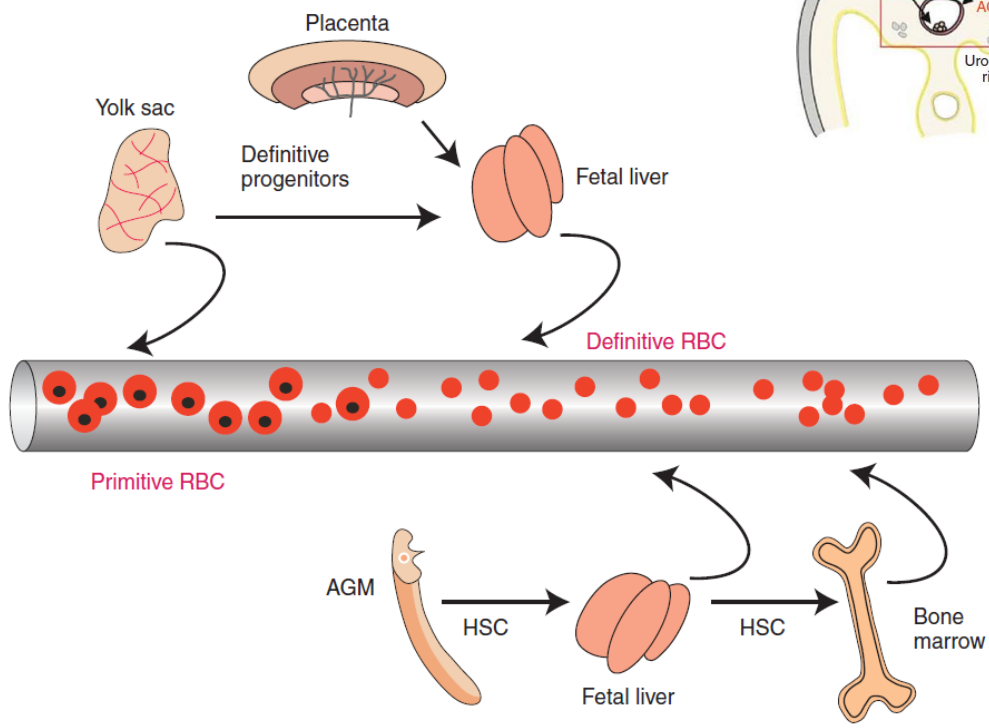


# INTRAEMBRYONIC HEMATOPOIESIS

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



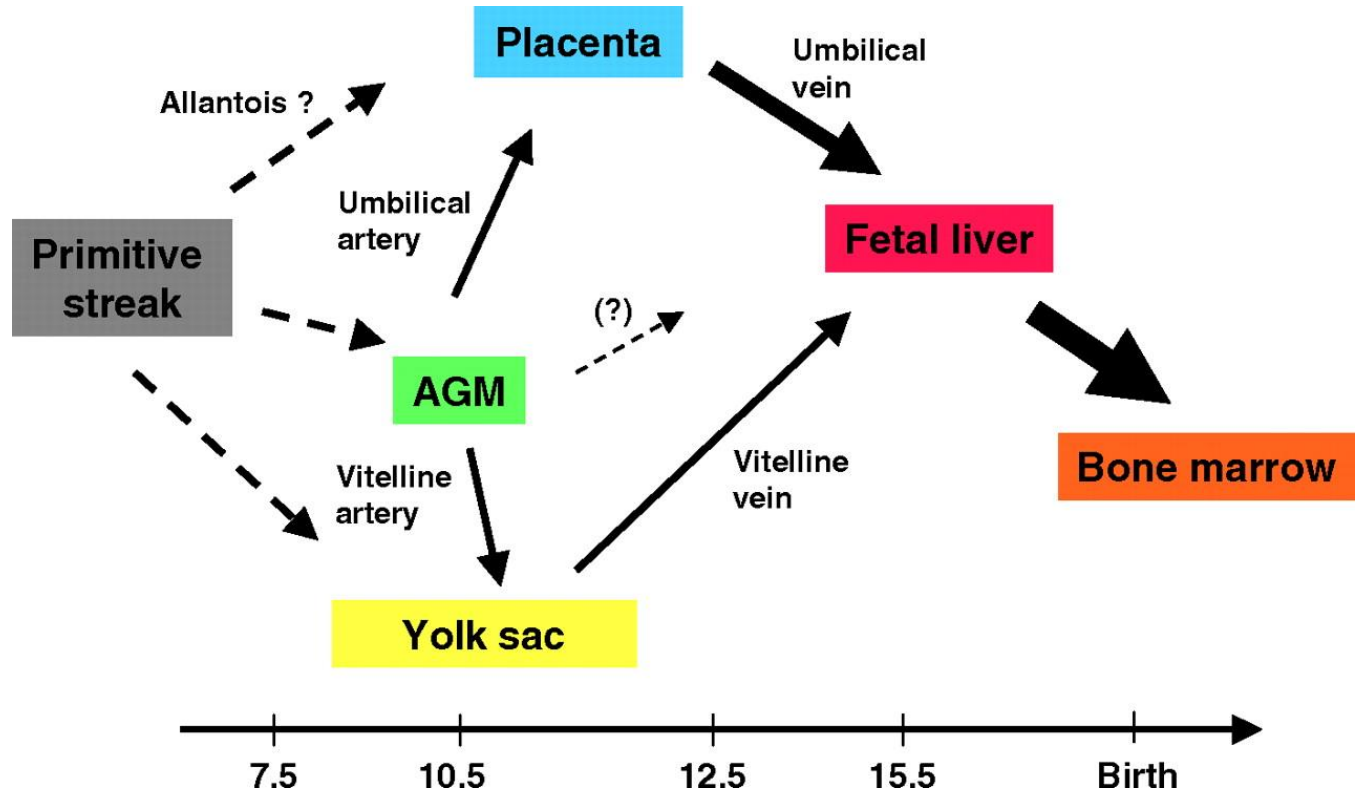
- **Placenta**



# 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

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