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Blood and Bone Marrow

M1 – Immunology Sequence

J. Matthew Velkey, Ph.D.

Fall 2008

Learning Objectives

Reading assignment: Ross and Pawlina, Ch. 10 (Blood and Hemopoiesis)

1. Be able to recognize all of the formed elements found in peripheral blood by light and electron microscopy.
2. Know the approximate abundance and life span of the formed elements.
3. Understand the functions of major plasma proteins and all of the formed elements.
4. Be familiar with the general process of hematopoeisis.
5. Describe the organization of the bone marrow.
6. Be able to recognize megakaryocytes in the bone marrow and understand their function in platelet production.

Functions of the Blood

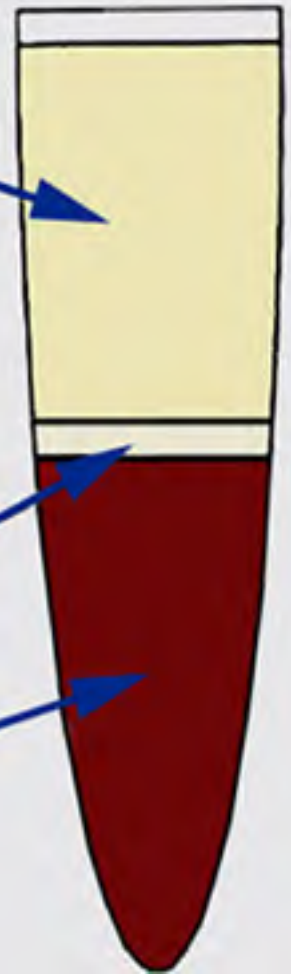
1. To transport nutrients, oxygen, wastes, and carbon dioxide to and from the tissues.

2. To convey hormones, cytokines, chemokines, and other soluble regulatory molecules.

3. To transport leukocytes and antibodies through the tissues.

4. To maintain homeostasis.

Contents of 1 μl of Peripheral Blood



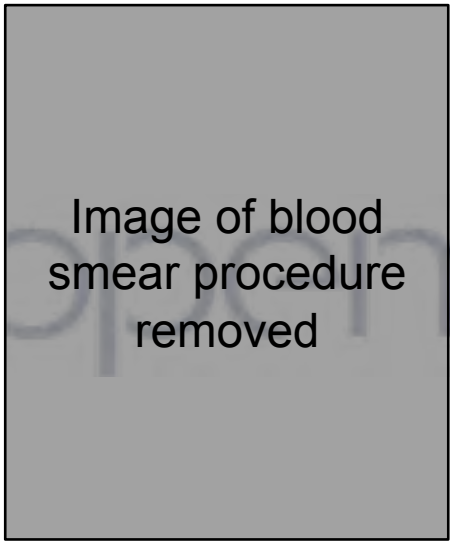
Major Plasma Proteins

Protein	Function
Albumin	Maintain colloid osmotic pressure;
Globulins	
α and β	Transport metal ions, protein-bound
γ	Antibodies for host defense
Complement proteins	Destruction of microorganisms
Clotting factors	Formation of blood clots
Plasma lipoproteins	Transport of triglycerides and

Cells of the blood

- **Erythrocytes** (red blood cells, RBC)
- **Platelets** (thrombocytes)
- **Leukocytes** (white blood cells, WBC)
  - **Granulocytes** (with specific granules)
    - **Neutrophil (~60% of WBC)**
    - **Eosinophil (~4% of WBC)**
    - **Basophil (<1% of WBC)**
  - **Agranulocytes** (without specific granules)
    - **Lymphocyte (B-cell, T-cell) (~27% of WBC)**
    - **Monocyte (~8% of WBC)**

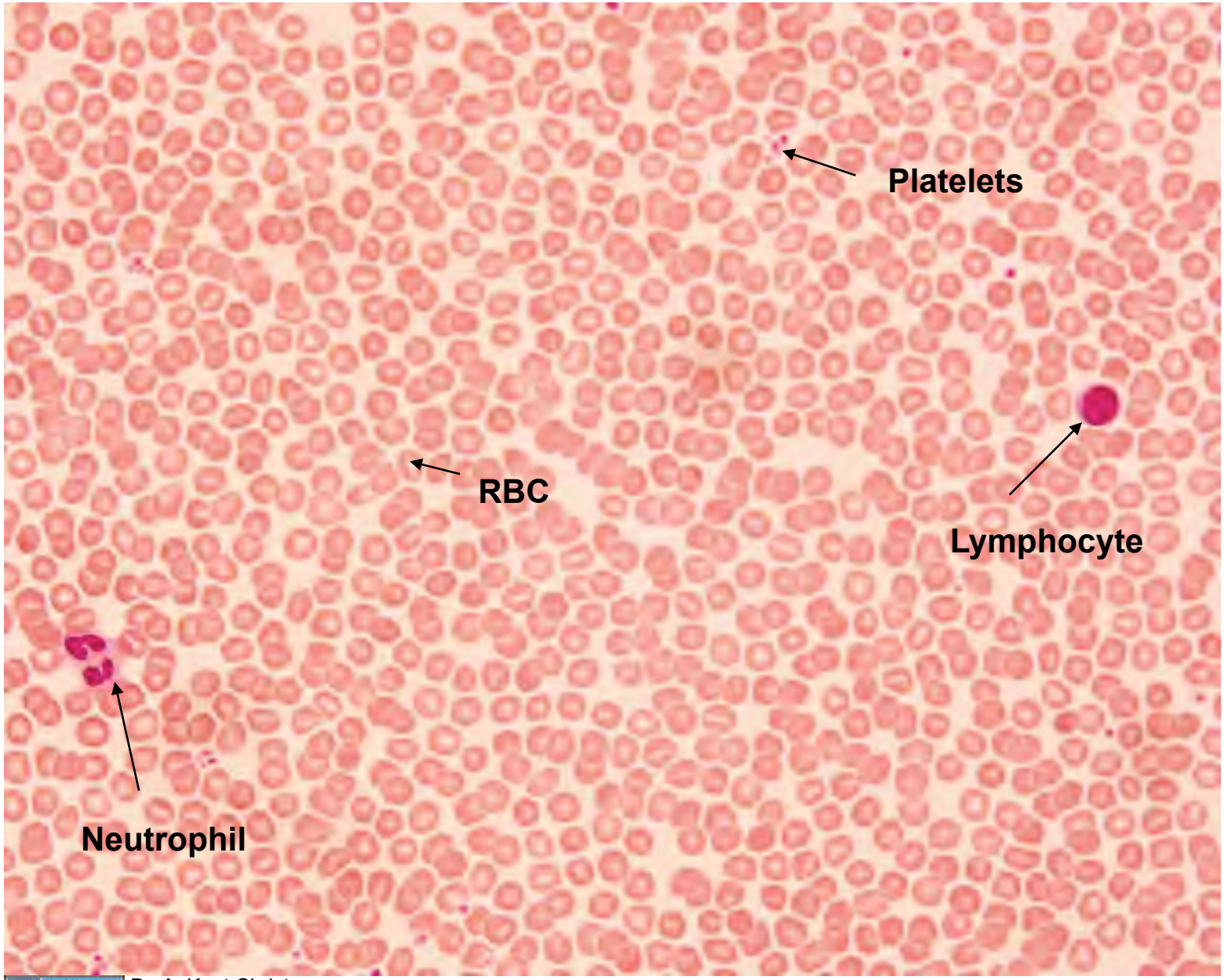
FYI, blood smear procedure



Original Source: Junqueira's histology text, 6th ed., page 231. BloodSmear-23J91(2).tif.

- The procedure for making a blood smear is shown at left.
- After the smear is made, it is air-dried and then stained. Common stains are Wright's stain and Giemsa stain. The stains generally include two or more dyes, one of them a basic dye (often methylene blue) and another an acidic dye (usually eosin). Reddish-blue azures are formed when methylene blue is oxidized (metachromasia). Cells usually stain pink/red with acidic dye and nuclei stain purple/black with basic dye, while specific granules stain characteristically.
- Remember that the cells you see in a blood smear have not been sectioned. Instead you are seeing whole cells dried down on the glass.

Human blood smear, with RBCs, WBCs and platelets

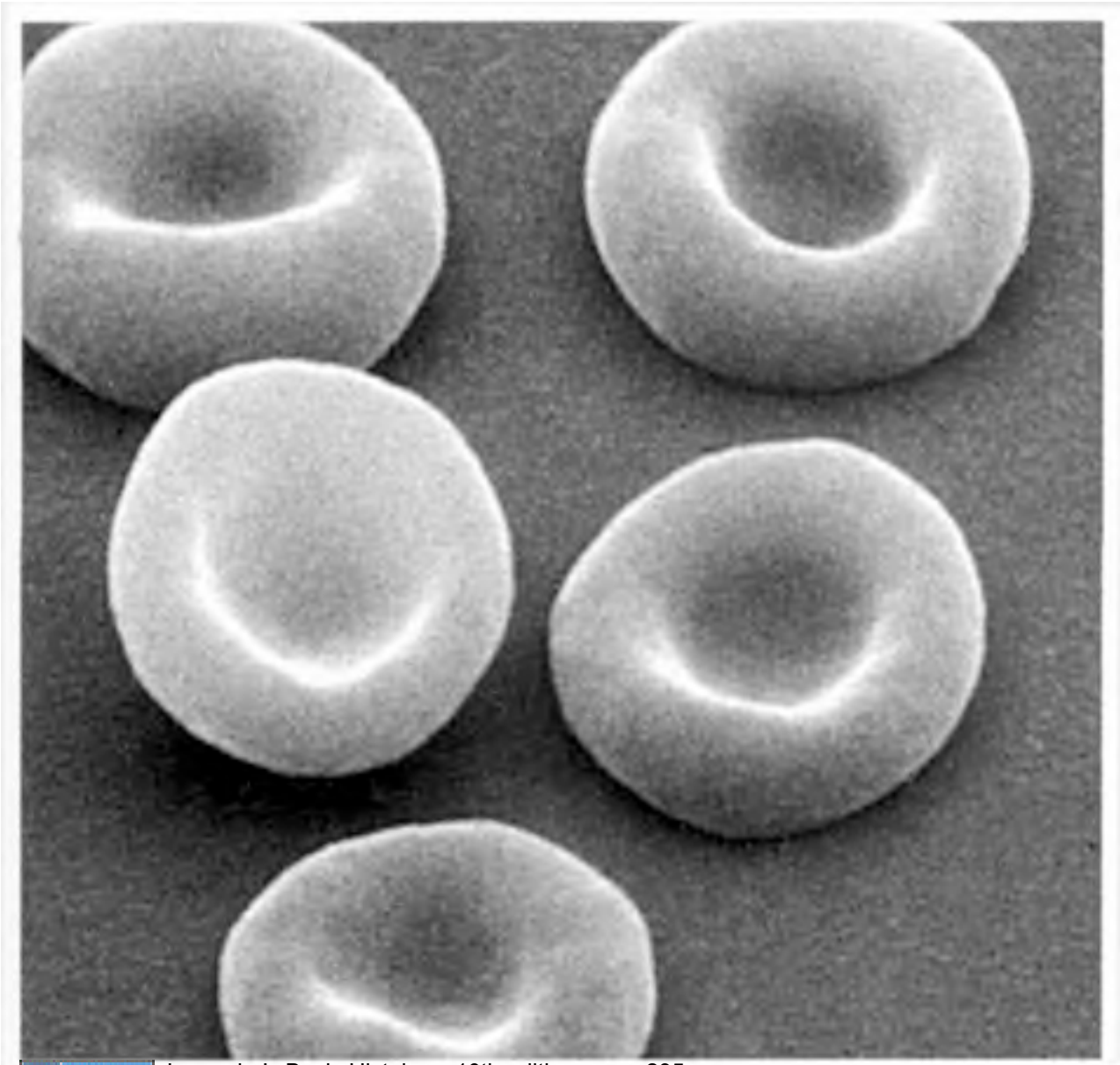


PD-INEL Dr. A. Kent Christensen

Erythrocyte (red blood cell, RBC)

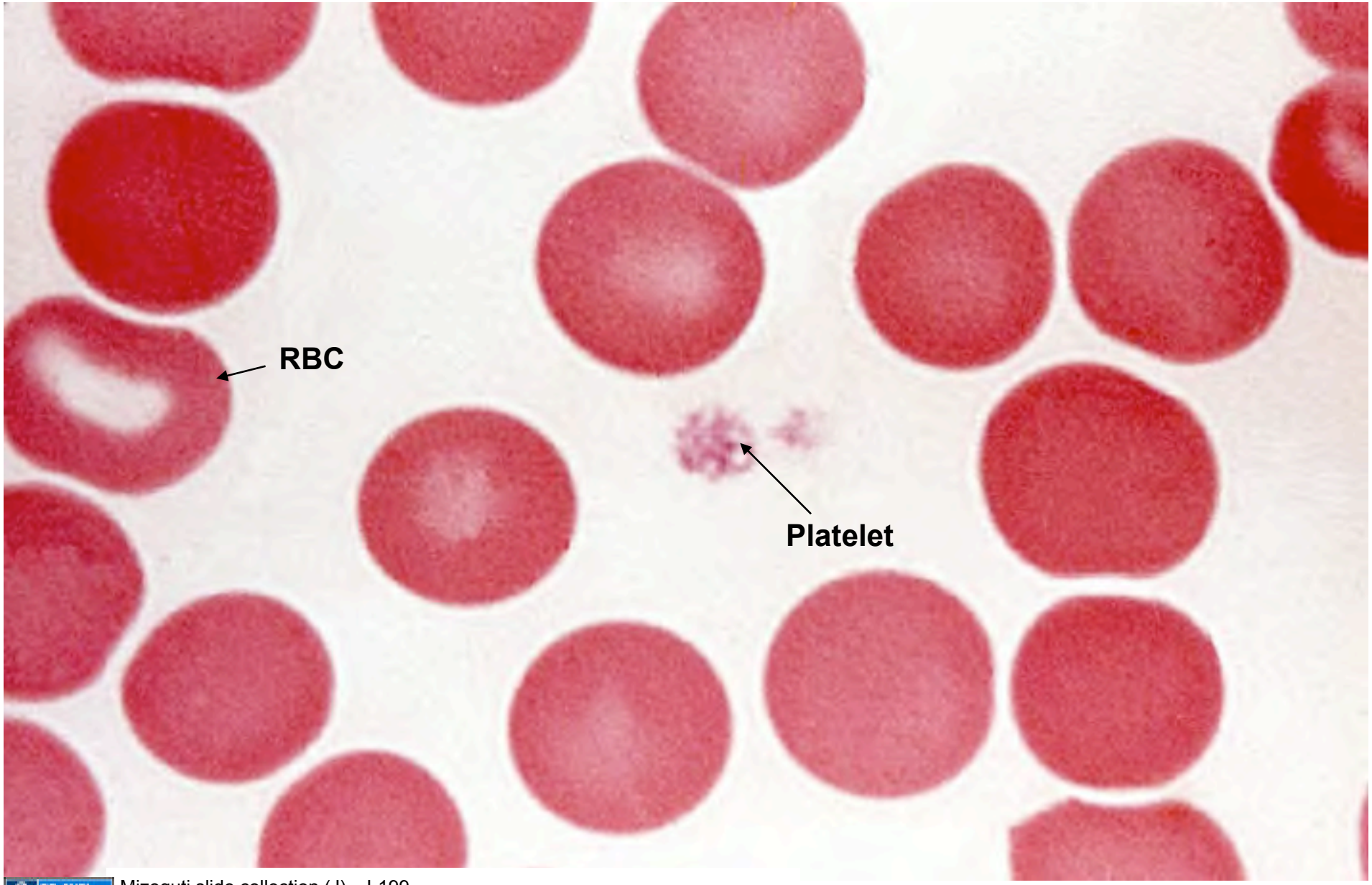
1. **Life span in blood:** About 120 days.
2. **Size and shape:**
   - biconcave disk, 8 μm diameter, 2μm at thickest point, 1 μm at thinnest
   - shape maintained by a cytoskeletal complex inside the plasma membrane (involving spectrin, actin and other components)
   - flexible: RBC's normally bend to pass through small capillaries
3. **LM appearance in smear:** Pink circle with light center (center is thinner because of the biconcave shape). No nucleus.
4. **TEM appearance:** Solid dark gray cytoplasm, because of highly concentrated hemoglobin.
5. **Function:**
   - Transport of oxygen and carbon dioxide
     - bound to hemoglobin (oxyhemoglobin and carboxyhemoglobin)
     - majority of CO_2 transported as HCO_3^-
   - pH homeostasis
     - carbonic anhydrase: $CO_2 + H_2O \rightarrow HCO_3^- + H^+$
     - band 3 membrane protein: exchanges HCO_3^- for extracellular Cl^-

RBCs, scanning electron microscopy



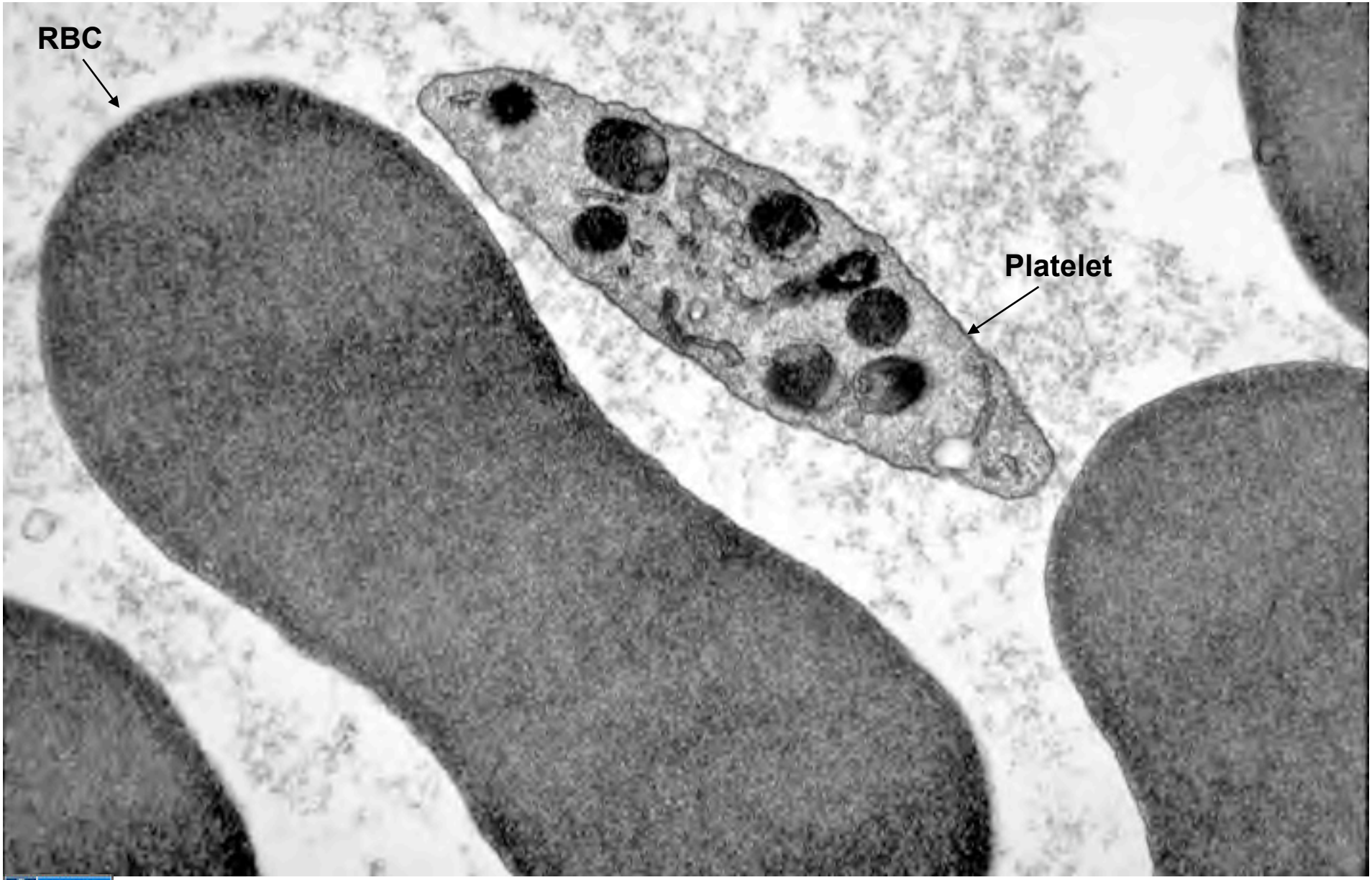
PD-INEL Junqueira's Basic Histology, 10th edition, page 235

Red blood cells in a blood smear



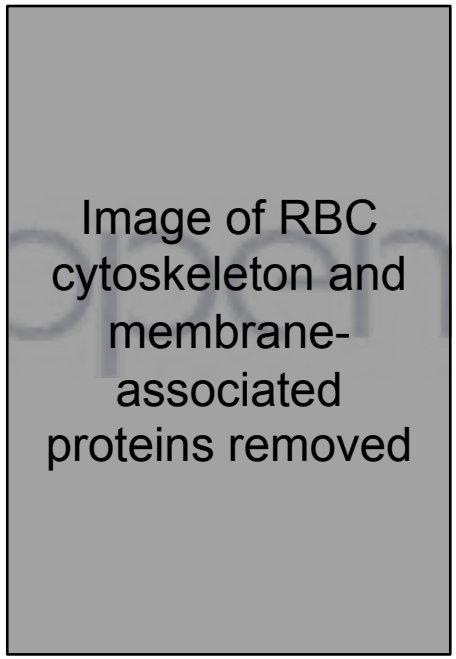
 Mizoguti slide collection (J). J-199.

RBC, transmission electron microscopy



 Erlandsen's slide set (MH). MH-2G3..

RBC Cytoskeleton and Membrane-Associated Proteins



Original Source: Ross' Histology, 4th edition, page 219. RBCmemb-Ross4-219.tif.

- Hereditary spherocytosis: defective spectrin; RBCs are fragile and destroyed in spleen leading to anemia.
- A,B,O blood antigens: antigenic carbohydrate chains on extracellular domain of glycophorins
- Rh antigen: multipass integral membrane protein (similar to band 3), also comprises a blood group

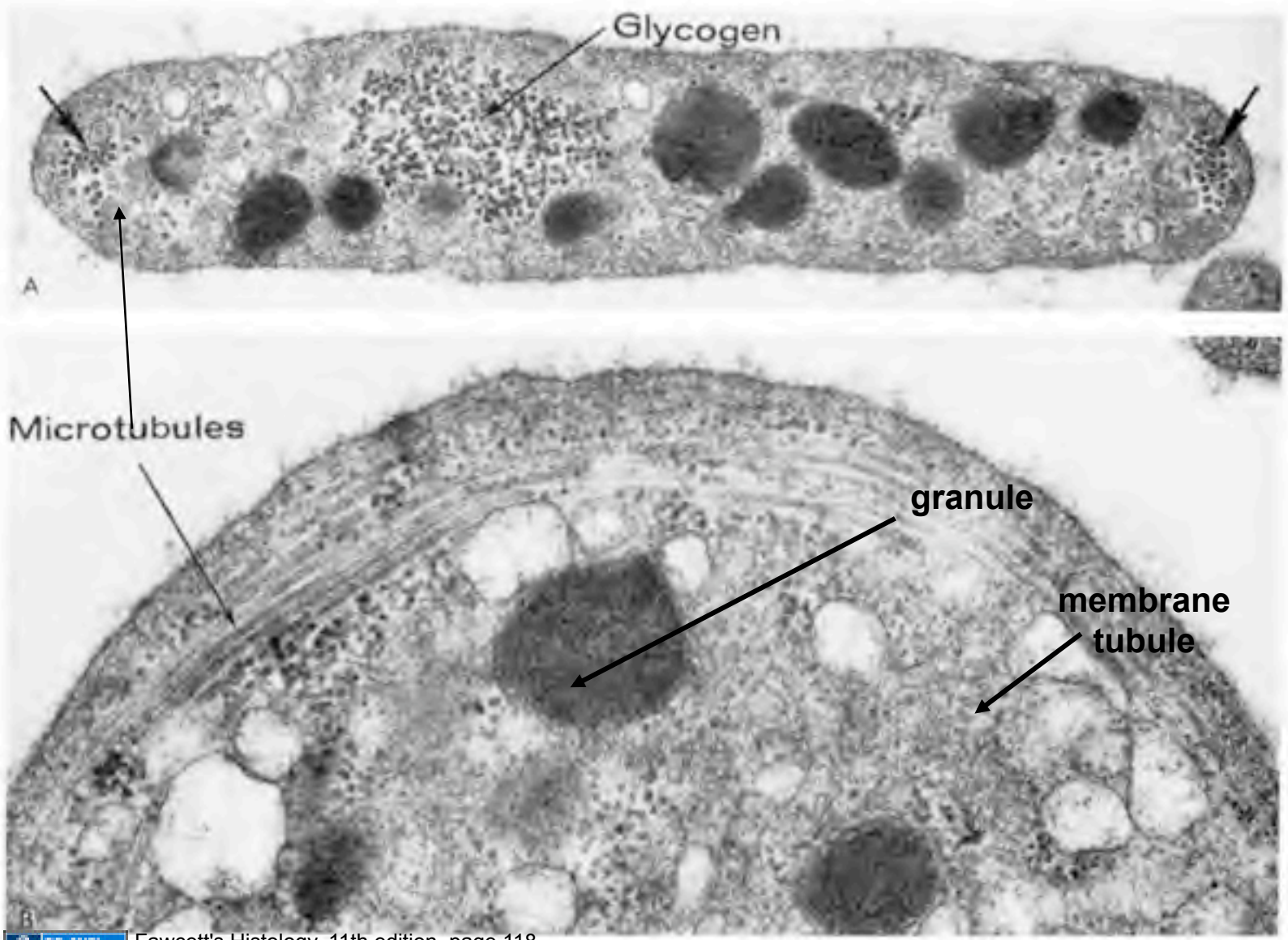
Platelets (thrombocytes)

1. **Life Span:** about 10 days
2. **Shape, size, and origin:** Small, biconvex disks, 2-3 μm 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.

Platelets (at right) in a blood smear

 Mizobuti histology slide set (J). J-186.

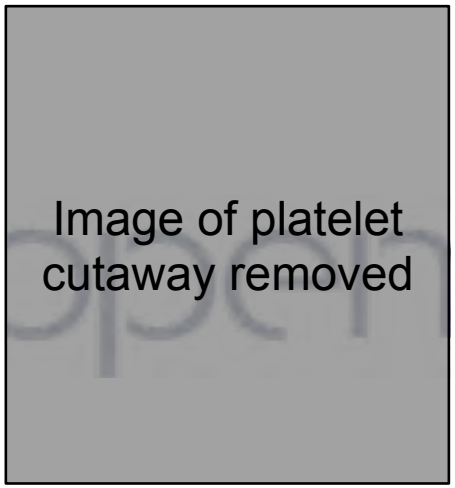
Transmission electron micrographs of a platelet seen in cross section (above) and in a section in the plane of the disk (below)



PD-INEL Fawcett's Histology, 11th edition, page 118.

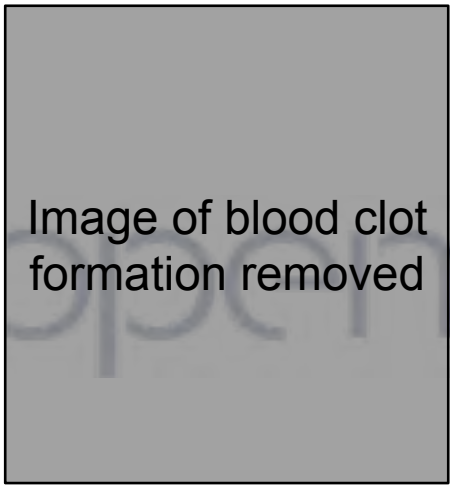
Cutaway diagram of a platelet

1. Peripheral microtubule bundle (maintains shape)
2. Actin and myosin (clot contraction)
3. Organelles facilitate clotting:
   - Mitochondria for ATP production
   - Granules contain clotting factors
   - Dense tubular system sequesters Ca^{++} for signaling (similar to SR in skeletal muscle)
   - Open canalicular system facilitates signaling and secretion



Original Source: Ross' Histology, 4th edition, page 230.

Platelets and blood clot formation



Original Source: Fawcett's Concise Histology, 2nd ed., page 45. BloodClot-FawcConc2-45.tif.

When a blood vessel wall is damaged, factors from the damaged endothelial cells and the ECM induce the clotting cascade. Platelets aggregate and release proteins for clot formation and resolution:

1. Vasoconstriction –via release of **serotonin**
2. Further platelet aggregation –mediated via **thromboxane A_2** and **ADP**
3. Fibrin polymerization –initiated by **thromboplastin** and free **Ca^{++}**

$$\text{Prothrombin} \xrightarrow{\text{thromboplastin}} \text{Thrombin}$$

$$\text{Fibrinogen} \xrightarrow[Ca^{++}]{\text{thrombin}} \text{Fibrin} \longrightarrow \text{Fibrin polymerization}$$

4. Clot contraction –via **actin**, **myosin**, and **ATP** released into the matrix of the clot
5. Clot resolution –**platelet plasminogen activator** (**pPA**, converts **plasminogen** into active fibrinolytic **plasmin**)
6. Tissue repair –**platelet derived growth factor** (**PDGF**, stimulates smooth muscle and fibroblast proliferation)

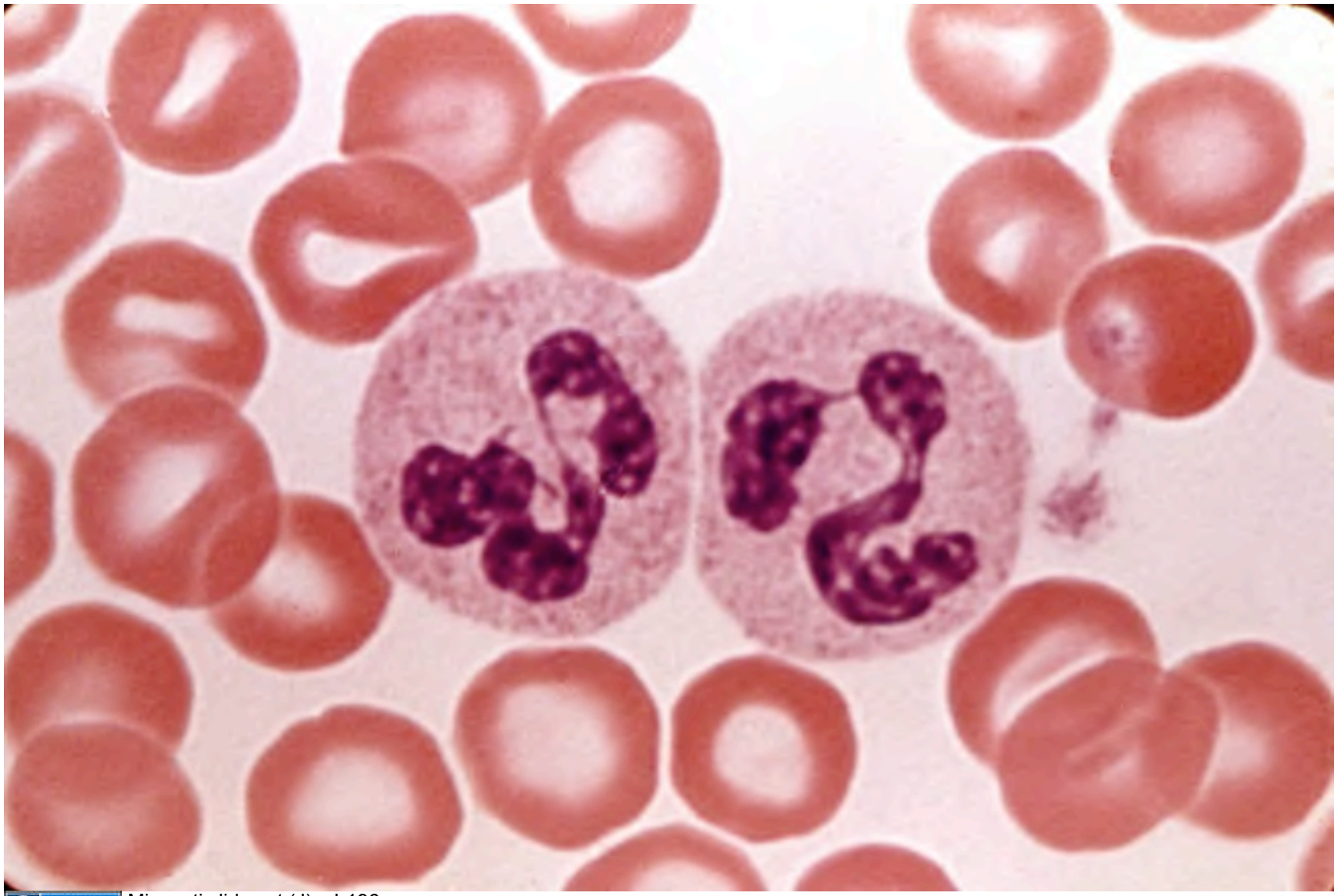
Neutrophil (polymorphonuclear leukocyte)

1. **Life Span:** < 1 week
2. **Granulocyte with specific and non-specific granules**

Specific granules	Non-specific granules (lysosomes)
• Type IV collagenase (aids migration)	• Lysozyme
• Lactoferrin (sequesters iron)	• Acid hydrolase
• Phospholipase A_2 (leukotriene synthesis)	• Myeloperoxidase
• Lysozyme (digests bacterial cell wall)	• 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

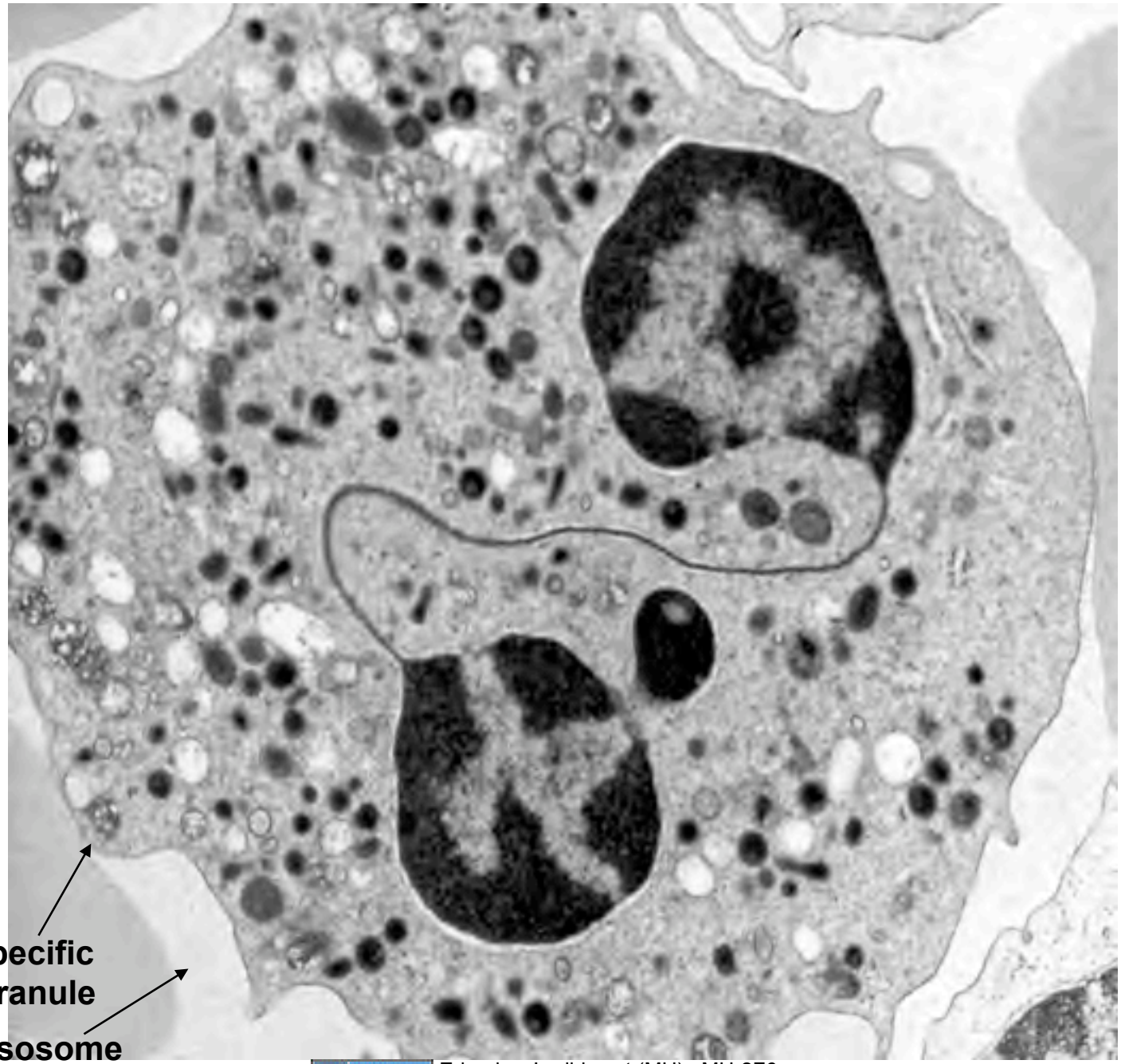


PD-INEL Mizoguti slide set (J). J-196.

LM appearance in smear: **About 9-12 µm 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.**

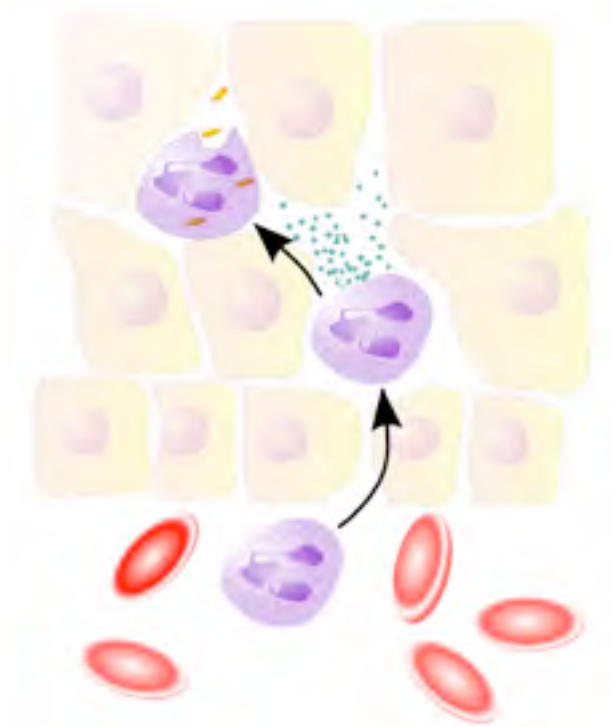
Neutrophil, transmission electron micrograph

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



 Erlandsen's slide set (MH). MH-2F6.

Extravasation via diapedesis



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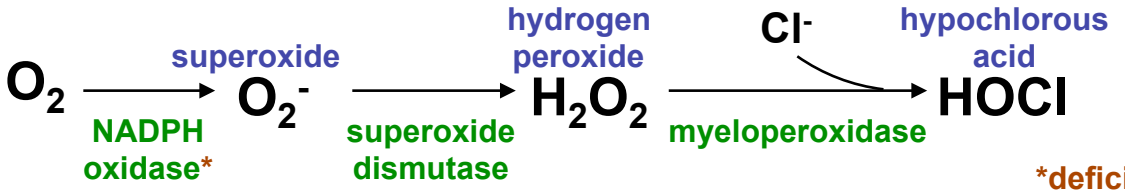
- Selectin-selectin receptor interaction causes neutrophil to slow & roll along surface.
- Chemokines from endothelium leads to expression of integrins & immunoglobulin family adhesion molecules on neutrophil cell membrane.
- Neutrophil firmly attached to vessel wall & extends pseudopod into vessel wall.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

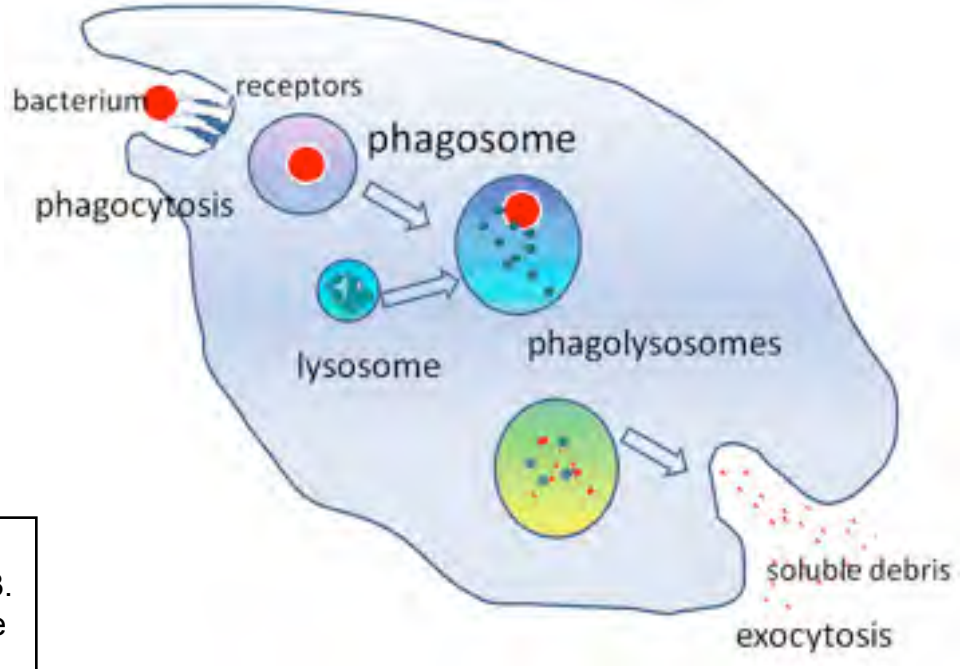
Neutrophil antibacterial activity

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

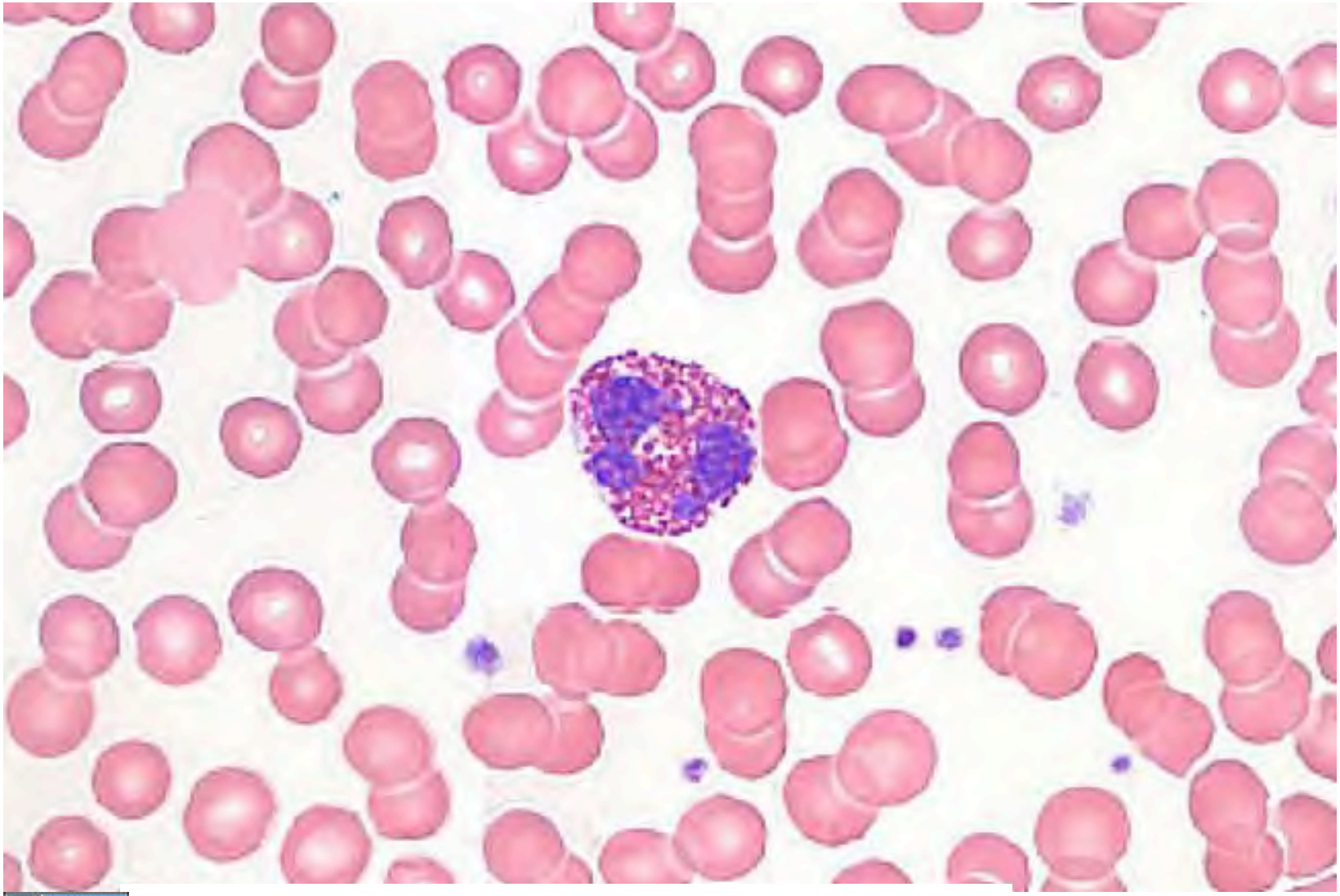
1. **Life Span:** < 2 weeks
2. **Granulocyte with specific and non-specific granules**

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 µm 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)

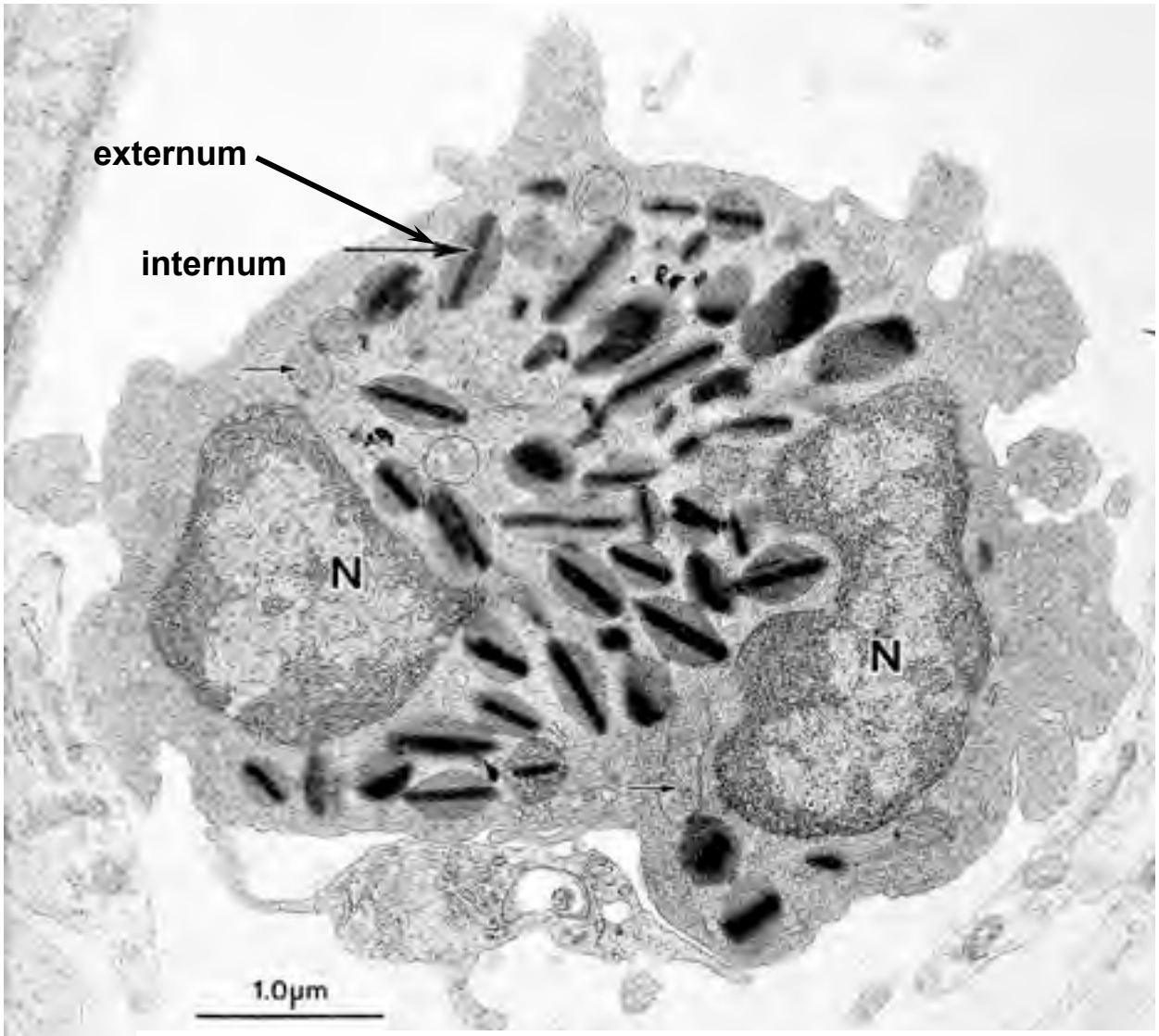
Eosinophil in a human blood smear



PD-INEL University of Michigan Virtual Slide Collection

LM appearance in smear: **About 10-14 µm 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.**

Eosinophil, transmission electron microscopy



PD-INEL Fawcett's Concise Histology, 2nd edition, page 49.

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 and histaminase. The cytoplasm also contains lysosomes (=azurophilic granules).**

Basophil

1. **Life Span:** 1-2 years (?)
2. **Granulocyte with specific and non-specific granules**

Specific granules

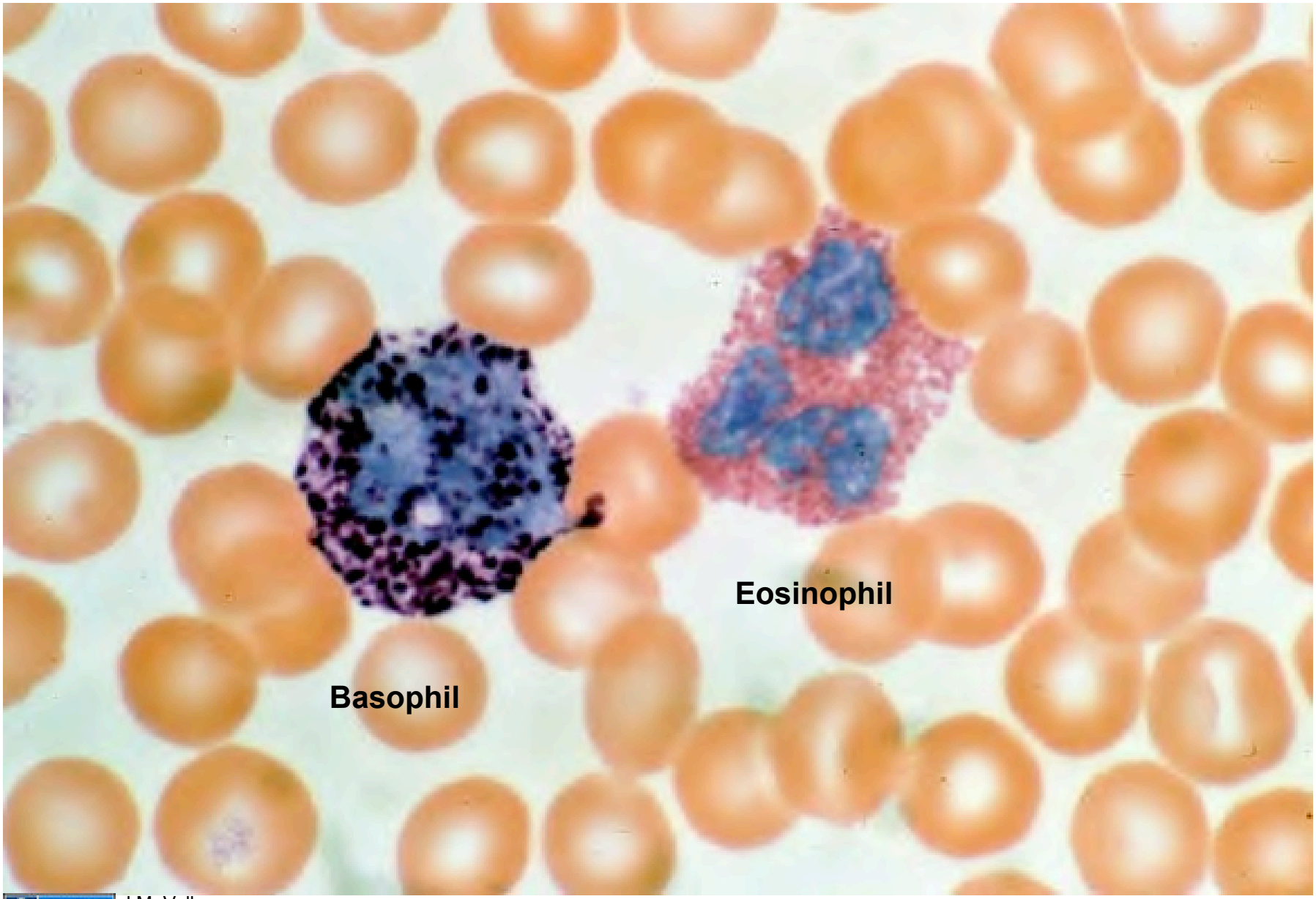
- Histamine
- Heparin
- Eosinophil chemotactic factor
- Phospholipids for synthesis of leukotrienes, e.g. slow-reacting substance of anaphylaxis (SRS-A)

Non-specific granules (lysosomes)

- Lysozyme
- Acid hydrolase
- Myeloperoxidase
- Elastase

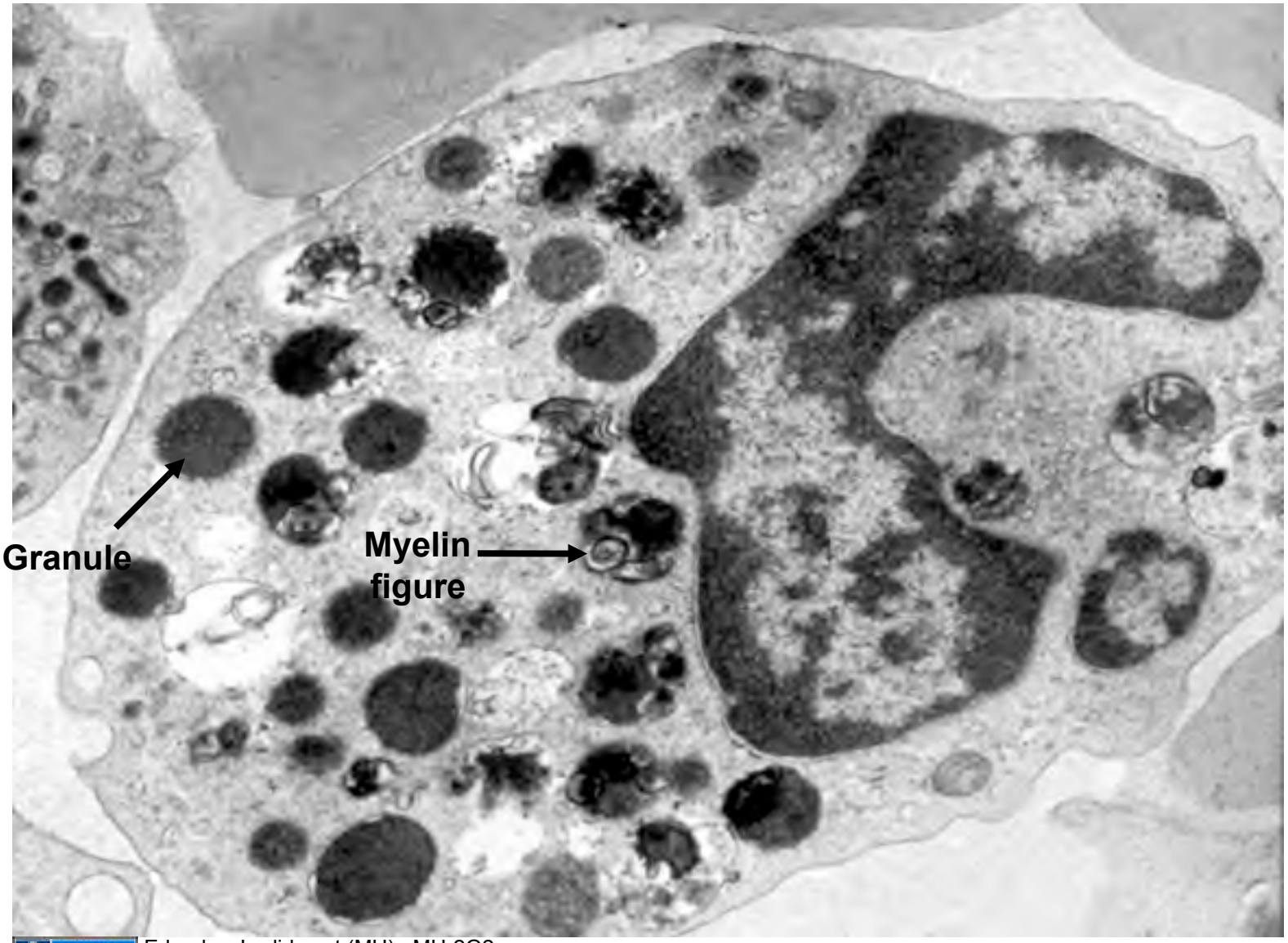
2. **LM appearance in smear:** About 8-10 µm in diameter. The cytoplasm contains large, purple/black specific granules (stained with the basic dye) that are larger but not as numerous as those of eosinophils. The nucleus is usually bilobed, but usually is partially obscured by granules, which can lie 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.
6. **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.

Comparison of basophil and eosinophil in a blood smear



PD-INEL J.M. Velkey.

Basophil, transmission electron microscopy



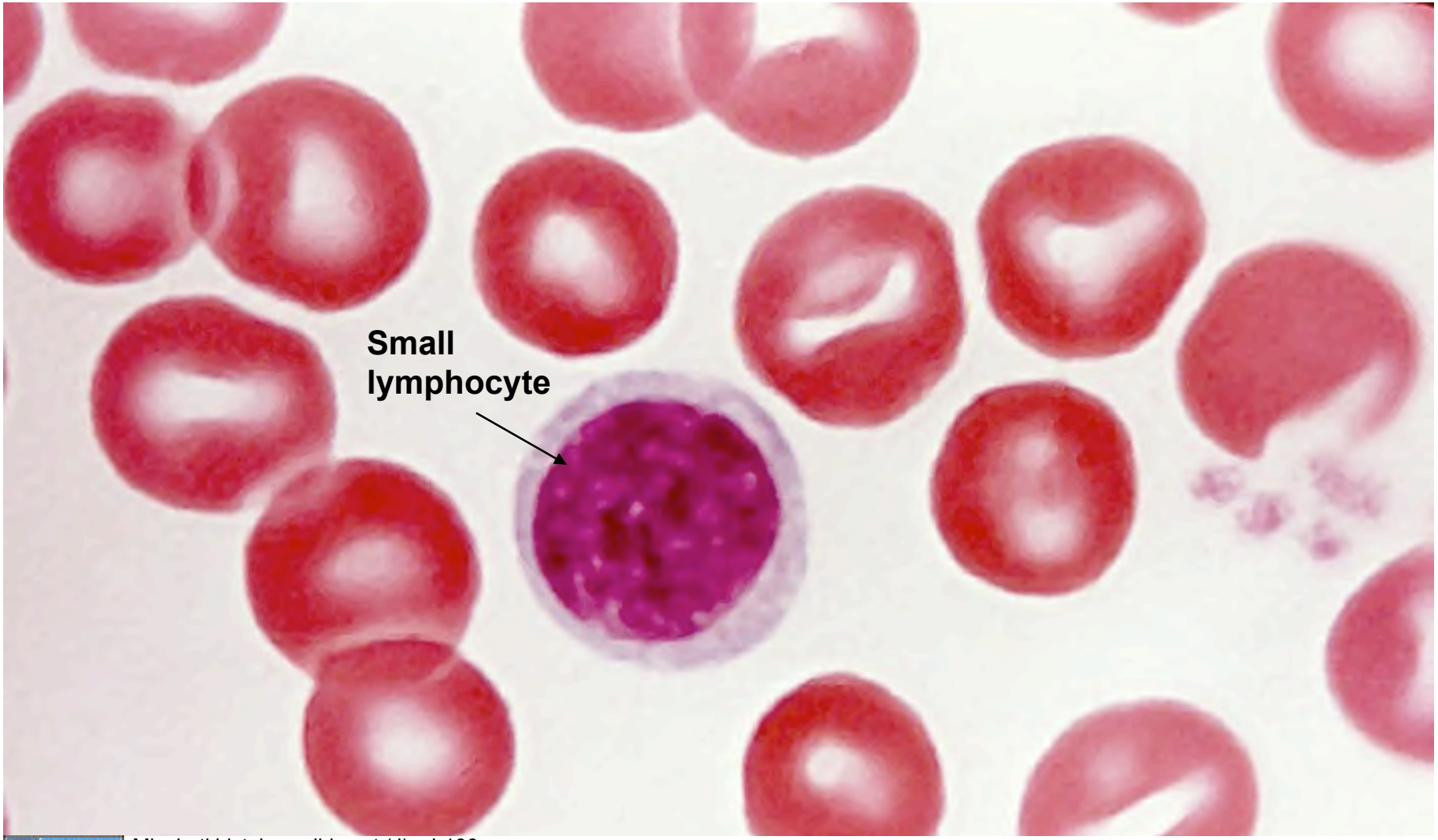
PD-INEL Erlandsen's slide set (MH). MH-2G2.

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).

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 µm in diameter, while large lymphocytes may be up to about 15 µm. 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.

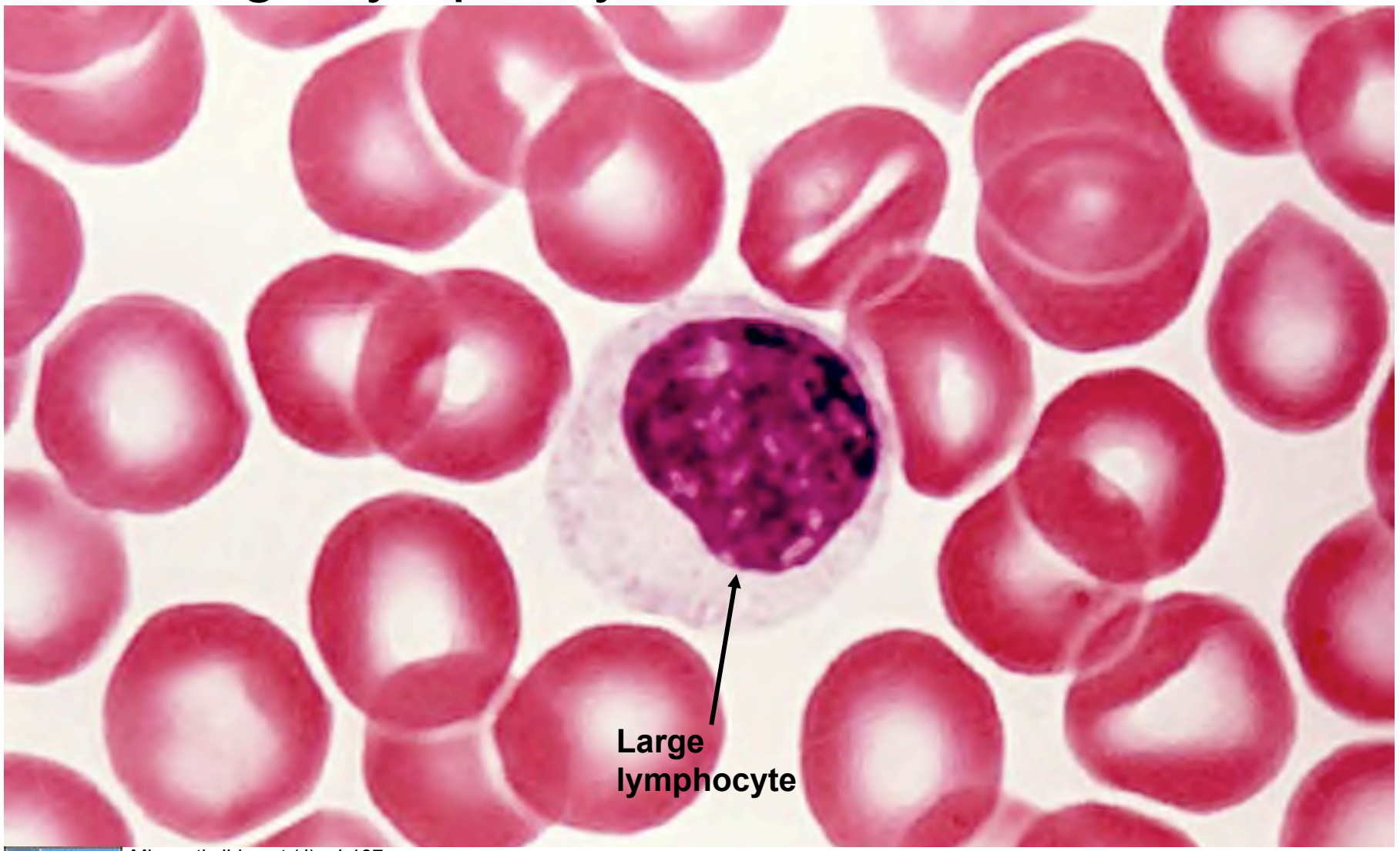
Small lymphocyte in a blood smear



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

LM appearance in smear: **Small lymphocyte (about 90% of lymphocytes you will see) are ~8 µm in diameter, while large lymphocytes may be up to about 15 µm. 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.**

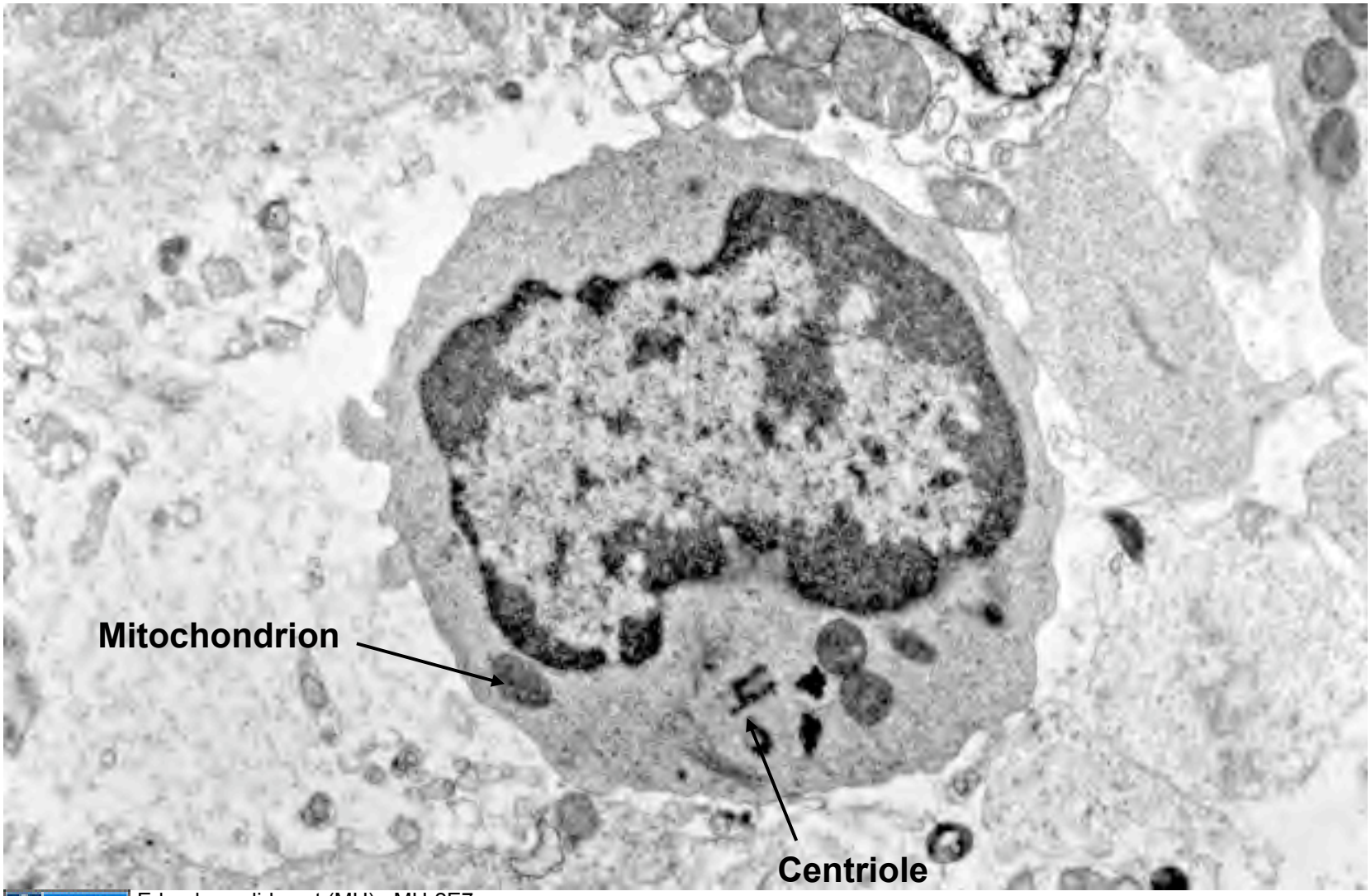
Large lymphocyte in a blood smear



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

LM appearance in smear: **Small lymphocytes (about 90% of lymphocytes you will see) are ~8 µm in diameter, while large lymphocytes may be up to about 15 µm with ovoid, dense nuclei (abundant heterochromatin).**

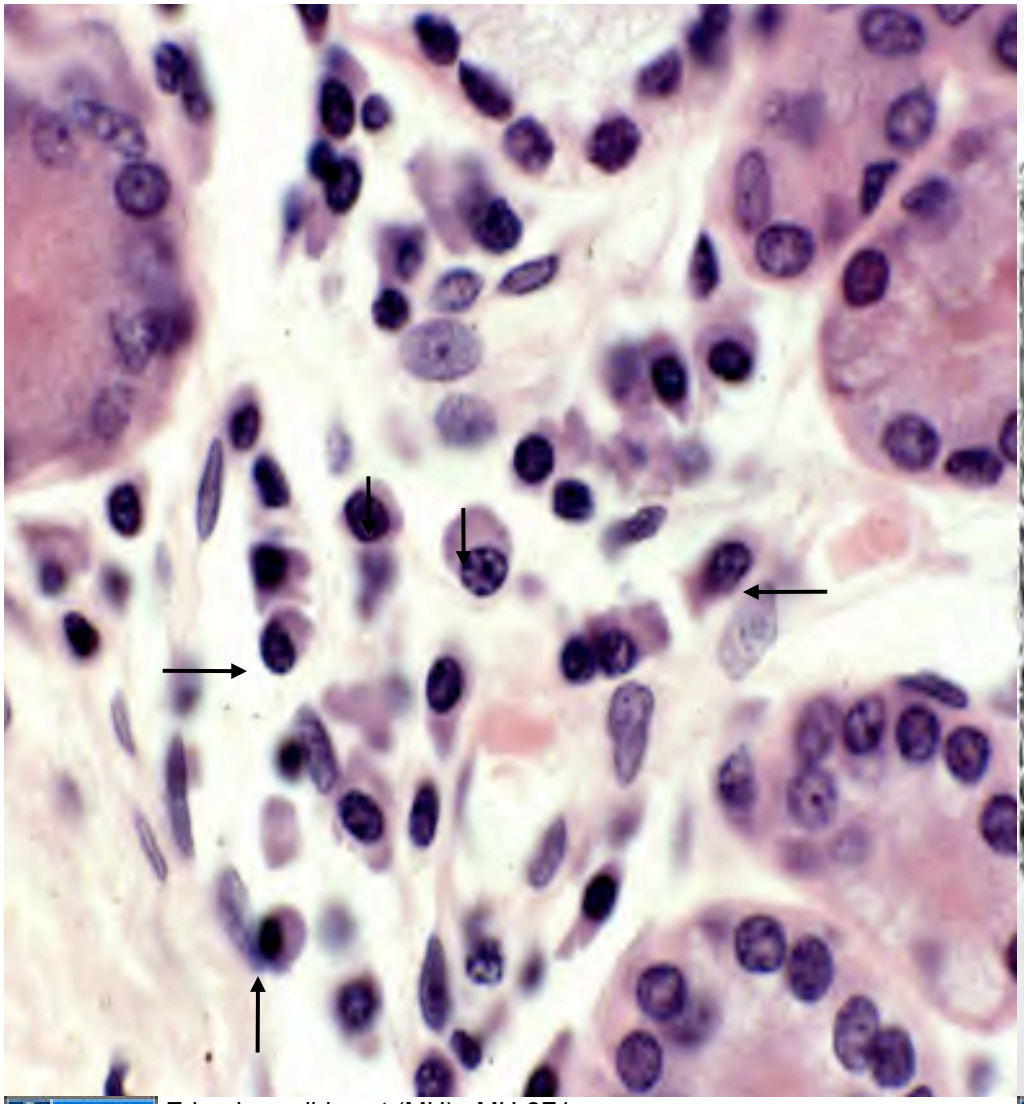
Electron micrograph of a lymphocyte



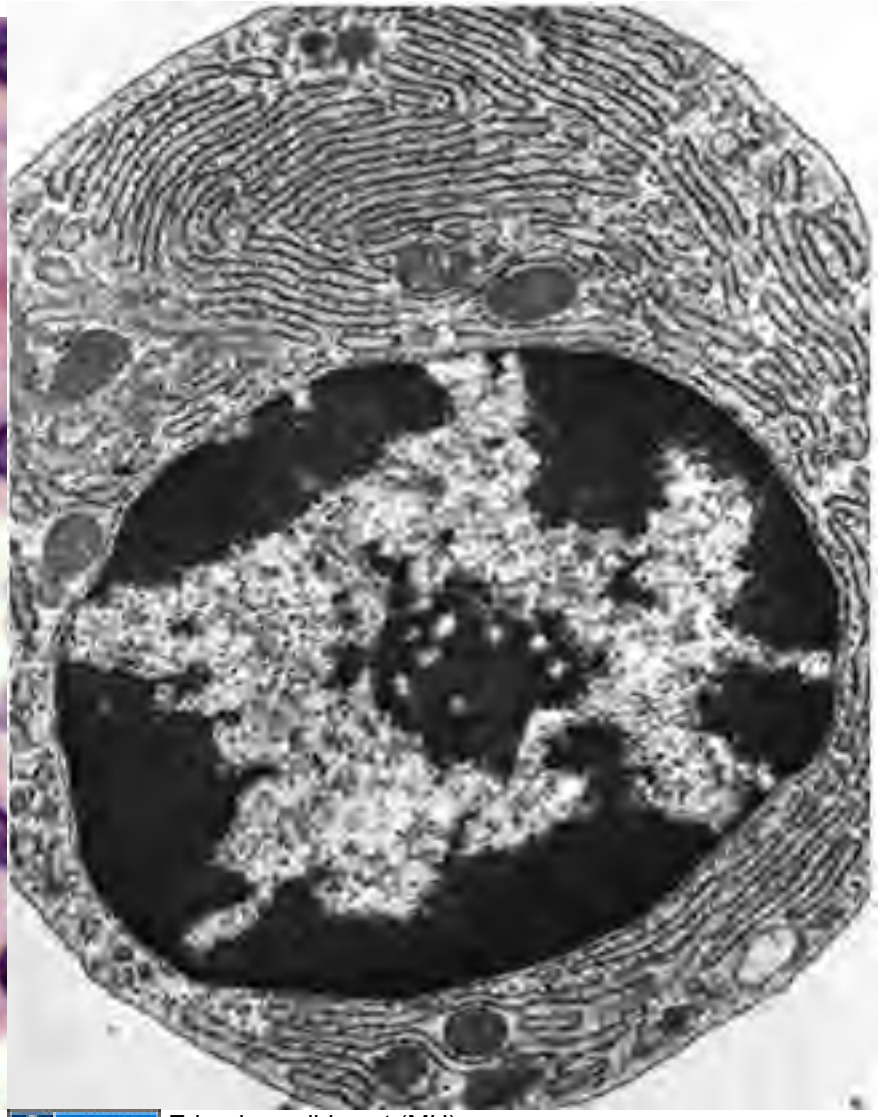
PD-INEL Erlandsen slide set (MH). MH-2E7

TEM appearance: **The cytoplasm doesn't appear to be very active, containing mainly mitochondria and free ribosomes.**

Tissue plasma cells (derived from B-lymphocytes)



PD-INEL Erlandsen slide set (MH). MH-2F1



PD-INEL Erlandsen slide set (MH).

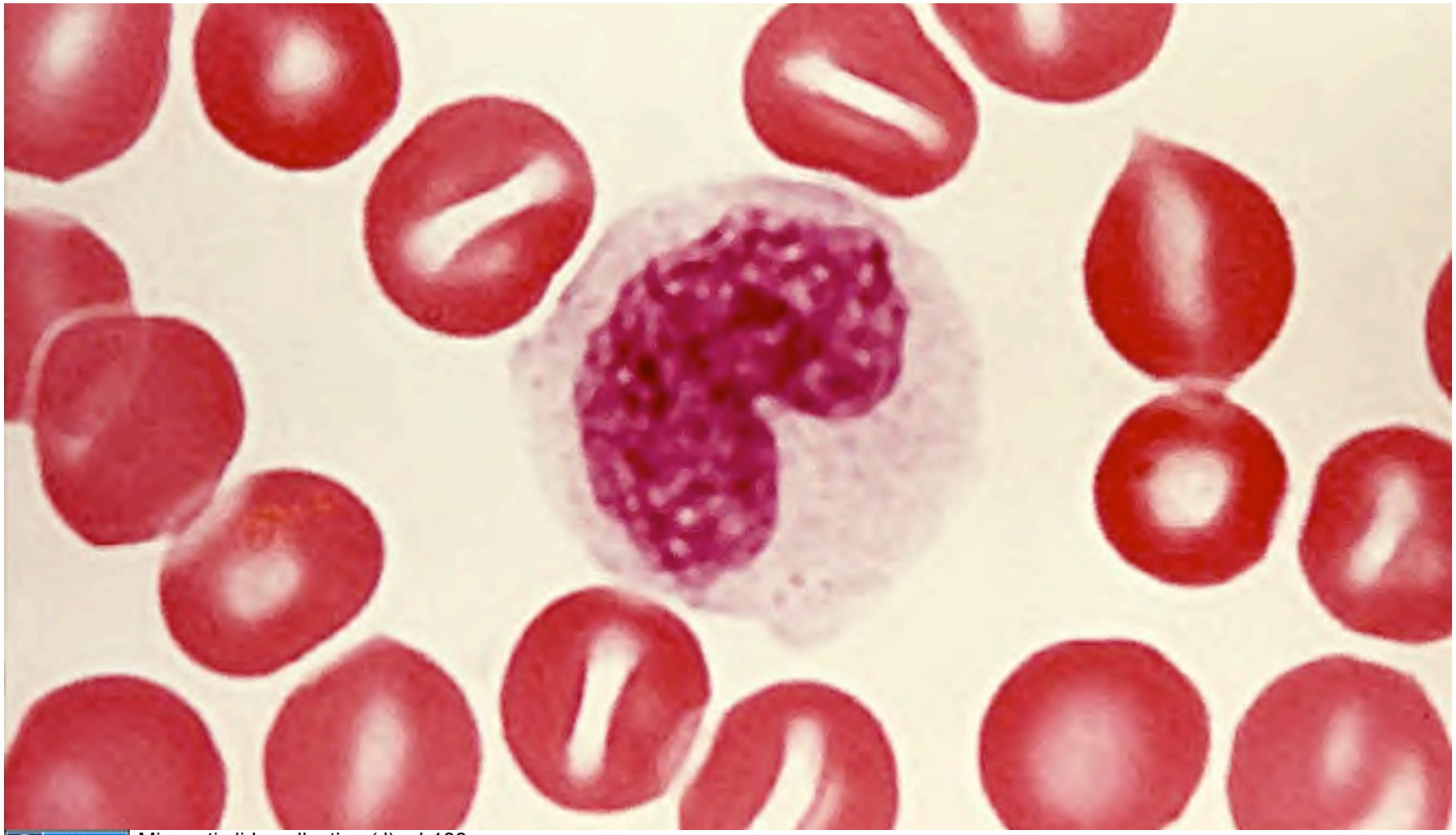
Monocyte

1. **Life Span:** few days in blood, several months in connective tissue
2. **LM appearance in smears:** About 16 µm 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

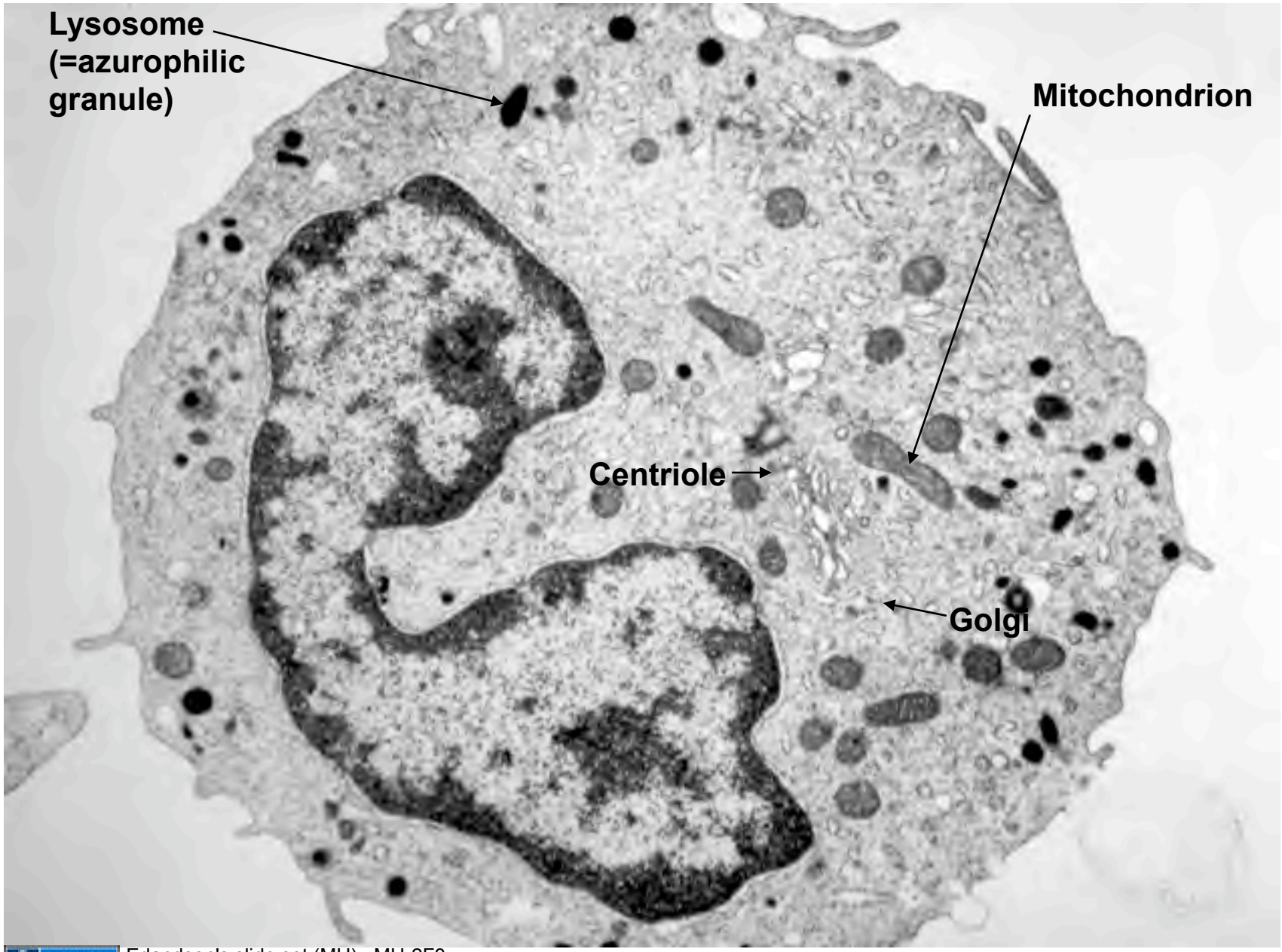
Monocyte in a blood smear



PD-INEL Mizoguti slide collection (J). J-188.

LM appearance in smears: About 16 µm 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.

Monocyte, transmission electron microscopy



PD-INEL Erlandsen's slide set (MH). MH-2F3.

TEM appearance: **Cytoplasm contains mitochondria and some small lysosomes.**

Blood cell development (hematopoiesis = hemopoiesis)

1. Normally occurs in red bone marrow in adult (also spleen & liver, if necessary)

   Phases: mesoblastic (yolk sac, 2 wks)* → hepatic (6 wks)* → splenic (12 wks) → myeloid (marrow, 24 wks)

   *** Erythrocytes still have nuclei; leukocytes do not appear until 8 wks**

2. Mitotic stem and progenitor cells undergo increasing lineage restriction to produce committed precursors.
3. Precursors undergo cell division and differentiation into mature cells.
4. Maturation involves (note exceptions for megakaryocytes below):
   - **decrease in cell size***
   - **shutting down transcription (nucleoli disappear and chromatin condenses)***
   - **adoption of morphological characteristics specific to that lineage.**

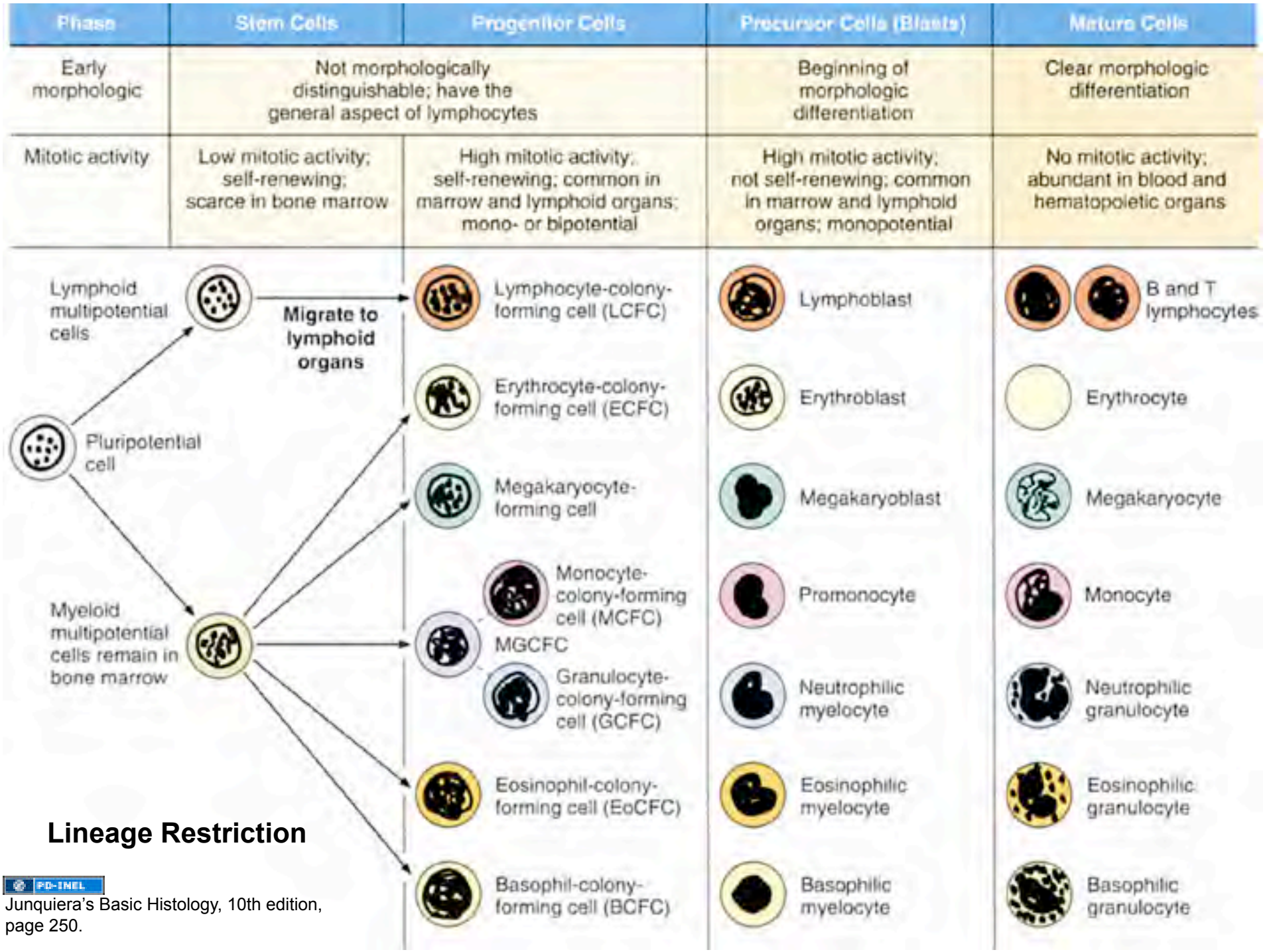
   – **Future granulocytes produce specific and non-specific granules, and then shape their nucleus.**

   – **Future monocytes produce non-specific granules and shape their nucleus.**

   – **Future small lymphocytes decrease their size and enter the blood, but then undergo extensive further maturation at another site (T-cells in the thymus, and B-cells in the "bursa equivalent" –to be discussed in immune system lecture).**

   – **Future erythrocytes fill cytoplasm with hemoglobin, synthesized on free polysomes (ribosomes on mRNA), and eventually extrude their nucleus.**
5. Mature cells enter marrow sinus; immature cells in peripheral blood typically indicates disease.

*** Megakaryocytes develop into large polyploid cells that remain transcriptionally active and extrude platelets as cytoplasmic fragments directly into marrow sinus.**



Lineage Restriction

Junquiera's Basic Histology, 10th edition, page 250.

Cellular Changes during Myeloid Differentiation

Mitotic Cell — *Postmitotic Cells*

Myelocyte | Metamyelocyte | Band Cell | Mature Neutrophil

Nuclear Changes-

Large, euchromatic, transcriptionally active nucleus → Smaller, euchromatic, less transcriptionally active nucleus → Condensed, heterochromatic, transcriptionally inactive nucleus

Cytoplasmic Changes-

Basophilic cytoplasm, active synthesis of specific and non-specific granules → Reduced basophilia, granule maturation → Pale bluish-pink cytoplasm, mature granules

Changes during Erythroblast Differentiation

Mitotic Cells | *Postmitotic Cells*

Proerythroblast | Early Erythroblast | Middle Erythroblast | Late Erythroblast | Erythrocyte (Reticulocyte)

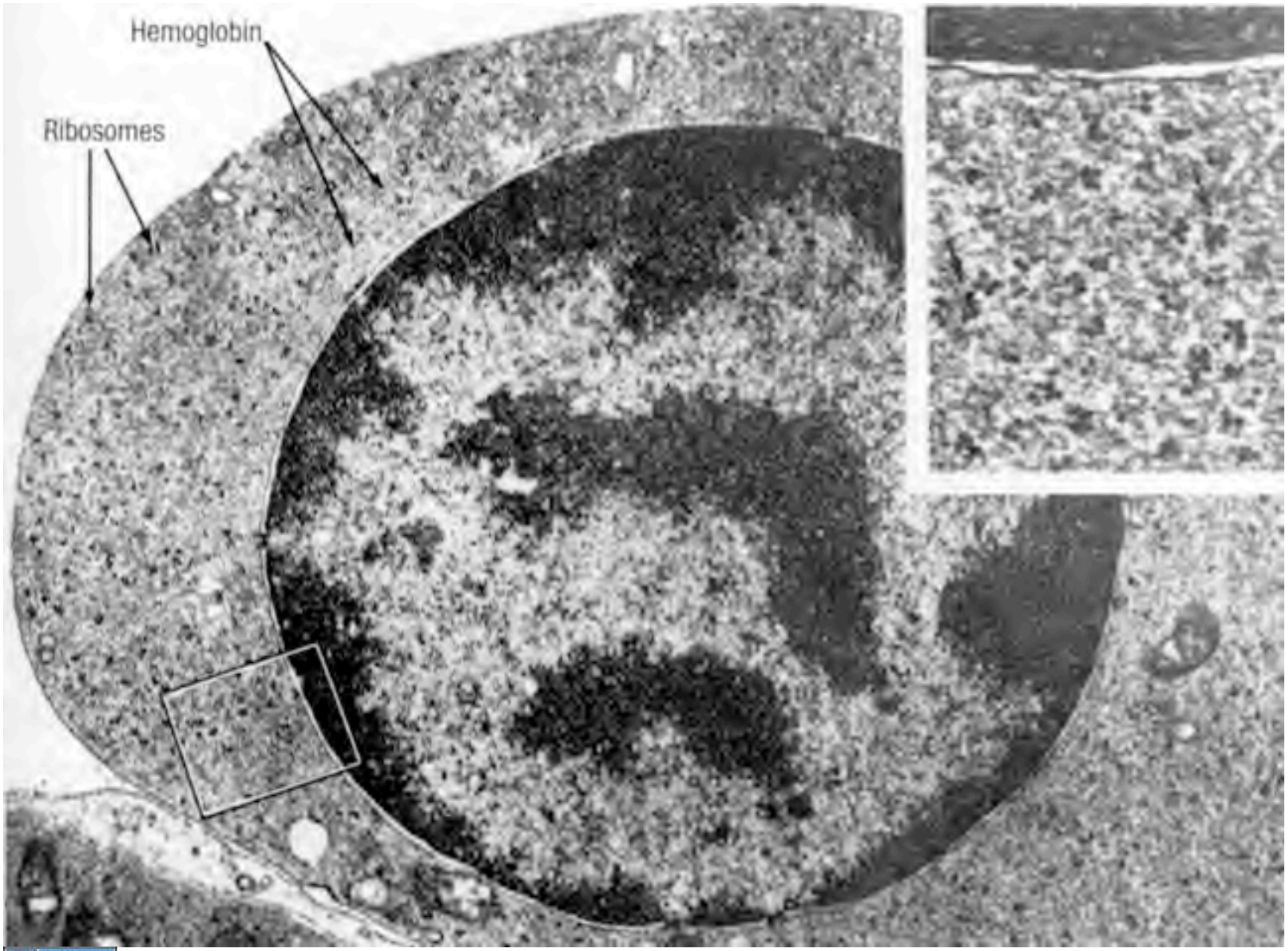
Nuclear Changes-

Large, euchromatic, and transcriptionally active → Smaller, heterochromatic, and transcriptionally inactive → Absent

Cytoplasmic Changes-

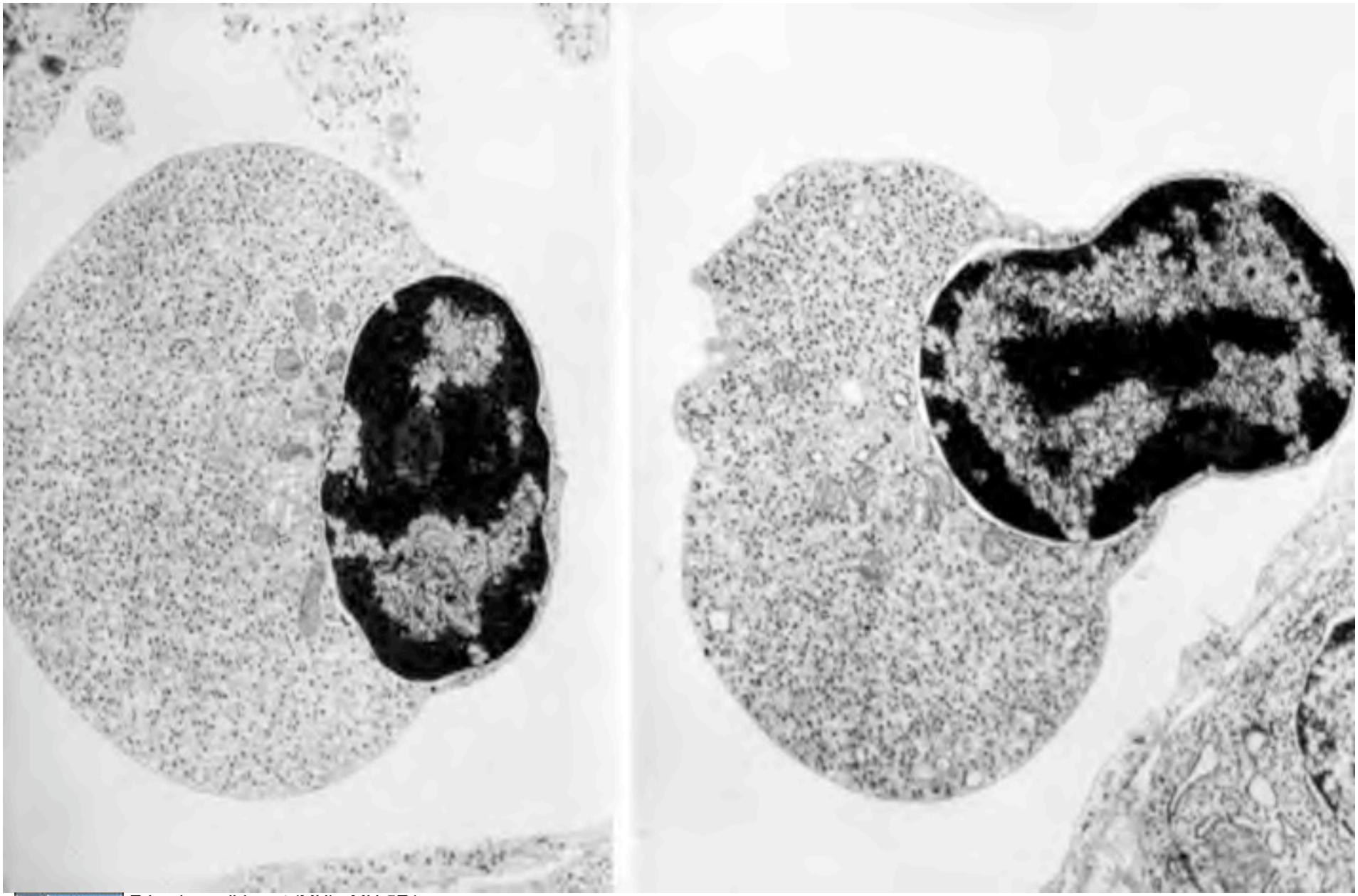
Basophilic with abundant RER → Polychromatic (basophilic and acidophilic) with abundant RER and hemoglobin → Acidophilic, with abundant hemoglobin

EM of developing erythrocyte, showing polyribosomes and hemoglobin in cytoplasm



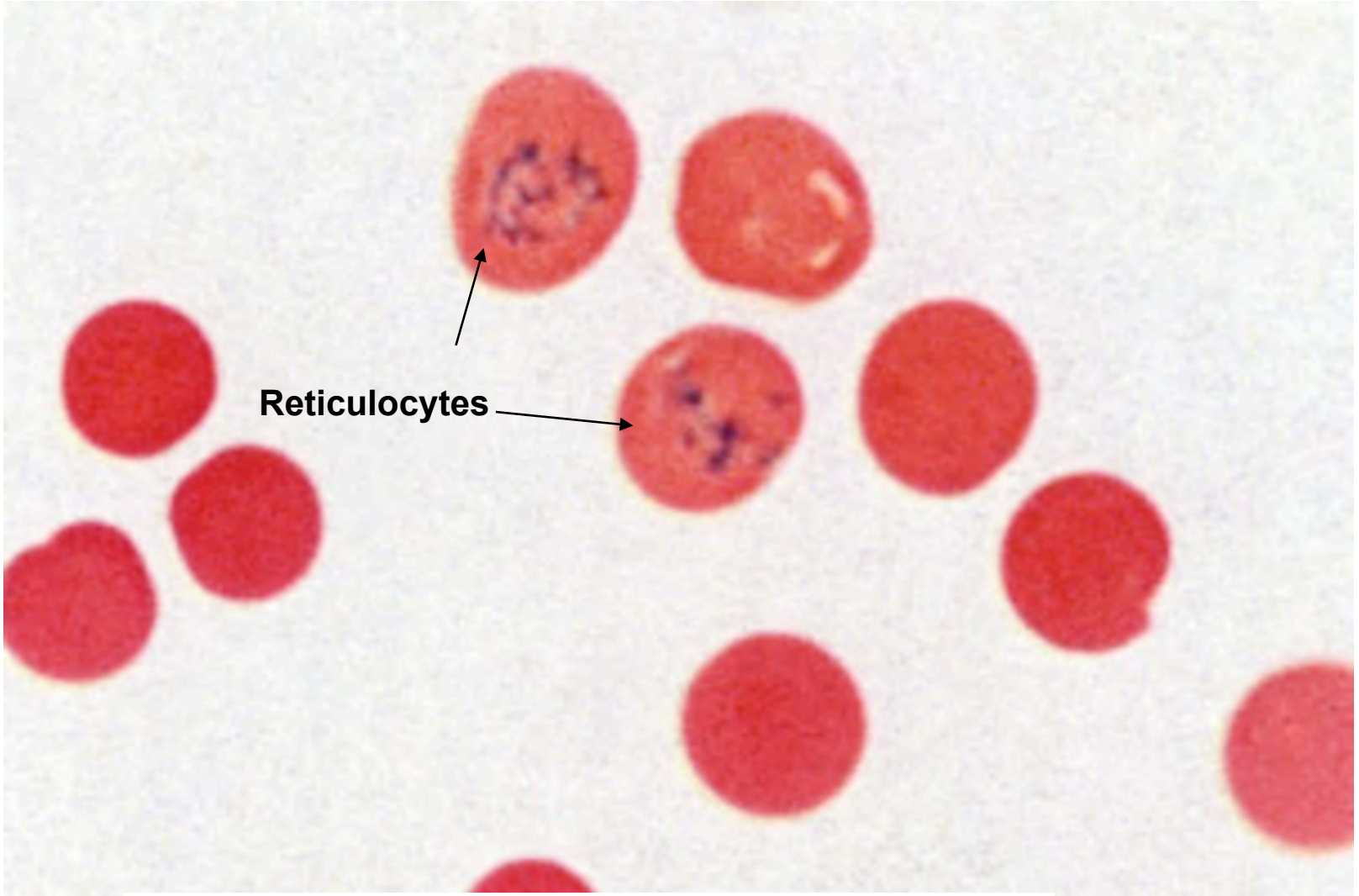
PD-INEL Fawcett's ConciseHistology, 2nd ed.,page 55.

Extrusion of nucleus from a developing erythrocyte in bone marrow, EM



 Erlandsen slide set (MH). MH-5E1.

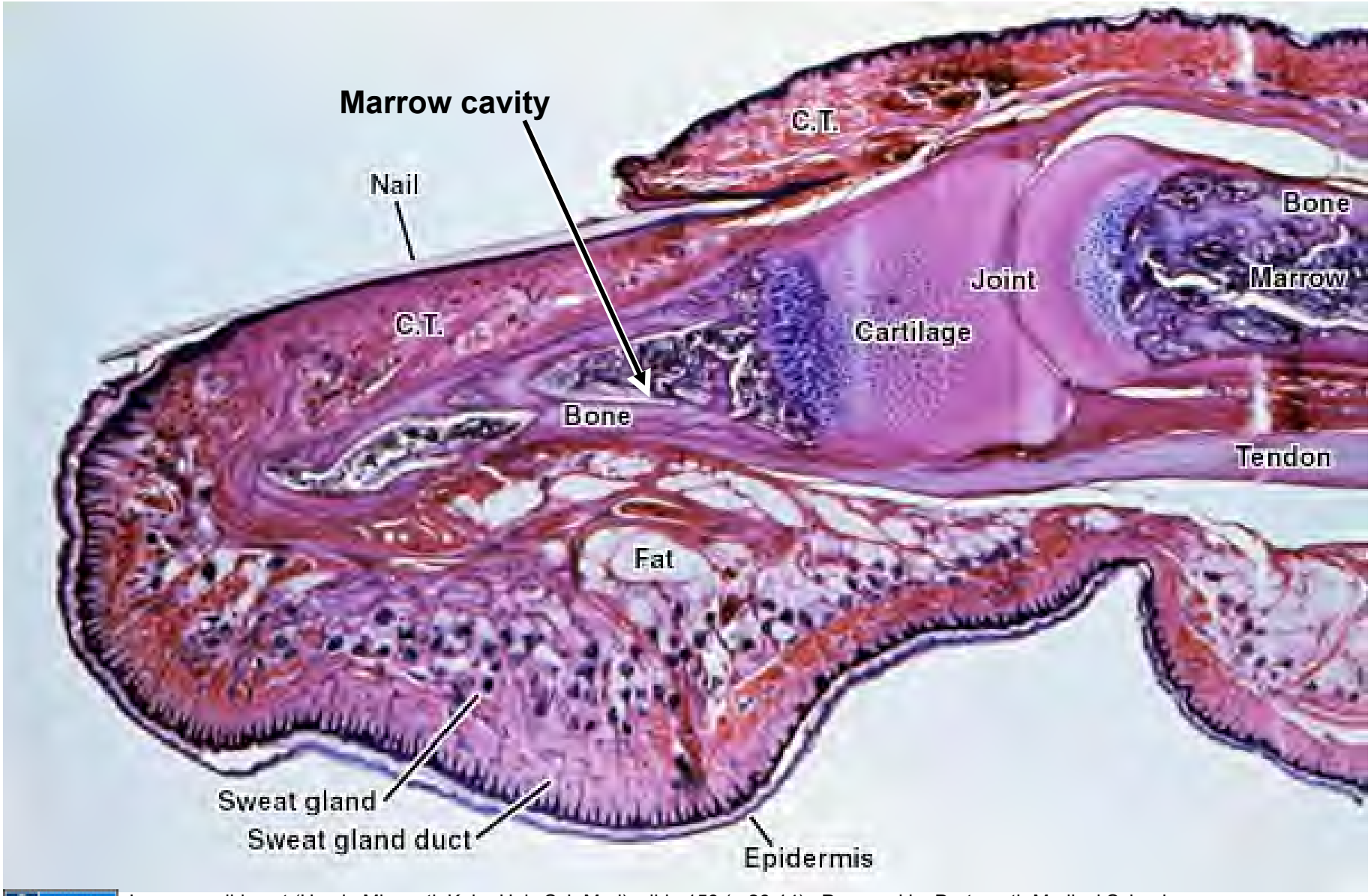
Reticulocytes (somewhat immature RBCs) in blood smear, cresyl blue stain



PD-INEL Wheater's Functional Histology, 4th edition, page 48.

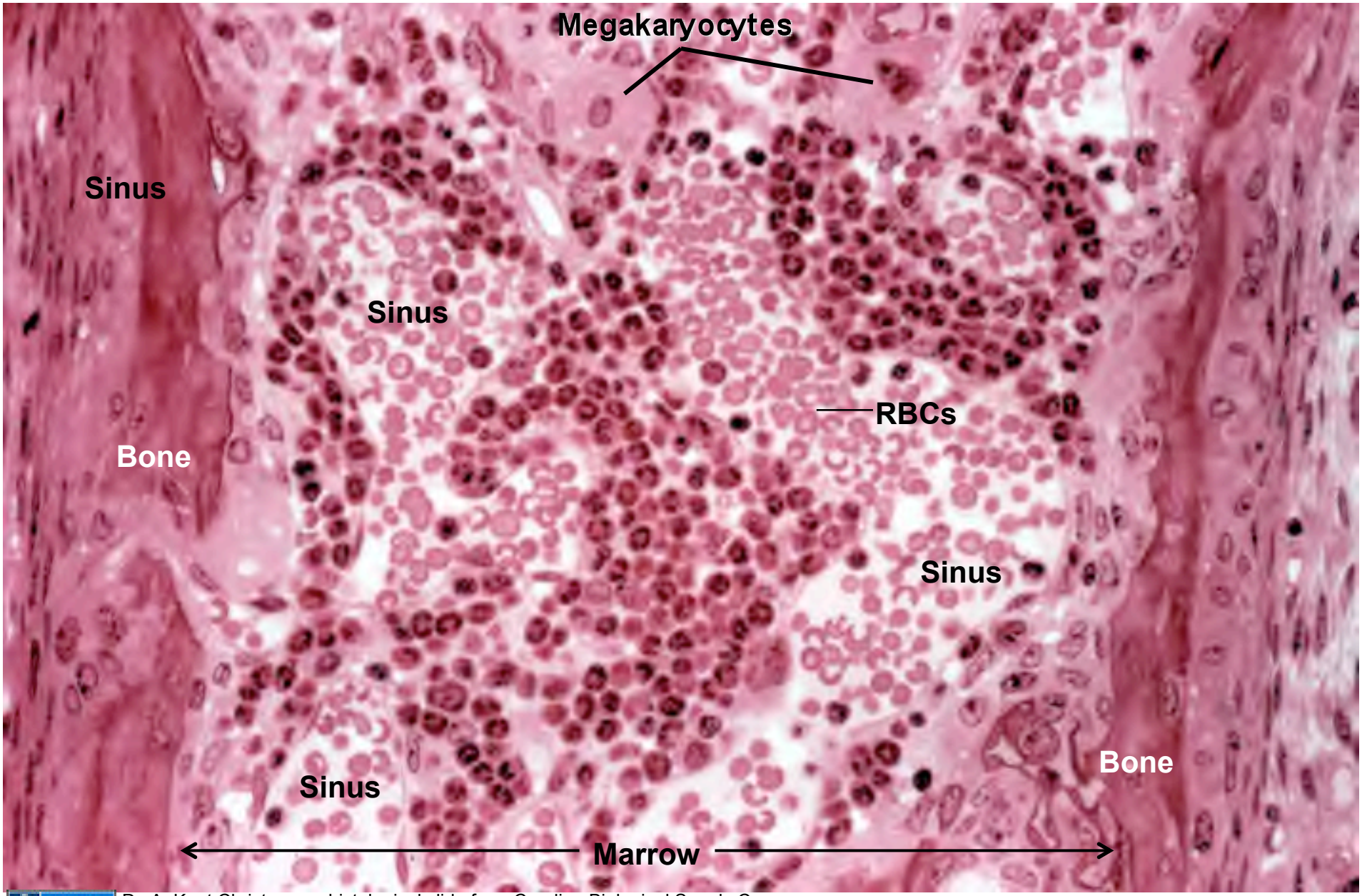
Residual ribosomes in cytoplasm are basophilic. Number of reticulocytes in peripheral blood reflects status of erythropoesis –generally increased by anemia and hypoxia.

Finger, bone marrow in phalanges



PD-INEL Japanese slide set (Humio Mizoguti, Kobe Univ Sch Med), slide 158 (= 26-14). Prepared by Dartmouth Medical School.

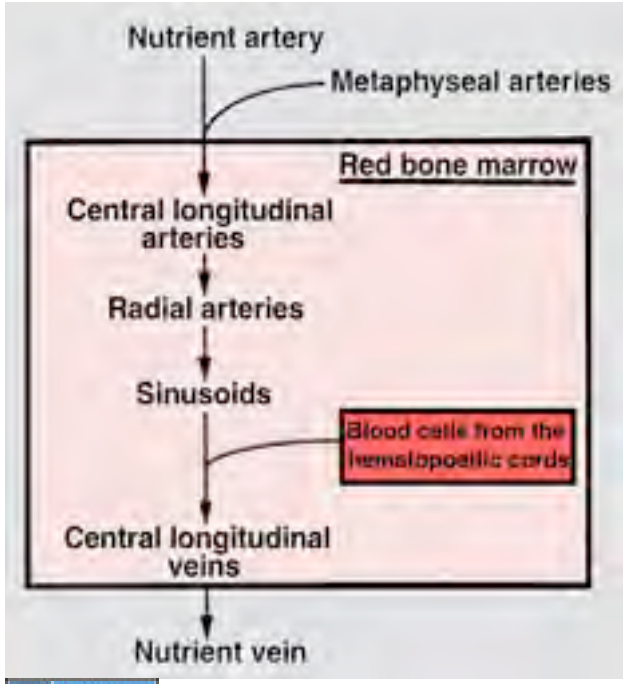
Section of bone marrow, LM



PD-INEL Dr. A. Kent Christensen, histological slide from Carolina Biological Supply Co.

Diagram of bone marrow

Blood flow through marrow:



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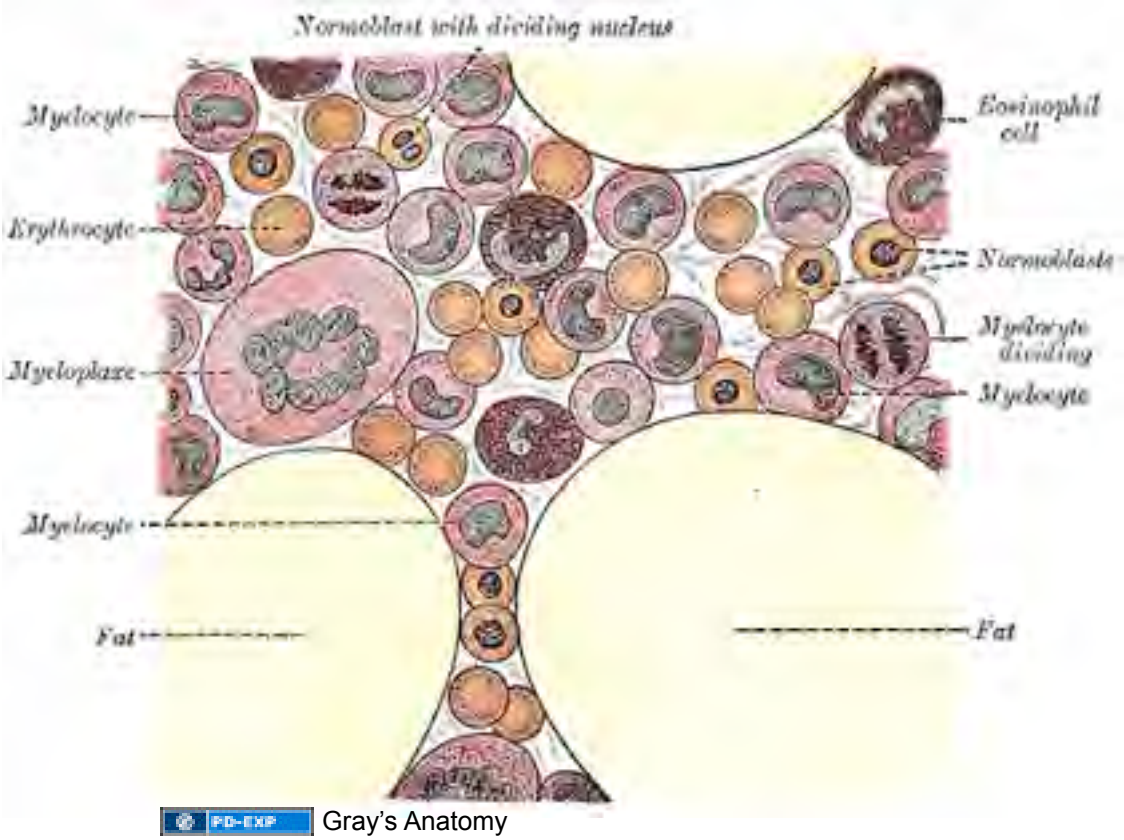


PD-EXP Gray's Anatomy

Original Source: Ross' Histology, 4th edition, page 241. BoneMarrow-Ross4-241.tif.

Marrow sinuses are sinusoidal, discontinuous capillaries. Mature cells enter the sinuses and are conveyed to the systemic circulation via nutrient veins.

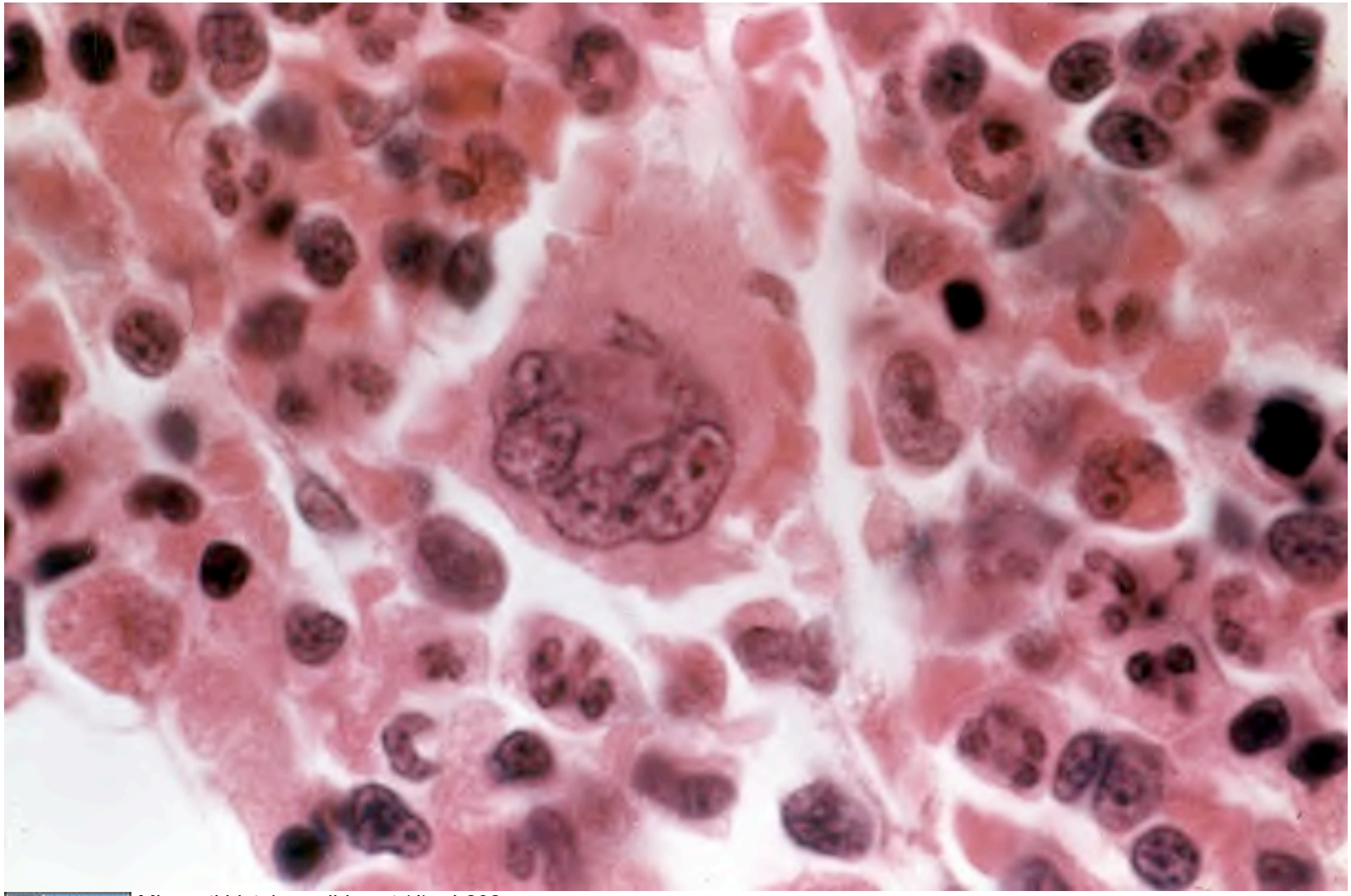
Diagram of bone marrow sinus showing intravasation of blood cells and megakaryocyte releasing platelets into bloodstream

Original Source: Junqueira's Basic Histology, 10th ed., page 253.
MegakarPlatelet-Junqueira10-253.tif.

Megakaryocytes in bone marrow produce blood platelets

- **LM appearance:** **A huge cell, up to 50 µm in diameter. Its long nucleus has several lobes (the nucleus is polyploid and can be up to 64N). The cytoplasm is pale pink/red, without visible granules. In bone marrow, megakaryocytes are situated adjacent to a marrow sinus (large capillary), although this may not be obvious in tissue sections.**
- **TEM appearance:** **Particularly striking in the cytoplasm are many curved white lines that are the platelet demarcation channels, membrane-bound spaces forming the boundaries between future platelets. The cytoplasm also contains granules of various sizes, that will be in the platelets.**
- **Function:** **Megakaryocytes produce blood platelets by fragmentation of their cytoplasm, extending cell processes through the endothelium of a marrow sinus, and releasing clusters of immature platelets into the blood, to become mature platelets.**

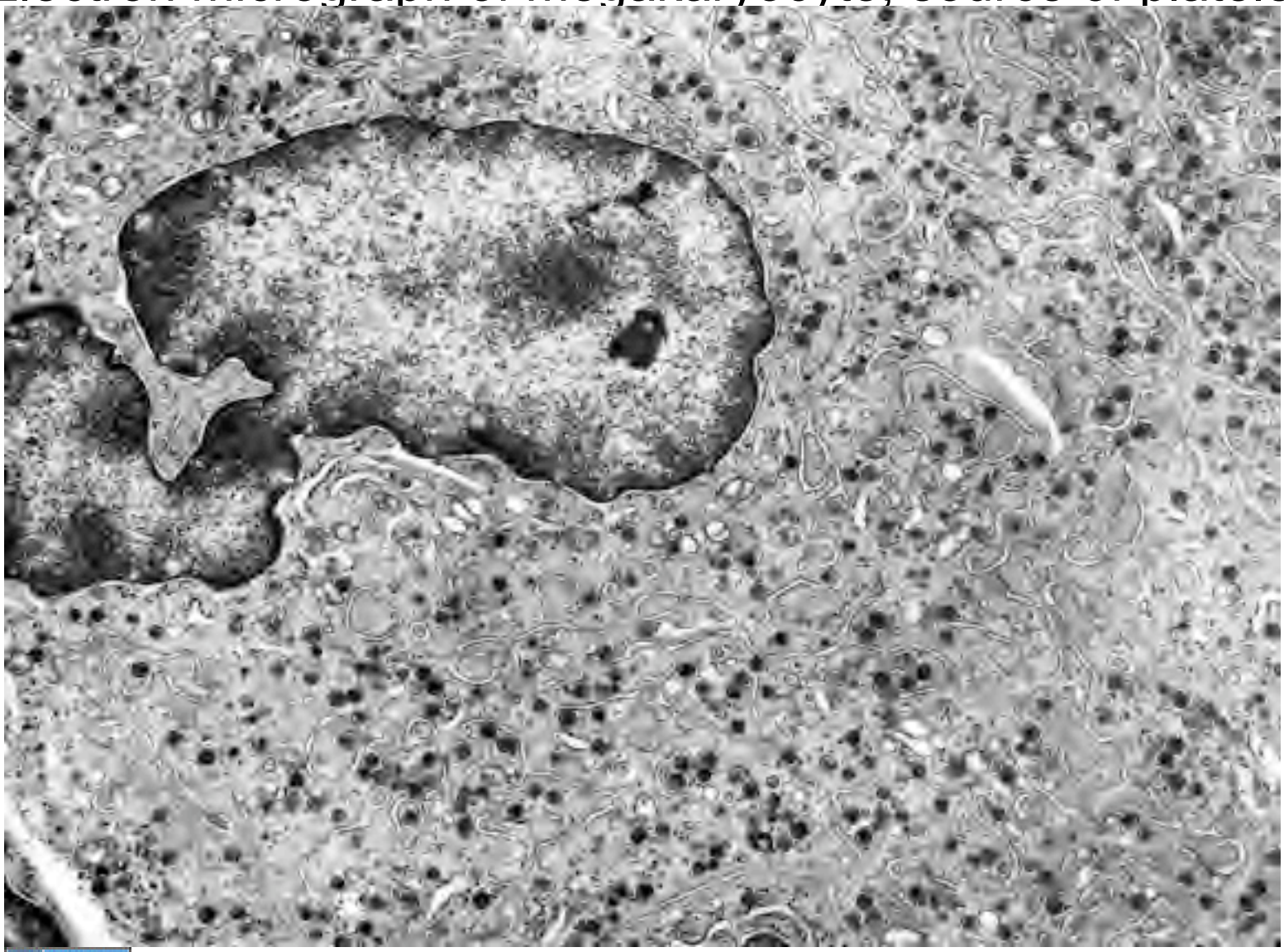
Megakaryocyte, LM section



PD-INEL Mizoguti histology slide set (J). J-202.

LM appearance: A huge cell, up to 50 µm in diameter. Its long nucleus has several lobes (the nucleus is polyploid and can be up to 64N). The cytoplasm is pale pink/red, without visible granules. In bone marrow, megakaryocytes are situated adjacent to a marrow sinus (large capillary), although this may not be obvious in tissue sections.

Electron micrograph of megakaryocyte, source of platelets

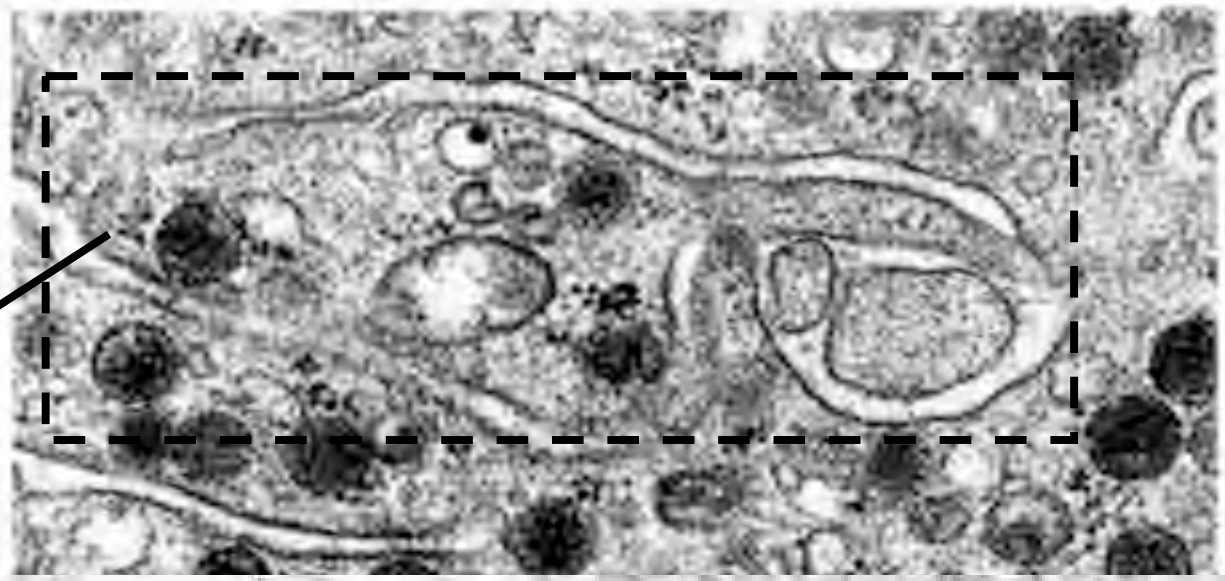


PD-INEL Fawcett's Concise Histology, 2nd ed., page 59

Particularly striking in the cytoplasm are many curved white lines that are the platelet demarcation channels, membrane-bound spaces forming the boundaries between future platelets. The cytoplasm also contains granules of various sizes that will be incorporated into the platelets.

EM detail of megakaryocyte cytoplasm

Will be extruded as a platelet



PD-INEL Fawcett's Concise Histology, 2nd ed., page 60.

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Slide 9: Original Source from Junqueira's histology text, 6th ed., page 231. BloodSmear-23J91(2).tif.

Slide 10: Dr. A. Kent Christensen

Slide 12: Junqueira's Basic Histology, 10th edition, page 235

Slide 13: Mizoguti slide collection (J). J-199.

Slide 14: Erlandsen's slide set (MH). MH-2G3

Slide 15: Original Source from Ross' Histology, 4th edition, page 219. RBCmemb-Ross4-219.tif.

Slide 17: Mizobuti histology slide set (J). J-186.

Slide 18: Fawcett's Histology, 11th edition, page 118.

Slide 19: Original Source: Ross' Histology, 4th edition, page 230.

Slide 20: Original Source: Fawcett's Concise Histology, 2nd ed., page 45. BloodClot-FawcConc2-45.tif

Slide 22: Mizoguti slide set (J). J-196

Slide 23: Erlandsen's slide set (MH). MH-2F6.

Slide 24: Uwe Thurmann, Wikipedia, http://en.wikipedia.org/wiki/File:NeutrophilerAktion.png GNU-FDL http://en.wikipedia.org/wiki/GNU_Free_Documentation_License

Slide 25: Wikipedia, Graham Colm; Original image from Ross' Histology, 4th ed., page 223. The labels to figure (a) have been modified slightly. PMNfunction-Ross4-223.tif.

Slide 27: University of Michigan Virtual Slide Collection

Slide 28: Fawcett's Concise Histology, 2nd edition, page 49.

Slide 30: J.M. Velkey

Slide 31: Erlandsen's slide set (MH). MH-2G2.

Slide 33: Mizobuti histology slide set (J). J-186.

Slide34: Mizoguti slide set (J). J-187.

Slide 35: Erlandsen slide set (MH). MH-2E7

Slide 36: Erlandsen slide set (MH). MH-2F1; Erlandsen slide set (MH).

Slide 38: Mizoguti slide collection (J). J-188.

Slide 39: Erlandsen's slide set (MH). MH-2F3.

Slide 41: Junquiera's Basic Histology, 10th edition, page 250.

Slide 42: Source Undetermined
Slide 43: Source Undetermined
Slide 44: Fawcett's ConciseHistology, 2nd ed.,page 55.
Slide 45: Erlandsen slide set (MH). MH-5E1.
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Slide 47: Japanese slide set (Humio Mizoguti, Kobe Univ Sch Med), slide 158 (= 26-14). Prepared by Dartmouth Medical School.
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Slide 49: Source Undetermined; Gray's Anatomy
Slide 50: Original Source: Junqueira's Basic Histology, 10th ed., page 253. MegakarPlatelet-Junqueira10-253.tif.
Slide 52: Mizoguti histology slide set (J). J-202.
Slide 53: Fawcett's Concise Histology, 2nd ed., page 59
Slide 54: Fawcett's Concise Histology, 2nd ed., page 60.