

# DARAH DAN SISTEM SIRKULASI (2)

# Sel Darah Putih .....

- Karakteristik Sirkulasi
  - 1. Gerak amoeboid
  - 2. Dapat bermigrasi keluar dari pembuluh darah
  - 3. Dipengaruhi oleh stimulus kimia spesifik (positif kemotaksis)
  - 4. Neutrophils, eosinophils, dan monocytes memiliki peran fagositosis

-

# LEUKOSIT













AMOEBOID ) → DAPAT MENINGGALKAN PEMBULUH DARAH KECIL,  
MENEMBUS  
→ GERAKAN SECARA DIAPEDEESIS ( GERAK DINDING PEMBULUH  
DARAH, MELALUI CELAH2 DIANTARA ENDOTEL → MASUK KE  
JARINGAN-JARINGAN.

## FUNGSI :

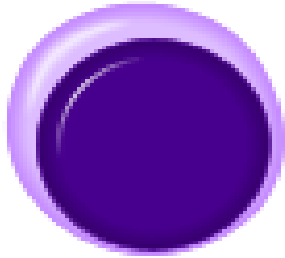
SEBAGAI PERTAHANAN TUBUH TERHADAP  
BENDA ASING

JUMLAH : 5000 – 9000 / MM<sup>3</sup>.

- Leukosit mempunyai kemampuan : Diapedesis, yaitu merembes keluar dari pembuluh darah, menuju ke jaringan radang karena daya tarik kemotaksis dari toksik kuman
- Peranan sel – sel lekosit
  - ^ Netrofil                      Fagositosis
  - ^ Eosinofil
  - ^ Basofil
    - Mengandung → Histamin : vasodilator
    - Heparin : antikoagulan
    - Tempat perlekatan Ig E
    - Banyak terdapat pada daerah peradangan

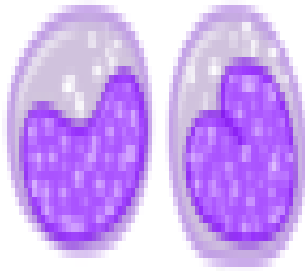
Tipe	Gambar	Diagram	% dalam tubuh manusia	Keterangan
Neutrofil			65%	Neutrofil berhubungan dengan pertahanan tubuh terhadap infeksi <b>bakteri</b> serta proses peradangan kecil lainnya, serta biasanya juga yang memberikan tanggapan pertama terhadap infeksi bakteri; aktivitas dan matinya neutrofil dalam jumlah yang banyak menyebabkan adanya nanah.
Eosinofil			4%	Eosinofil terutama berhubungan dengan infeksi <b>parasit</b> , dengan demikian meningkatnya eosinofil menandakan banyaknya parasit.
Basofil			<1%	Basofil terutama bertanggung jawab untuk memberi reaksi <b>alergi</b> dan <b>antigen</b> dengan jalan mengeluarkan <b>histamin</b> kimia yang menyebabkan <b>peradangan</b> .
Limfosit			25%	<p>Limfosit lebih umum dalam sistem limfa. Darah mempunyai tiga jenis limfosit:</p> <ul style="list-style-type: none"> <li>▪ <b>Sel B:</b> Sel B membuat <b>antibodi</b> yang mengikat <b>patogen</b> lalu menghancurkannya. (Sel B tidak hanya membuat antibodi yang dapat mengikat patogen, tapi setelah adanya serangan, beberapa sel B akan mempertahankan kemampuannya dalam menghasilkan antibodi sebagai layanan sistem 'memori'.)</li> <li>▪ <b>Sel T: CD4+ (pembantu)</b> Sel T mengkoordinir tanggapan ketahanan (yang bertahan dalam infeksi <b>HIV</b>) serta penting untuk menahan bakteri intraseluler. <b>CD8+ (sitotoksik)</b> dapat membunuh sel yang terinfeksi virus.</li> <li>▪ <b>Sel natural killer.</b> Sel pembunuh alami (<i>natural killer, NK</i>) dapat membunuh sel tubuh yang tidak menunjukkan sinyal bahwa dia tidak boleh dibunuh karena telah terinfeksi <b>virus</b> atau telah menjadi <b>kanker</b>.</li> </ul>
Monosit			6%	<b>Monosit</b> membagi fungsi "pembersih vakum" ( <b>fagositosis</b> ) dari neutrofil, tetapi lebih jauh dia hidup dengan tugas tambahan: memberikan potongan <b>patogen</b> kepada sel T sehingga patogen tersebut dapat dihafal dan dibunuh, atau dapat membuat tanggapan antibodi untuk menjaga.
Makrofag			(lihat di atas)	Monosit dikenal juga sebagai <b>makrofag</b> setelah dia meninggalkan aliran darah serta masuk ke dalam jaringan.

# Agranulosit



## *Limfosit*

- Berbentuk seperti bola dengan ukuran diameter 6-14 mikron
- Dibentuk di sumsum tulang (janin di hati)
- Limfosit, tidak dapat bergerak
- berinti satu
- berfungsi untuk membentuk antibodi



## *Monosit*

- *Berinti satu*
- *Berbentuk kepal kuda atau ginjal dengan ukuran diameter 12-20 mikron*
- *Bersifat fagosit*

# Lymphocytes

- *Lymphocytes* are cells involved in immune responses:
- B lymphocytes make antibodies;
- T lymphocytes kill virus-infected cells and regulate the activities of other white blood cells by secreting cytokines and by cell-to-cell contact.



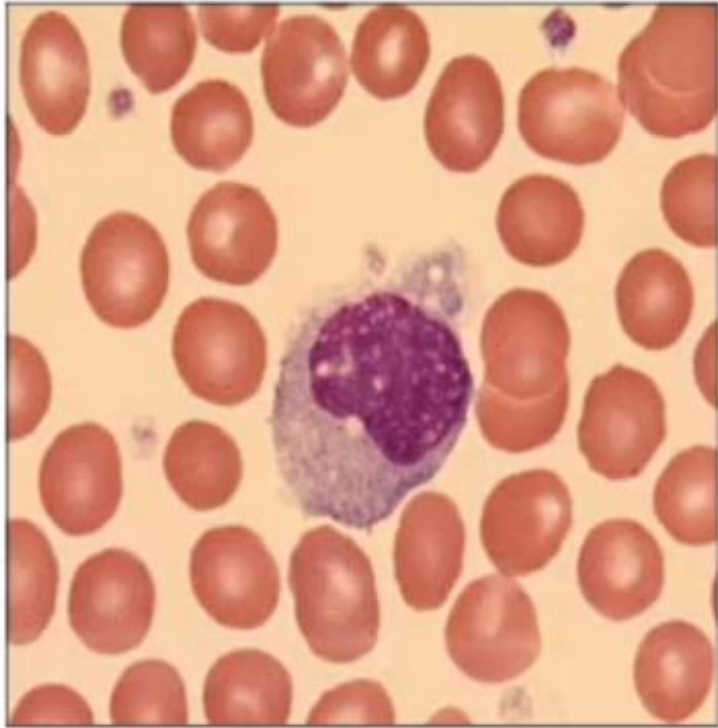
# LYMPHOCYTES

- These cells have receptors for antigen and confer specificity on an immune response.
- Lymphocytes express receptors with varying affinity for the antigen in question.
- The cell with the highest affinity for the most abundant antigen will have growth advantage and will preferentially generate progeny of itself.
- This process is called clonal expansion and is antigen driven.





## MONOSIT (MONOCYTES )



- Sel darah terbesar, diameter :
- 3-8% dari total leukosit
- Nukleus : ukuran besar, berada dipinggir , berbentuk seperti ginjal
- Granul : granul azurophlic
- Fungsi : Lukosit migrasi ke jaringan ikat → berubah menjadi Makrofag → fagositosis dan sebagai APC (Antigen precenting cells)

# Lymphocyte

1. **Life Span:** variable (few days to several years)
2. **LM appearance in smear:** Small lymphocyte (about 90% of lymphocytes you will see) are ~8  $\mu\text{m}$  in diameter, while large lymphocytes may be up to about 15  $\mu\text{m}$ . Round, dense nucleus (abundant heterochromatin). The cytoplasm of a small lymphocyte is a narrow rim around the nucleus, and when well stained is pale blue. T-lymphocytes and B-lymphocytes cannot be distinguished in a smear.
3. **TEM appearance:** The cytoplasm doesn't appear to be very active, containing mainly mitochondria and free ribosomes.
4. **Function:** Cellular and humoral immunity (more detail in the lecture and lab on lymphatic system histology). In general:
  - B-lymphocytes (B-cells): may differentiate into tissue [plasma cells](#) which make antibodies. Some B-cells become memory cells.
  - T-lymphocytes (T-cells): cytotoxic T cells and helper T cells.

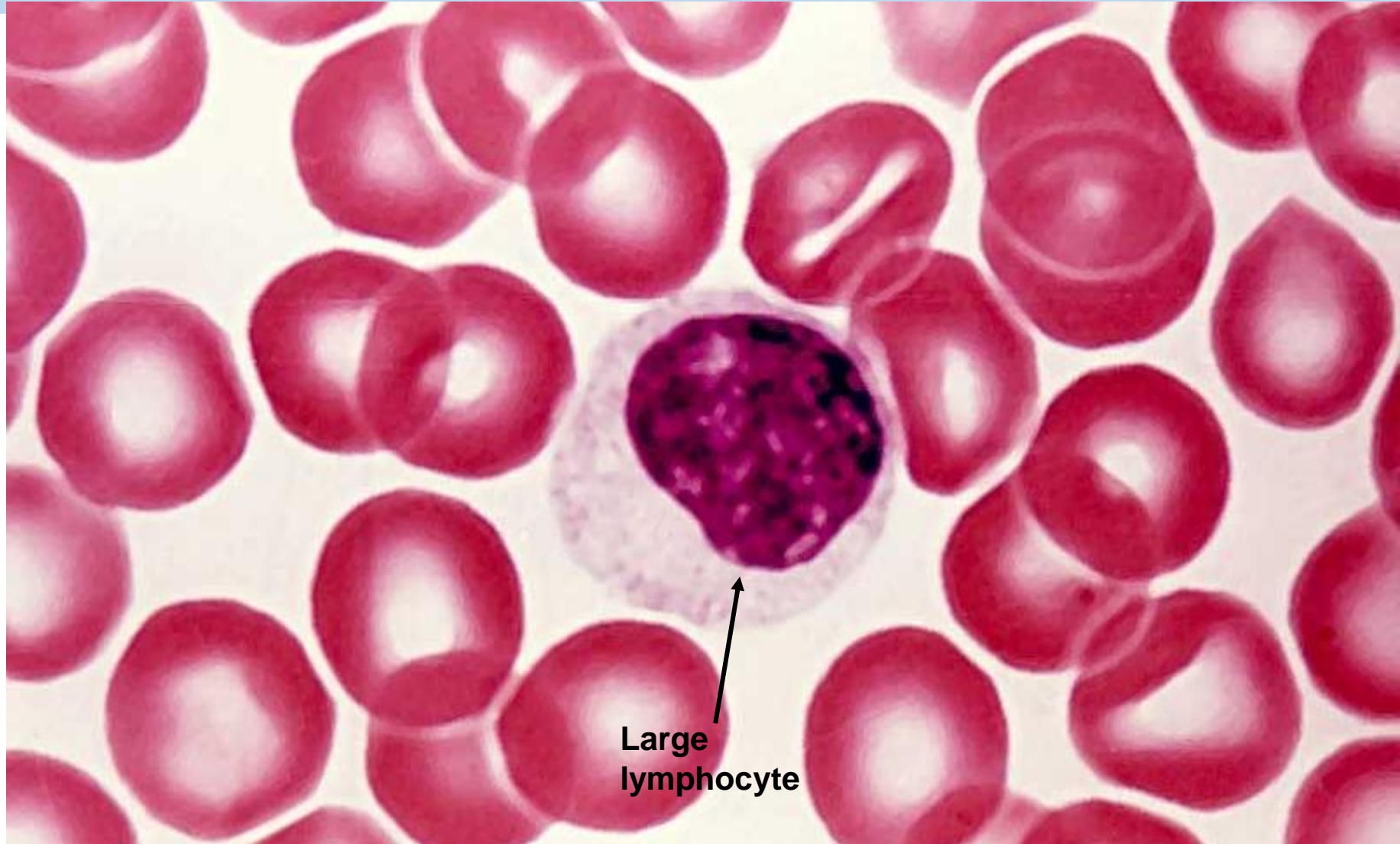
# Small lymphocyte in a blood smear



© PD-INEL Mizobuti histology slide set (J). J-186.

**LM appearance in smear:** Small lymphocyte (about 90% of lymphocytes you will see) are  $\sim 8 \mu\text{m}$  in diameter, while large lymphocytes may be up to about  $15 \mu\text{m}$ . Round, dense nucleus (abundant heterochromatin). The cytoplasm of a small lymphocyte is a narrow rim around the nucleus, and when well-stained is pale blue.

# Large lymphocyte in a blood smear



© PD-INEL Mizoguti slide set (J). J-187.

**LM appearance in smear:** Small lymphocytes (about 90% of lymphocytes you will see) are  $\sim 8 \mu\text{m}$  in diameter, while large lymphocytes may be up to about  $15 \mu\text{m}$  with ovoid, dense nuclei (abundant heterochromatin).

# Jenis Limfosit

- Ada tiga jenis limfosit :
  - **Limfosit B** (15% dari total limfosit). Bertanggung jawab pada humorally mediated immune response. Ketika distimulasi oleh antigen akan berubah menjadi sel yang memproduksi antibodi yaitu sel plasma .
  - **Limfosit T** ( 80 % dari total limfosit) bertanggung jawab pada cell-mediated immune response. Limfosit T harus melewati pematangan di organ Timus sebelum kompeten secara imunologis
  - **Null cells** ( 5% dari total limfosit), ada dua jenis yaitu *stem cells* dan *natural killer (NK) cells*.

# Rangkuman Jenis, Jumlah dan Fungsi Leukosit

Type	Nucleus	Specific Granules*	Differential Count <sup>b</sup> (%)	Life Span	Major Functions
<b>Granulocytes</b>					
Neutrophils	3-5 lobes	Faint/light pink	57-67	1-4 d	Kill and phagocytose bacteria
Eosinophils	Bilobed	Red/dark pink	1-3	1-2 wk	Kill helminthic and other parasites; modulate local inflammation
Basophils	Bilobed or S-shaped	Dark blue/purple	0-0.75	Several months	Modulate inflammation, release histamine during allergy
<b>Agranulocytes</b>					
Lymphocytes	Rather spherical	(none)	25-33	Hours to many years	Effector and regulatory cells for adaptive immunity
Monocytes	Indented or C-shaped	(none)	3-7	Hours to years	Precursors of macrophages and other mononuclear phagocytic cells

# Lokasi perkembangan leukosit

LEUKOSIT DIBENTUK DALAM SUMSUM TULANG DAN BERKEMBANG DALAM DUA ORGAN :

## 1. BURSA FABRICIUS.

ORGAN INI TERDAPAT PADA UNGGAS, PADA MANUSIA DISEBUT BURSA EQUIVALENT YANG LETAKNYA DIDUGA DI DALAM SALURAN CERNA, TEPATNYA BELUM DIKETAHUI PASTI LIMFOSIT DISINI AKAN MENJADI BURSA DEPENDENT LEUKOSIT ( **B-LIMFOSIT = B CELL** ), PADA KEADAAN TERTENTU BERUBAH MENJADI PLASMOSIT, YANG BERFUNGSI MEMBENTUK ANTIBODI (IMMUNOGLOBULIN) TERHADAP ANTIGEN – ANTIGEN SPESIFIK.

## 2. THYMUS

LIMFOSIT YANG BERKEMBANG DISINI AKAN MENJADI THYMUS – DEPENDENT LEUKOSIT ( T- LIMFOSIT = T – CELL ).

**FUNGSI : IMMUNITAS CELLULER.**

CONTOH : GRAFT REJECTION → SUATU REAKSI PENOLAKAN TERHADAP CANGKOK ORGAN.

## monosit

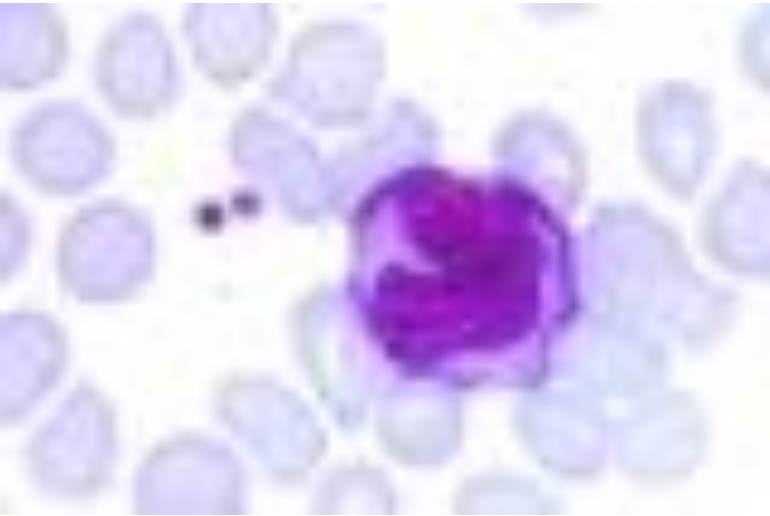
SEL DARAH TERBESAR DENGAN DIAMETER 12 –15 MIKRON, KADANG2 MENCAPAI 20 MIKRON.

JUMLAH 2 – 8 % DARI JUMLAH LEUKOSIT.

- INTI MONOSIT SEPERTI GINJAL ATAU KADANG BERGELAMBIR, SUSUNAN CHROMATIN LONGGAR HINGGA INTI TAMPAK SEPERTI BERBUIH.
- SITOPLASMA BIRU MUDA, MENGANDUNG BUTIR2 AZUROFIK.
- FUNGSI : FAGOSITOSIS, TERMASUK DALAM R.E.S ( RETICULO ENDOTHELIAL SYSTEM ).
- MONOSIT SETELAH DIKELUARKAN DARI SUTUL, AKAN BEREDAR DALAM DARAH, KEMUDIAN MASUK DALAM JARINGAN → MENJADI MACROFAG.



# Monocytes




- Monocytes circulate in the blood and pass through blood vessel walls to enter tissues, where they become macrophages.
- Macrophages along with neutrophils, are scavengers in the body. These cells dispose of debris from dead cells as well as bacteria and other foreign cells by engulfing these in a process called phagocytosis.

# Monocyte

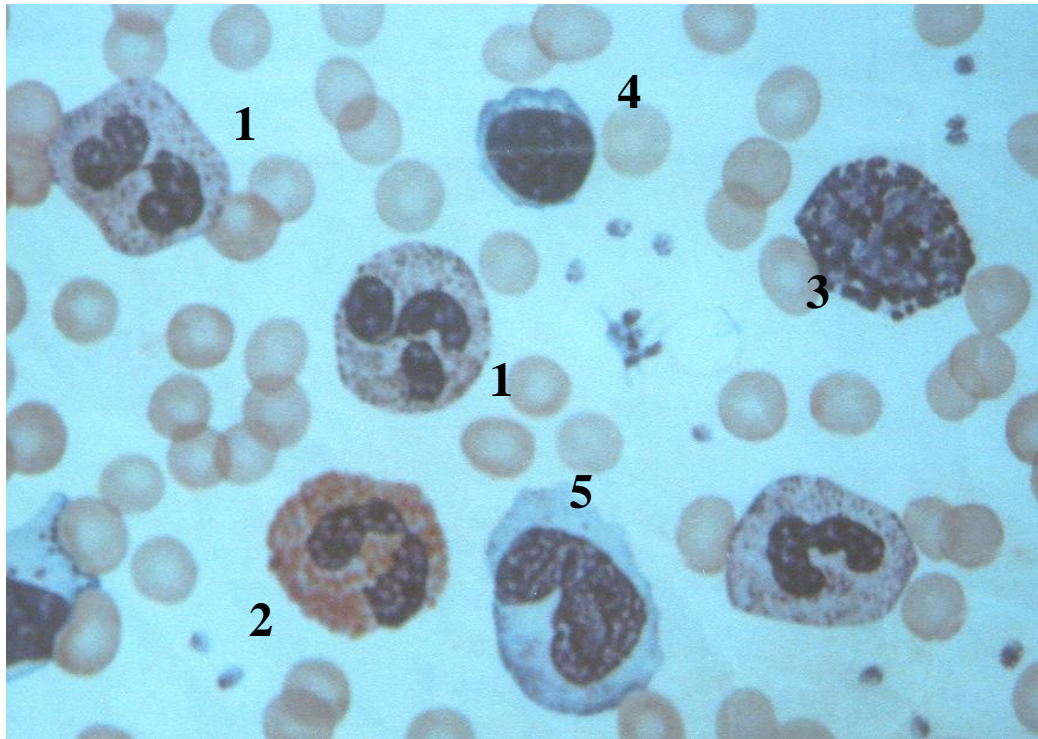
1. **Life Span:** few days in blood, several months in connective tissue
2. **LM appearance in smears:** About 16  $\mu\text{m}$  in smears, thus the largest leukocyte. Large, eccentric nucleus either oval, kidney-shaped or horseshoe-shaped, with delicate chromatin that is less dense than that of lymphocytes. Pale cytoplasm, often grayish, may contain occasional stained granules (lysosomes = azurophilic granules). Large lymphocytes may resemble monocytes, but the lymphocyte nucleus is usually more dense.
3. **TEM appearance:** Cytoplasm contains mitochondria and some small lysosomes.
4. **Function**
  - Migrate into tissues and constitute mononuclear phagocyte system that help destroy foreign bodies and maintain or remodel tissues  
Tissue macrophages    Kupfer cells (liver)                      Osteoclasts (bone)  
Dust cells (lungs)                      Microglia (brain)
  - Mediate inflammatory response
  - Antigen presenting cells: **Dendritic Cells, Langerhans cells**

# Monocyte in a blood smear

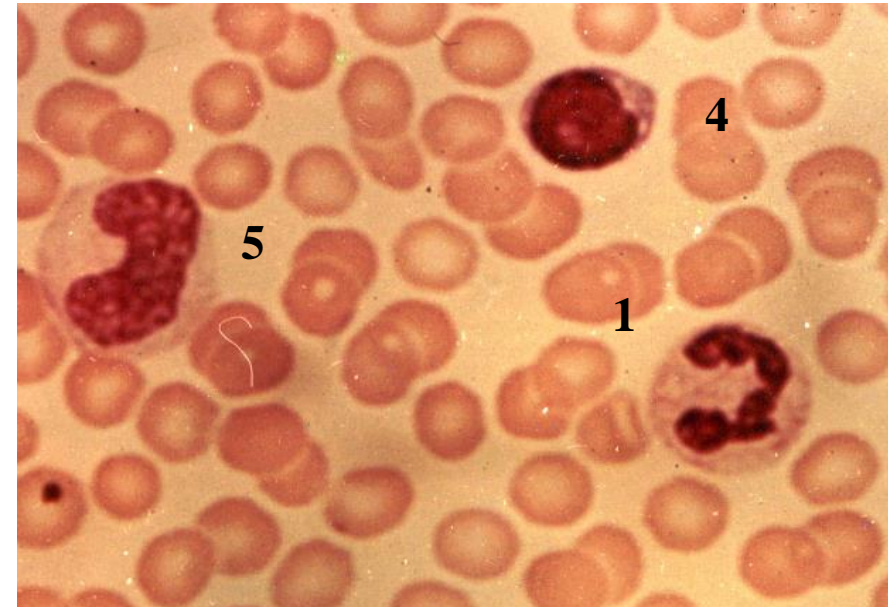


 Mizoguti slide collection (J). J-188.

**LM appearance in smears:** About  $16\ \mu\text{m}$  in smears, thus the largest leukocyte. Large, eccentric nucleus either oval, kidney-shaped or horseshoe-shaped, with delicate chromatin that is less dense than that of lymphocytes. Pale cytoplasm, often grayish, may contain occasional stained granules (lysosomes = azurophilic granules). Large lymphocytes may resemble monocytes, but the lymphocyte nucleus is usually more dense.



1. Segmen neutrofil
2. Segmen eosinofil
3. Segmen basofil
4. Limfosit
5. Monosit



## PENYAKIT - PENYAKIT DARAH

### 1. Erythroblastosis foetalis

Ayah (Rh +) X Ibu (Rh -) → Anak (Rh +)

→ anak II letal (lahir mati)

### 2. Thalasemia : - gen

- umur erythrosit pendek

### 3. Hemofilia : gangguan proses pembekuan darah

## PENYAKIT - PENYAKIT DARAH

4. Leukemia : jumlah lekosit meningkat &  
ganas

5. Anemia : kadar Hb rendah

Penyebab : - kekurangan nutrisi

- kelainan bawaan

- perdarahan

Akut : luka yang hebat

Kronis : - Hemorhoid

- Menstruasi

- Cacingan

# Granulosit



- ***Neutrofil***
- Memiliki inti
- Berukuran sekitar 8 mikron
- Bersifat fagosit dengan cara masuk ke jaringan yang terinfeksi
- Aktif selama 6-20 jam



- ***Eusinoofil***
- memiliki inti
- Bersifat fagosit lemah
- Berbentuk hampir seperti bola
- Berukuran sekitar 9 mikron

## NEUTROFIL (NEUTROPHILS )



- 60-70% dari total leukosit
- Diameter : 9-12  $\mu\text{m}$
- Nukleus Multilobe
- Pada Wanita : drum stick/Barr Body
- Granul:
  - Granul Spesifik ukuran kecil
  - Granul Azurophilic (Lysosomes)
  - Tertiary granules (gelatine and cathepsins)
- Fungsi :
  - Phagocytes



# Neutrophil (polymorphonuclear leukocyte)

1. **Life Span:** < 1 week

2. **Granulocyte with specific and non-specific granules**

Specific granules

- Type IV collagenase (aids migration)
- Lactoferrin (sequesters iron)
- Phospholipase A<sub>2</sub> (leukotriene synthesis)
- Lysozyme (digests bacterial cell wall)

Non-specific granules (lysosomes)

- Lysozyme
- Acid hydrolase
- Myeloperoxidase
- Elastase

3. **LM appearance in smear:** About 9-12 µm in diameter (thus larger than RBC). Nucleus long and multi-lobed (usually 2-4 lobes).

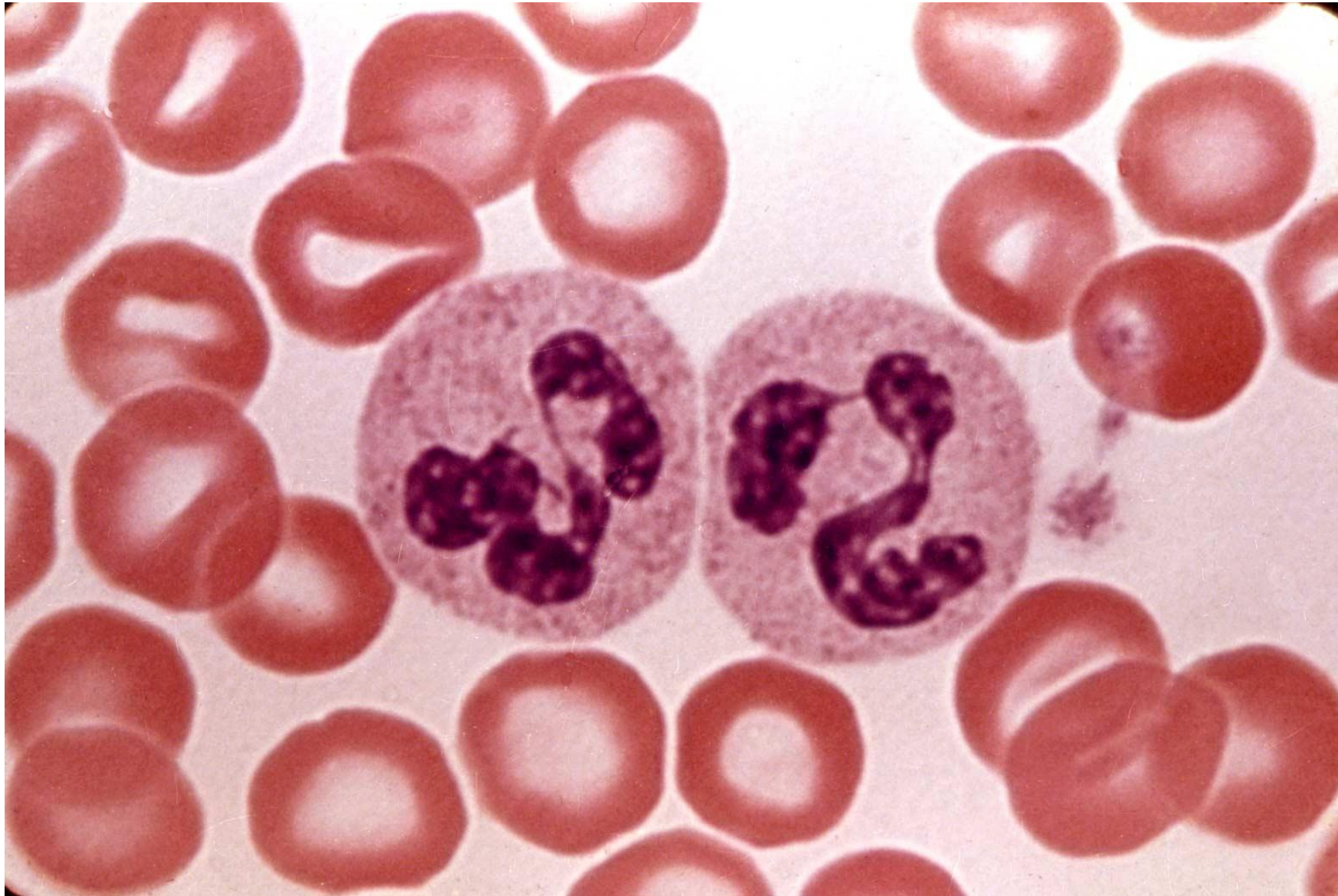
4. Cytoplasm has small, neutrally stained specific granules. Non-specific granules are azurophilic.


5. **TEM appearance:** Multi-lobed nucleus and numerous specific granules and lysosomes (=azurophilic granules in LM).

6. **Function:** Primarily antibacterial

- Neutrophils leave the blood and follow chemotaxic signals to sites of wounding or other inflammation, and phagocytose foreign agents such as bacteria. Pus is composed largely of dead neutrophils.

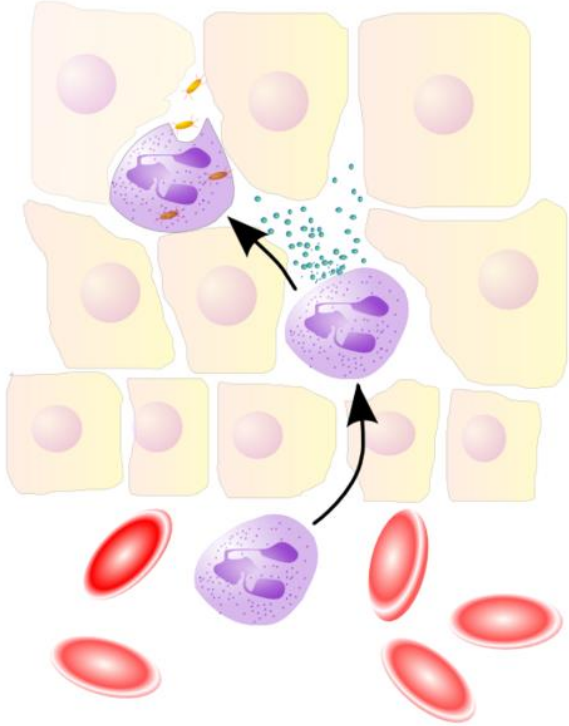
## Two neutrophils in a blood smear



 Mizoguti slide set (J). J-196.

**LM appearance in smear:** About 9-12  $\mu\text{m}$  in diameter (thus larger than RBC). Nucleus long and multi-lobed (usually 2-4 lobes). Cytoplasm has small, neutrally stained specific granules. Non-specific granules are azurophilic.

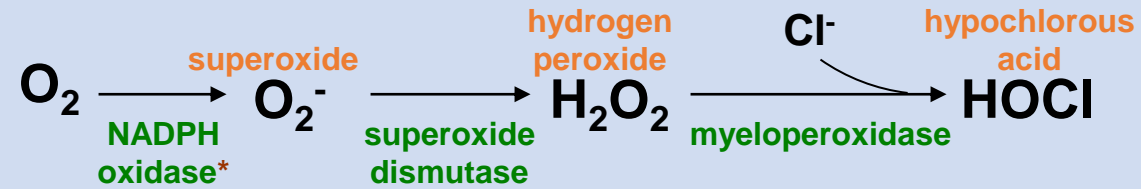
# Extravasation via diapedesis



- Selectin-selectin receptor interaction causes neutrophil to slow & roll along surface.
- Chemokines from endothelium leads to expression of integrins & immunoglobulin family adhesion molecules on neutrophil cell membrane.
- Neutrophil firmly attached to vessel wall & extends pseudopod into vessel wall.
- Vascular permeability mediated by heparin & histamines released by mast cells/basophils.
- Once in connective tissue, neutrophils respond to chemoattractants & migrate to injury site.

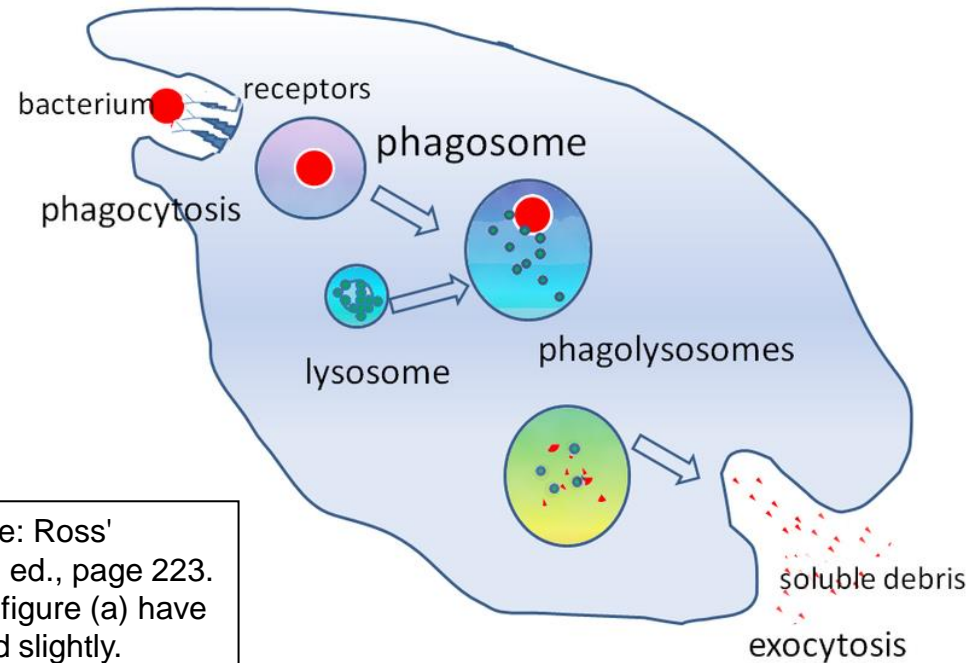
# Neutrophil antibacterial activity

1. Chemotaxis and migration (chemokine synthesis and matrix proteolysis)
2. Phagocytosis and bacterial destruction
  - Digestion via lysozymes
  - Production of reactive oxygen compounds (respiratory burst)



\*deficiency increases risk of persistent bacterial infections

- Iron sequestration via lactoferrin
3. Release factors to increase inflammatory response (and increase neutrophil production)



Original image: Ross' Histology, 4th ed., page 223. The labels to figure (a) have been modified slightly. PMNfunction-Ross4-223.tif.

# Eosinophil

1. **Life Span:** < 2 weeks

2. **Granulocyte with specific and non-specific granules**

Specific granules

- Major basic protein
- Eosinophilic cationic protein
- Neurotoxin
- Histaminase

Non-specific granules (lysosomes)

- Lysozyme
- Acid hydrolase
- Myeloperoxidase
- Elastase

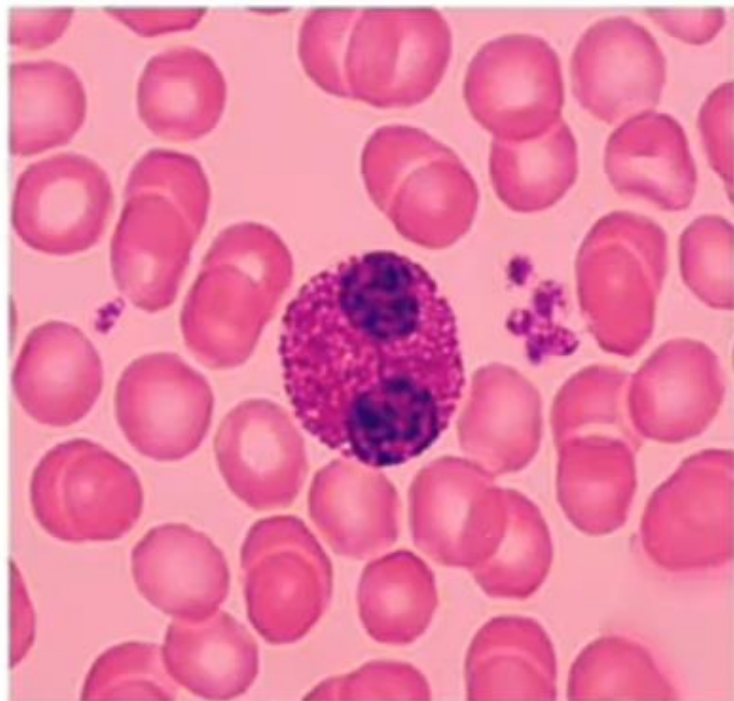
2. **LM appearance in smear:** About 10-14  $\mu\text{m}$  in diameter. Bilobed nucleus. The cytoplasm has prominent pink/red specific granules (stained with eosin dye). If the smear is not stained properly, the granules may be brownish.

3. **TEM appearance:** The specific granules are ovoid in shape, and contain a dark crystalloid body composed of major basic protein (MBP), effective against parasites. The rest of the granule contains other anti-parasitic substances. The cytoplasm also contains lysosomes (=azurophilic granules).

4. **Function:**

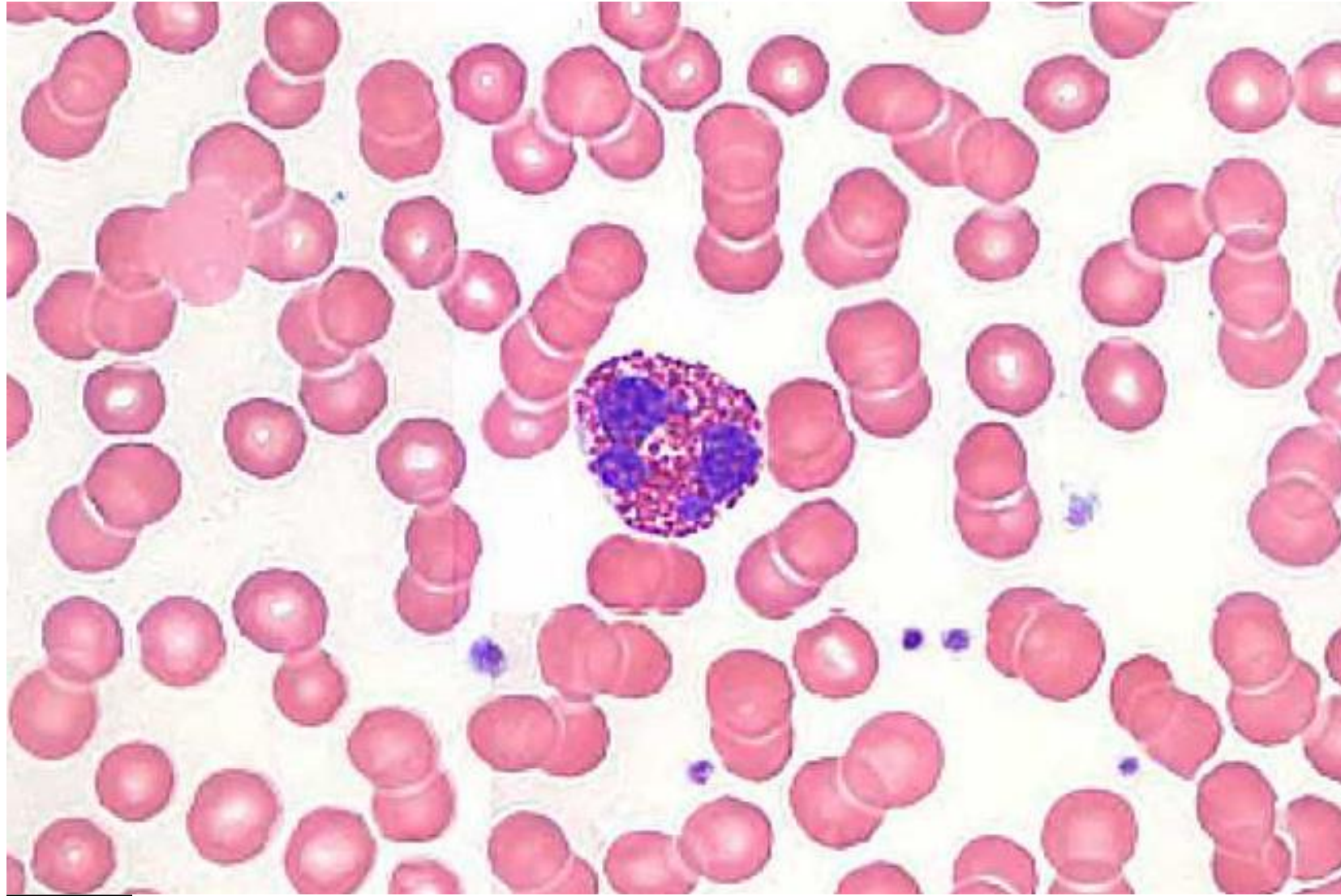
- Anti-parasitic activity
- Mediators of inflammatory/allergic responses in tissues
  - Inactivate leukotrienes and histamine secreted by basophils
  - Engulf and sequester antigen-antibody complexes
  - Inflammatory stimulus increases production/release of eosinophils from bone marrow, whereas inflammatory suppression decreases eosinophil numbers in peripheral blood.
  - But, they also secrete PRO-inflammatory chemokines AND they can degranulate inappropriately to cause tissue damage (as in reactive airway disease)

## EOSINOFIL (EOSINOPHILS)



- 4% dari total leukosit
- Diameter : 10 - 14  $\mu\text{m}$
- Nukleus : Bilobus
- Granule :
  - Granul spesifik ukuran besar tercat ke merahan (eosin).
  - Granul Azurophilic
- Pada membran ditemukan reseptor IgG, IgE, dan komplemen
- Fungsi :
  - Mengeliminasi kompleks antigen-antibodi
  - Pertahanan terhadap parasit/cacing

# Eosinophil in a human blood smear



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**LM appearance in smear:** About 10-14  $\mu\text{m}$  in diameter. Bilobed nucleus. The cytoplasm has prominent pink/red specific granules (stained with eosin dye). If the smear is not stained properly, the granules may be brownish.

- ***Basofil***

Bentuknya bulat atau oval

Meninggalkan sistem sirkulasi dan terakumulasi dalam cairan interstitial pada tempat infeksi atau peradangan, melepas toksin yang membunuh mikroorganisme penyusup dan parasit.





# Basophil

1. **Life Span:** 1-2 years (?)

2. **Granulocyte with specific and non-specific granules**

Specific granules

- Histamine
- Heparin
- Eosinophil chemotactic factor
- Phospholipids for synthesis of leukotrienes, e.g. slow-reacting substance of anaphylaxis ( SRS-A )

Non-specific granules (lysosomes)

- Lysozyme
- Acid hydrolase
- Myeloperoxidase
- Elastase

2. **LM appearance in smear:** About 8-10  $\mu\text{m}$  in diameter. The cytoplasm contains large, purple/black specific granules (stained with the basic dye) that are larger but not as numerous as those of eosinophils. The nucleus is usually bilobed, but usually is partially obscured by granules, which can lie over it.

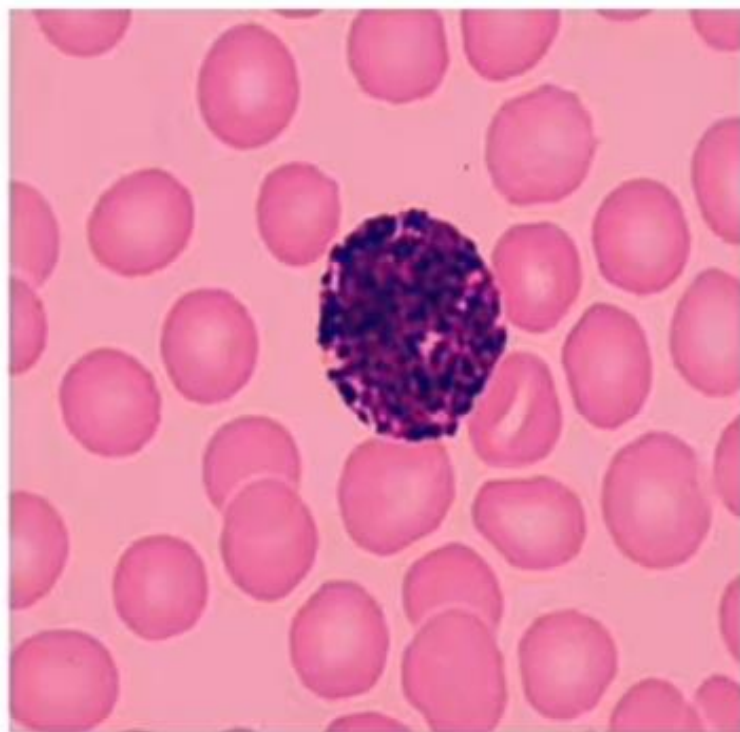
3. **TEM appearance:** The specific granules vary in size and shape, and have occasional myelin figures (usually formed from phospholipids). The cytoplasm also has some lysosomes (=azurophilic granules).

4. **Function:** Allergies and anaphylaxis (hypersensitivity reaction)

- Binding of antigens to membrane-bound IgE antibodies induces degranulation of specific granules, which leads to allergic reaction.
- In hypersensitivity reaction, widespread vasodilation (arteriolar) and vessel leakiness induce circulatory shock. Bronchial spasms cause respiratory insufficiency; combined effect is anaphylactic shock.

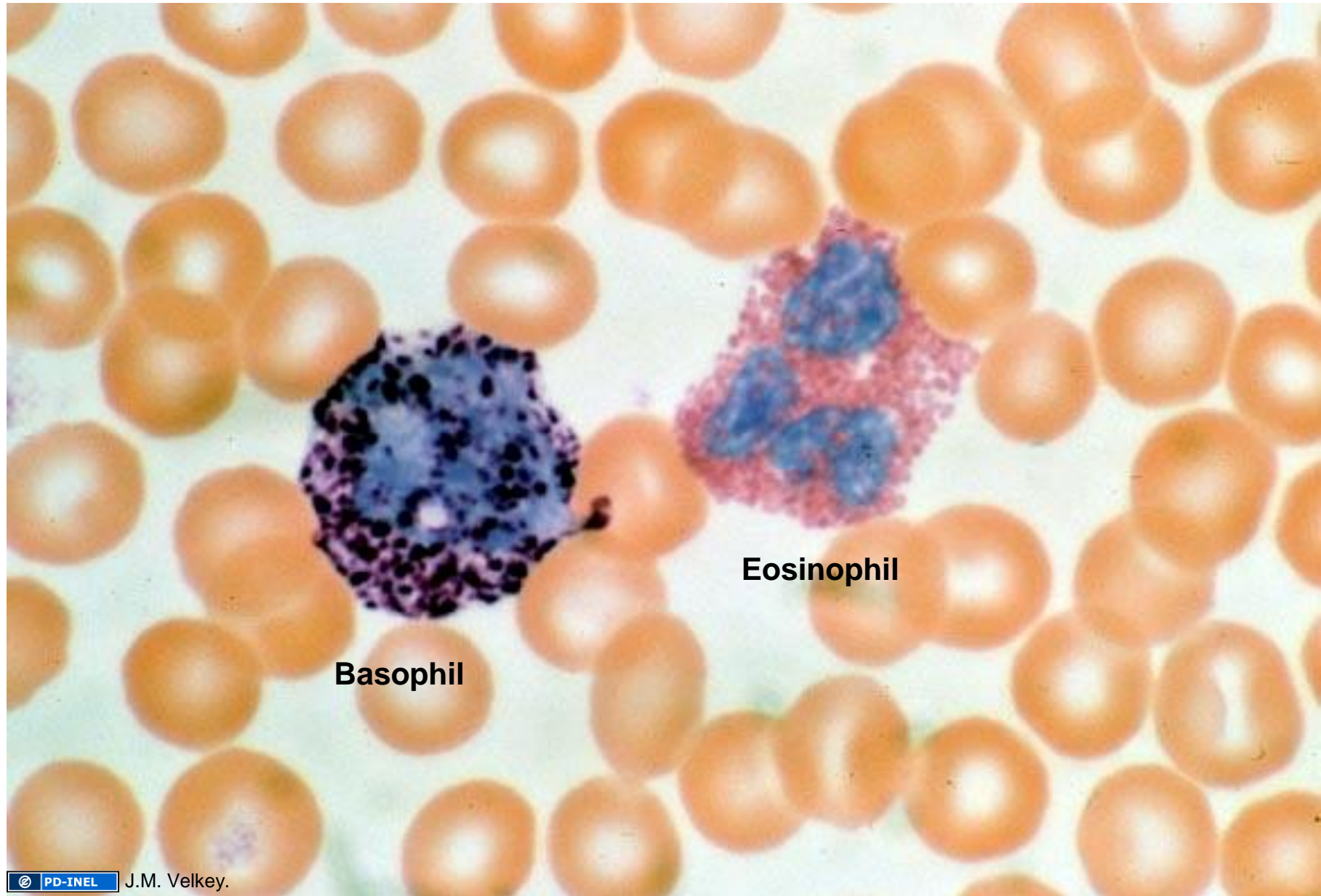
5. **Similarity to tissue mast cells:** Tissue mast cells also have IgE receptors and similar (though not identical) granule content. Mast cells and basophils have a common precursor in bone marrow.

# BASOFIL (BASOPHILS)



- kurang dari 1% total leukosit
  - diameter :8-10  $\mu\text{m}$
  - Nukleus : berbentuk S-s (irregular lobes)
  - Granul :
    - Spesifik granul, besar-besar  $\rightarrow$  menutupi nukleus .  
Berwarna biru gelap menandung heparin dan histamin
    - Granul Azurophilic
- Pada permukaan sel ditemukan reseptor Ig E
- Fungsi :
  - Inisiasi proses inflamasi

# Comparison of basophil and eosinophil in a blood smear



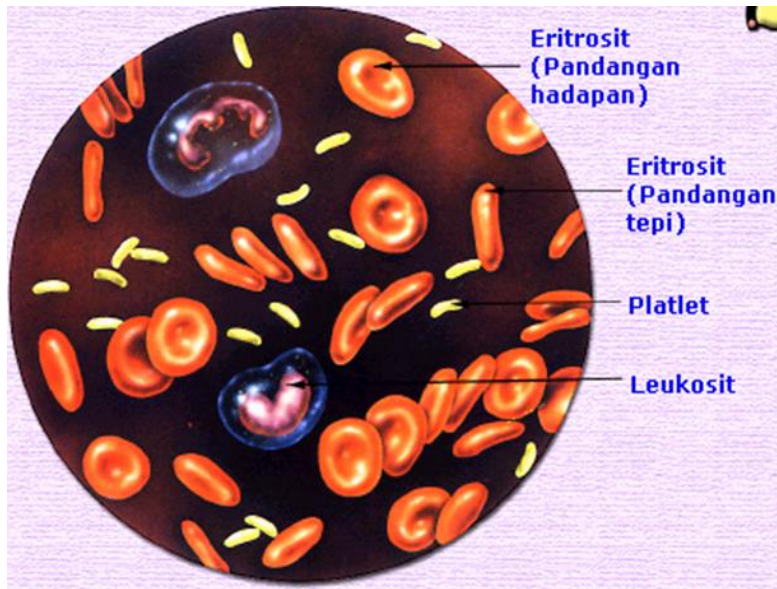
# PLATELET

- Platelet disebut juga trombosit
- Berada dalam sirkulasi 9-12 hari
- N : 350.000/ $\mu$ l
- 1/3 berada di limpa
- Fungsi :
  1. Transport zat-zat kimia penting dalam proses pembekuan darah.
  2. Perlindungan sementara dari kebocoran pembuluh darah
  3. Kontraksi aktif setelah terbentuknya bekuan darah.

# Platelets (thrombocytes)

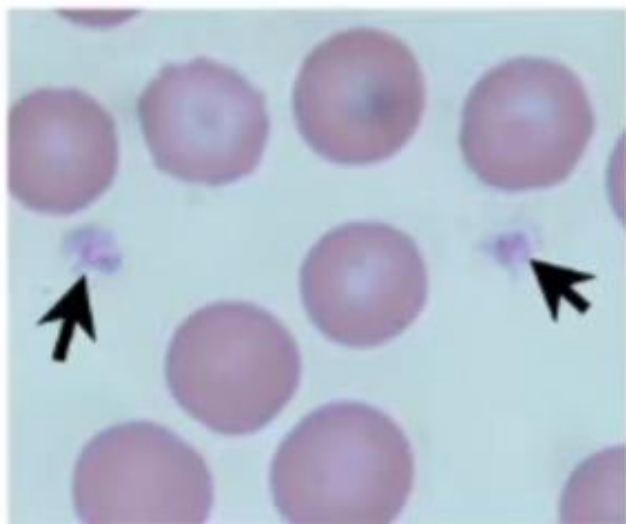
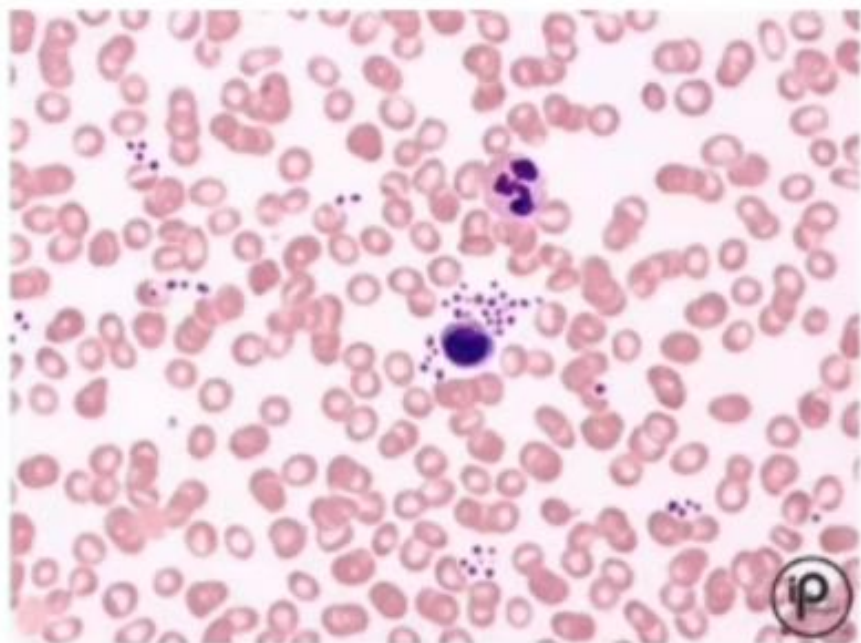
1. **Life Span:** about 10 days
2. **Shape, size, and origin:** Small, biconvex disks, 2-3  $\mu\text{m}$  in diameter. Non-nucleated cell fragments derived from cytoplasm of a very large cell, the megakaryocyte, in bone marrow. Platelets have a life span of about 10 days.
3. **LM appearance in smears:** Small basophilic fragments, often appearing in clusters.
4. **TEM appearance:** The platelet is bounded by a plasma membrane, and has a bundle of microtubules around the margin of the disk (which maintains the disk shape). There are three types of granules, containing fibrinogen, plasminogen, thromboplastin and other factors for clotting. There are also membrane tubules and glycogen.
5. **Function:** Platelets initiate blood clots.

# Trombosit



- Masa hidupnya 5-9 hari
- Memainkan peran penting dalam pembekuan darah.

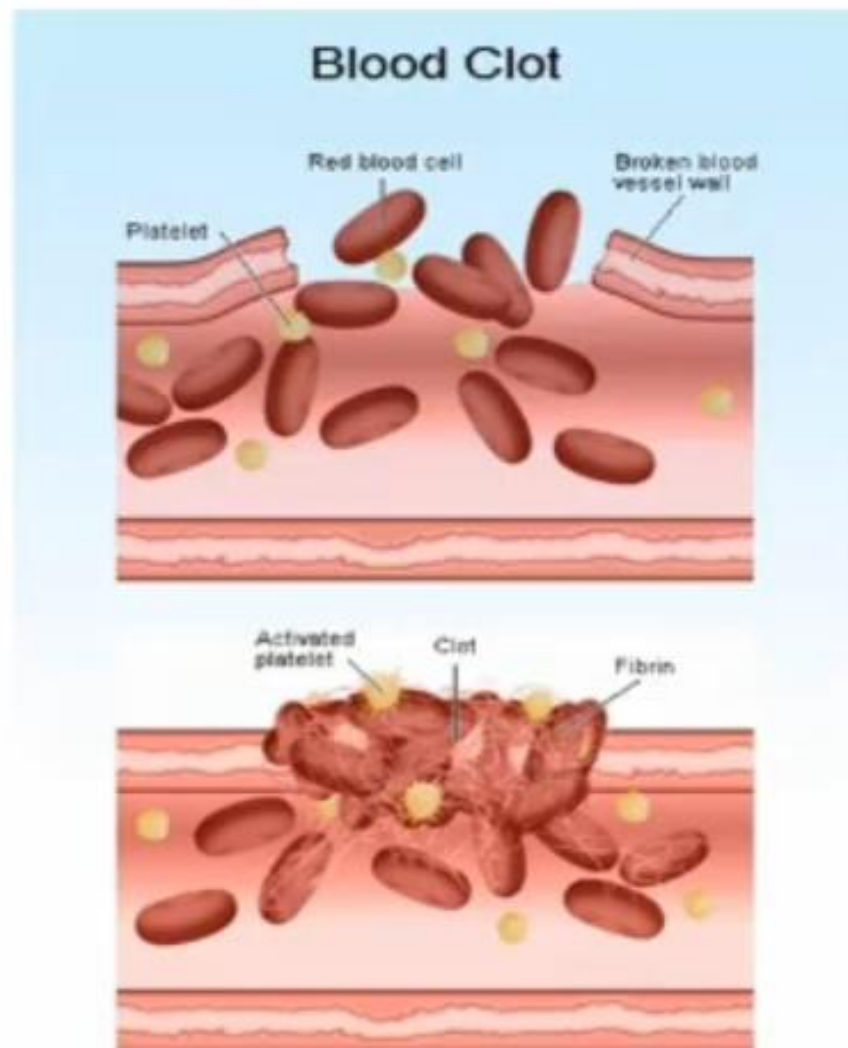
## Keping darah (PLATELETS)



- Jumlah : 250.000-400.000 /mm<sup>3</sup>
- Bentuk : Discoid, diameter 2 - 4  $\mu\text{m}$
- Daerah terang di pinggir (**hyalomere**) dan gelap di tengah(**granulomere**)
- Masa hidup :10 hari
- Diproduksi oleh : sel megakaryosit

# Fungsi Platelet

Berperan dalam proses pembekuan darah (Hemostasis)





## Karakteristik Trombosit

<i>Terdapat</i>	Dalam pembuluh darah
Dihasilkan	Sumsum tulang
<i>bentuk</i>	Berbentuk bulat, bulat lonjong atau spindle, cakram
<i>umur</i>	5-9 hari
<i>inti</i>	Tidak memiliki inti

# Perbandingan sel-sel darah

No	Pembeda	Eritrosit	Leukosit	Trombosit
1.	Tempat Produksi	Sumsum tulang	Sumsum tulang & buku limfa	Sumsum tulang
2.	Jumlah	5.000.000/mm <sup>3</sup>	7.000/mm <sup>3</sup>	250.000/mm <sup>3</sup>
3.	Ukuran	7,5 μm	5 – 9 μm	2 – 4 μm
4.	Bentuk	Bulat pipih, bikonkaf	Tidak beraturan	Tidak beraturan
5.	Struktur	<ul style="list-style-type: none"> <li>○ Tanpa nukleus</li> <li>○ Ada hemoglobin (Hb)</li> </ul>	<ul style="list-style-type: none"> <li>○ Ada Nukleus</li> <li>○ Tanpa Hemoglobin</li> </ul>	<ul style="list-style-type: none"> <li>○ Tanpa Nukleus</li> <li>○ Tanpa Hb</li> </ul>
6.	Fungsi	Membawa O <sub>2</sub> dari paru-paru ke seluruh bagian tubuh	<ul style="list-style-type: none"> <li>○ Memakan kuman</li> <li>○ Menghasilkan antibodi untuk membunuh kuman</li> </ul>	Pembekuan darah