

Krvetvorba

MUDr. Andrea Vajsová

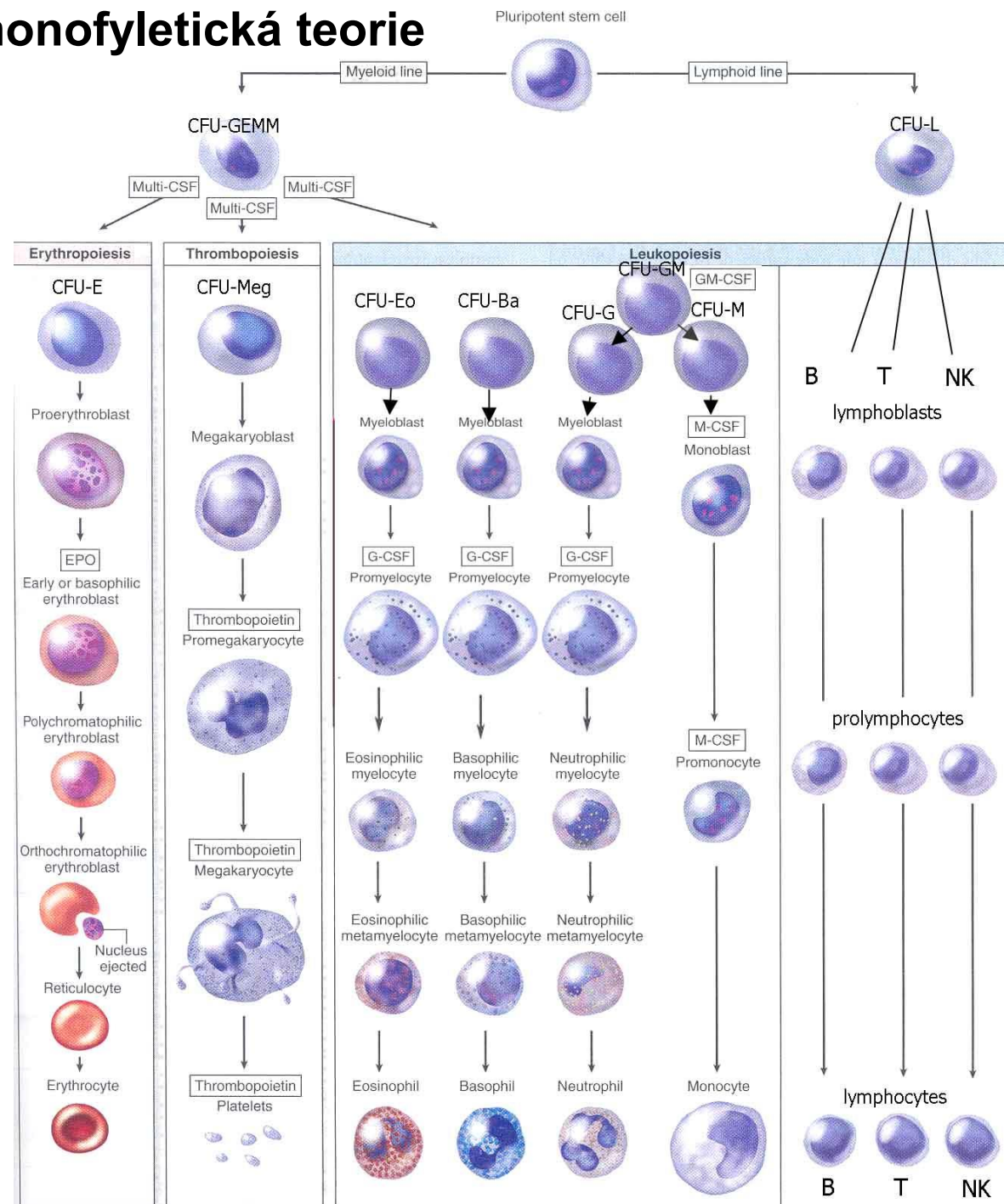
monofyletická teorie

Kmenové buňky

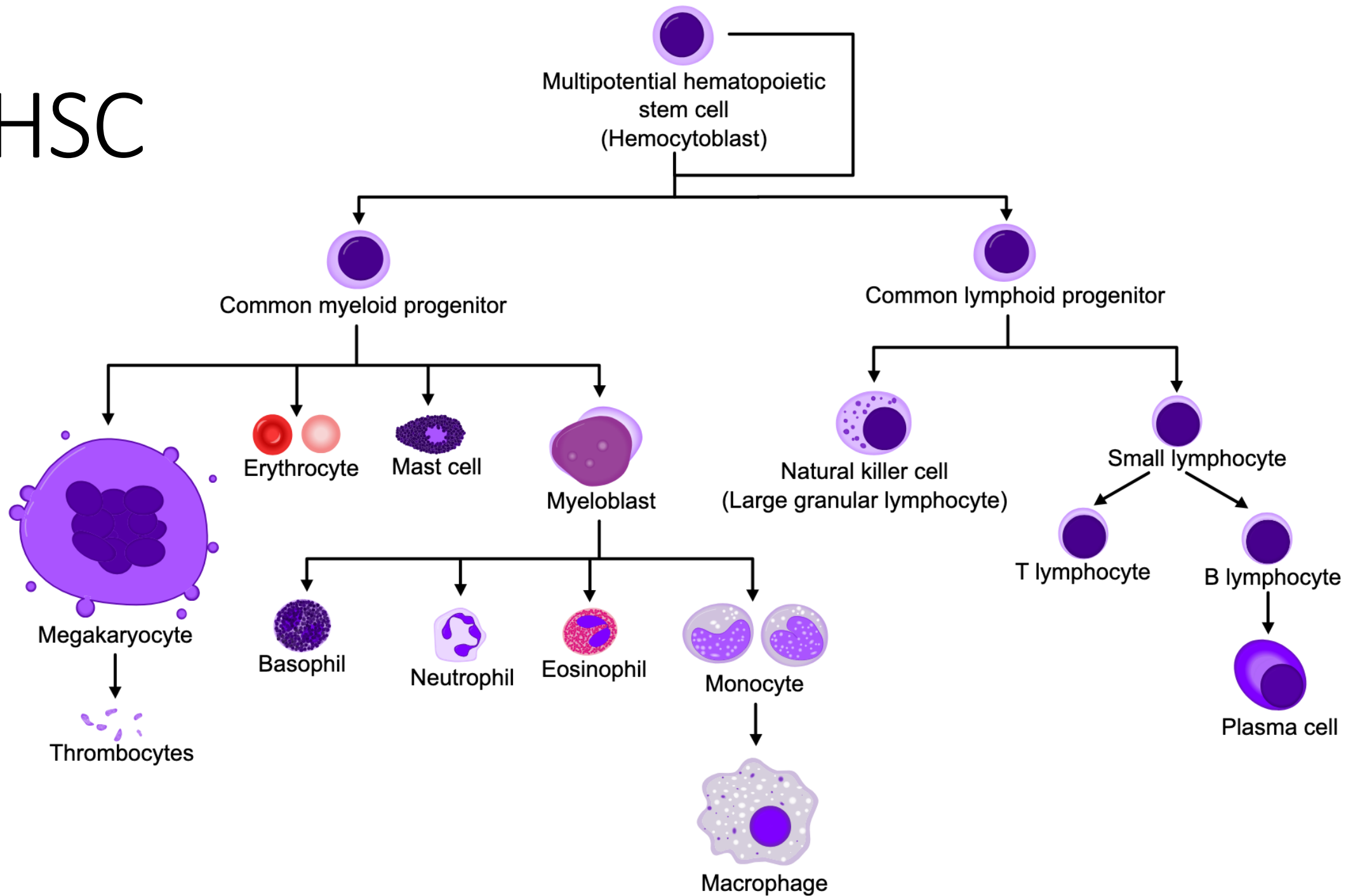
Progenitorové buňky (CFU)

Prekursorové buňky (blasty)

Zralé buňky

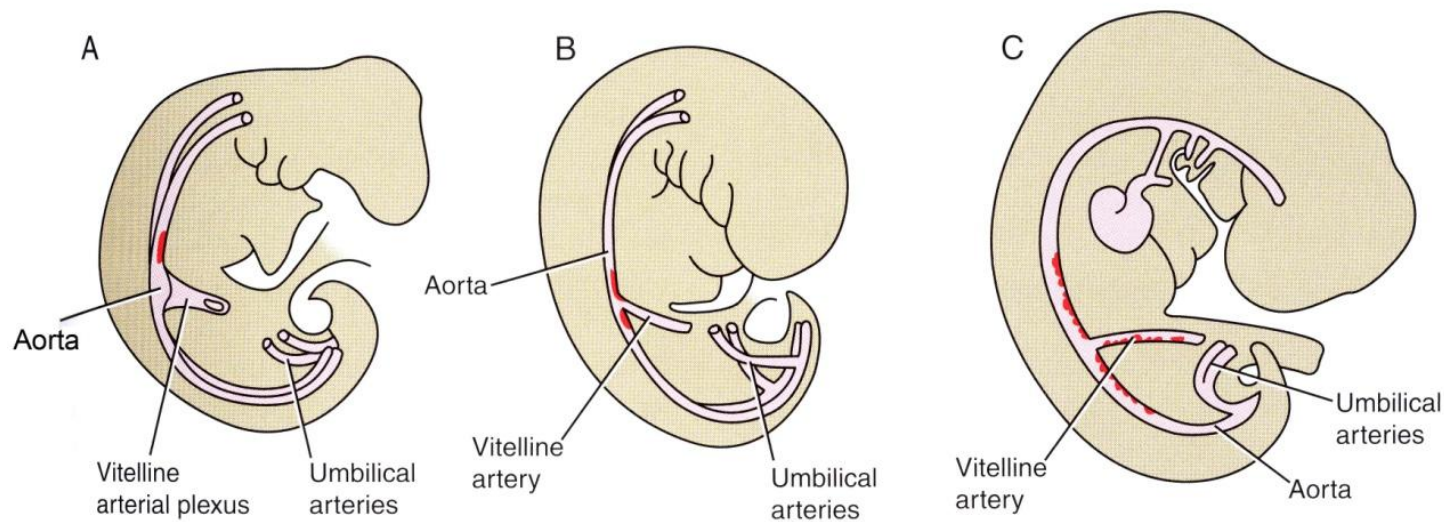
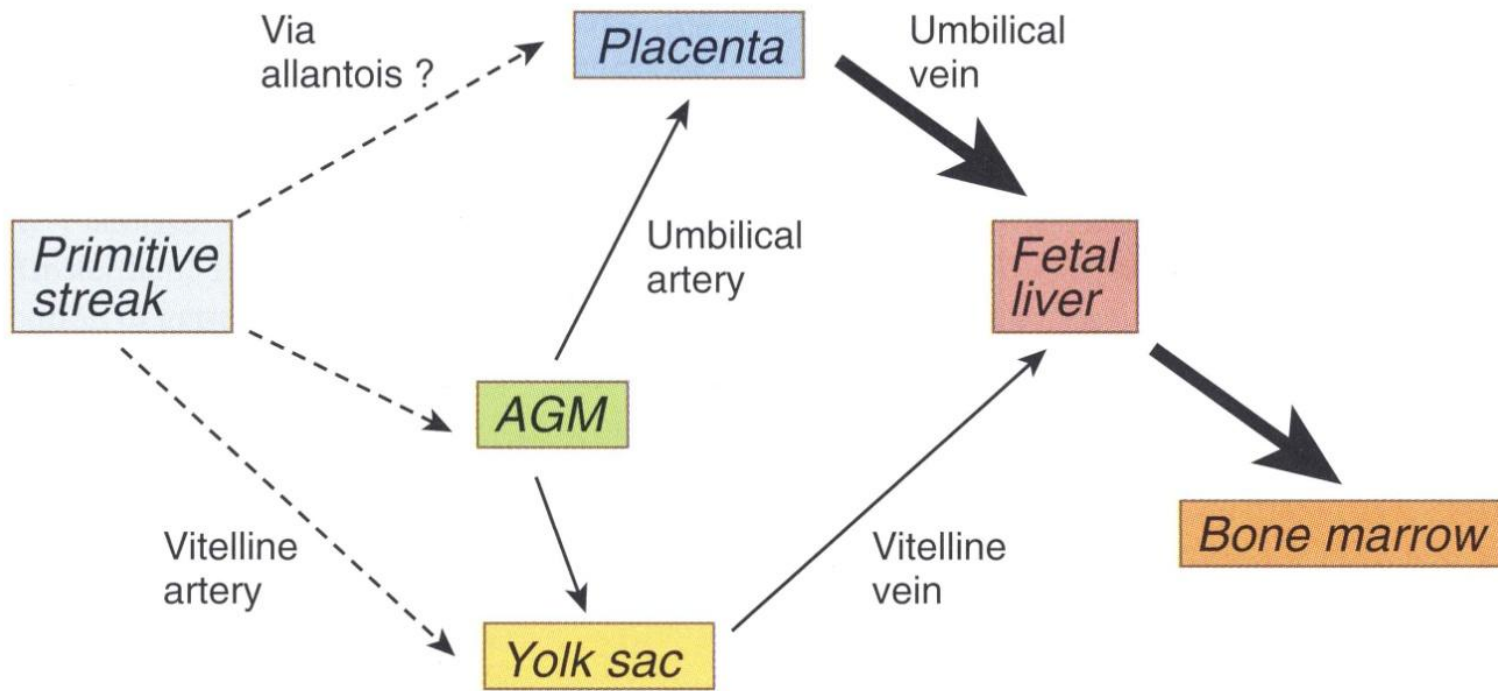


HSC



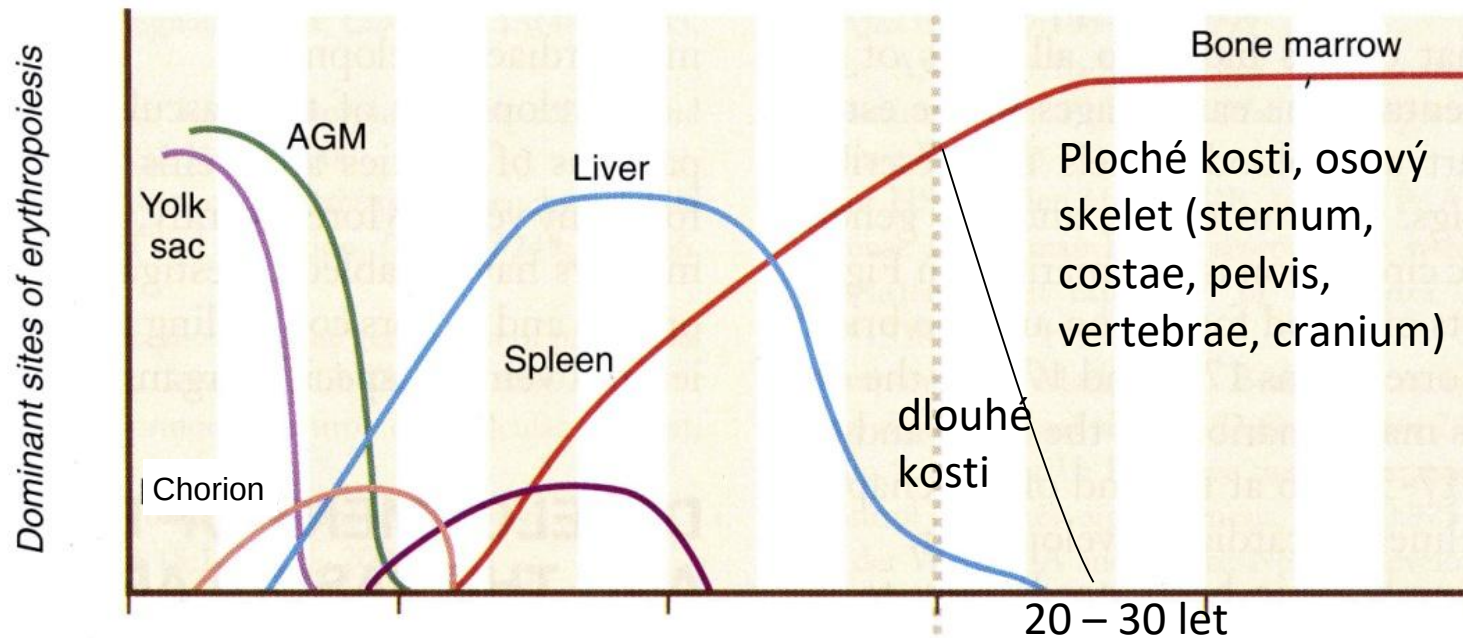
Hematopoéza - úvod

- **Monofyletická** teorie – leukocyty, erytrocyty a trombocyty pocházejí z HSC
- Další úroveň diferenciací jsou 2 společné progenitory – **lymfoidní CLP** a **myeloidní CMP**
- Z **progenitorů** vznikají **prekursorové** buňky určitého konkrétního typu
- Následuje několik stádií postupně získávajících znaky příslušných diferencovaných buněk

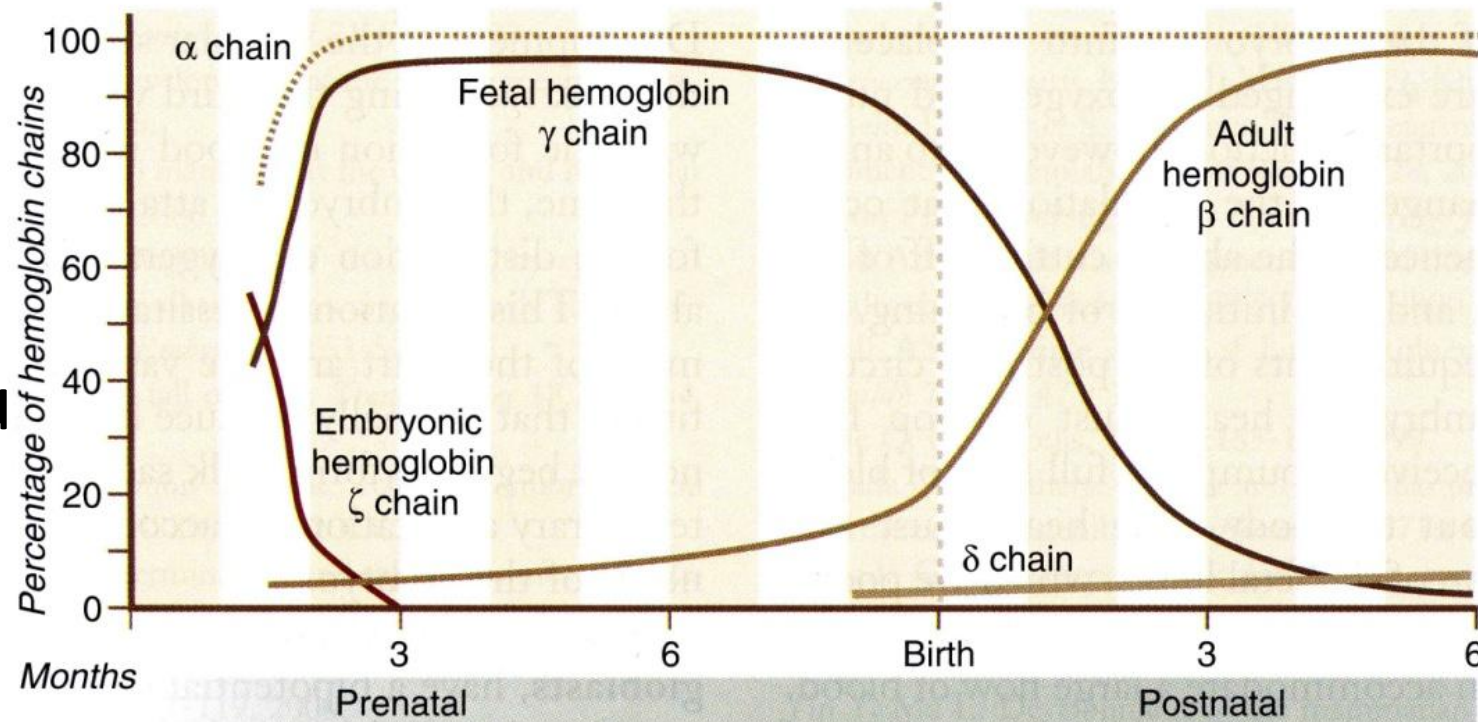


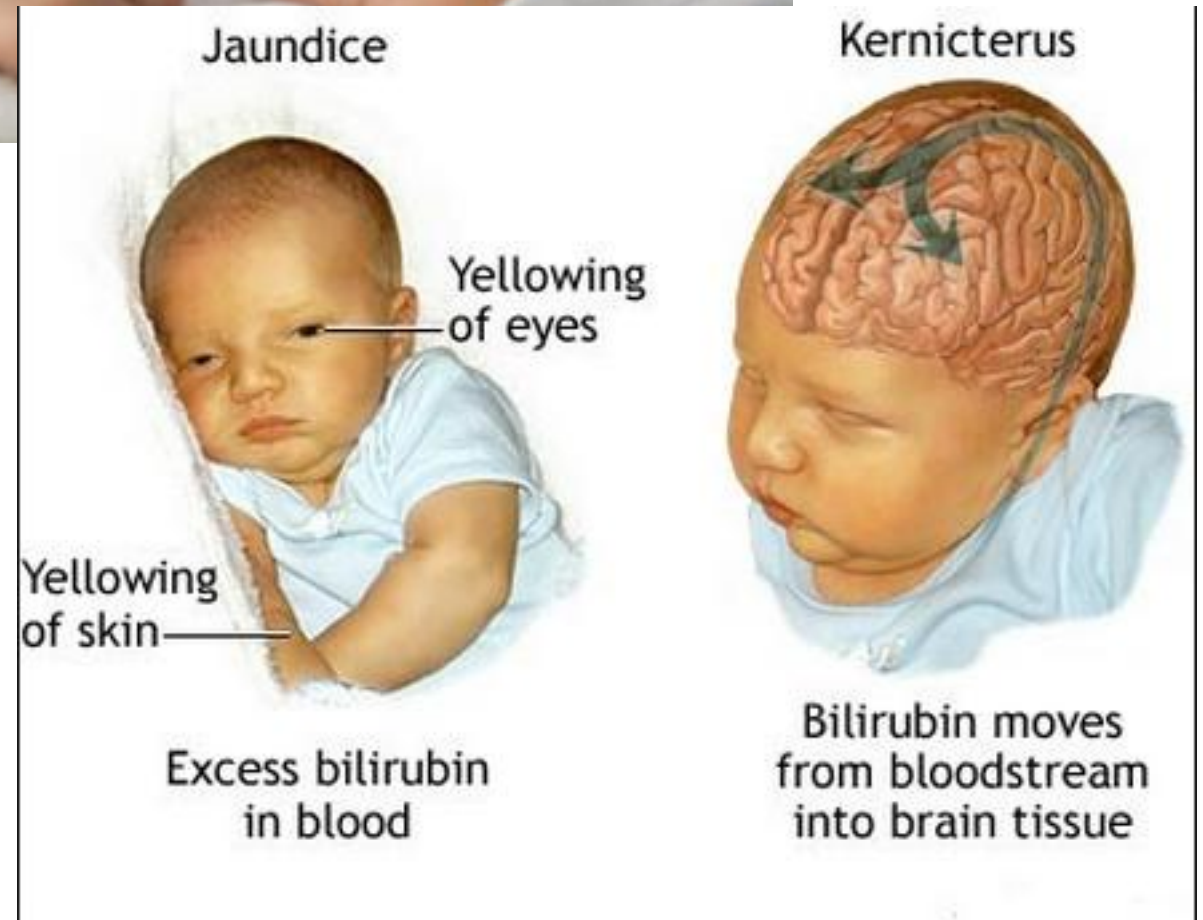
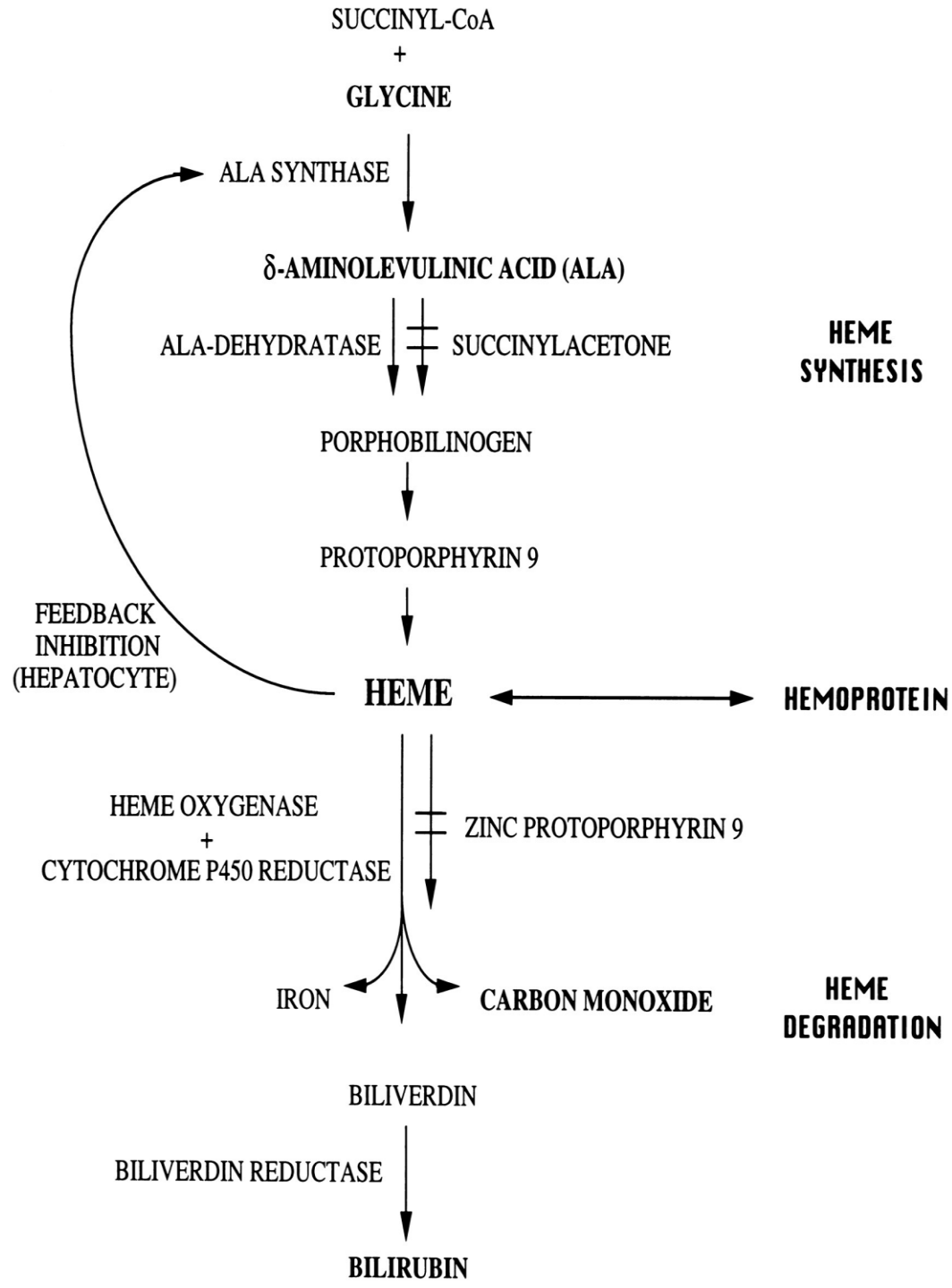
AGM
= aorta-gonad-mesonephros

Vývoj krvetvorby

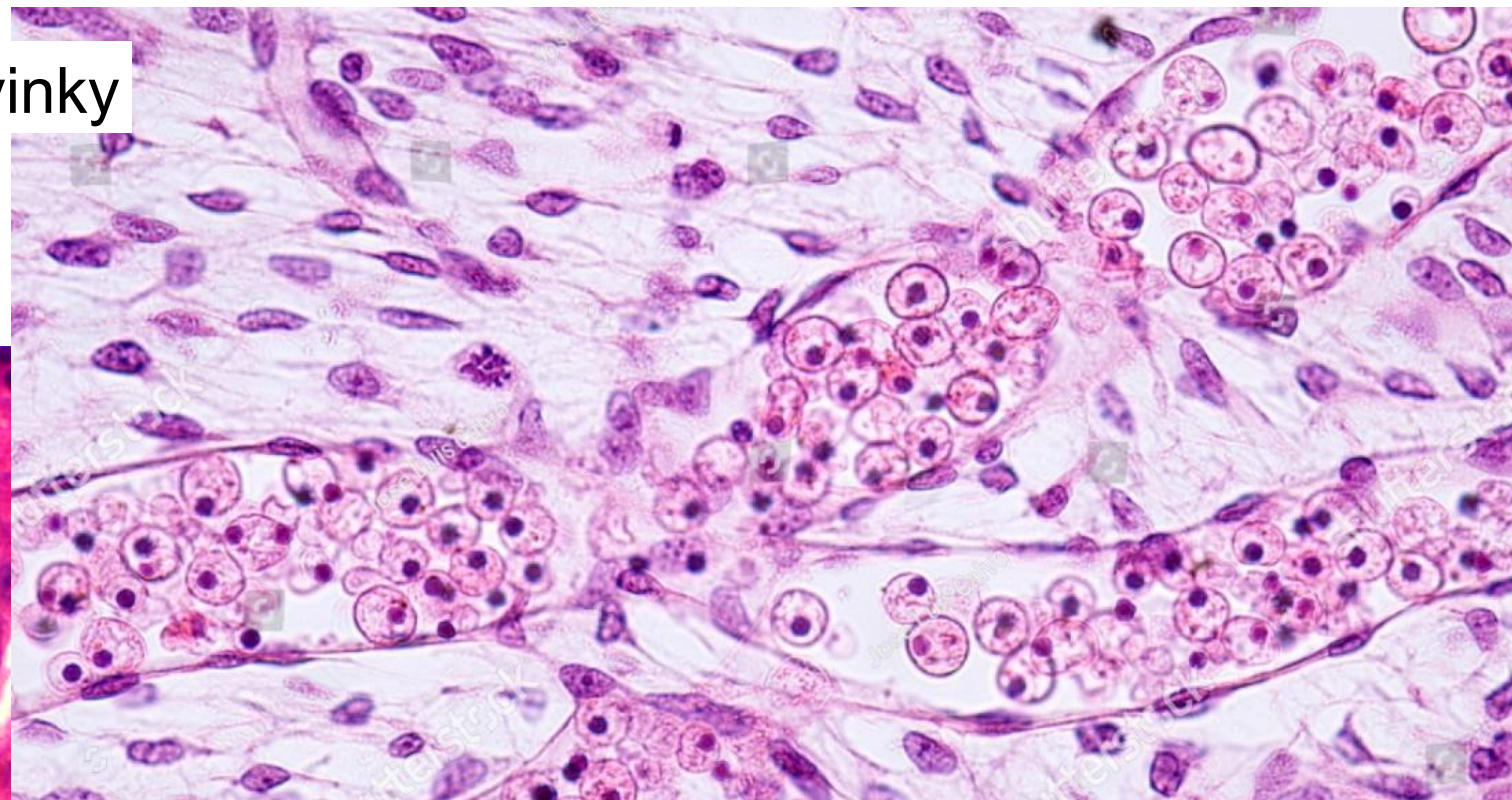
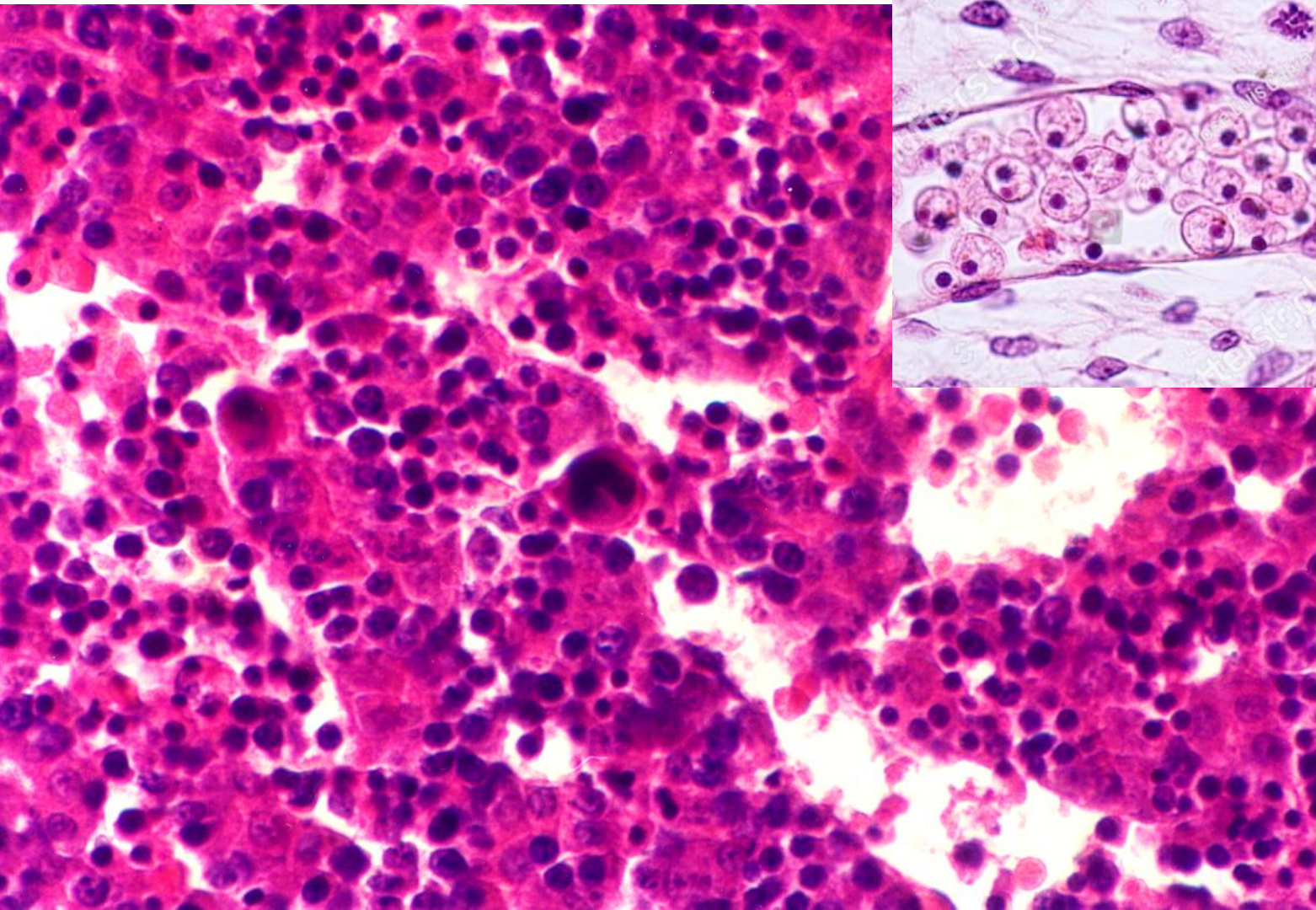


Vývoj typu hemoglobinu



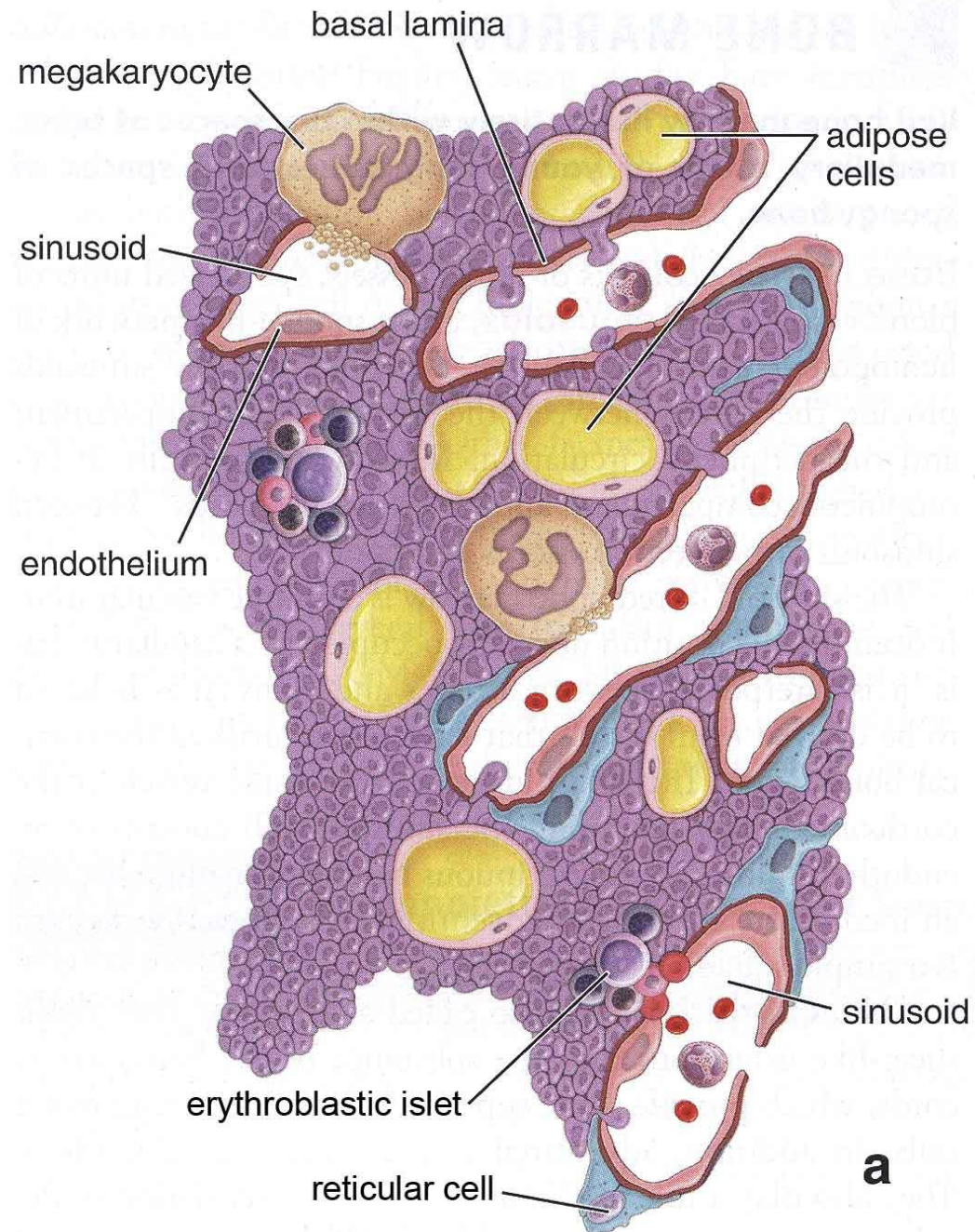


Embryonální krvinky

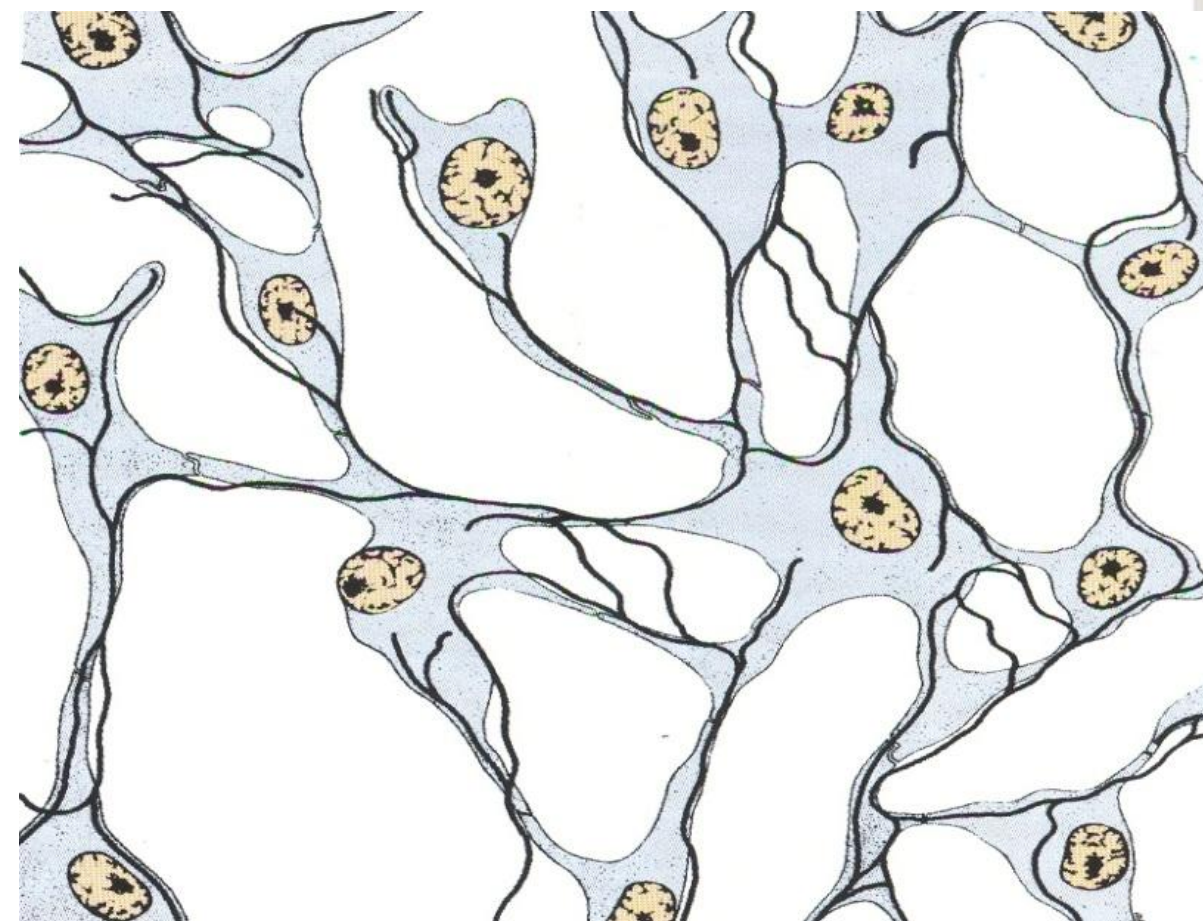


Fetální játra

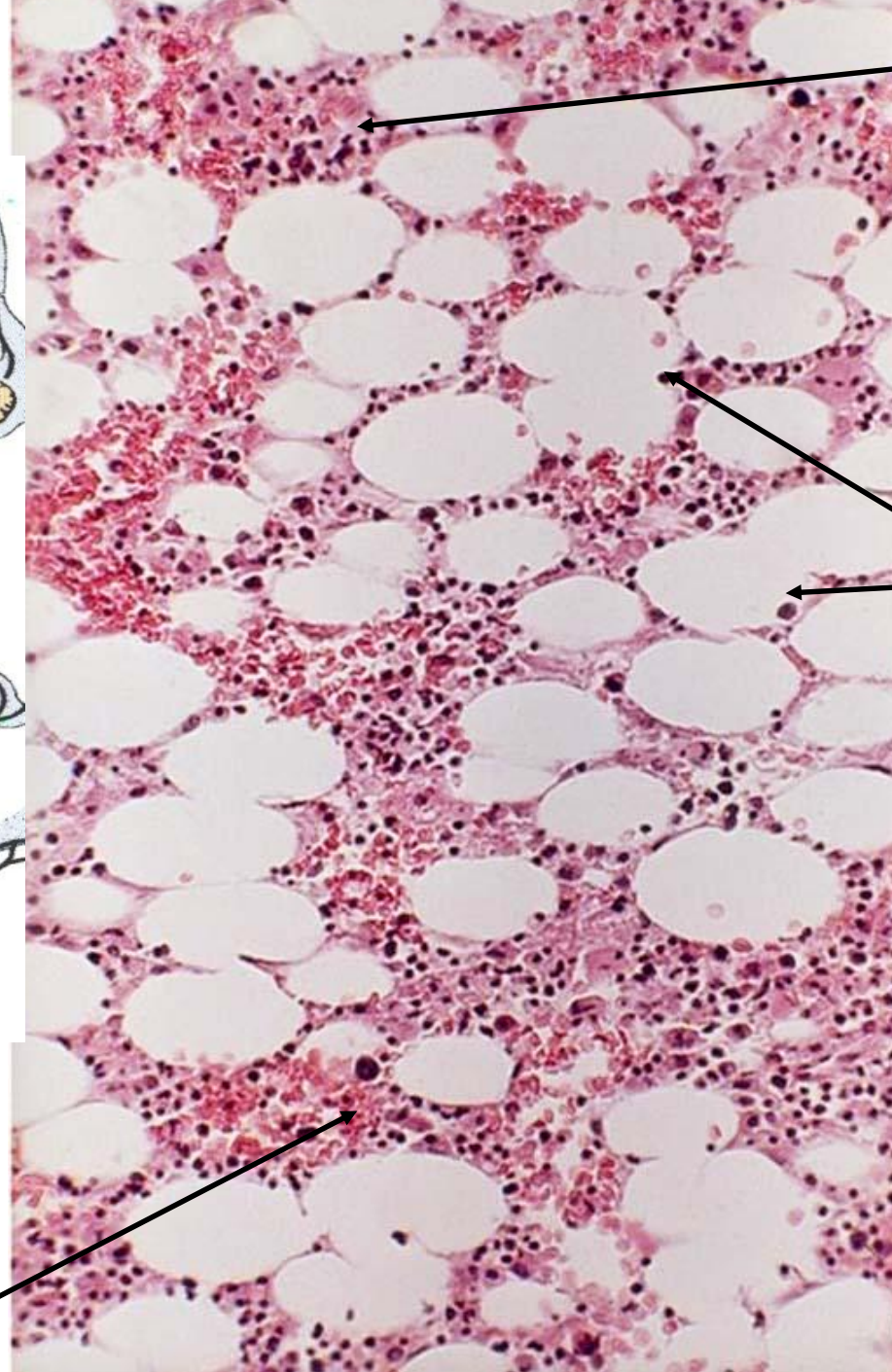
Kostní dřeň



a



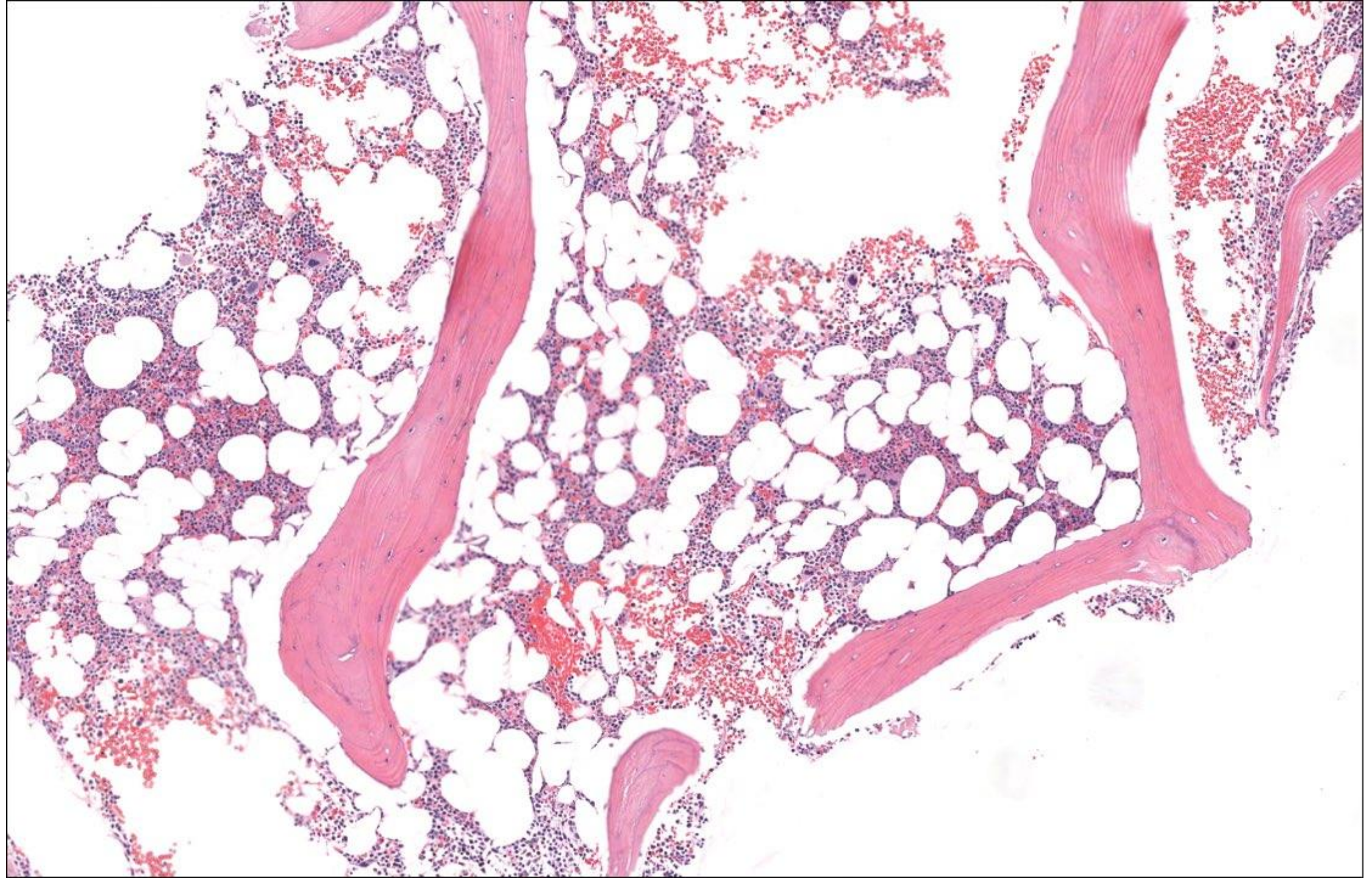
retikulární vazivo

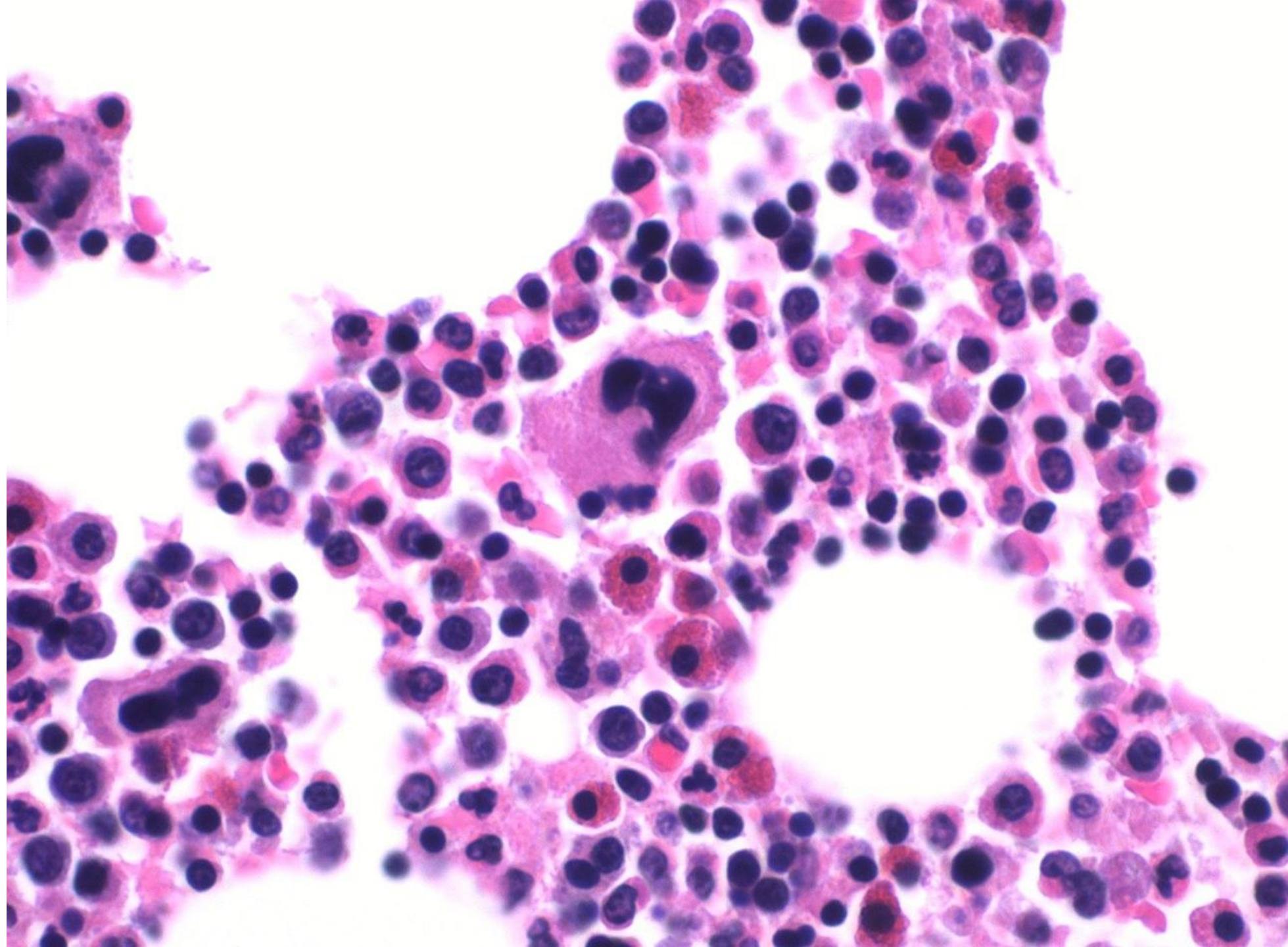


hemopoetické
ostrůvky

adipocyty

sinusoidy





Aspirace kostní dřeně vs trepanobiopsie

Bone Marrow Aspiration

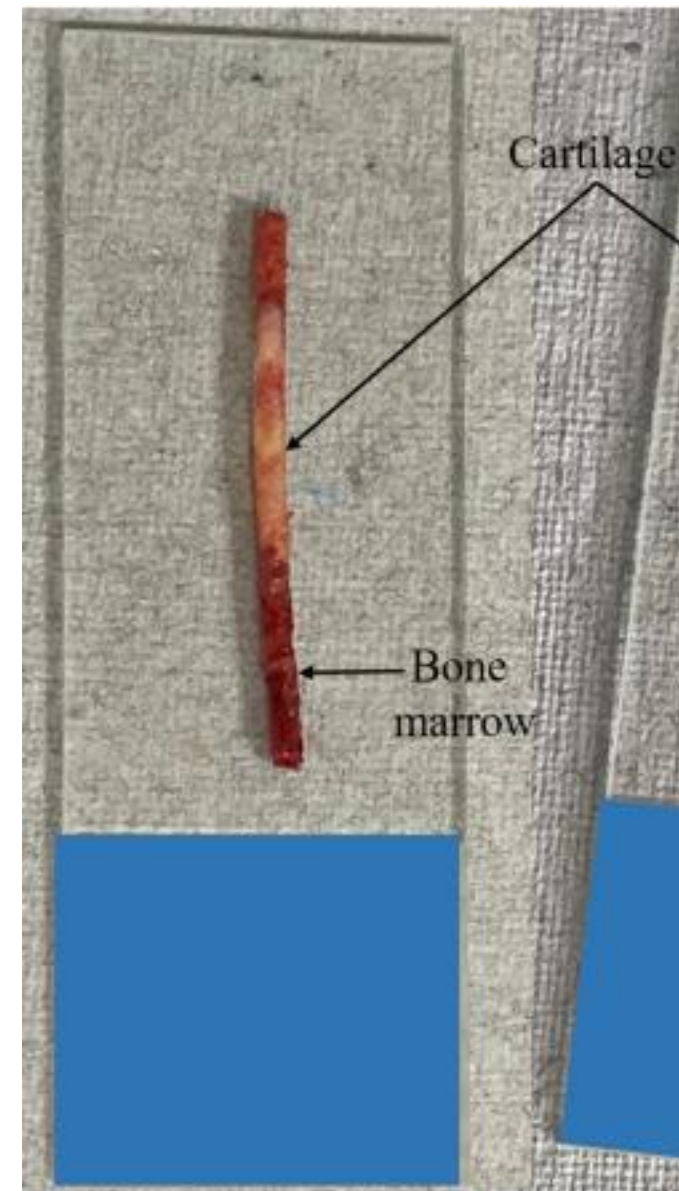
Trephine Biopsy

Cytology

Histology

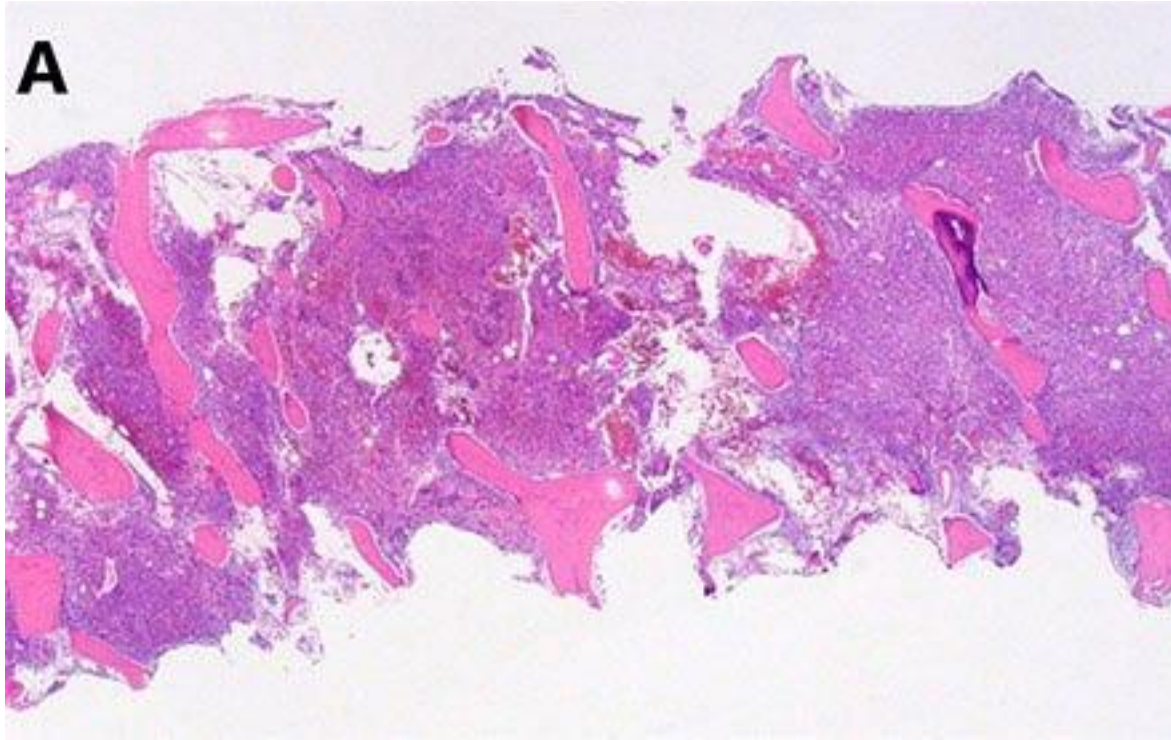


IM
INTERESTING
MEDICINE



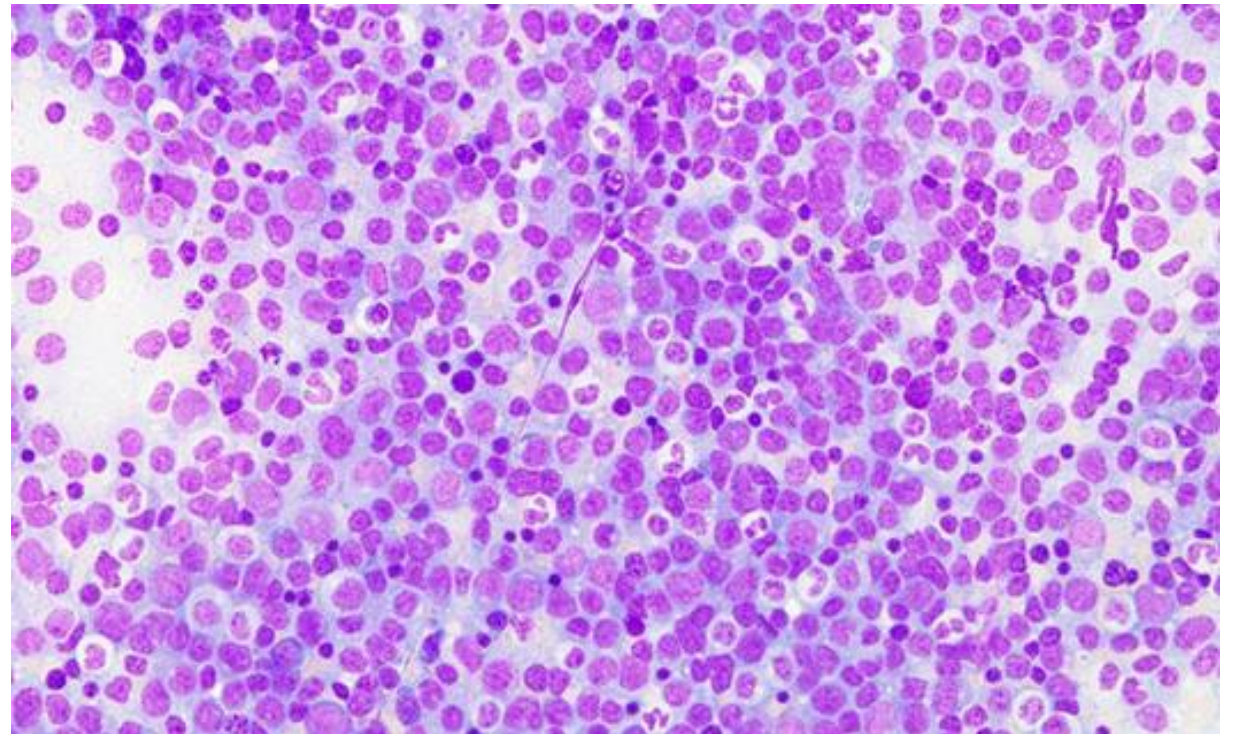
(a) Adult bone marrow

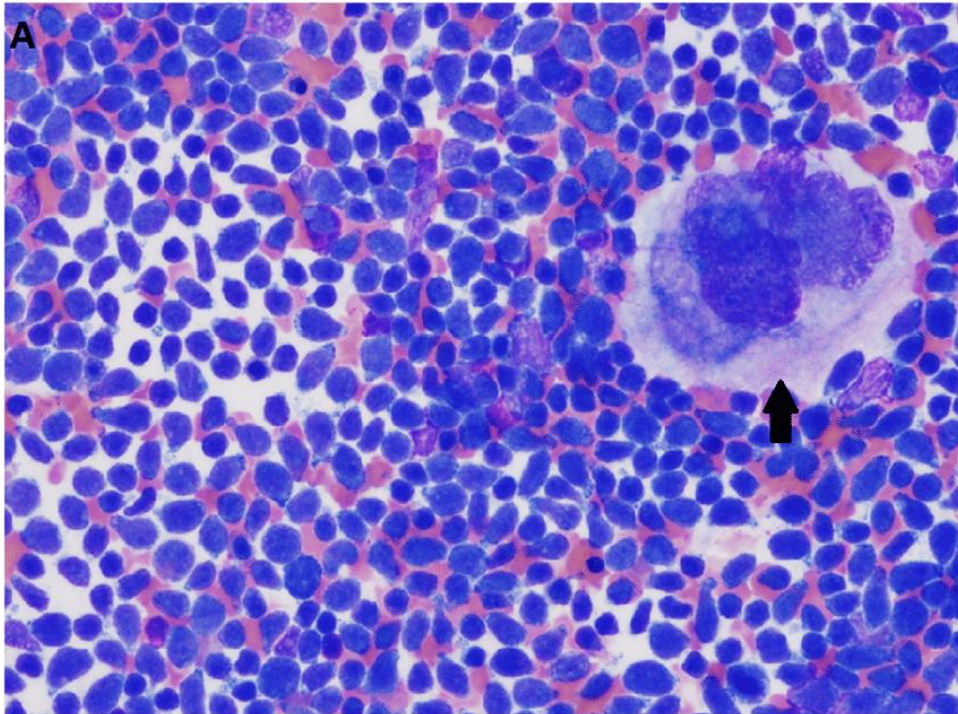
(b)



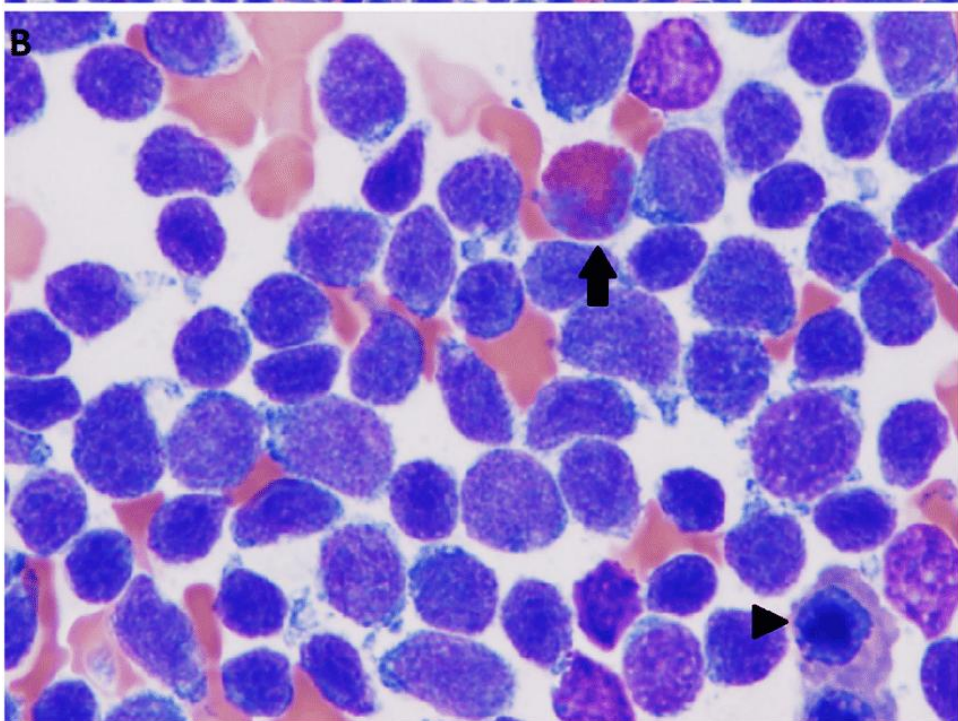
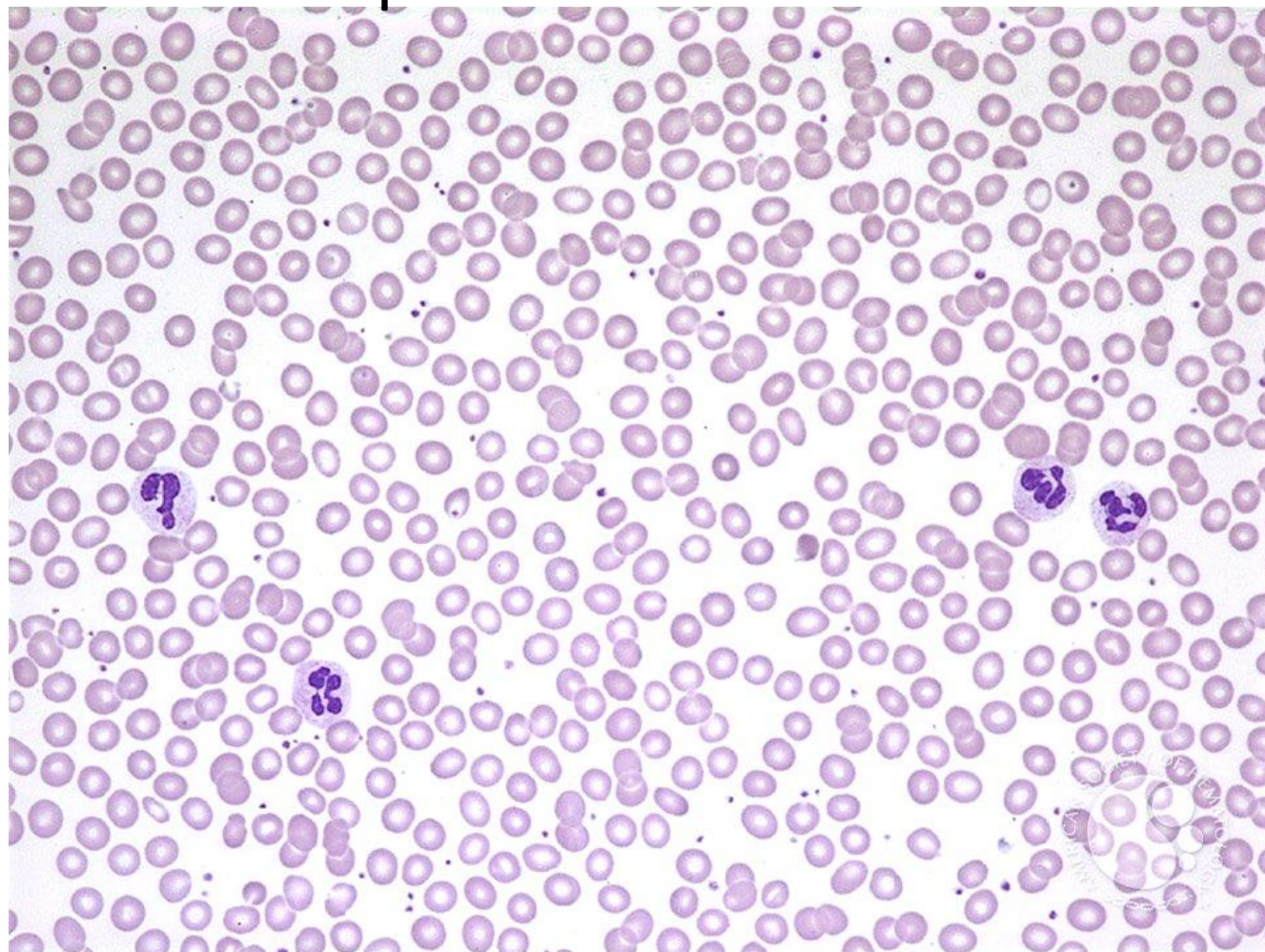
trepanobiopsie

aspirace

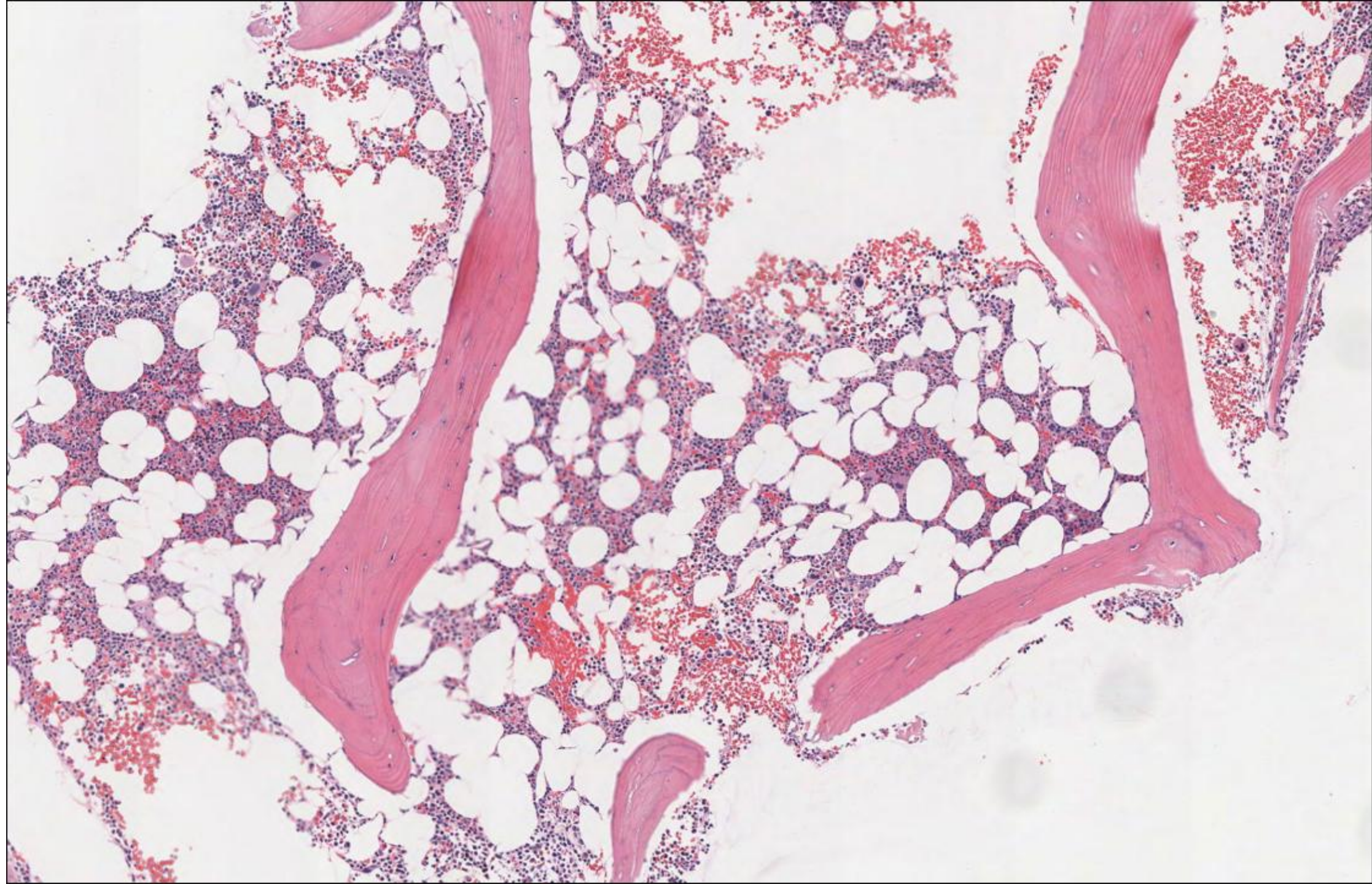




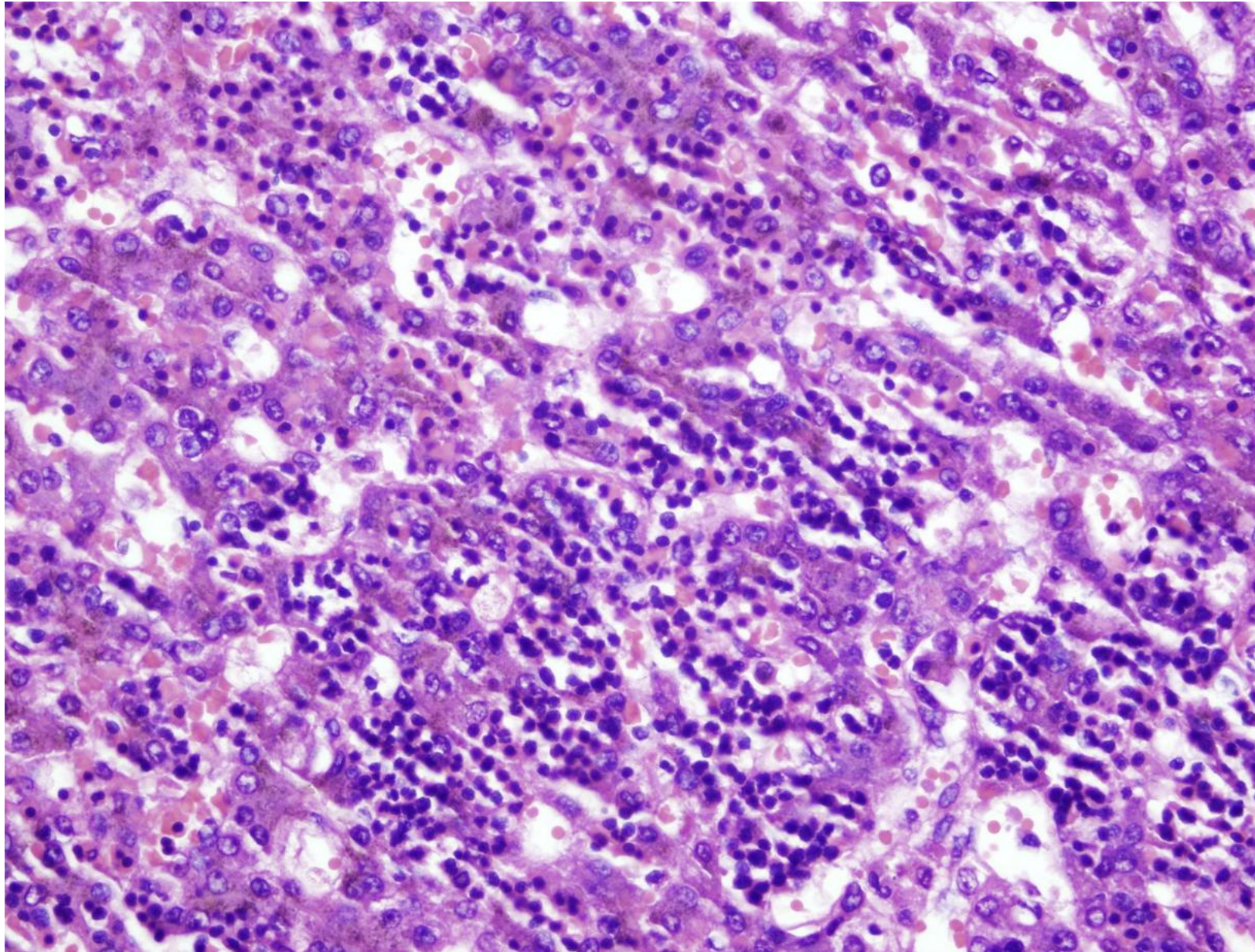
periferní krev



kostní dřeň

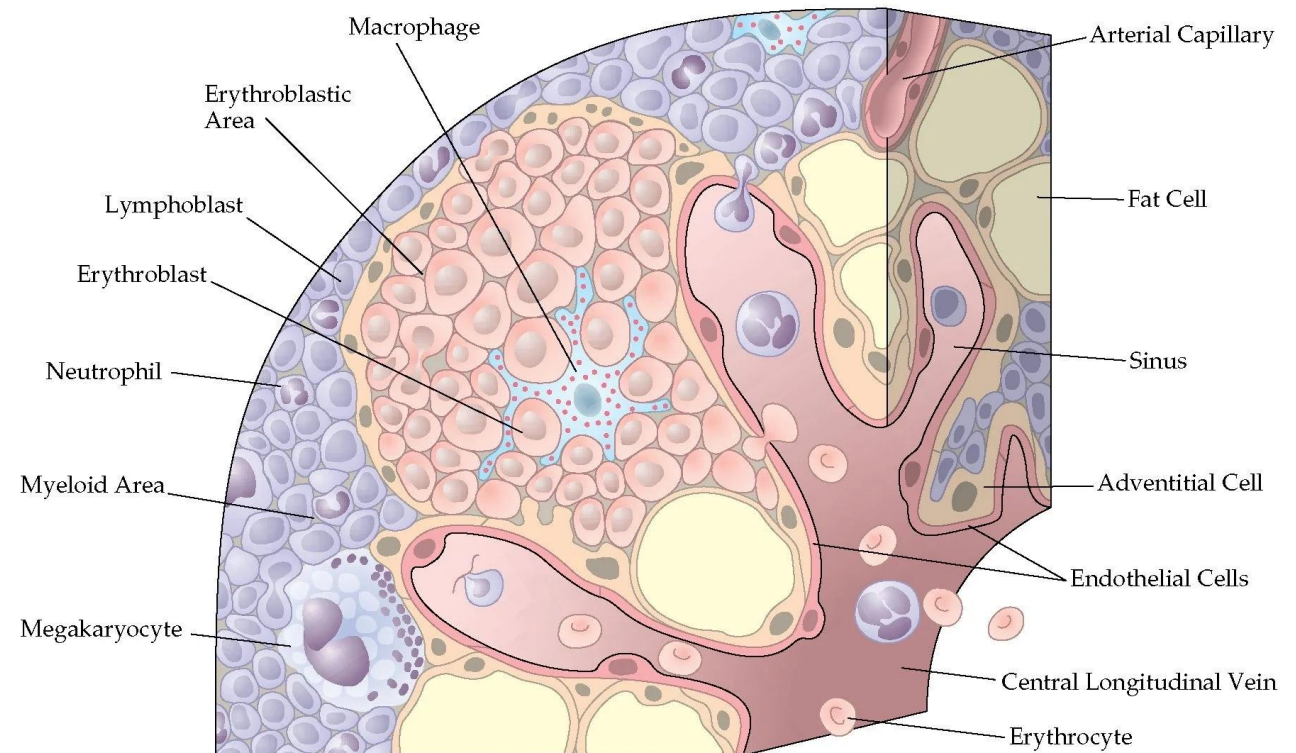


extramedulární hematopoéza

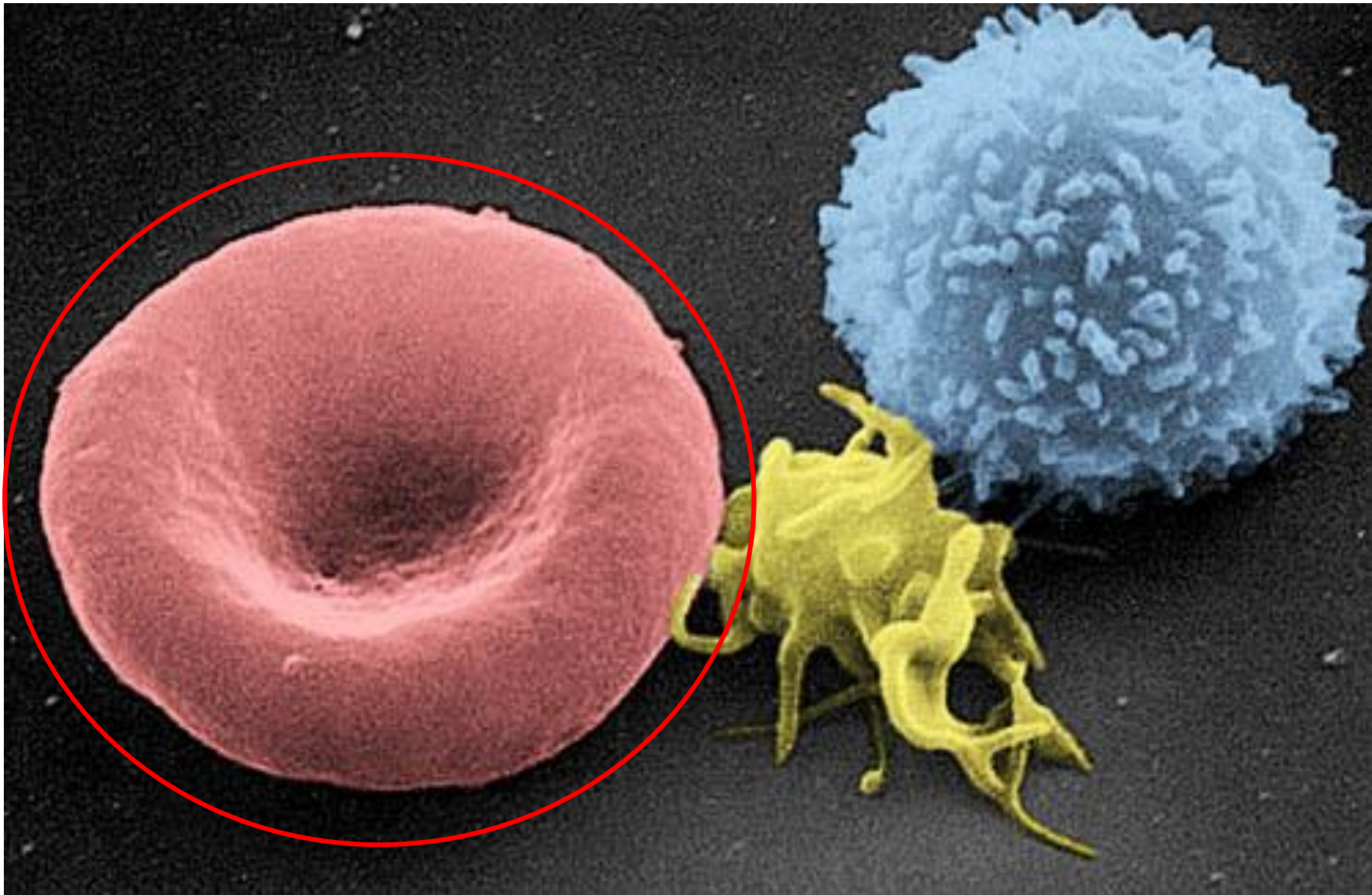


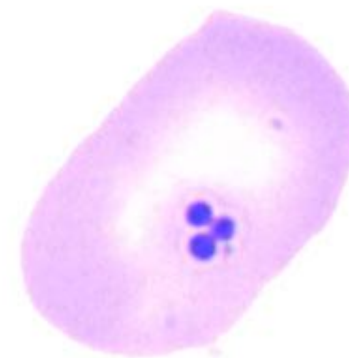
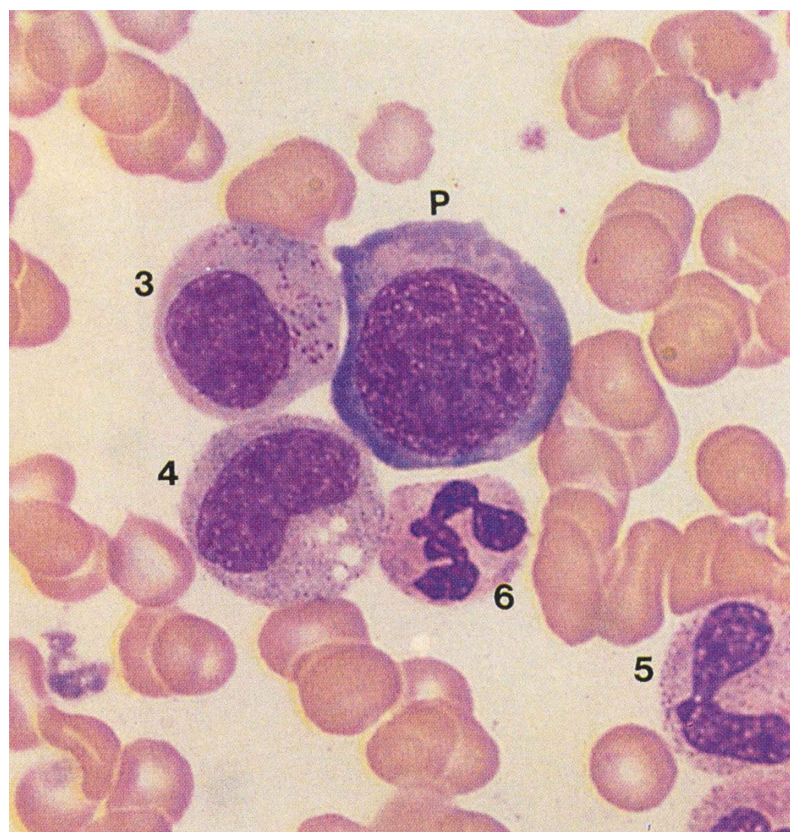
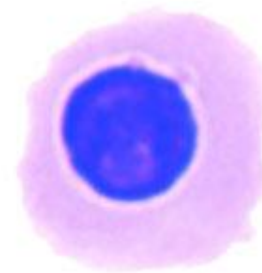
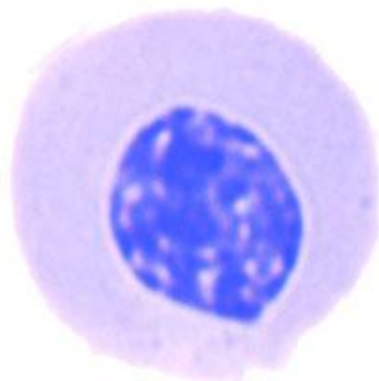
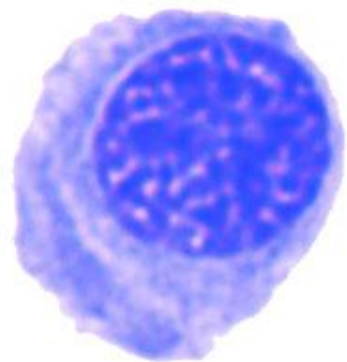
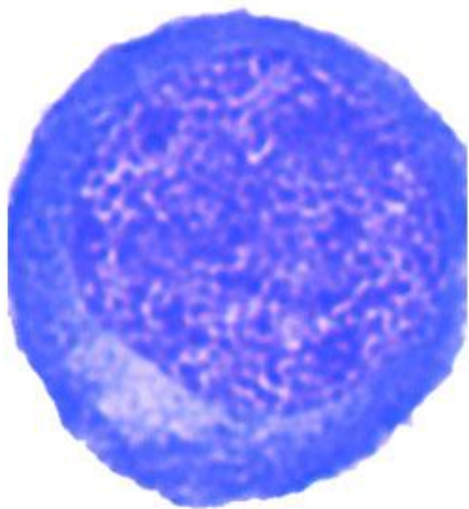
Kostní dřeň

- Červená kostní dřeň je místem krve tvorby (hlavně osový skelet), žlutá kostní dřeň je tukově přeměněná
- Základem je retikulární vazivo, které je kolonizováno HSC a z ní odvozenými typy buněk
- Obsahuje sinusoidy (kapiláry s velkým průsvitem)



Erytropoéza





- **Vývoj červených krvinek,**
- **erythropoéza**

- velikost buňky



- velikost jádra



- kondenzace jádra



- basofilie (ribosomy)



- eosinofilie (hemoglobin)

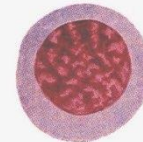


mitóza



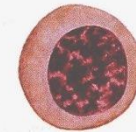
Proerythroblast

12 – 20 μm
24 h



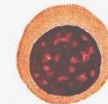
Basophilic erythroblast

10 – 17 μm
24 h



Polychromatophilic erythroblast

10 – 15 μm
30 h



Orthochromatophilic erythroblast

8 – 12 μm
48 h



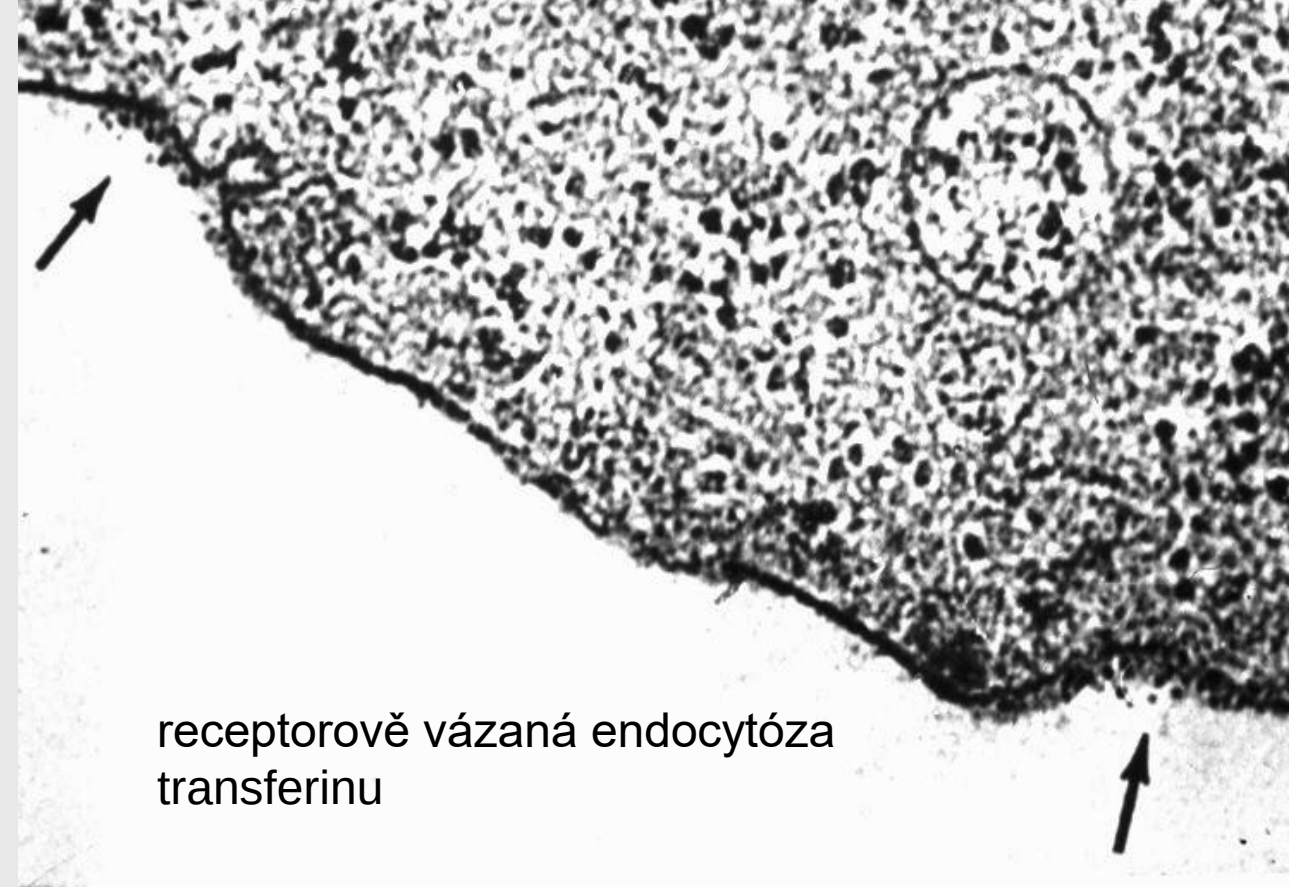
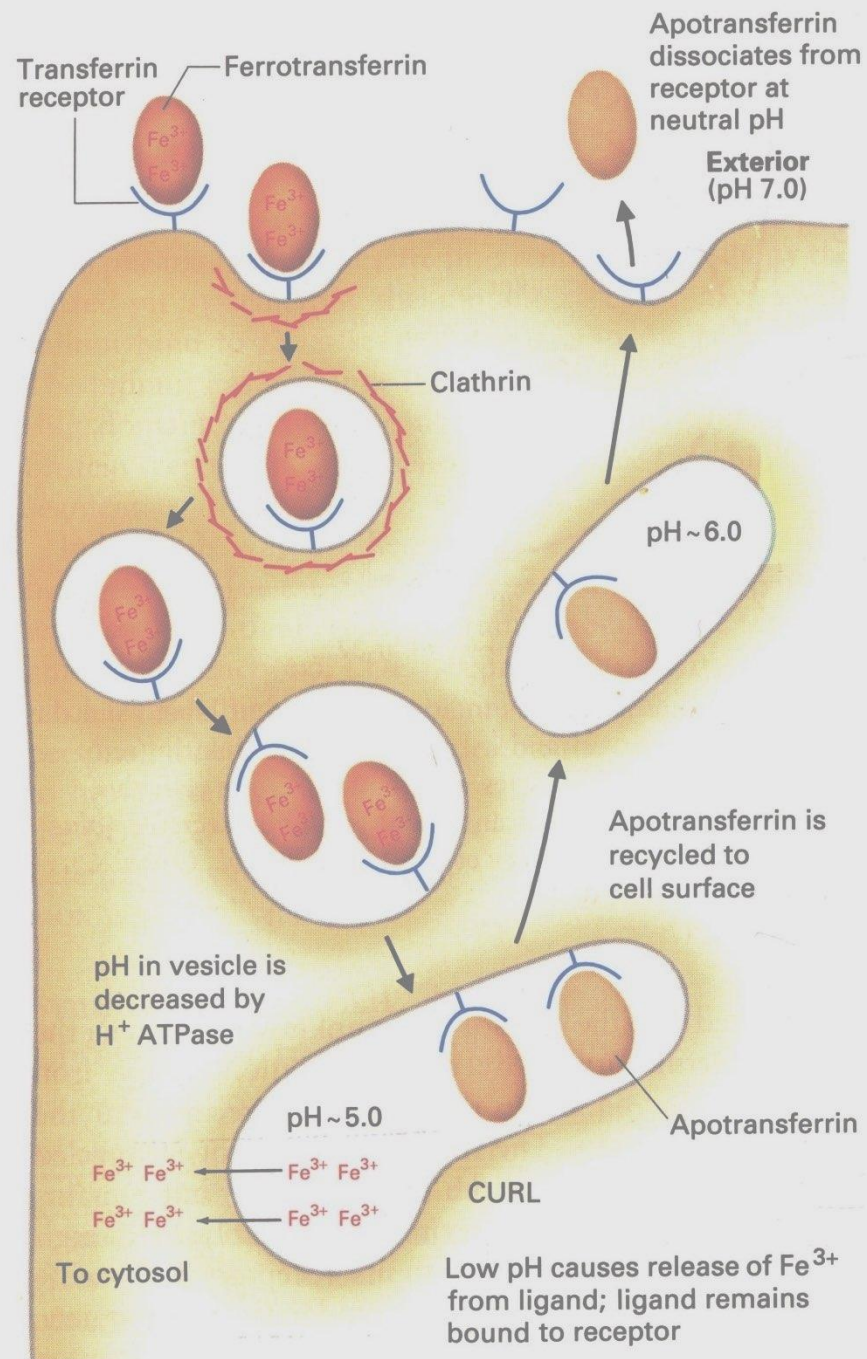
Reticulocyte

Cca 8 μm
2 – 3 dny

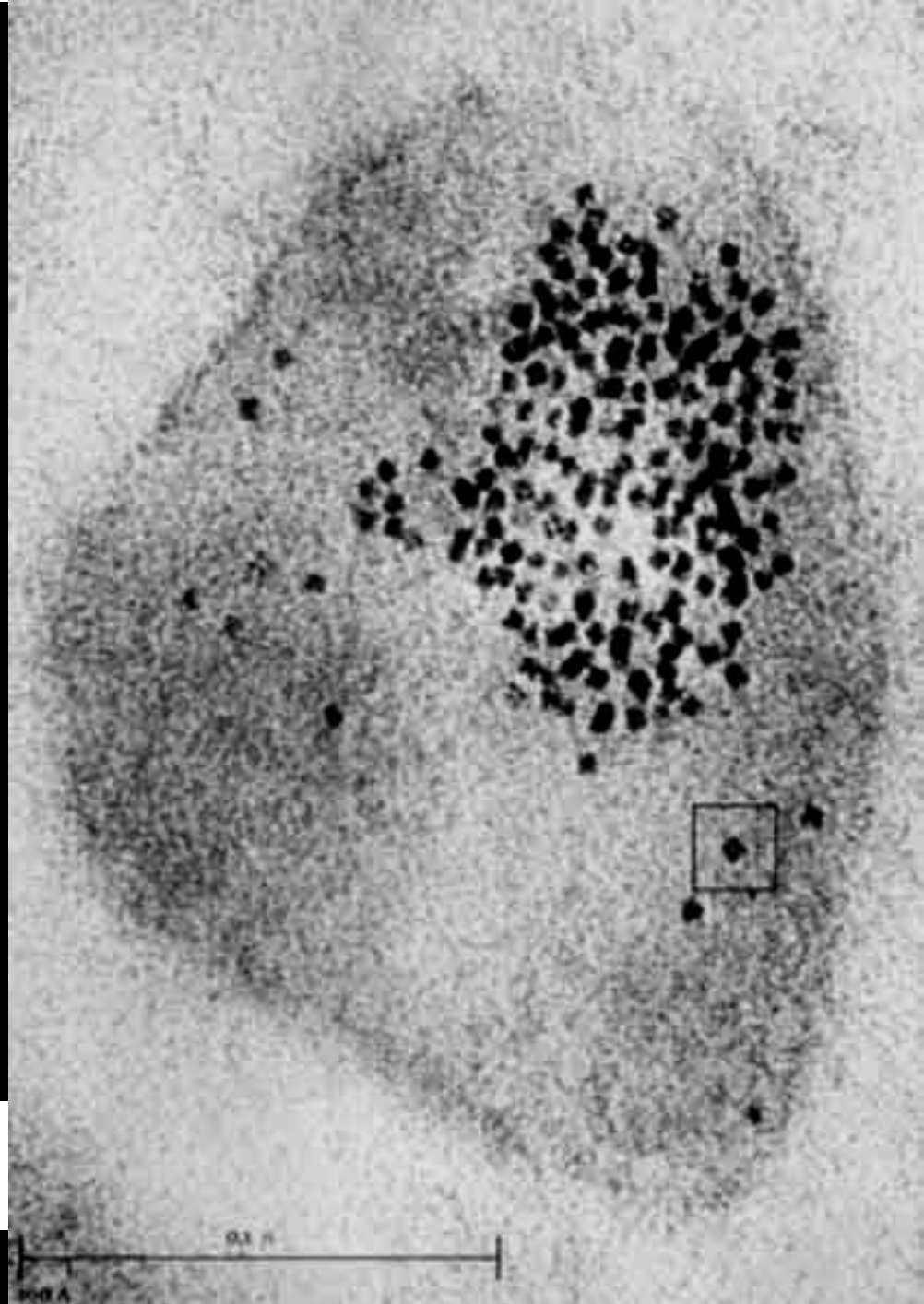
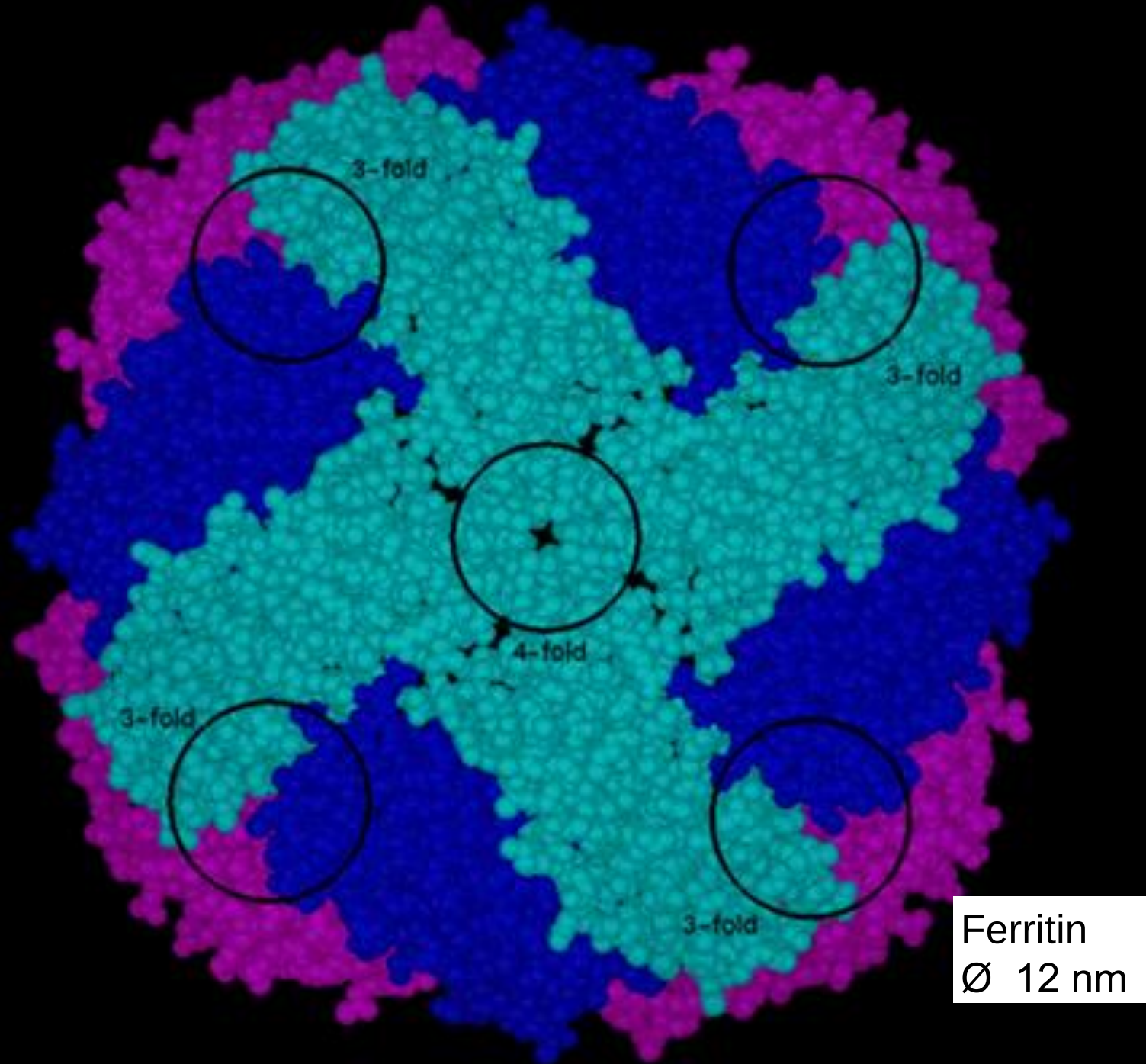


Erythrocyte

7,8 μm
120 dnů



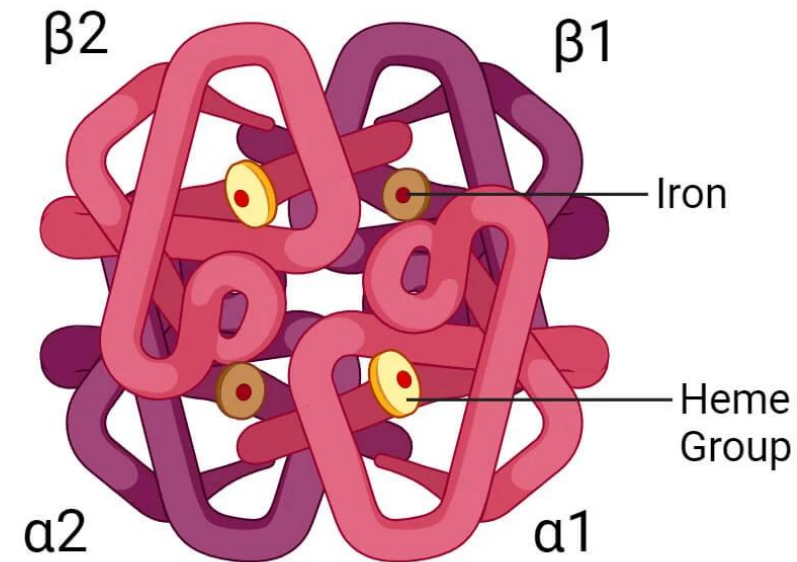
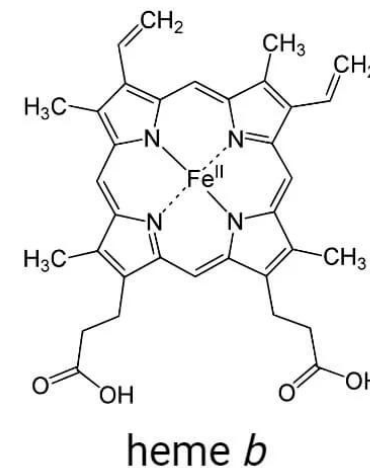
receptorově vázaná endocytóza transferinu



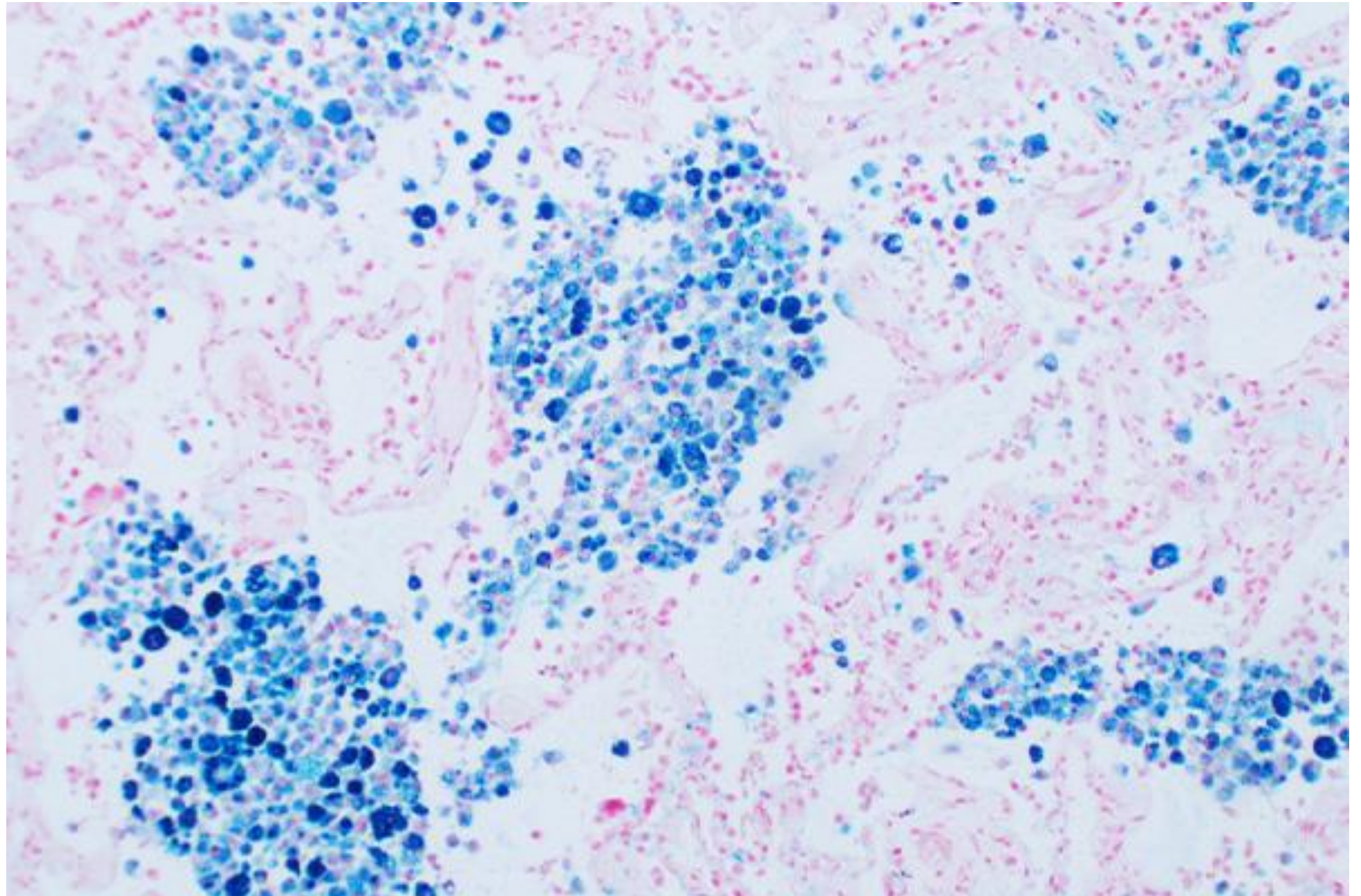
Hemoglobin a hospodaření s železem

- Hemoglobin vzniká z proteinu globinu (syntéza na polyribosomech) a z hemu, který obsahuje porfyrinové jádro s centrálně „zabudovaným“ atomem železa
- Po zániku erytrocytu je globin metabolizován proteázami, hem se rozpadá na barviva (biliverdin, bilirubin) a atomy železa, které jsou následně uloženy ve feritinu
- K transportu železa oběhem slouží transferin, který je zachycován receptory na erytroblastech
- Ke zobrazení železa v histologii můžeme použít Perlsovu reakci (Fe modře)

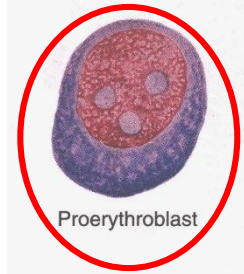
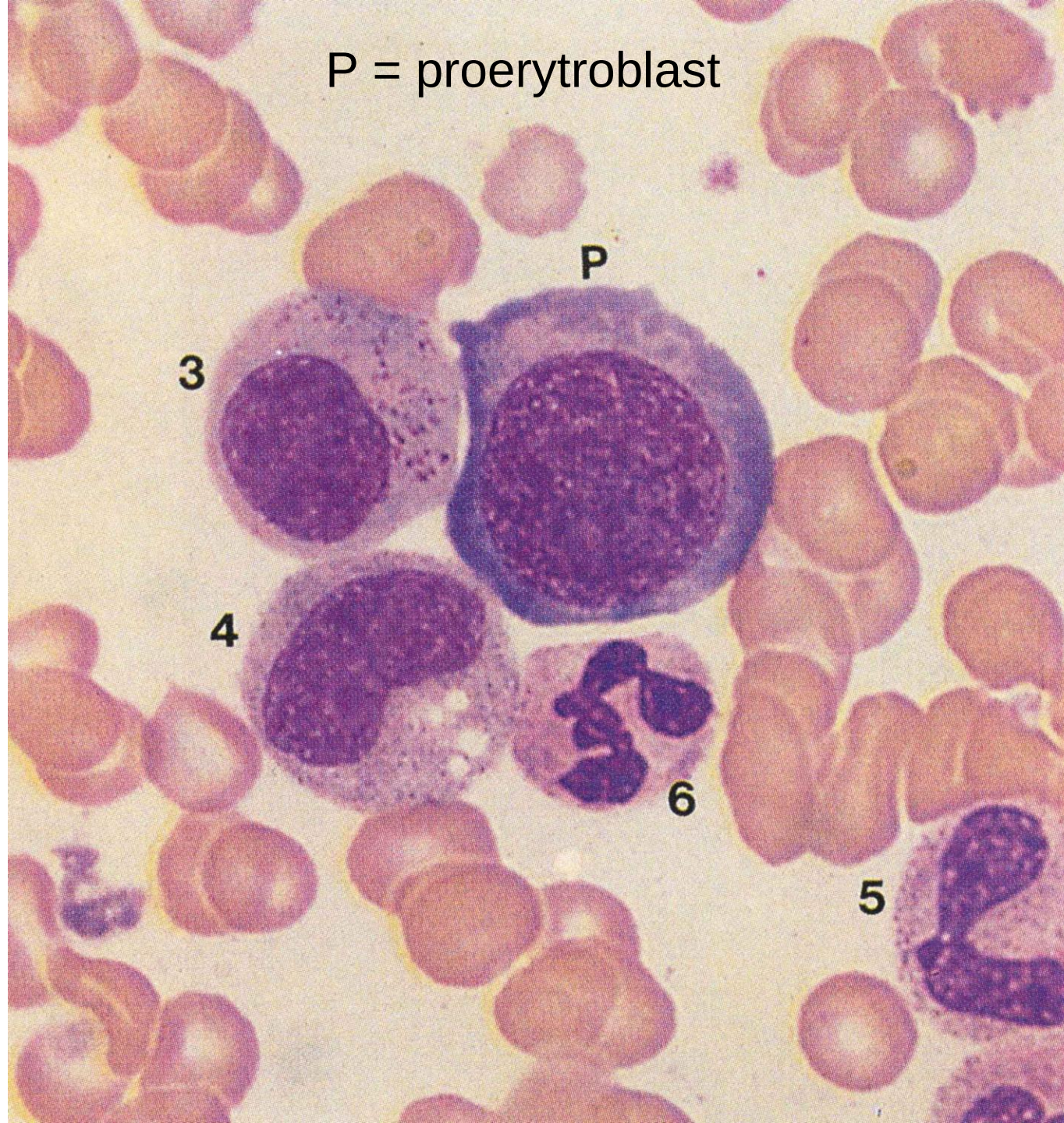
Hemoglobin



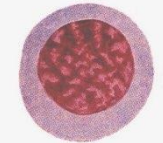
- Perlsova reakce



P = proerythroblast



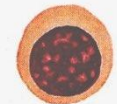
Proerythroblast



Basophilic
erythroblast



Polychromatophilic
erythroblast



Orthochromatophilic
erythroblast

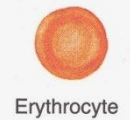
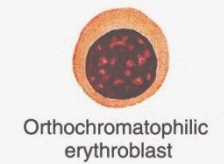
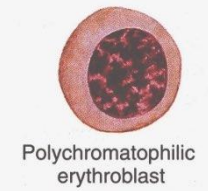
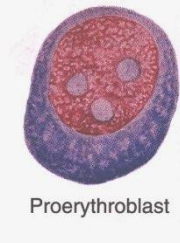
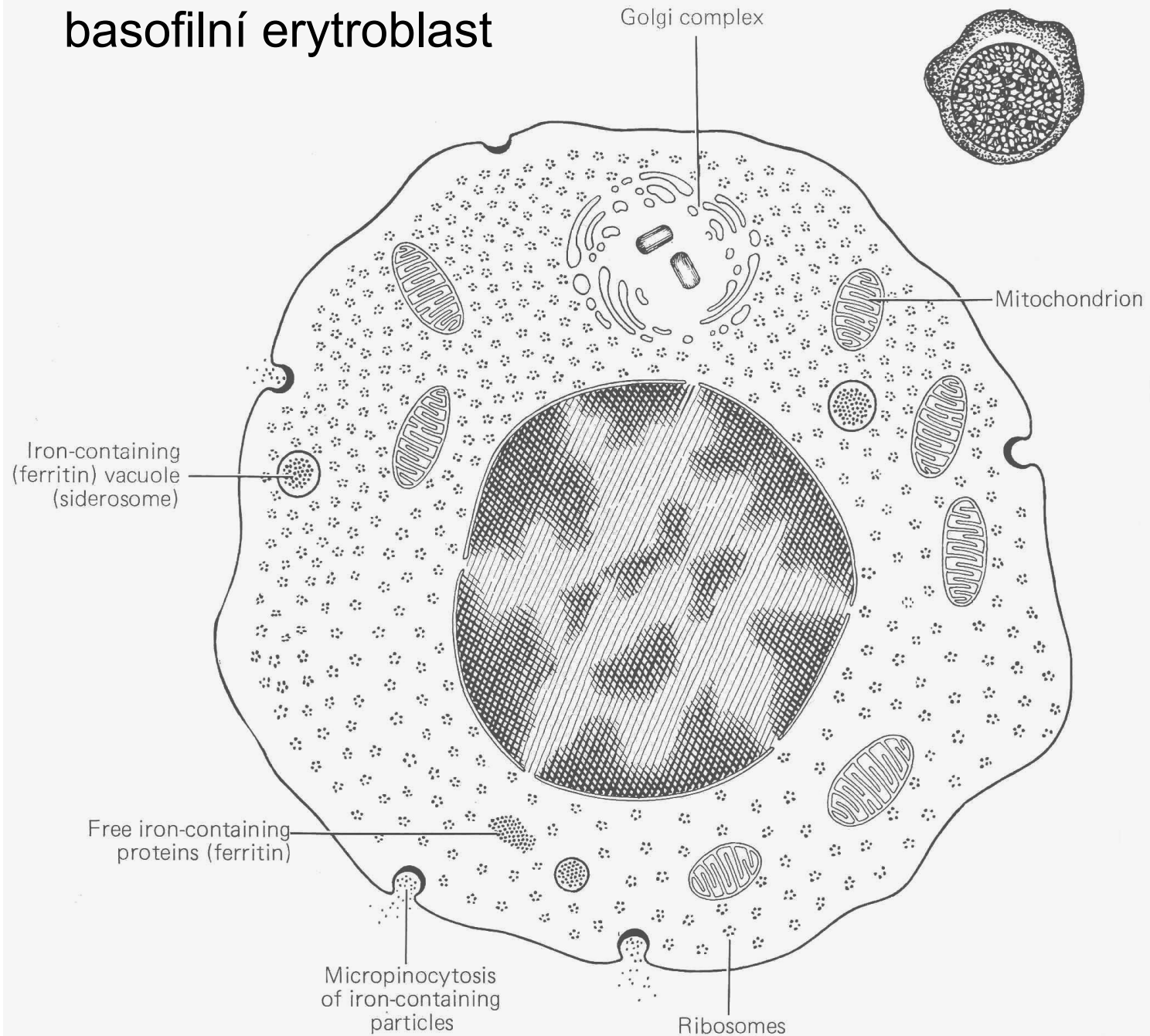


Reticulocyte

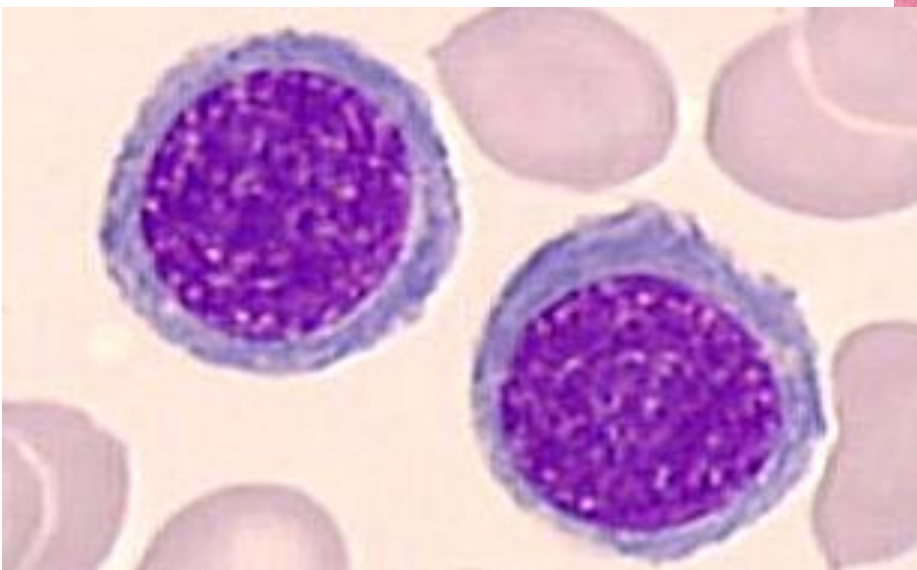


Erythrocyte

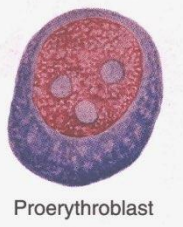
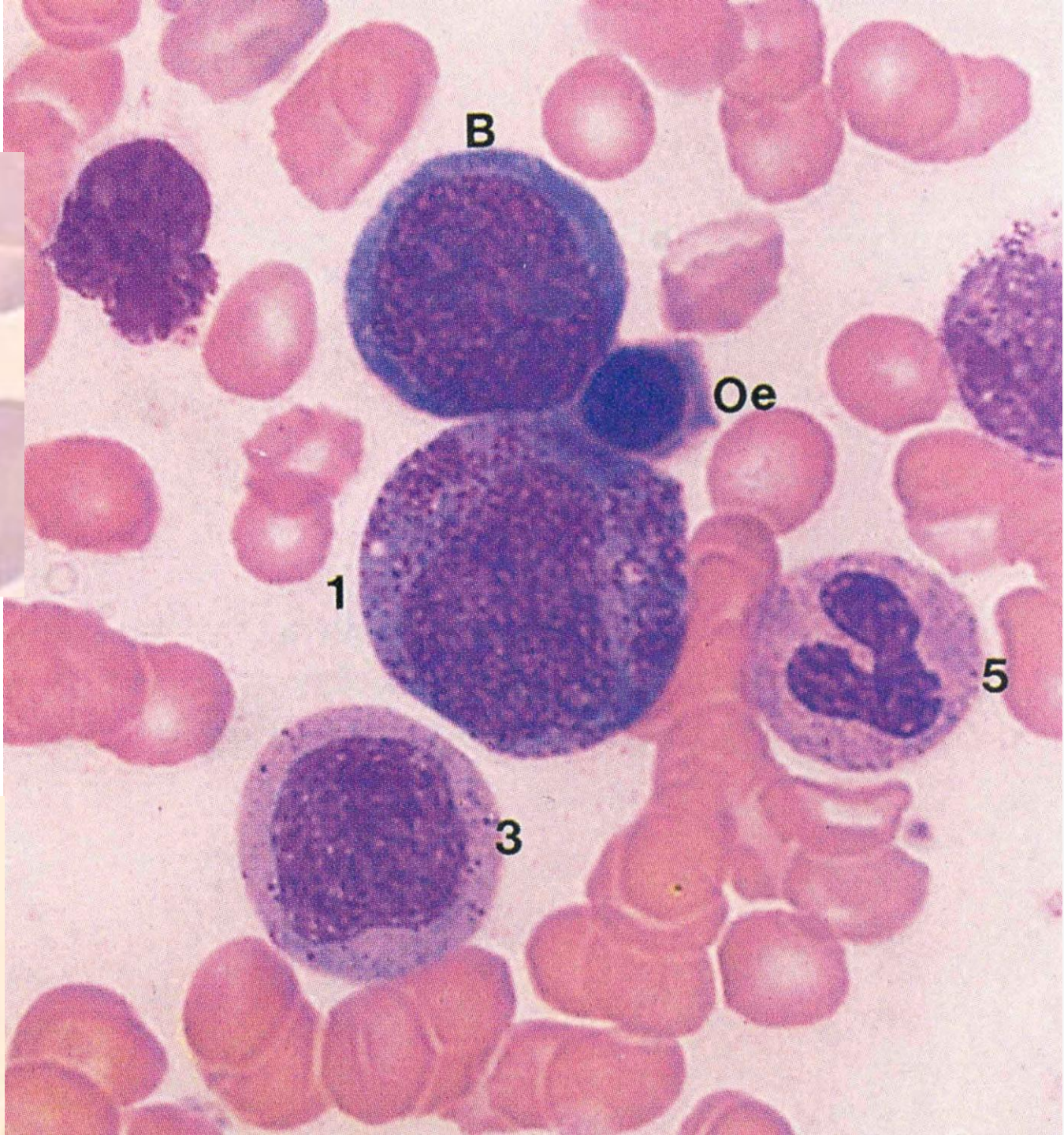
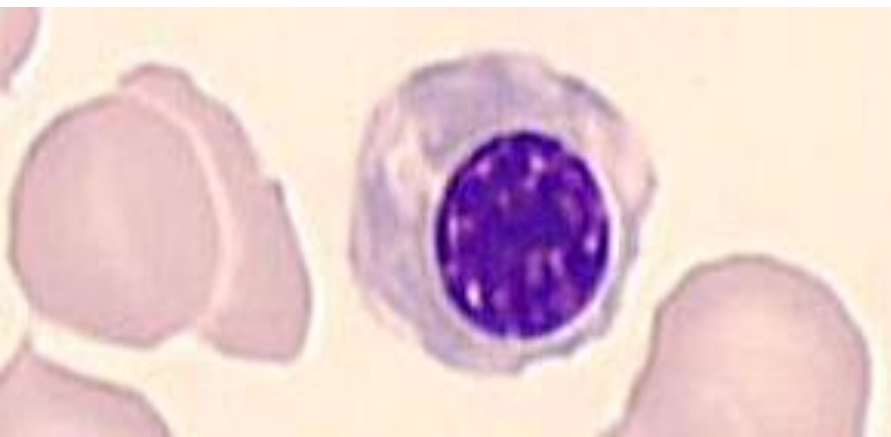
basofilní erythroblast



B = bazofilní erytroblast 10 – 17 μm



Oe = časné ortochromatofilní erytroblasty 8 – 12 μm



Proerythroblast



Basophilic erythroblast



Polychromatophilic erythroblast



Orthochromatophilic erythroblast

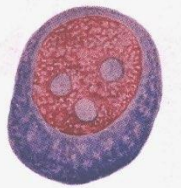
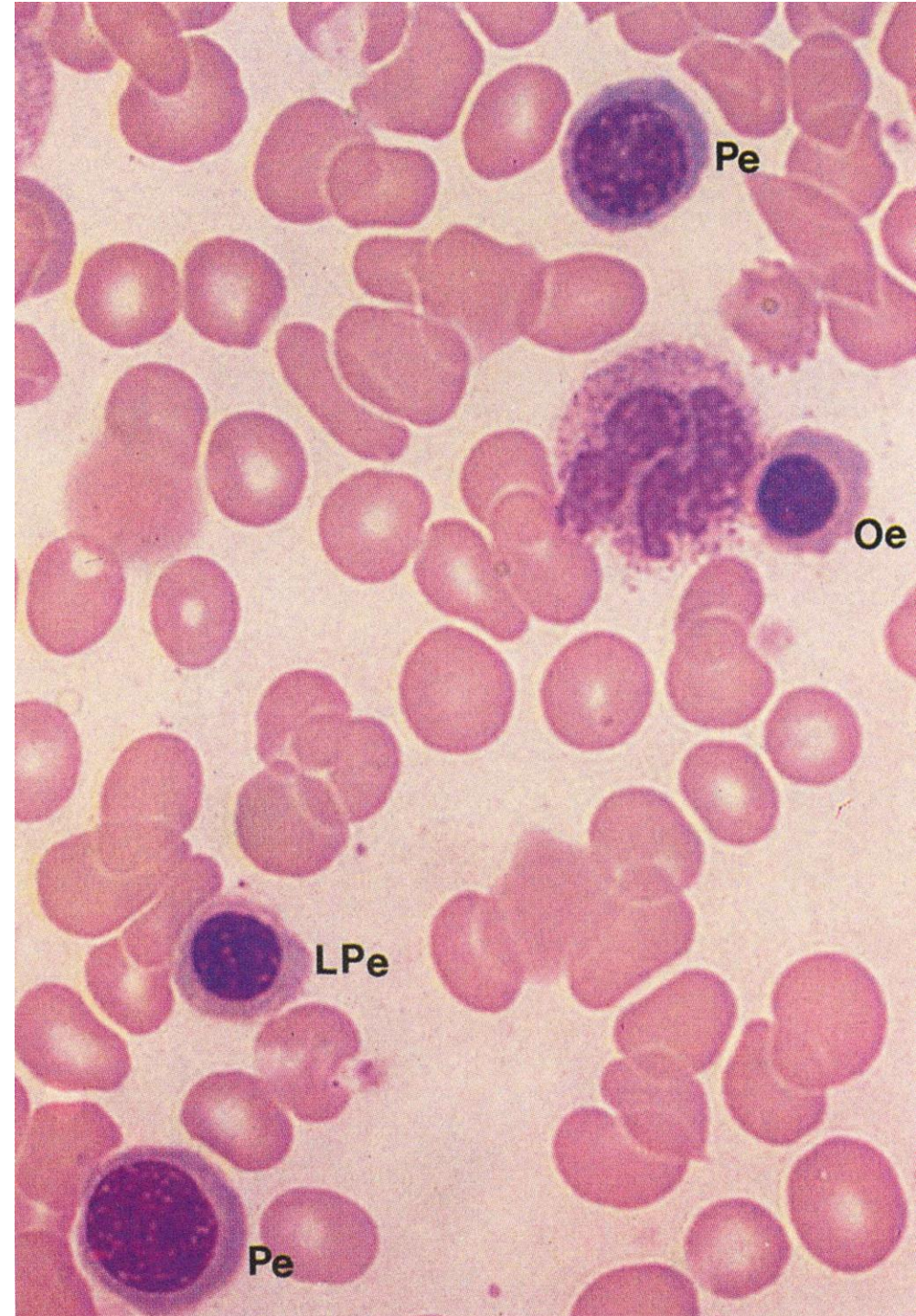


Reticulocyte

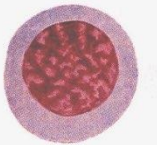


Erythrocyte

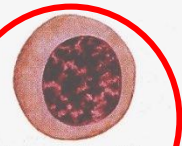
Pe = polychromatofilní erytroblast
LPe = pozdní polychromatofilní
erytroblast
Oe = pozdní ortochromatofilní
erytroblast



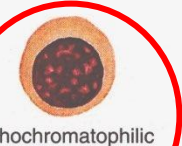
Proerythroblast



Basophilic
erythroblast



Polychromatophilic
erythroblast



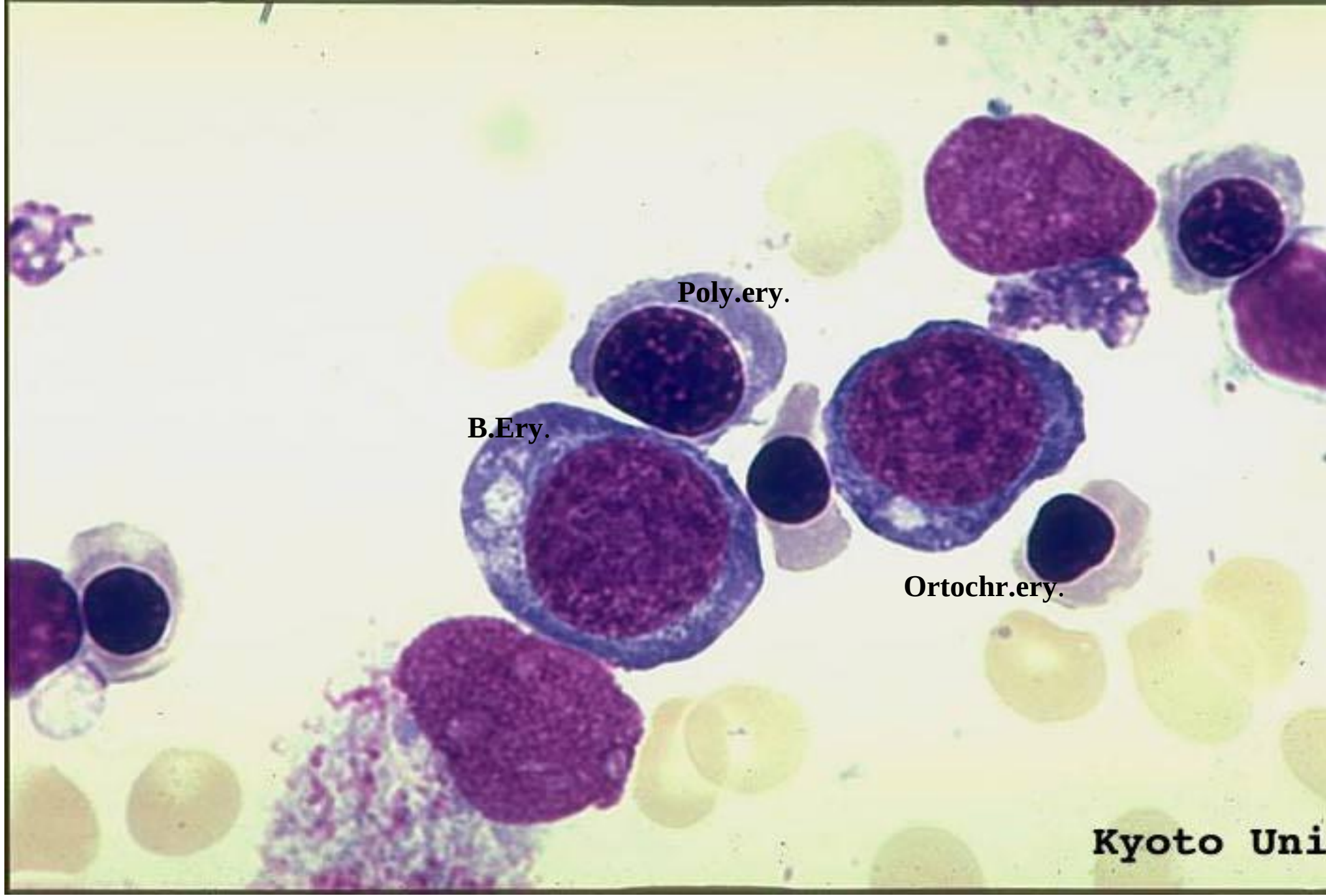
Orthochromatophilic
erythroblast



Reticulocyte



Erythrocyte



Proerythroblast



Basophilic erythroblast



Polychromatophilic erythroblast



Orthochromatophilic erythroblast

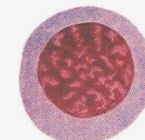
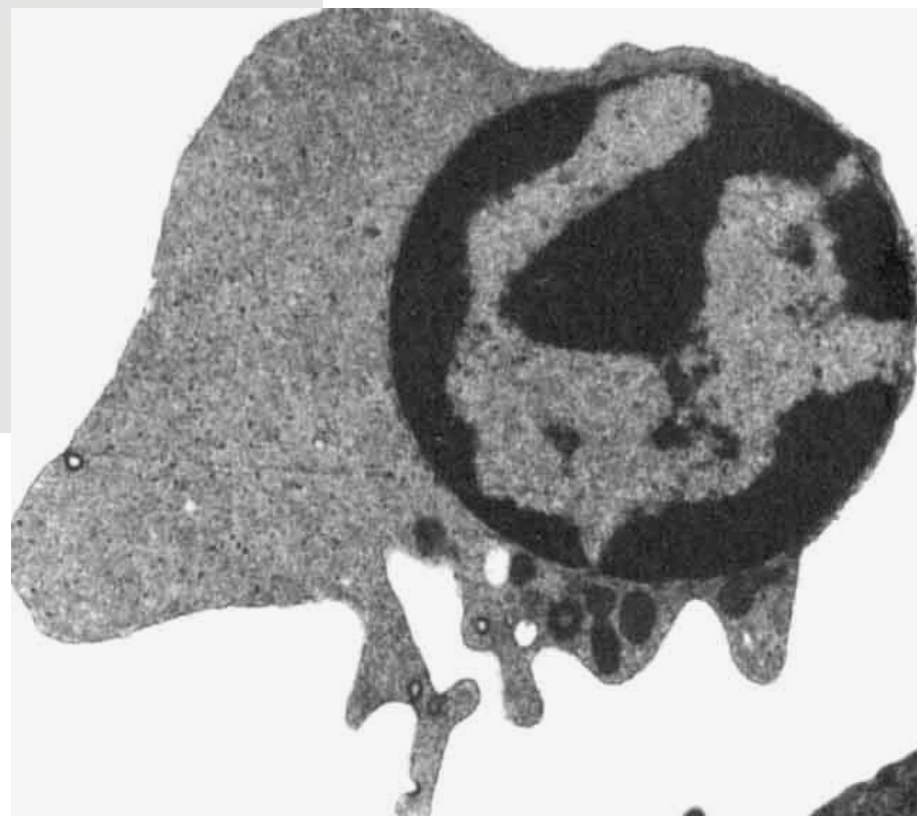
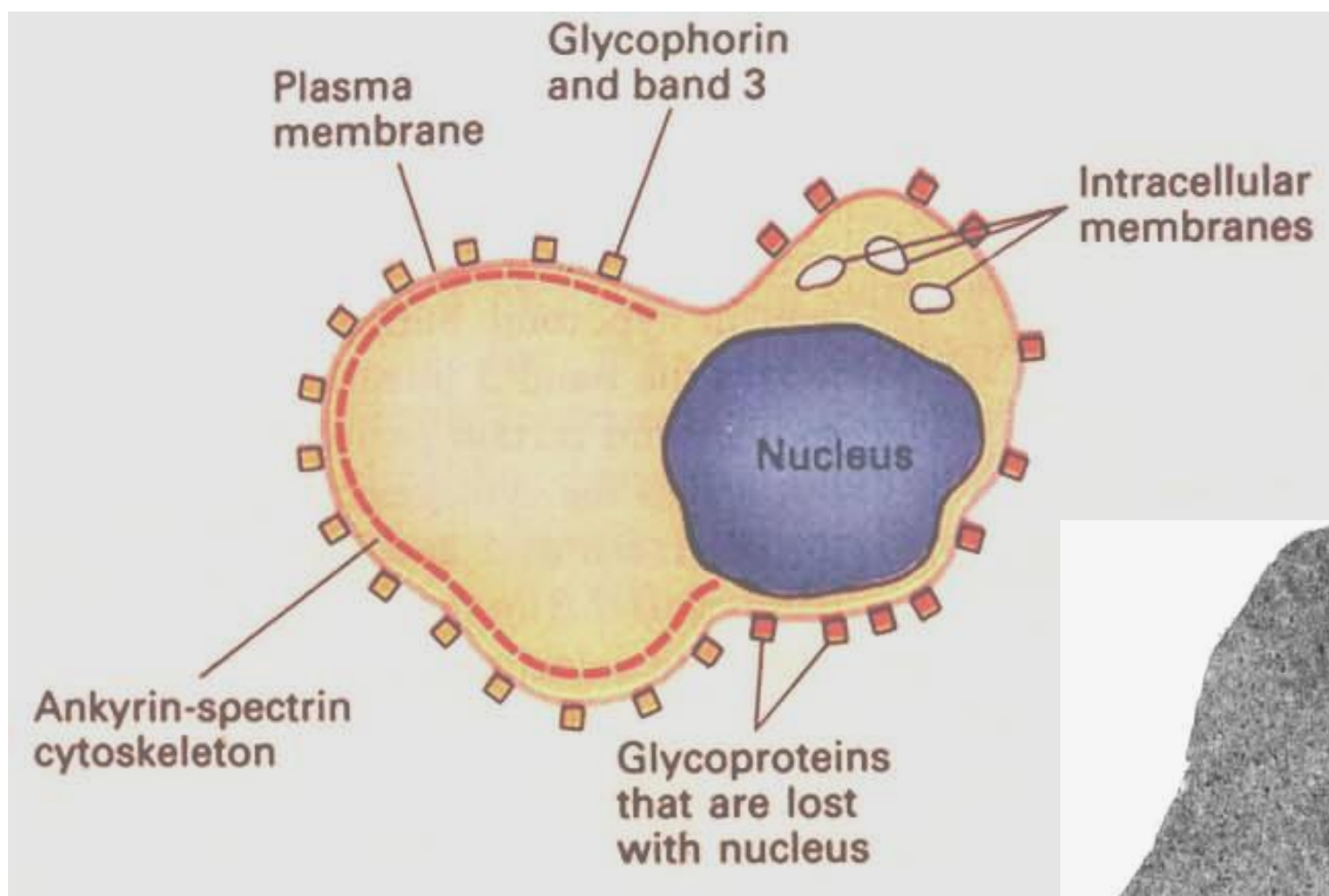


Reticulocyte

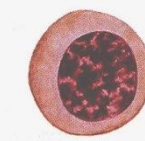


Erythrocyte

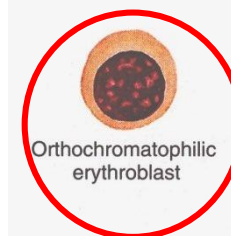
Kyoto Uni



Basophilic erythroblast



Polychromatophilic erythroblast



Orthochromatophilic erythroblast



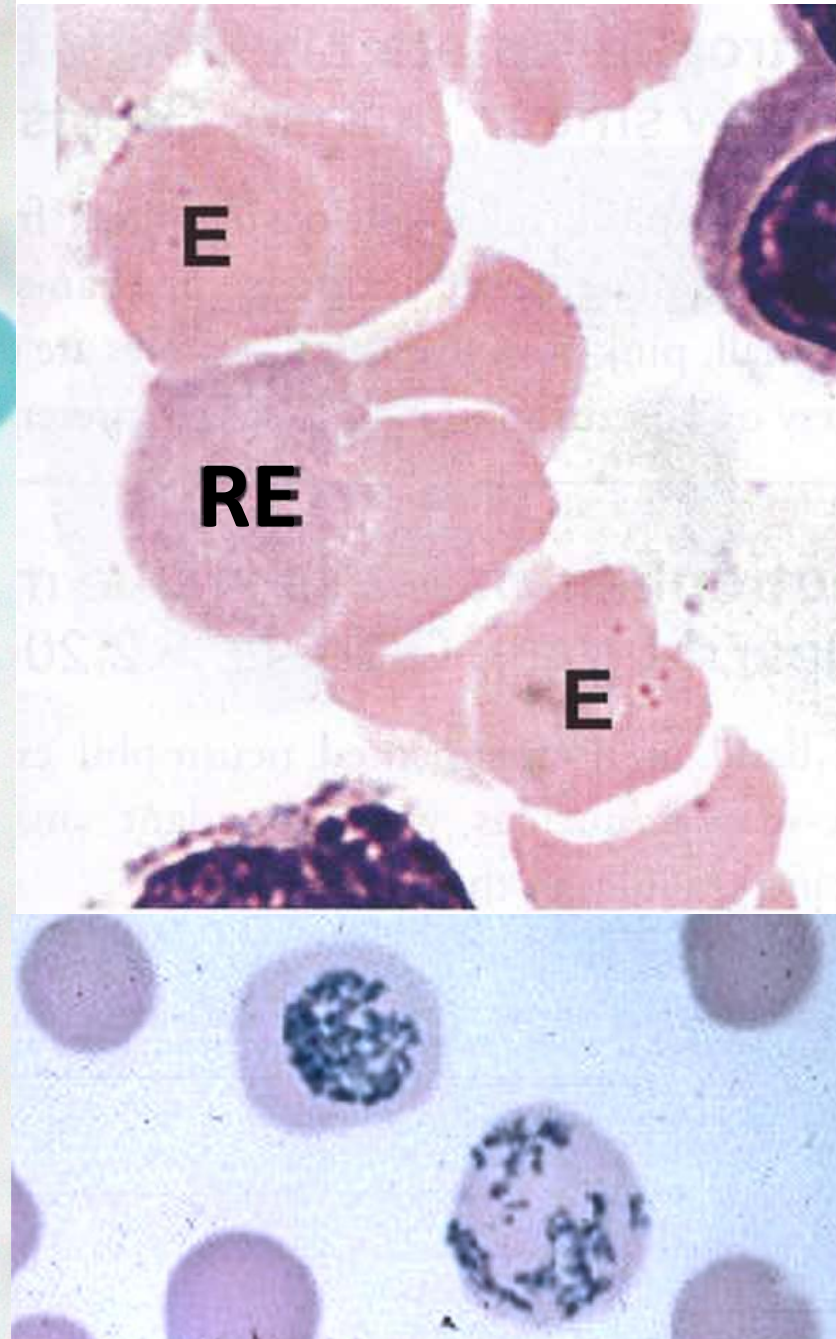
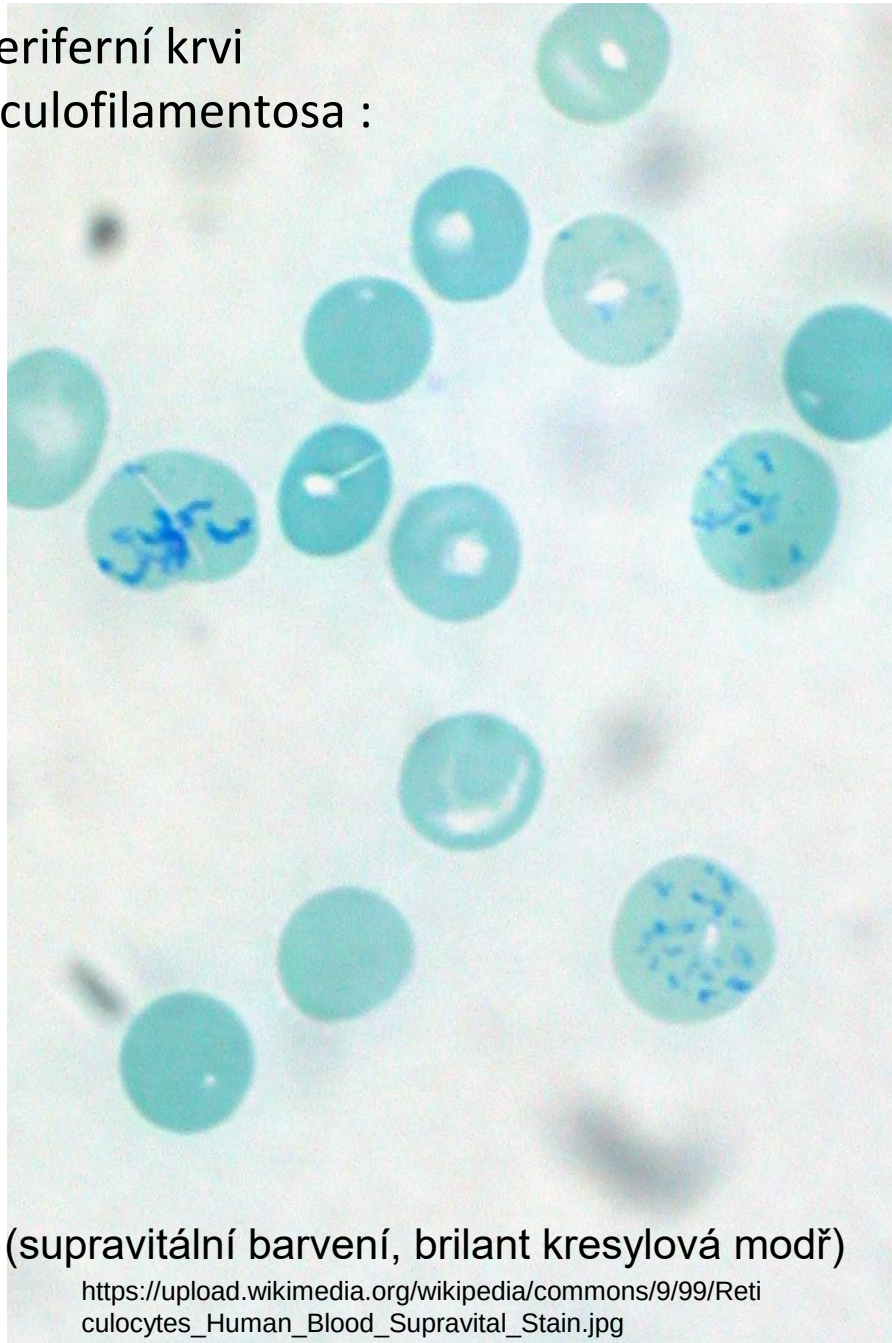
Reticulocyte



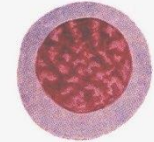
Erythrocyte

Retikulocyty

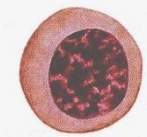
0,5 – 2,5 % v periferní krvi
Substantia reticulofilamentosa :
Zbytky RNA



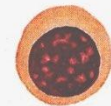
Proerythroblast



Basophilic erythroblast



Polychromatophilic erythroblast



Orthochromatophilic erythroblast

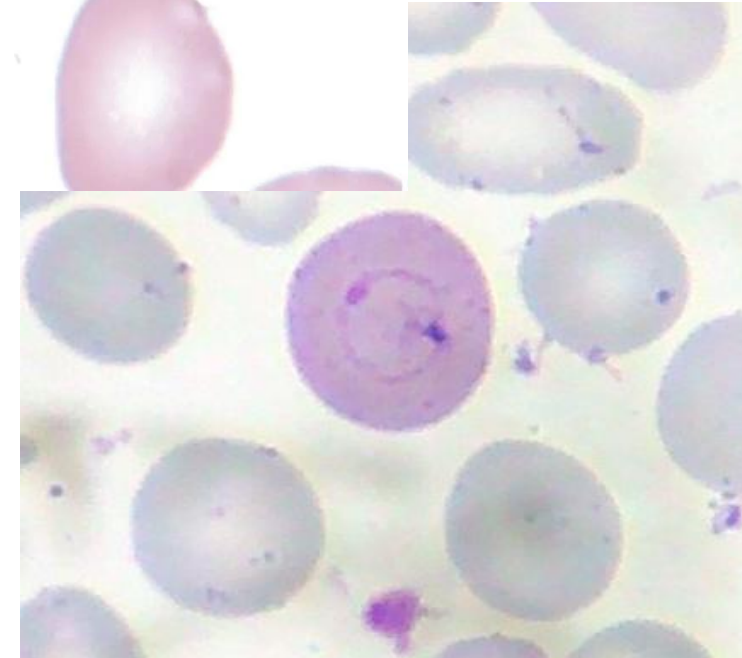
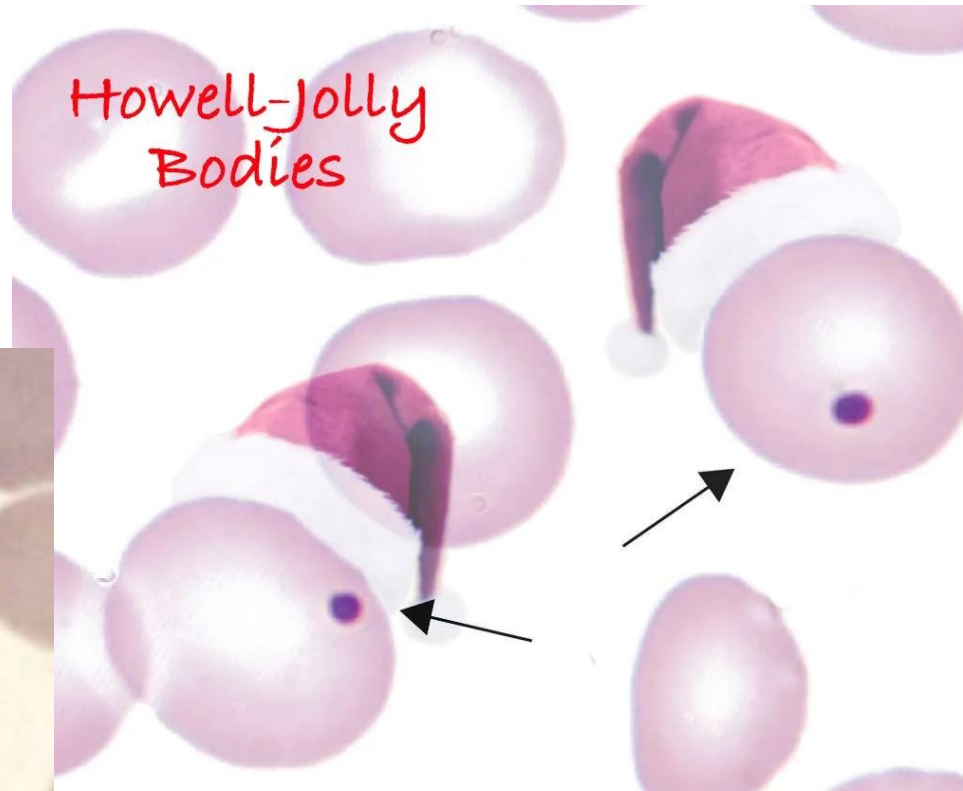
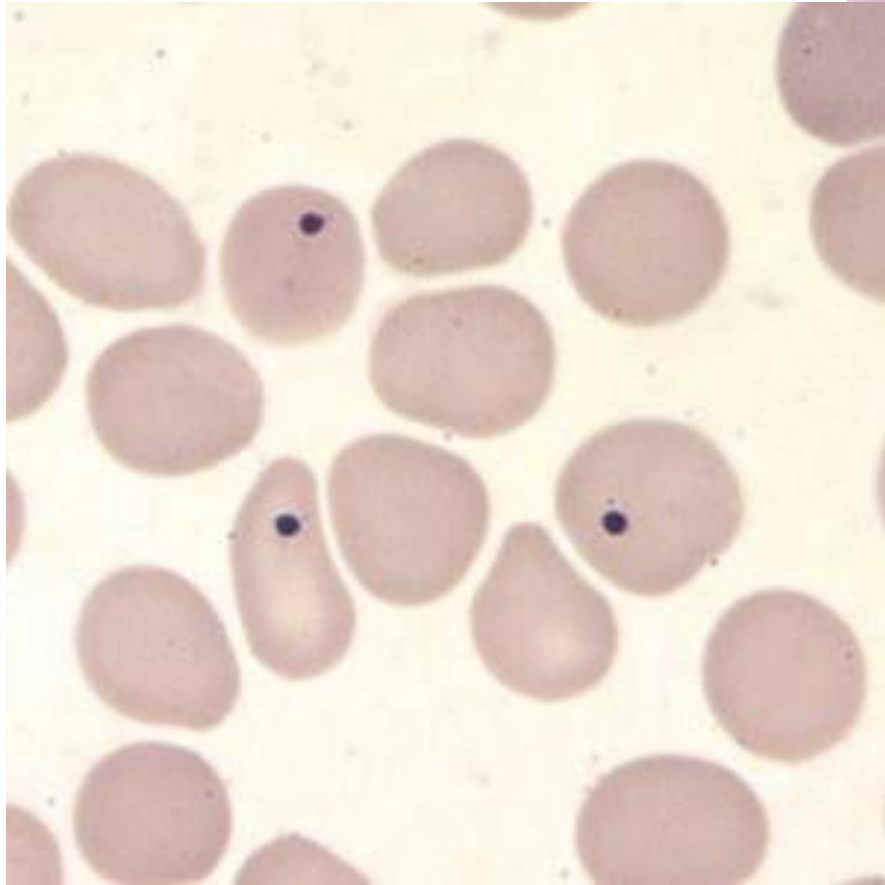


Reticulocyte

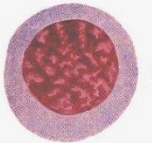


Erythrocyte

Fragmenty jádra: Howell – Jolly bodies



Proerythroblast



Basophilic erythroblast



Polychromatophilic erythroblast



Orthochromatophilic erythroblast

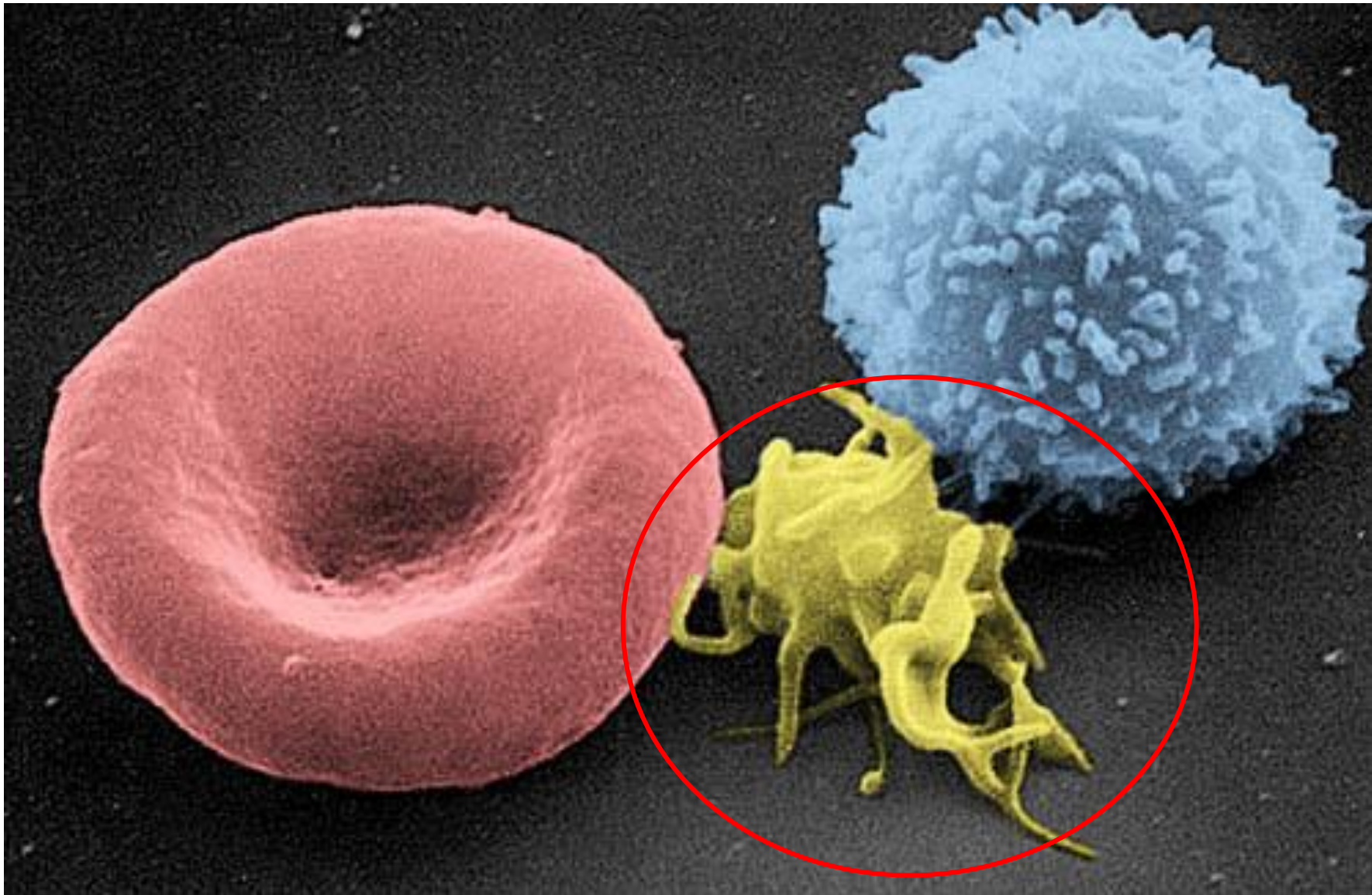


Reticulocyte



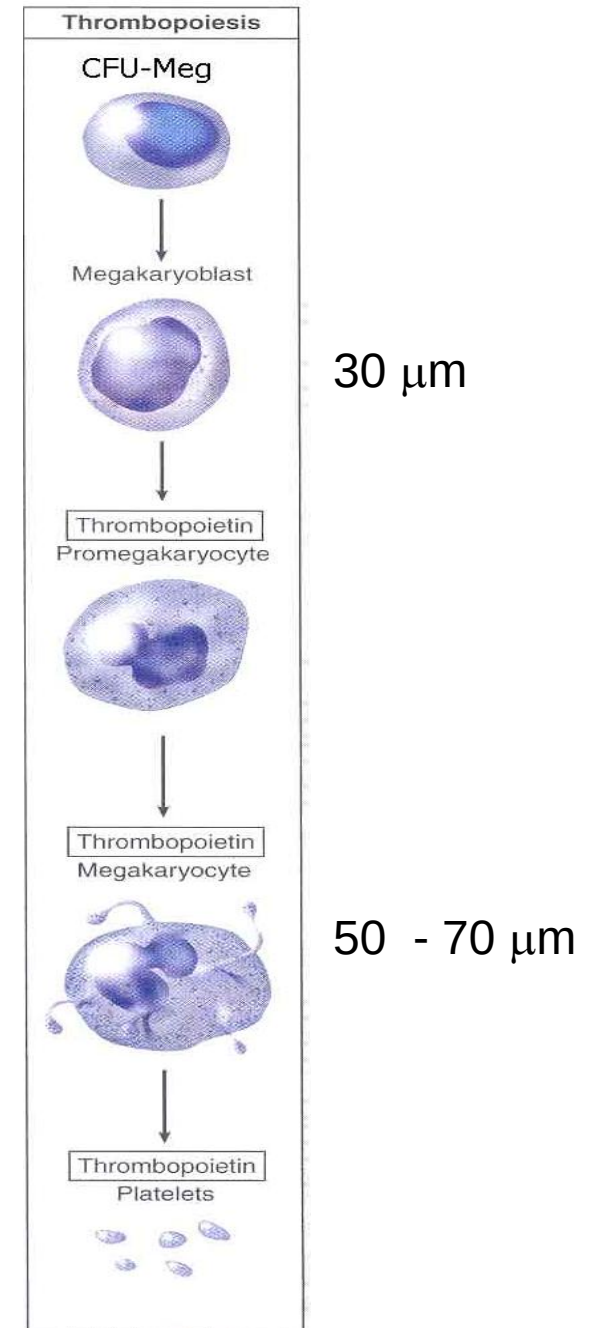
Erythrocyte

Trombopoéza



• Trombopoéza

- velikost buňky ↑
- velikost jádra ↑
- ploidie ↑
- lobulace jádra ↑



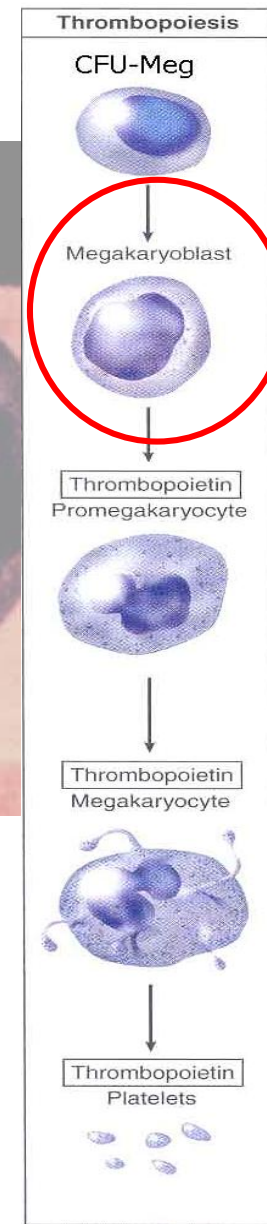
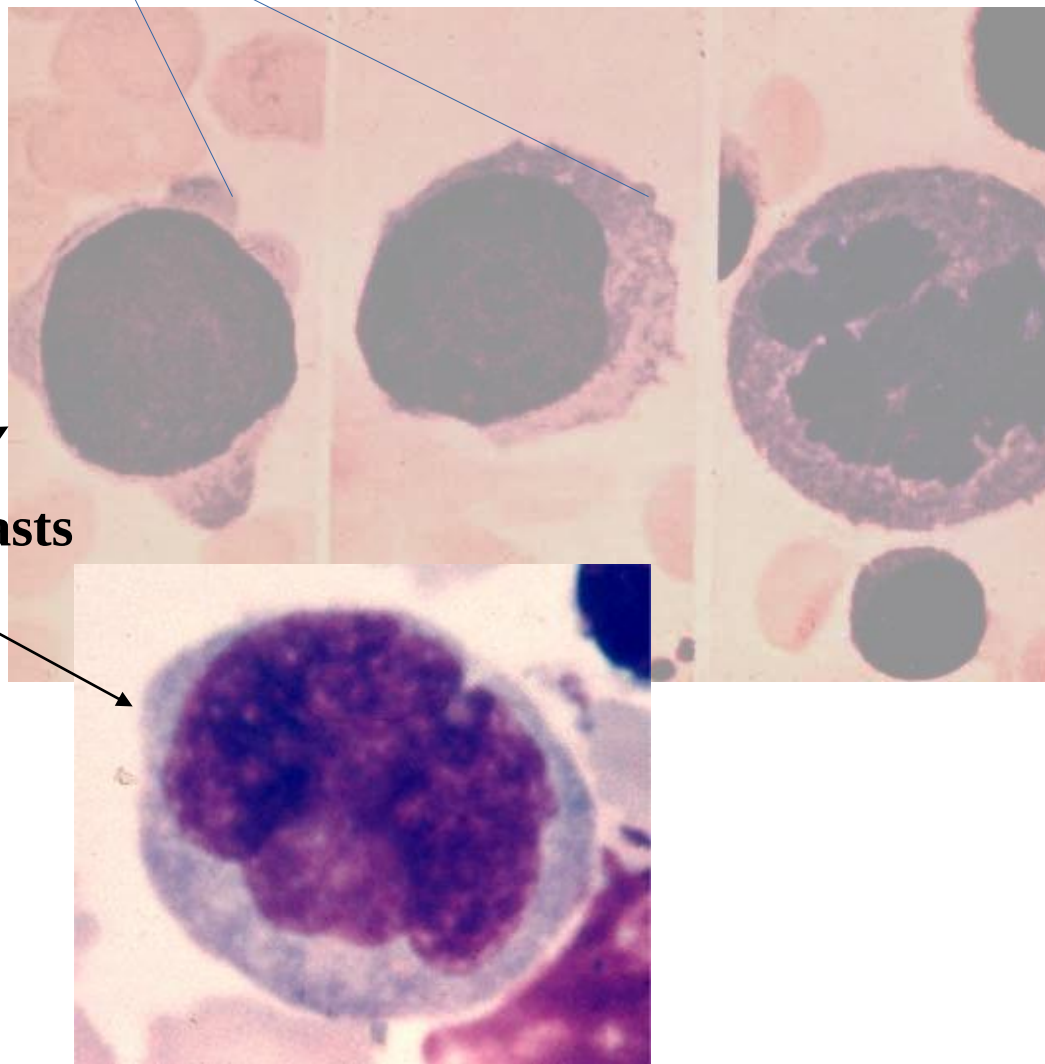
Thrombocytes Thrombopoiesis

endomitózy

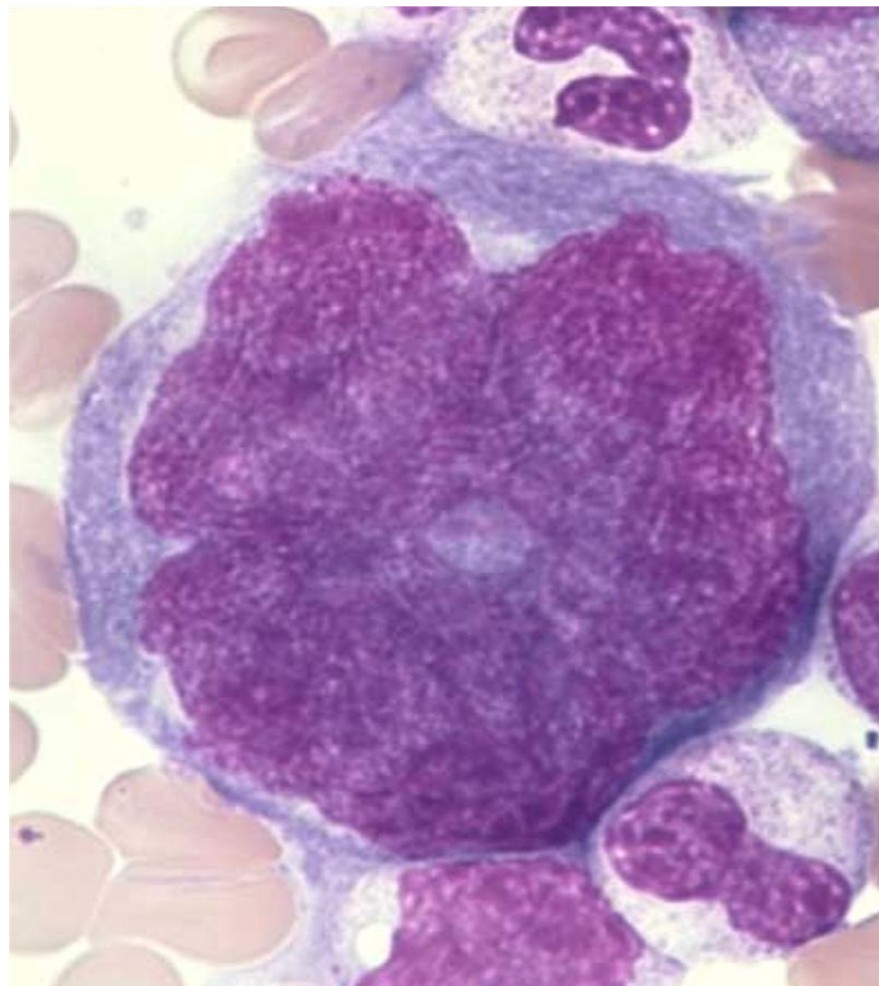
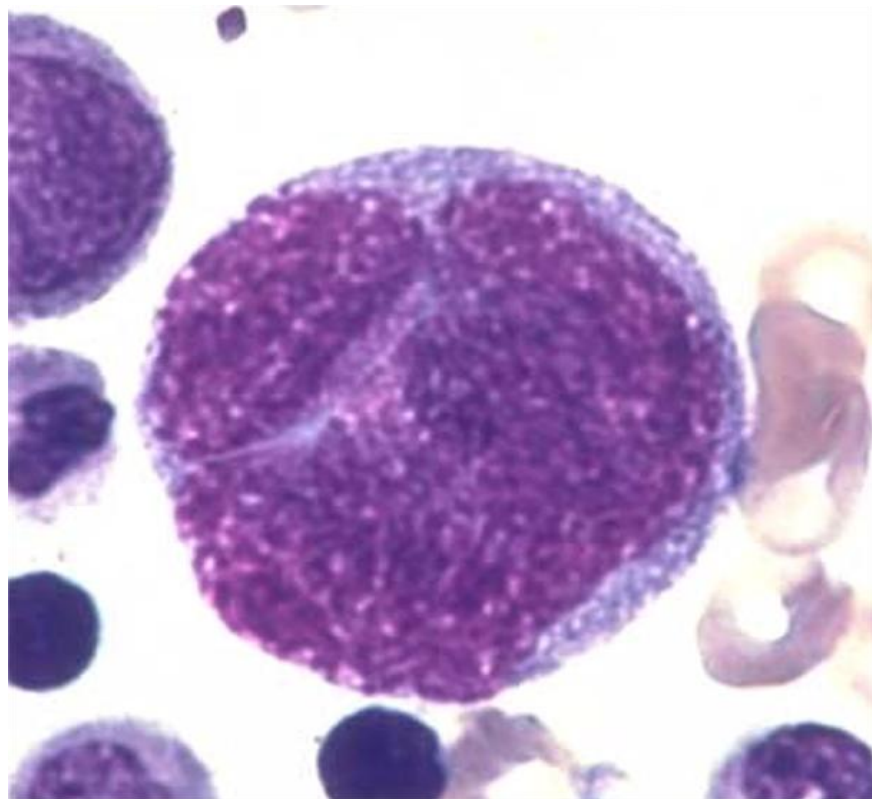
Megakaryoblasts
15 – 35 μm

polyploidy 64n
Basofilní cytoplasma
Ještě nemá granula

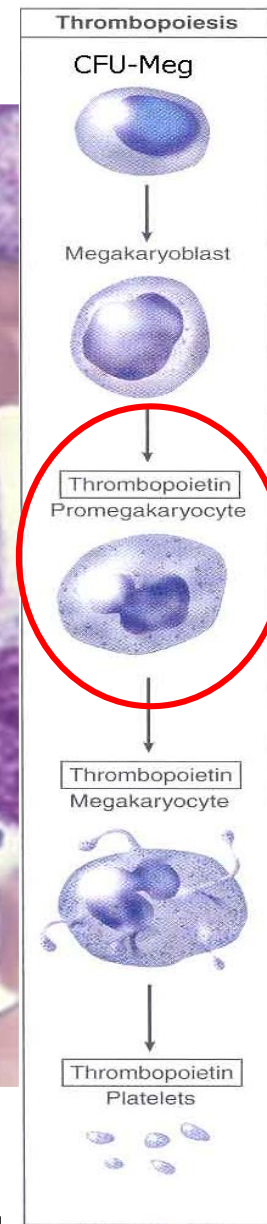
ouška



Promegakaryocytes
30 – 60 μm



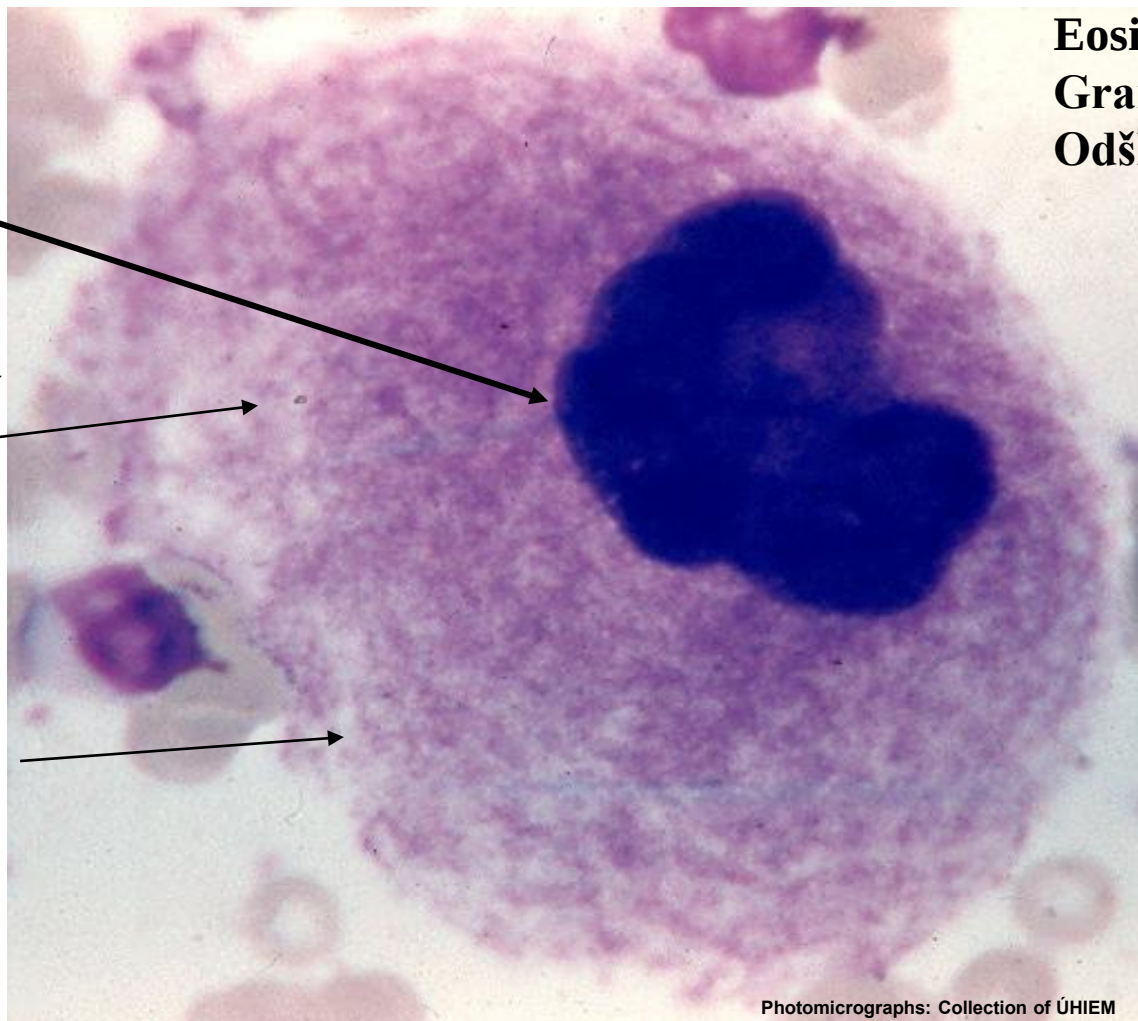
**Basofilní cytoplasma s granuly
ještě nedochází k oddělování destiček**



MEGAKARYOCYTE - size : 50 - 100 μm

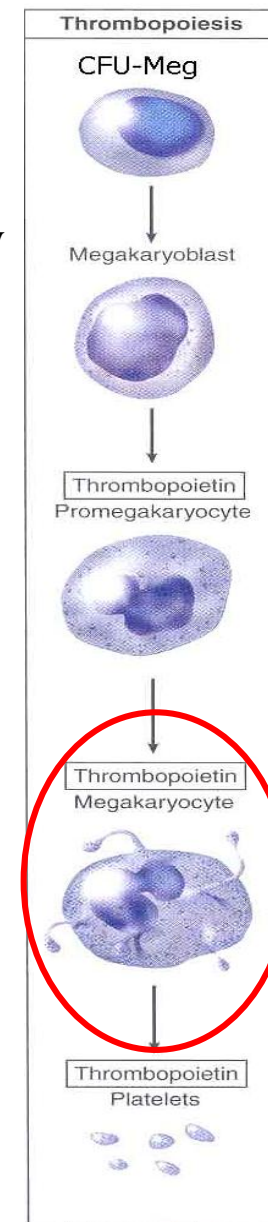
Azurofilní granula

Demarkační linie

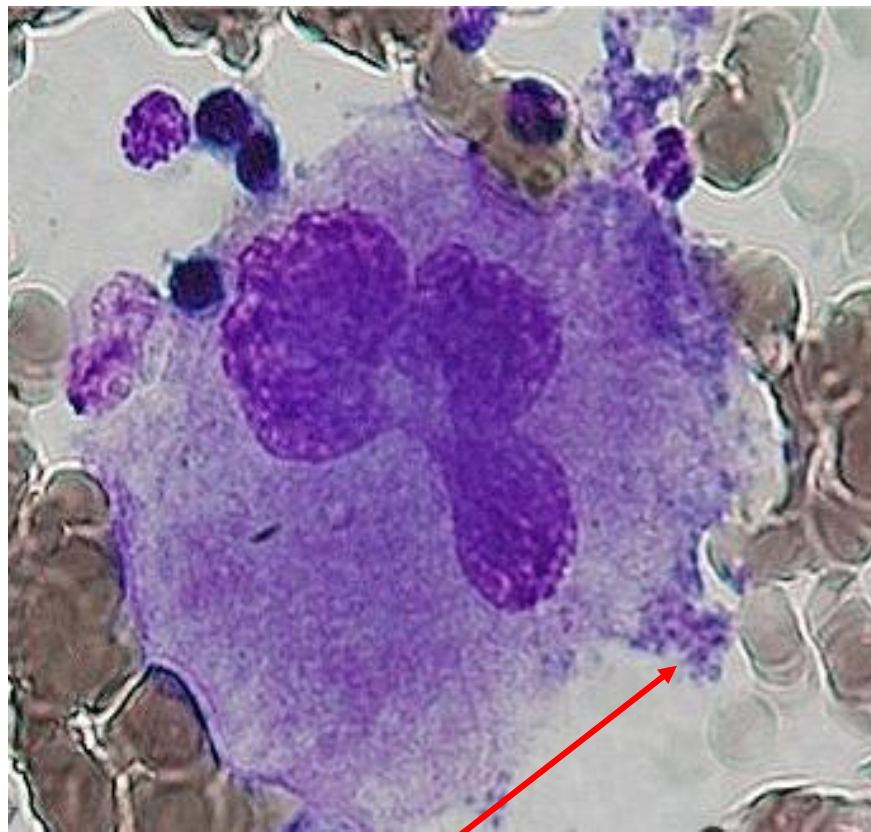
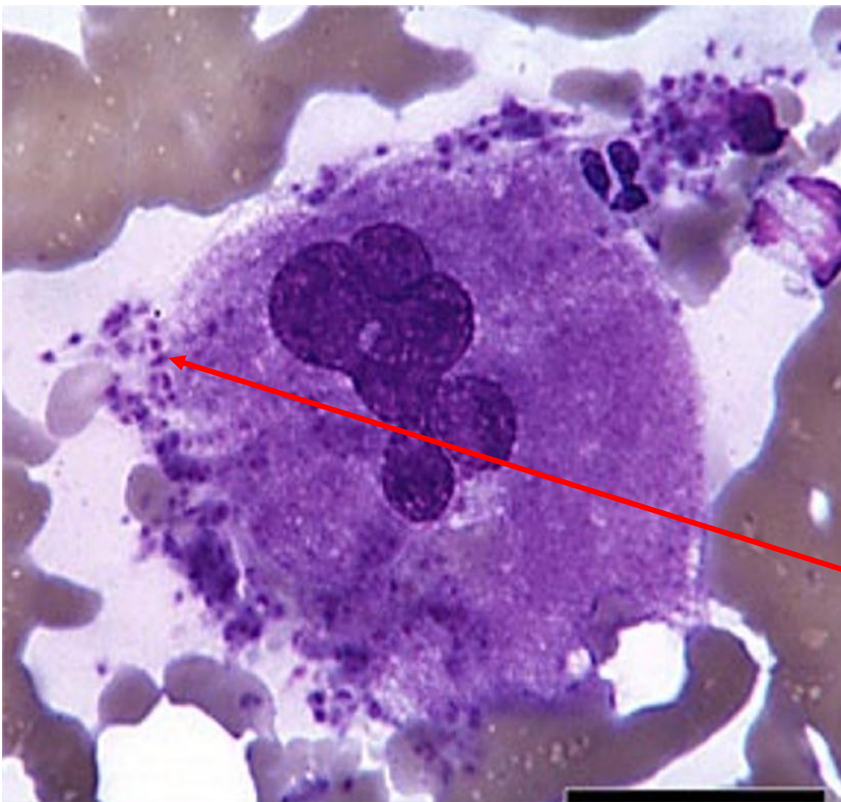


Photomicrographs: Collection of ÚHIEM

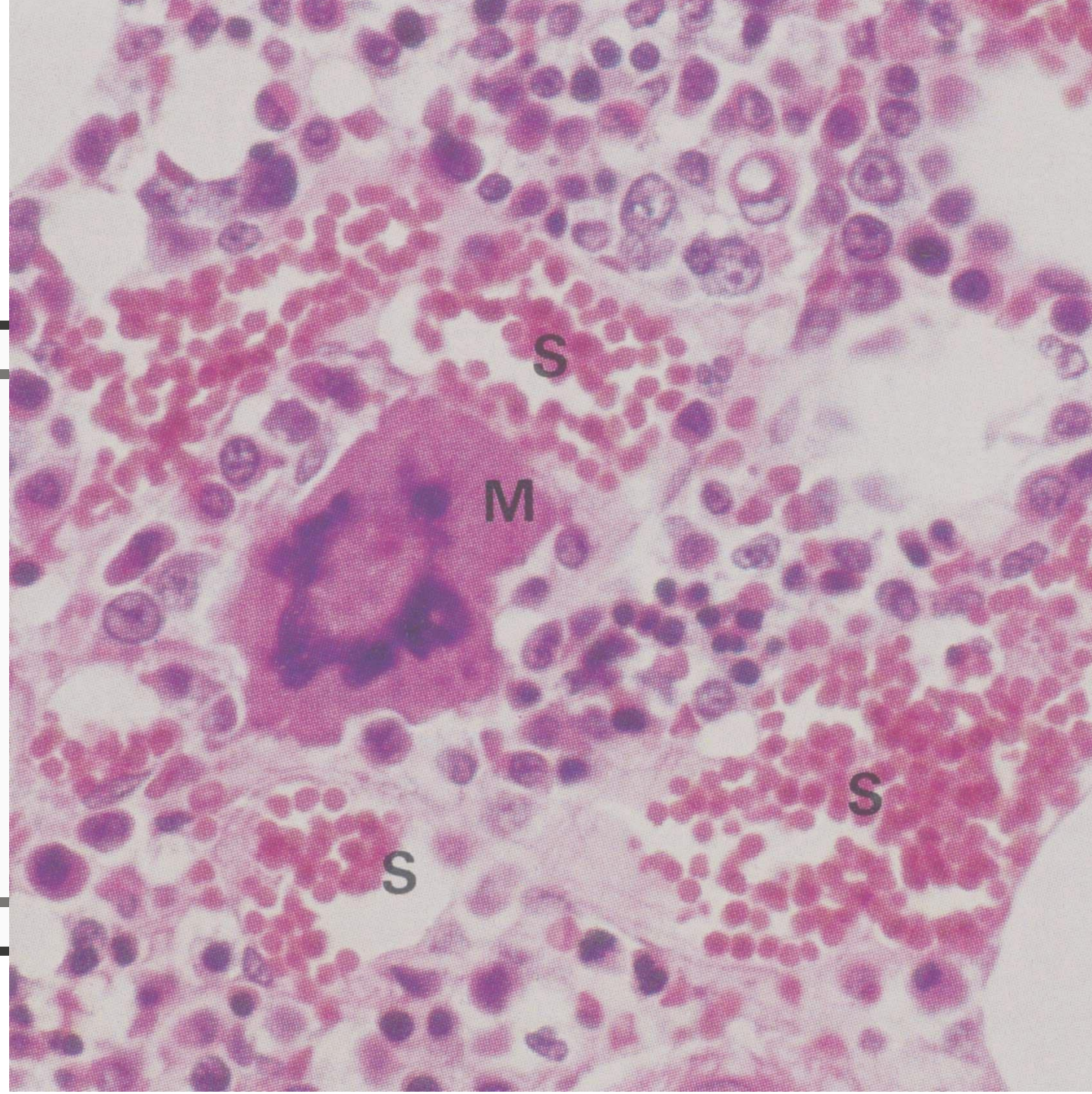
Laločnaté, tmavé jádro
Eosinofilie cytoplasmu
Granula, invaginace membrány
Odškrcující se trombocyty

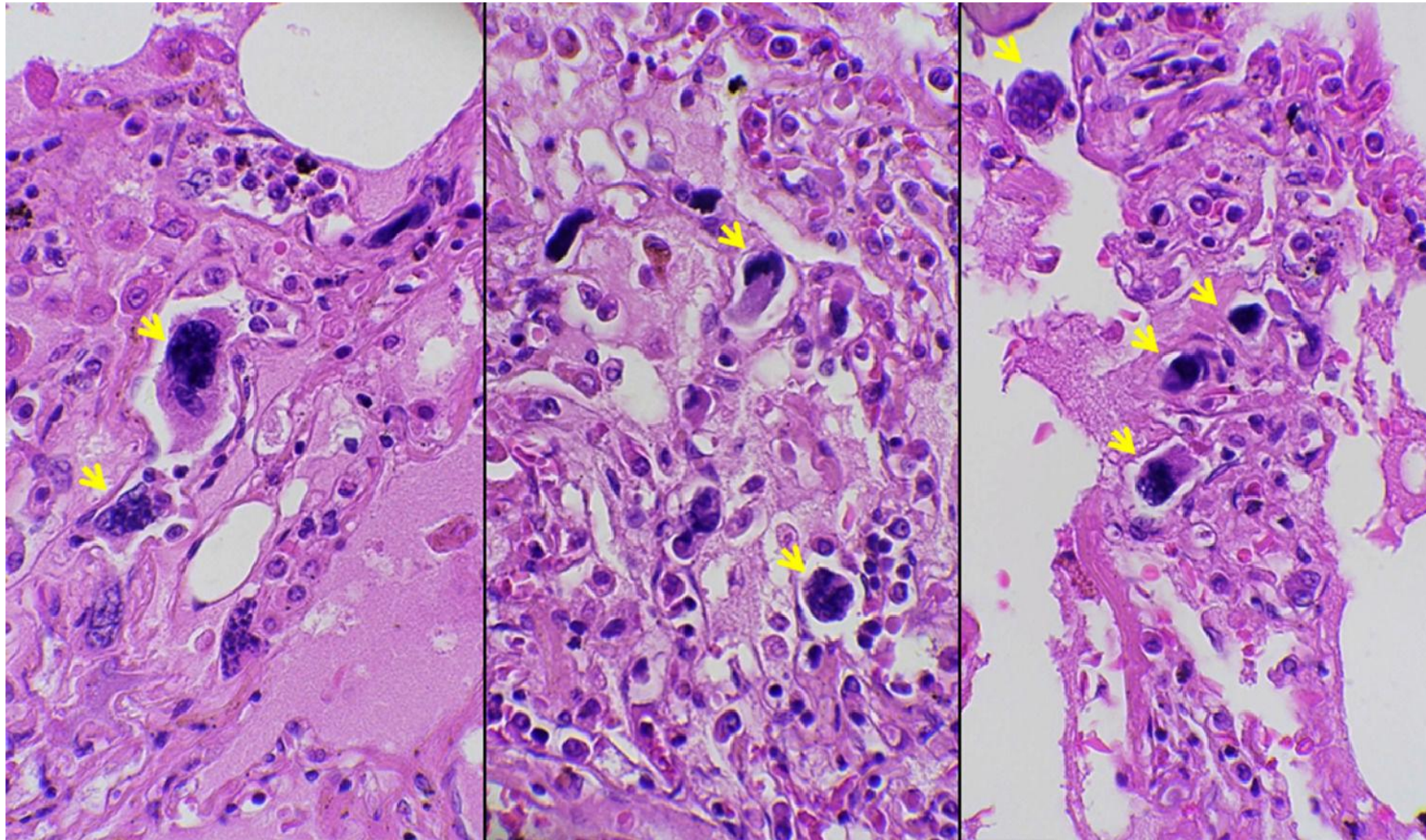


Megakaryocyty



**fragmentace trombocytů
(2000 - 4000)**



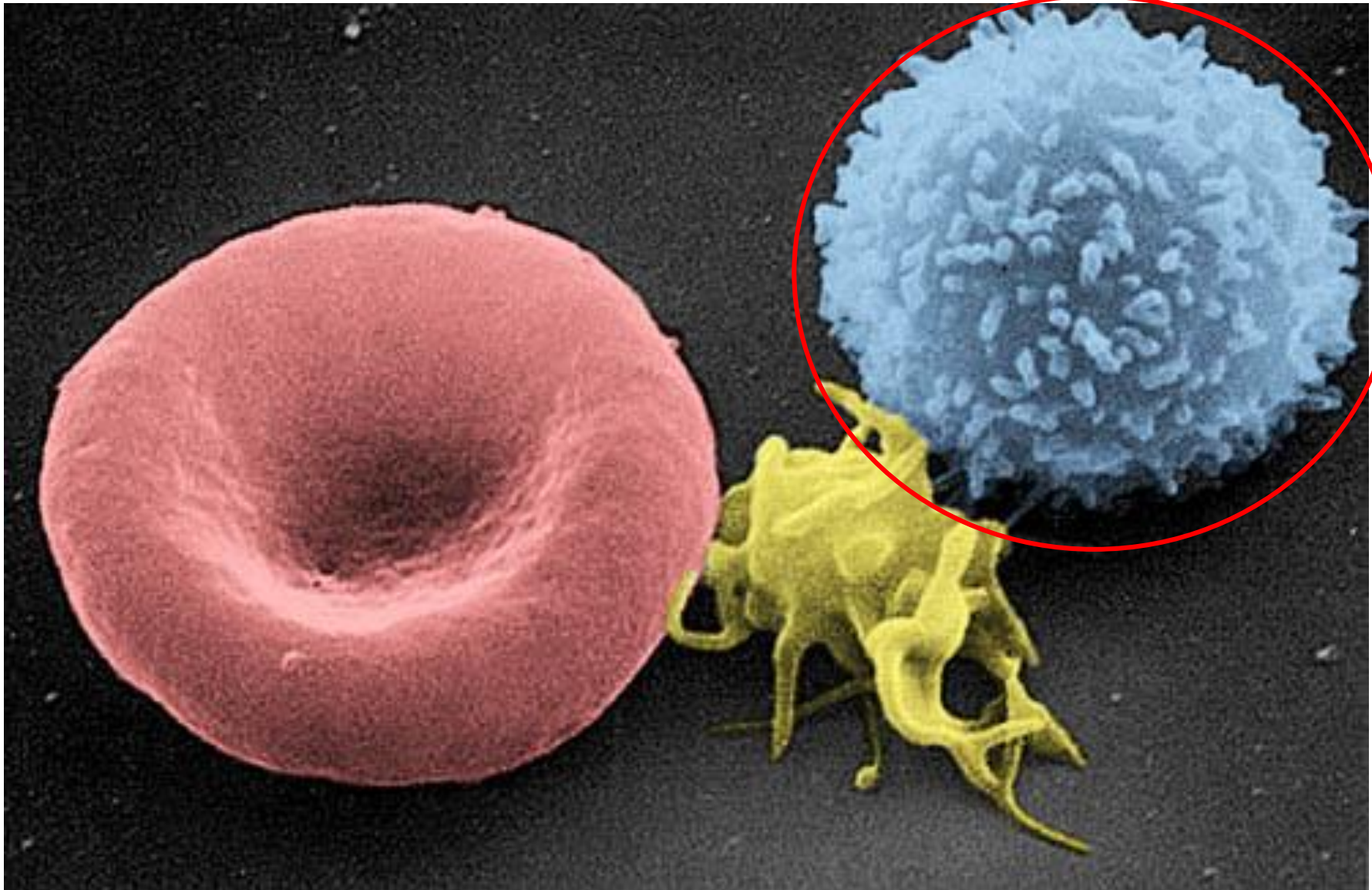


Megakaryocyty - plíce

Trombopoéza

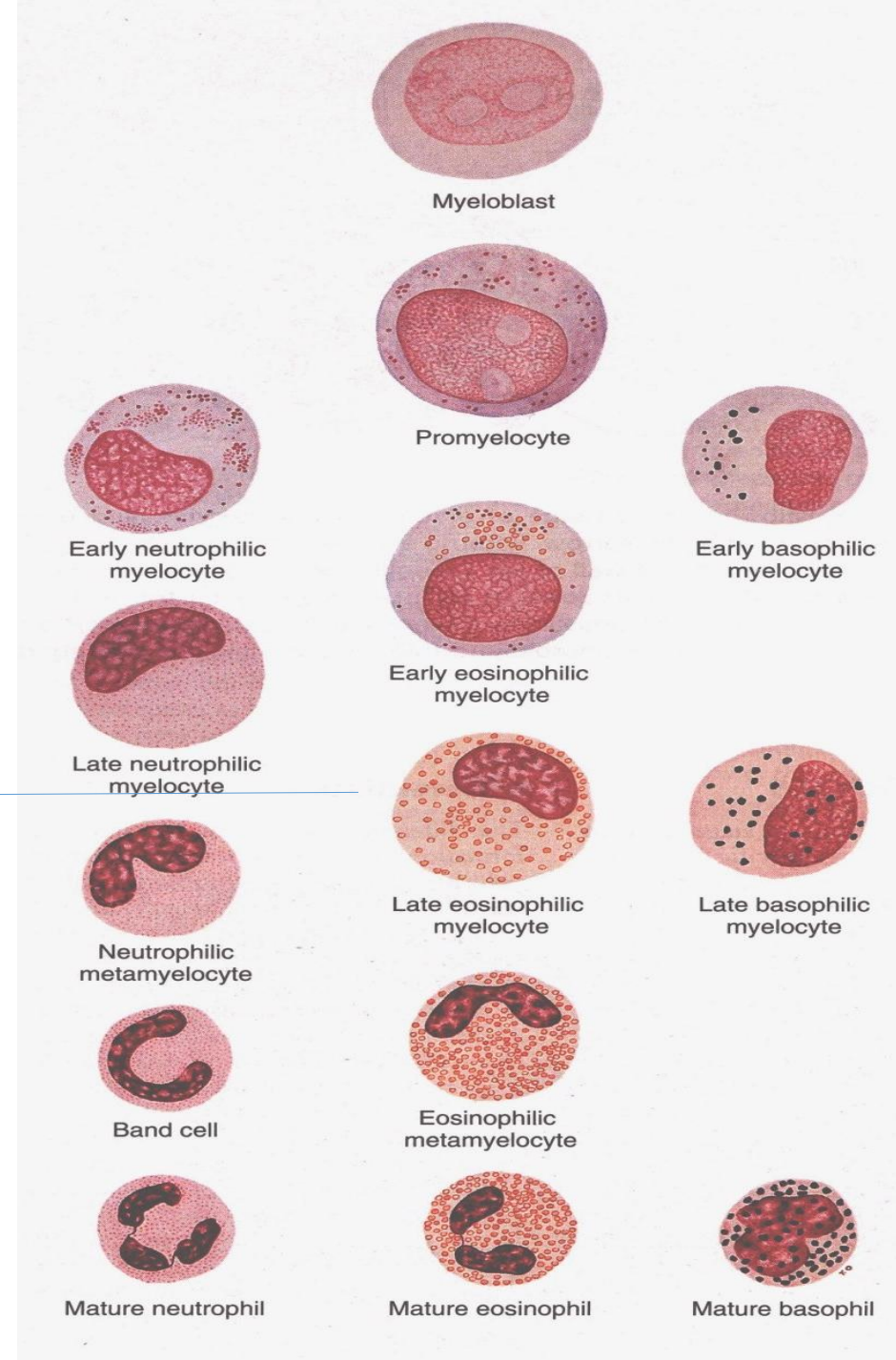
- Prekurzor je společný s červenou řadou (MEP)
- Megakaryoblast podstupuje endomitózy a mění se v promegakaryocyt a dále v megakaryocyt
- Megakaryocyt je polyploidní obrovská buňka s eosinofilní cytoplasmou, postupně odškrcuje jednotlivé destičky
 - Lze pozorovat granula a demarkační linie
- Z jednoho megakaryocytu se do krevních sinusoid uvolňují tisíce destiček

Leukopoéza



- Vývoj granulocytů,
- granulopoéza, myelopoéza

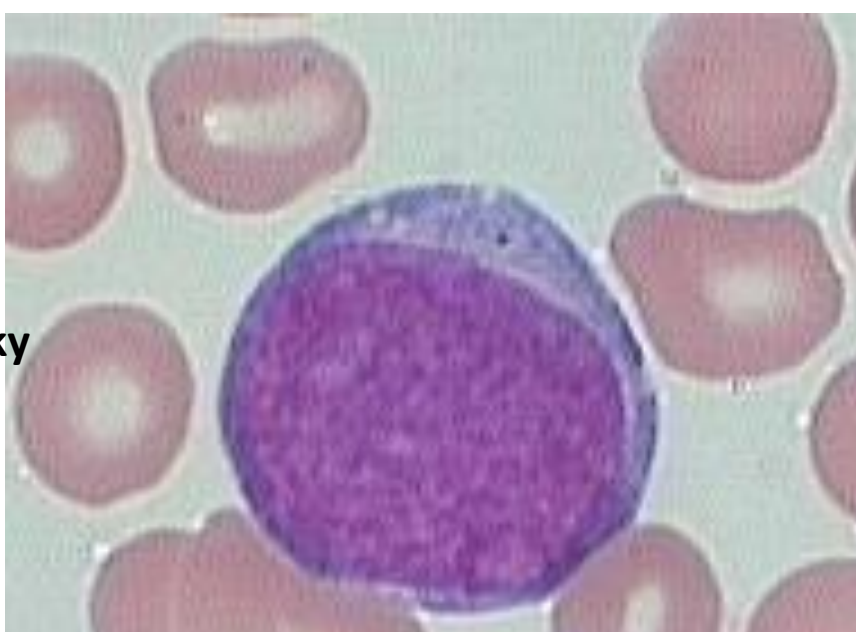
- velikost buňky ↙ ↘
- velikost jádra ↓
- kondenzace a segmentace jádra ↑ mitóza
- azurofilní granula ↑ — ↓
- specifická granula ↑



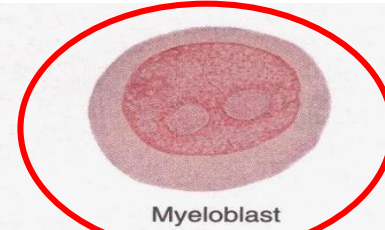
Granulopoiesis

Myeloblast
10 – 20 μm

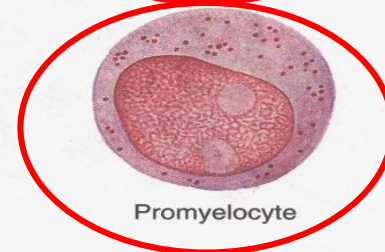
Velké sferické jádro s jadérky
Basofilní cytoplasma



Promyelocyt
15 – 24 μm
Azurofilní granula



Myeloblast



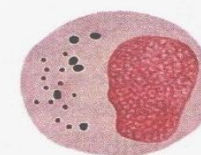
Promyelocyte



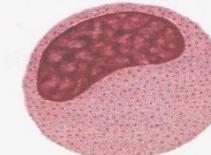
Early neutrophilic
myelocyte



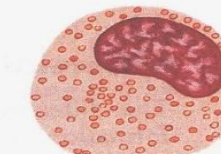
Early eosinophilic
myelocyte



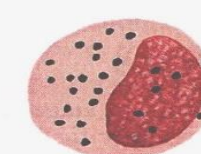
Early basophilic
myelocyte



Late neutrophilic
myelocyte



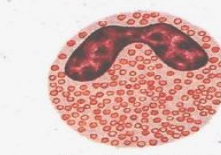
Late eosinophilic
myelocyte



Late basophilic
myelocyte



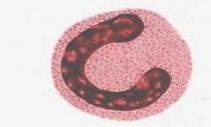
Neutrophilic
metamyelocyte



Eosinophilic
metamyelocyte



Mature neutrophil



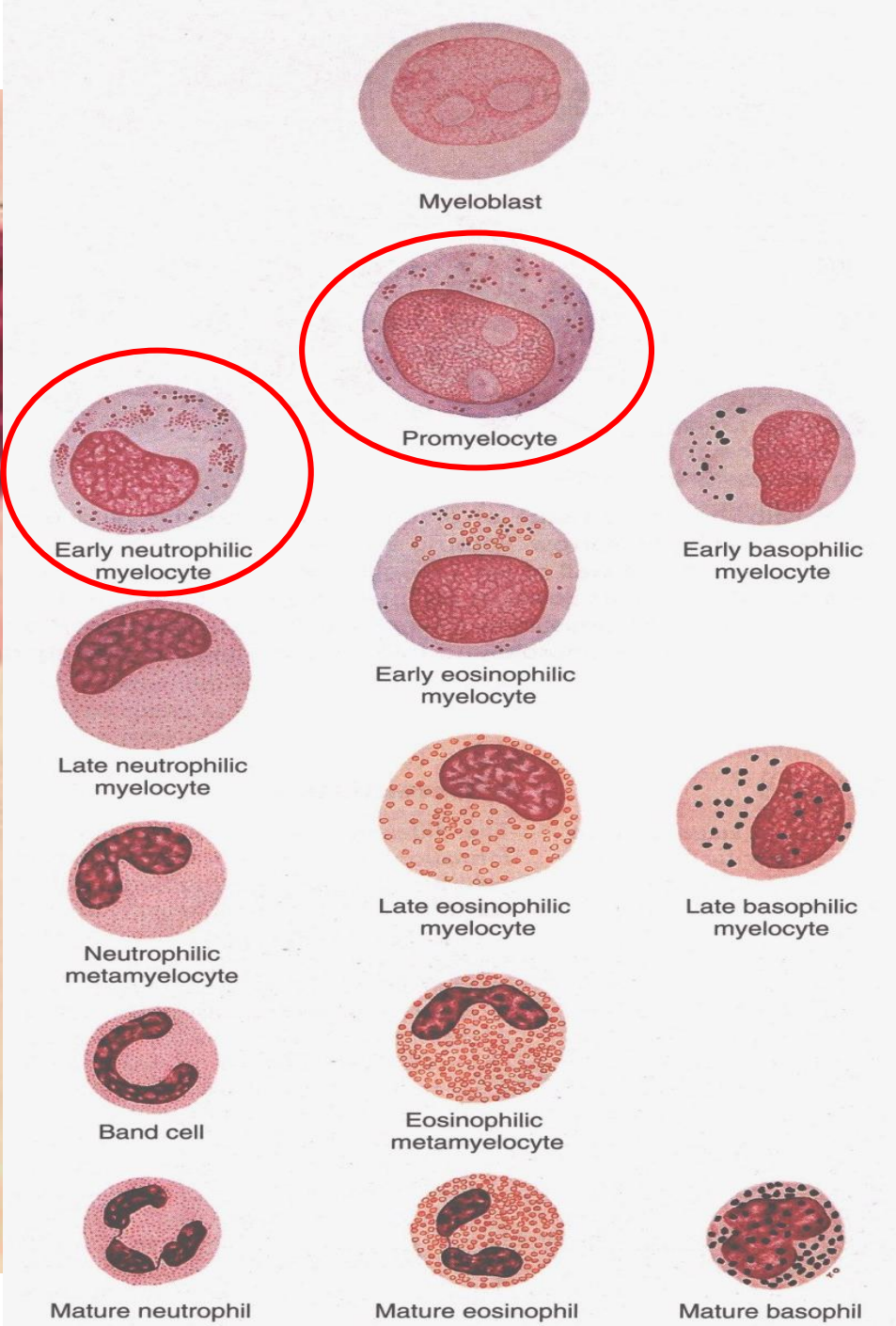
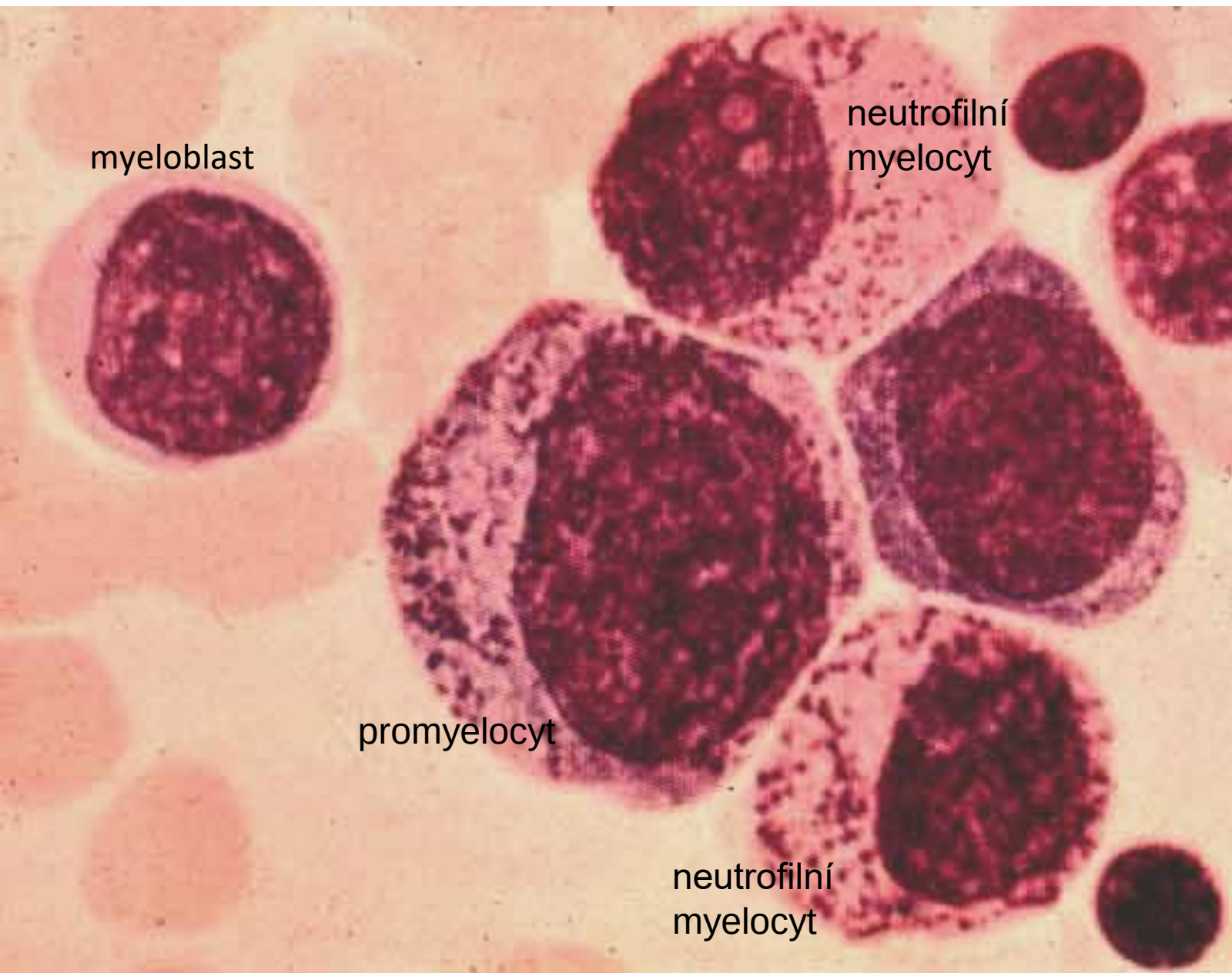
Band cell



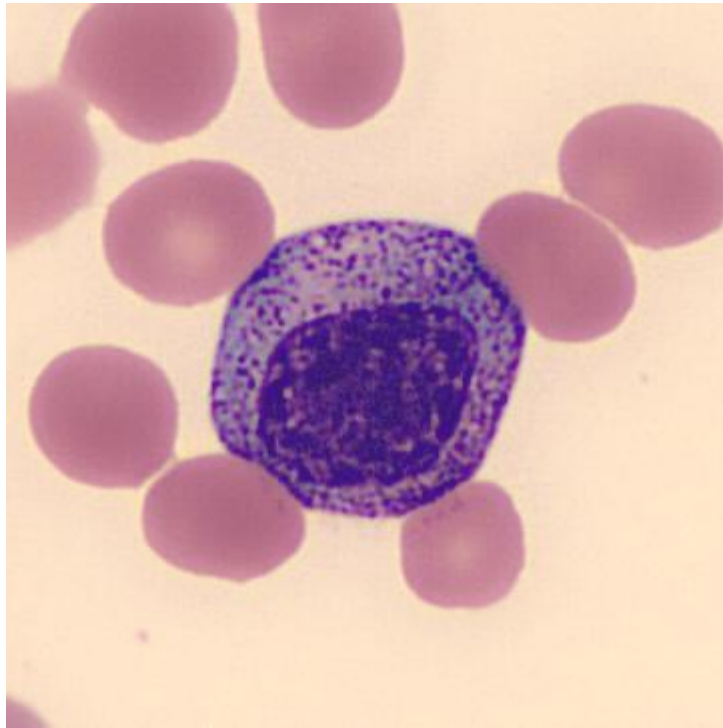
Mature eosinophil



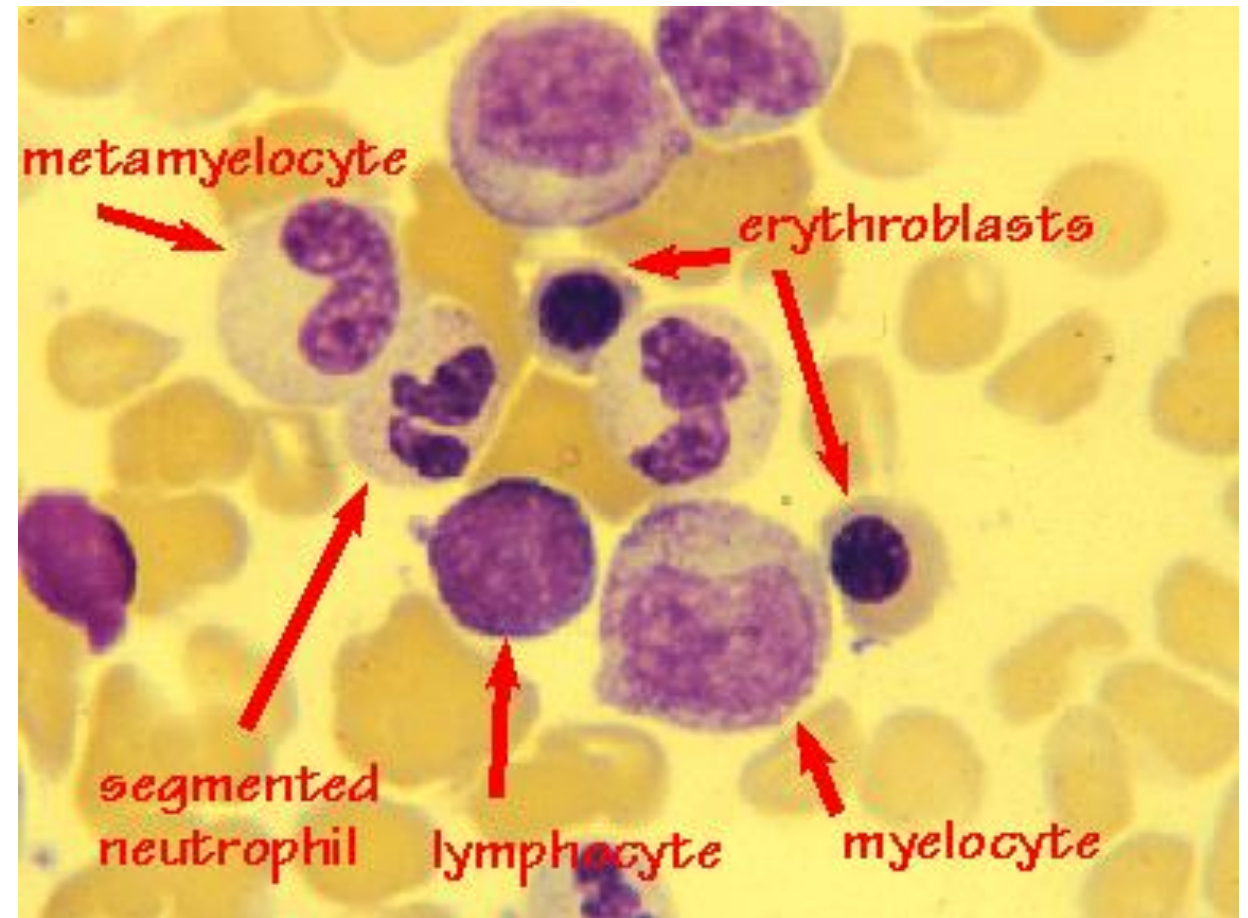
Mature basophil



myelocyt



Postupná kondenzace a změna tvaru jádra
Tvoří se specifická granula
Ještě se dělí





neutrofilní
metamyelocyty

Ledvinovité až
podkovovité jádro
Se segmentací jádra
vyzraje v granulocyt



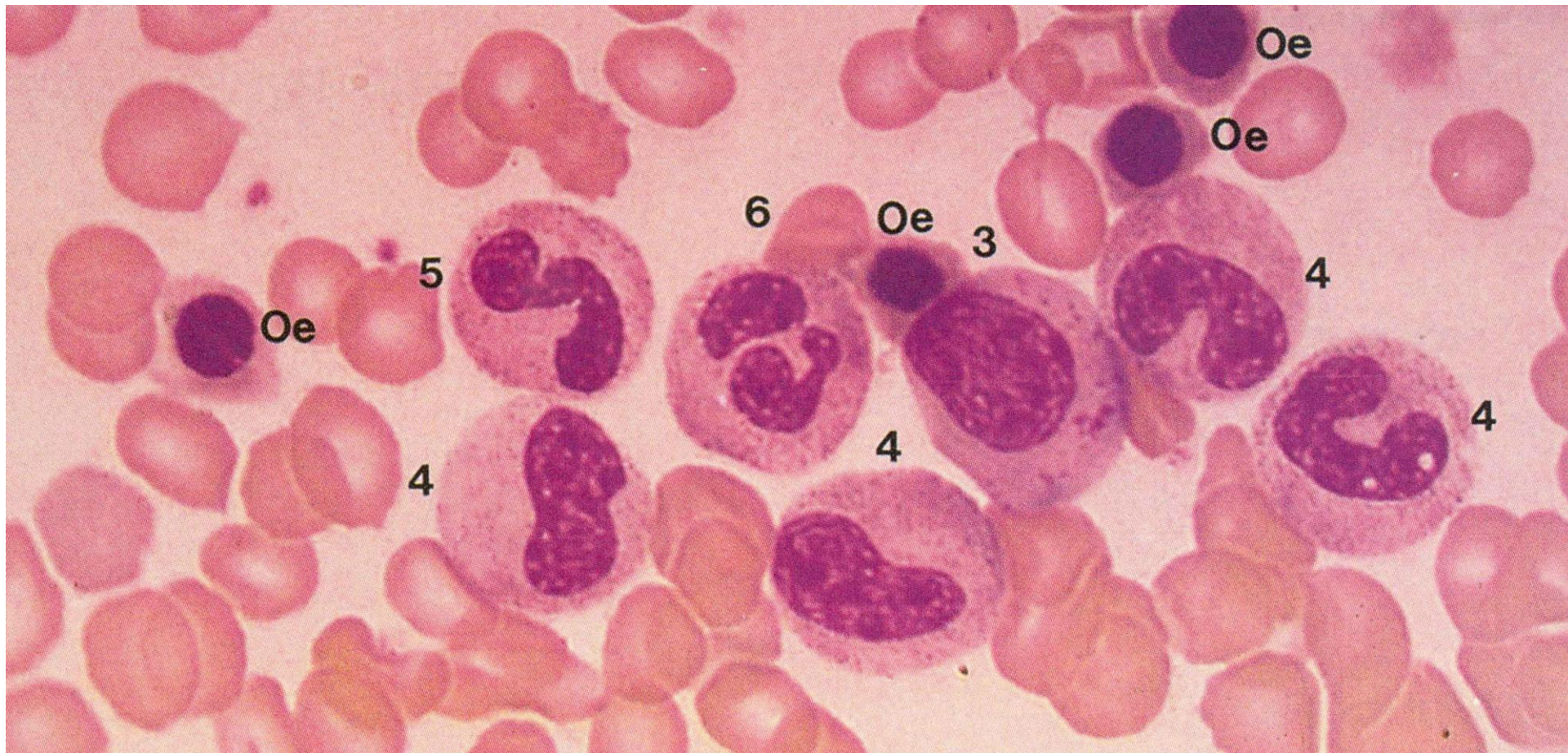
neutrofilní
metamyelocyty

3 = neutrofilní myelocyt

4 = neutrofilní metamyelocyt

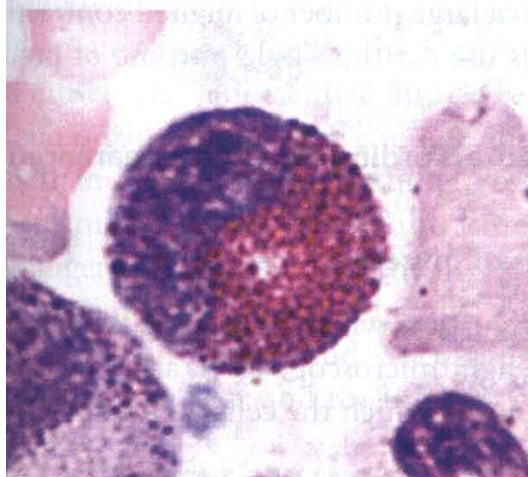
5 = neutrofilní tyč

6 = neutrofilní granulocyte

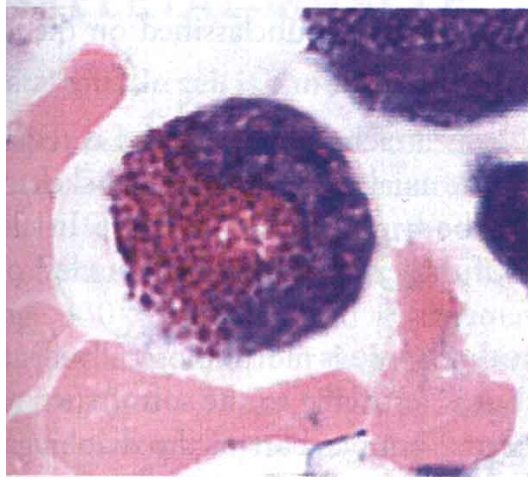




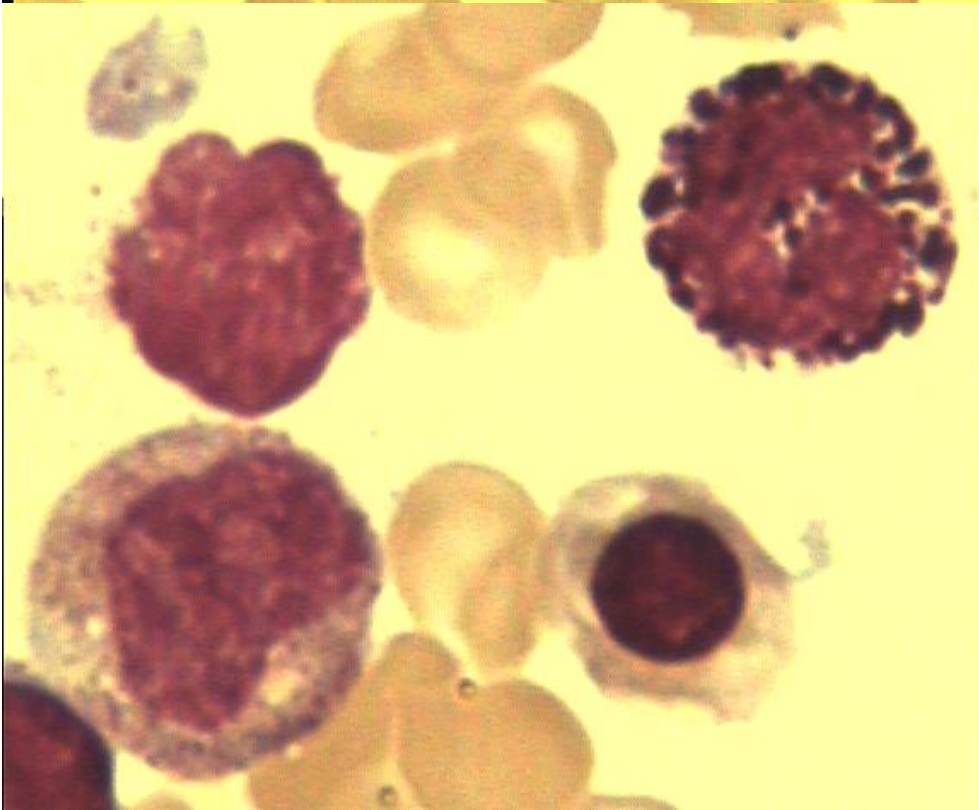
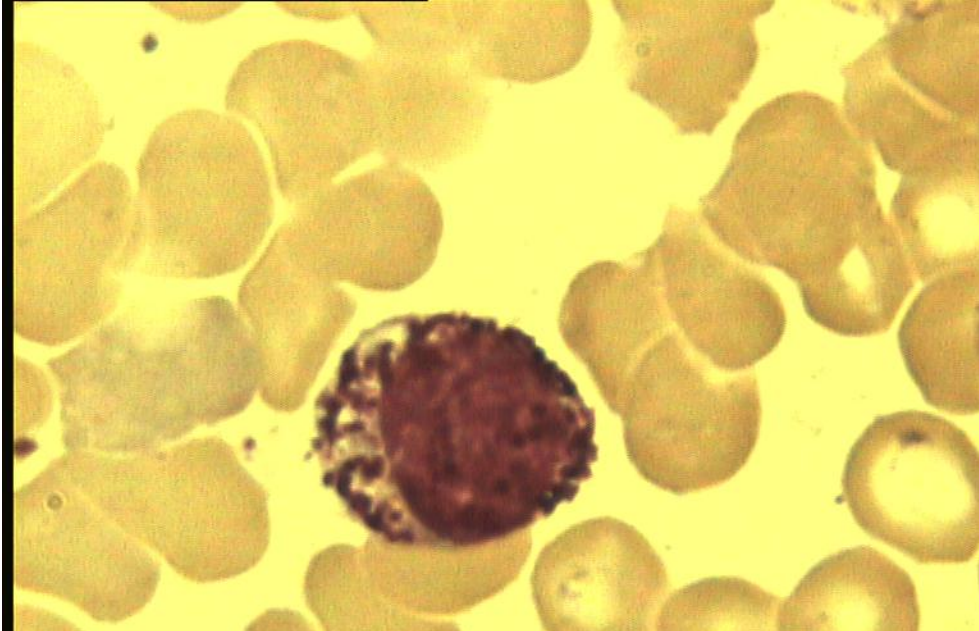
— eosinophilic
myelocyte



— eosinophilic
metamyelocyte



— eosinophilic
band cell

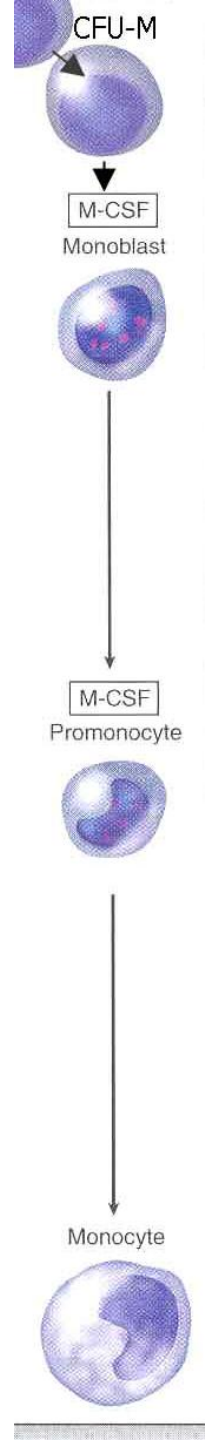


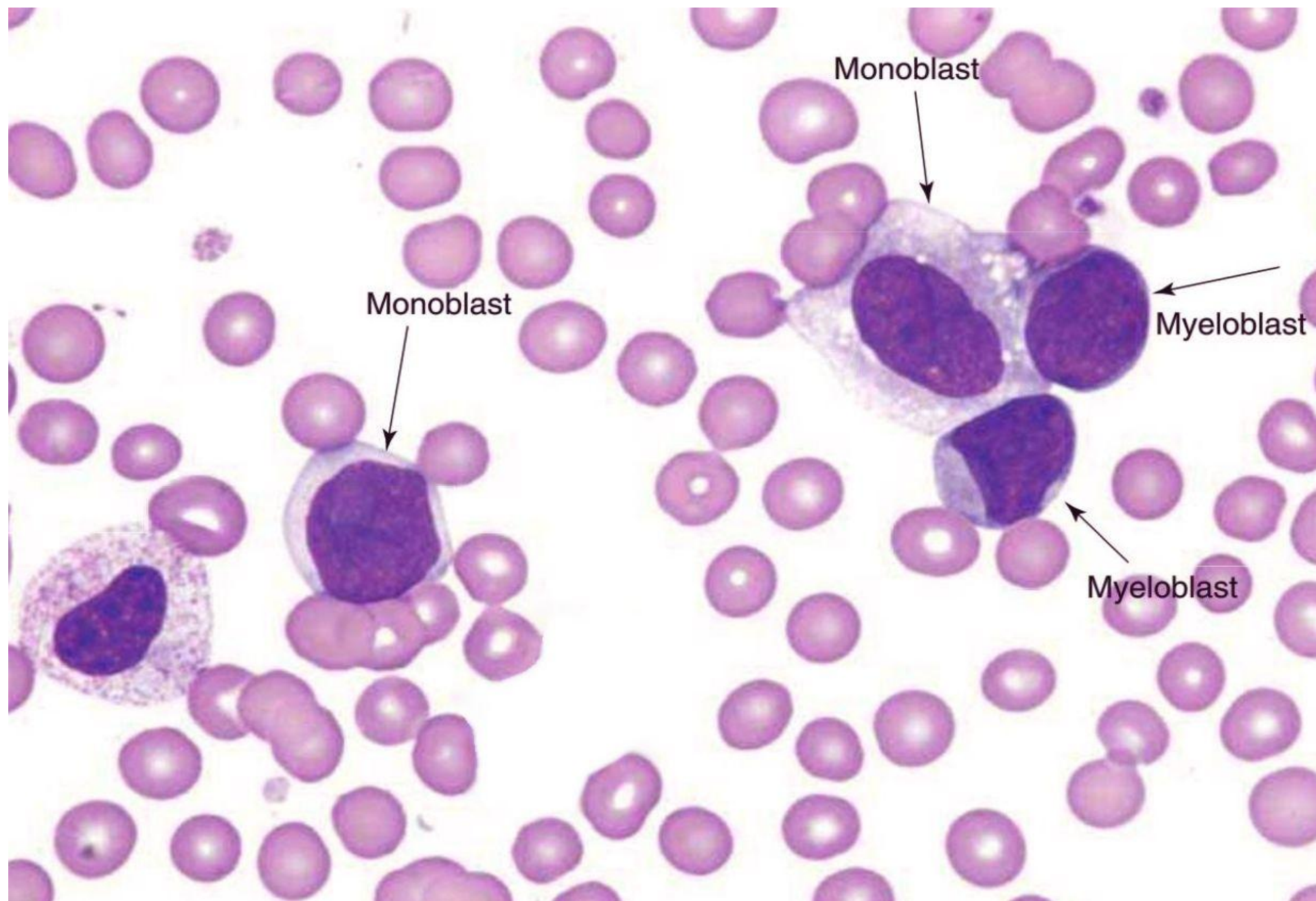
Myelopoéza

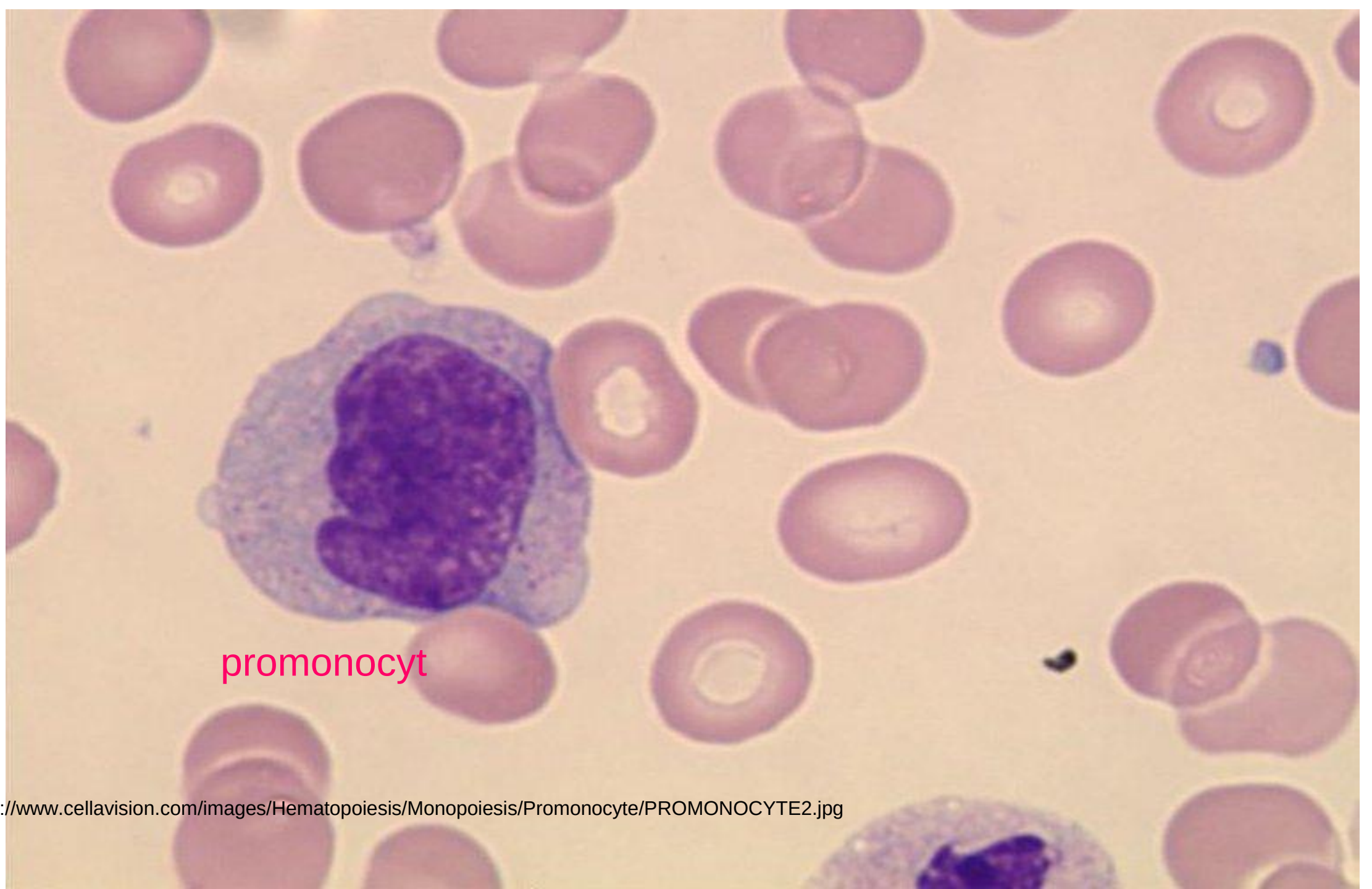
- Myeloblast s basofilní cytoplasmou je společným prekursorem pro všechny granulocyty
- Největší buňkou řady je promyelocyt, pouze v tomto stadiu se tvoří azurofilní granula, při následných děleních jejich hustota klesá
- Myelocyt je posledním dělícím se stadiem, tvoří se v něm specifická granula (lze rozlišit druhy granulocytů)
 - Jádro se mění do tvaru D
- Metamyelocyt má cytoplasmu odpovídající zralému granulocyту, ale podkovovité jádro stále není segmentováno
- Mladý granulocyt s nesegmentovaným jádrem se nazývá tyč

Vývoj monocytů, monopoéza

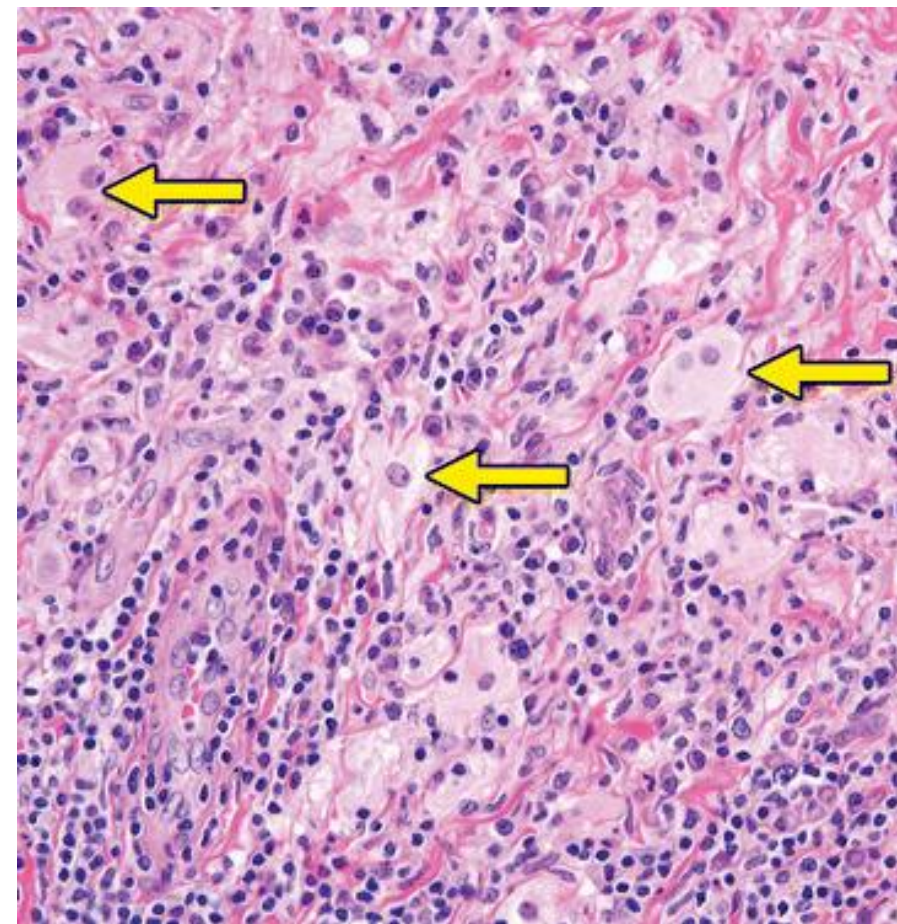
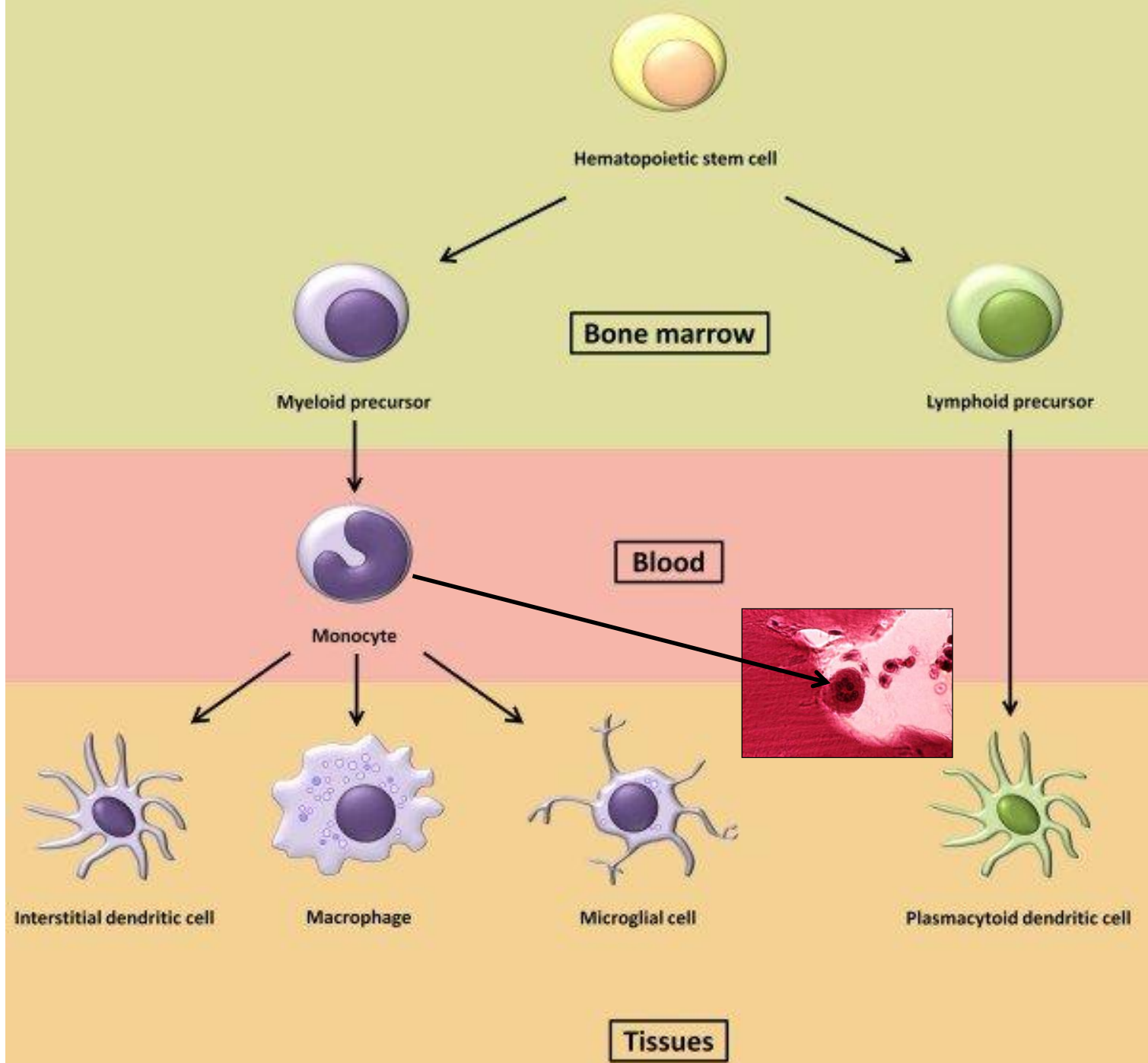
- Monoblast je prakticky nerozlišitelný od myeloblastu
- Promonocyty jsou větší s vpáčeným jádrem







promonocyt



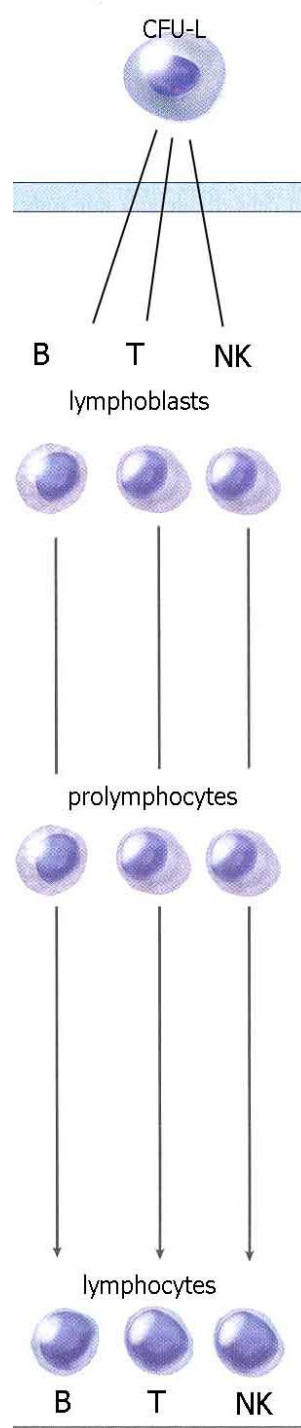
makrofágy, histiocyty

Vývoj lymfocytů, lymfopoéza

- velikost buňky ↓

- velikost jádra ↓

- kondenzace jádra ↑



Morfologicky jsou jednotlivá stadia značně podobná, odlišují se pomocí povrchových markerů

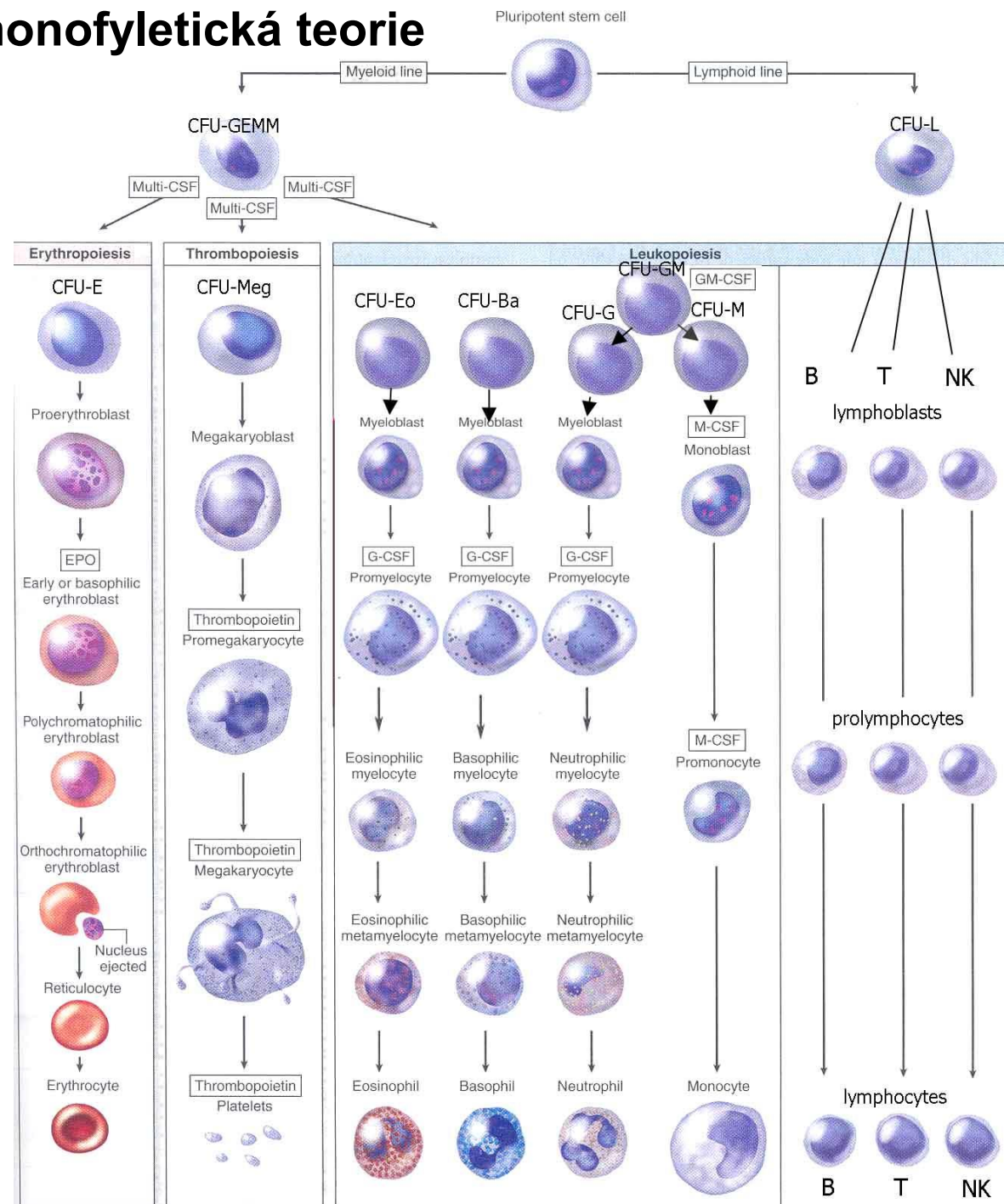
monofyletická teorie

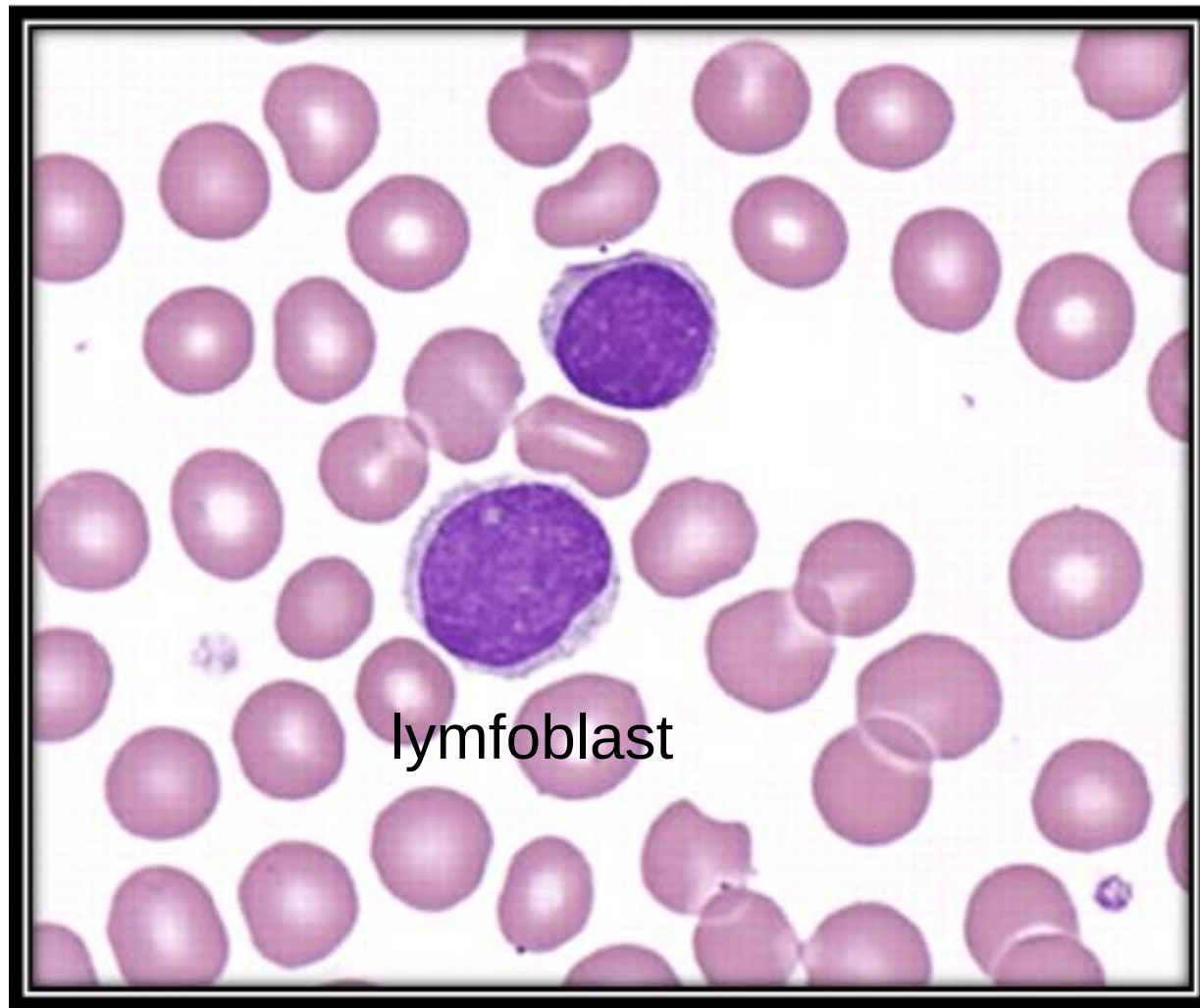
Kmenové buňky

Progenitorové buňky (CFU)

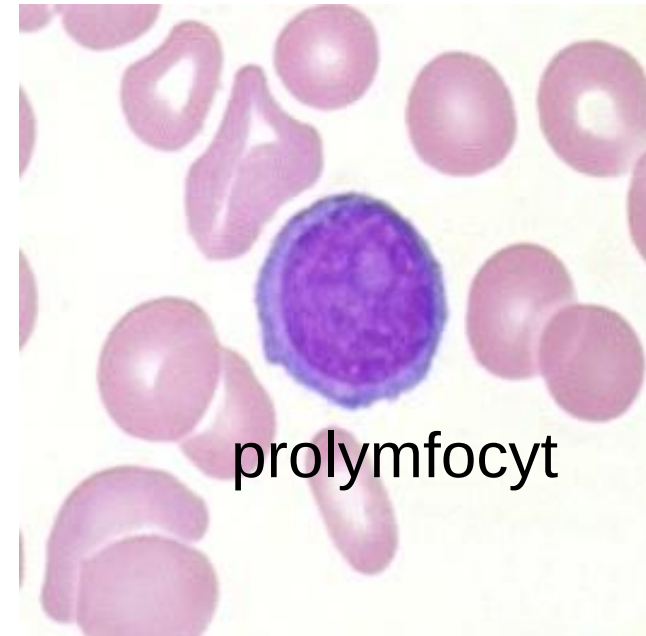
Prekursorové buňky (blasty)

Zralé buňky





lymfoblast

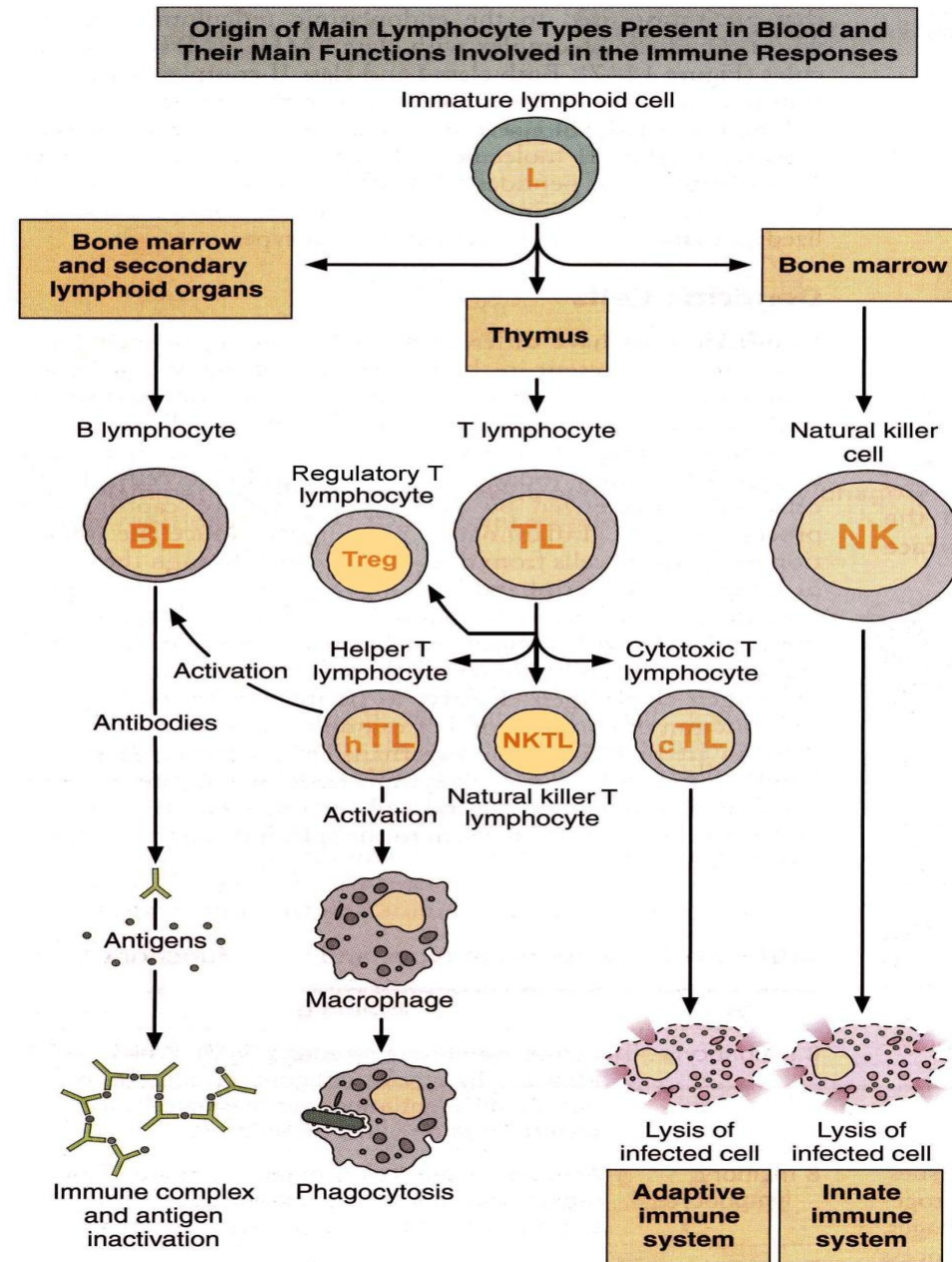


prolymfocyt

Lymphoblast
(in bone marrow)

Places of maturation
(immunocompetency
acquisition)

Types
of lymphocytes



SURFACE ANTIGENS

all B- lymphocytes
CD20,23,(19) BCR
MHC II

all T-lymphocytes
CD3 TCR

T_hL CD4

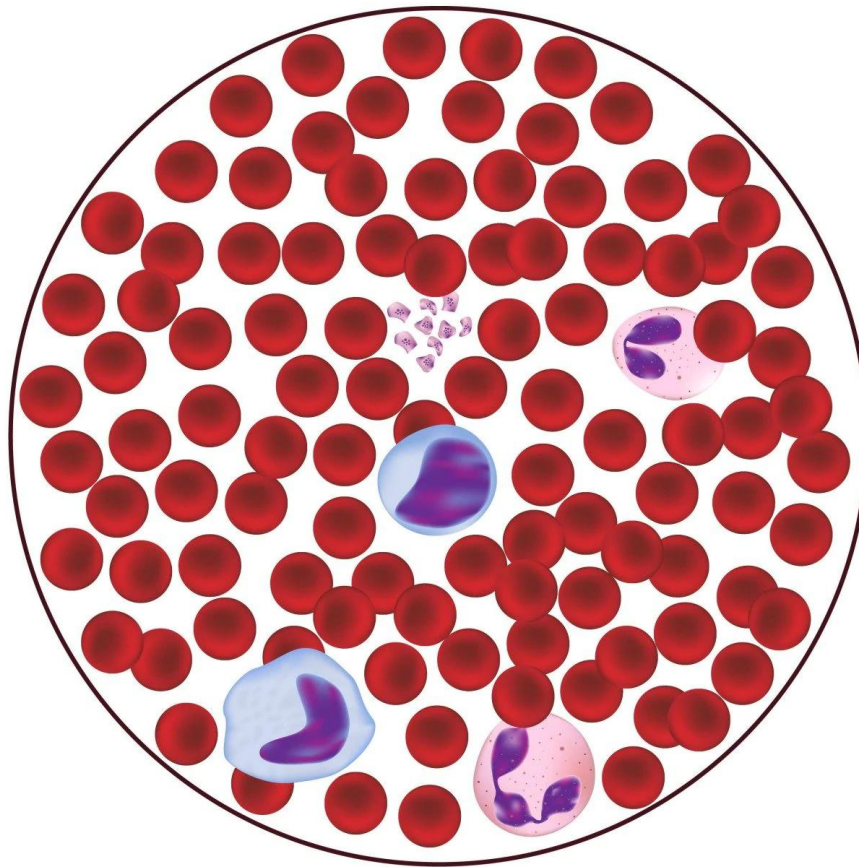
T_cL CD8

T_{reg}L CD4 or CD8
CD25 and FOXP3

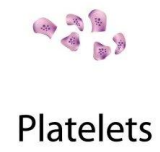
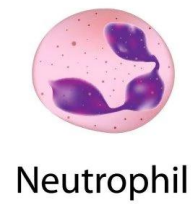
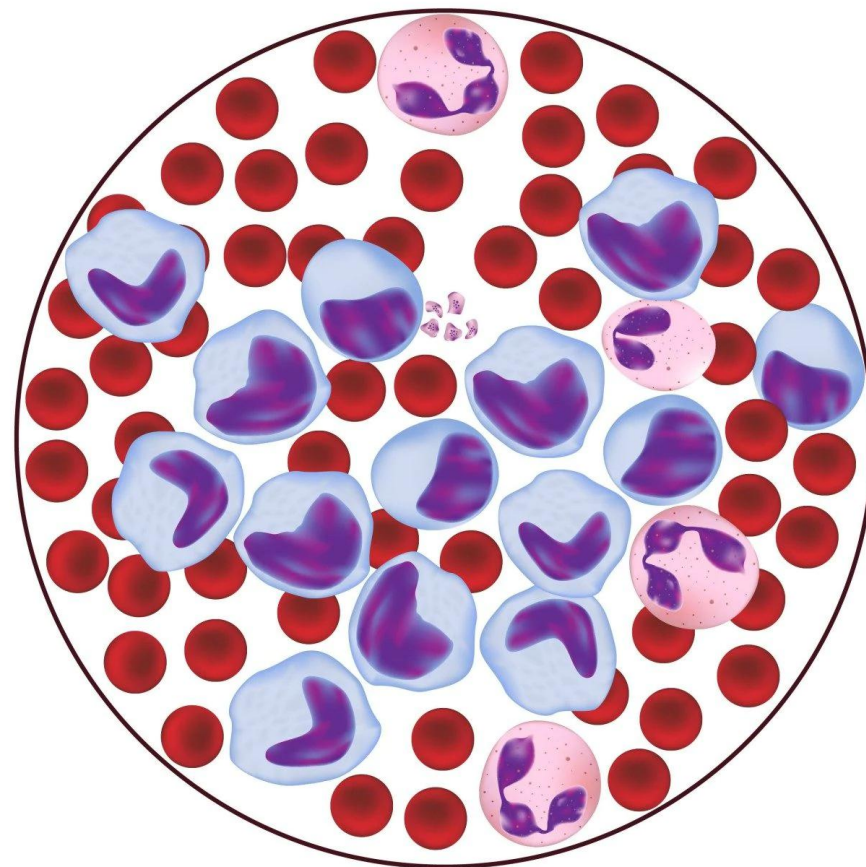
NKTL and other
unconventional TL (MAIT)
CD1d CD16

NK-cells CD16
CD56

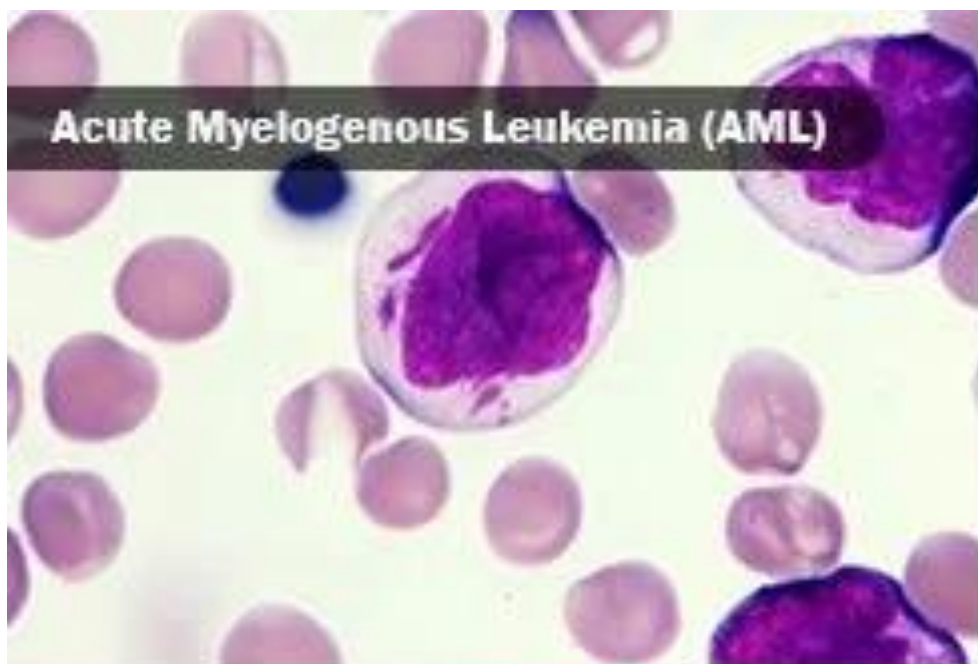
Normal Blood



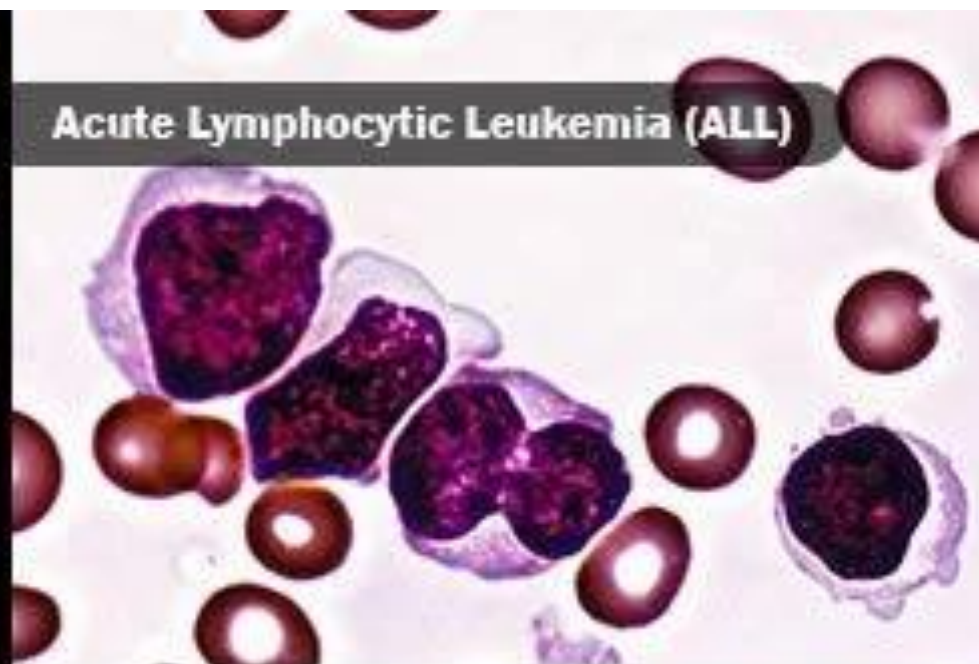
Leukemia



Acute Myelogenous Leukemia (AML)



Acute Lymphocytic Leukemia (ALL)



Chronic Myelogenous Leukemia (CML)



Chronic Lymphocytic Leukemia (CLL)



NO STRESS



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