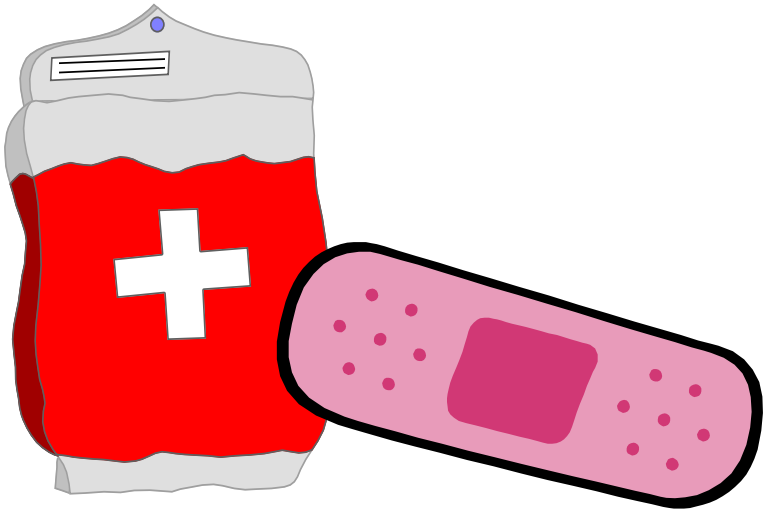
FNS 1108 PATHOPHYSIOLOGY 3(3-0-6)

HEMATOLOGICAL DISORDERS



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Learning Objectives

- Composition & functions of Blood cells & Lymphatic system
- Red blood cell and bleeding disorders
  - Anemias:

    Diminished erythropoiesis: Iron def. anemia, Vitamin B_{12} def. anemia

    Hemolytic anemia: Hereditary spherocytosis, Thalassemia
  - Bleeding disorders:

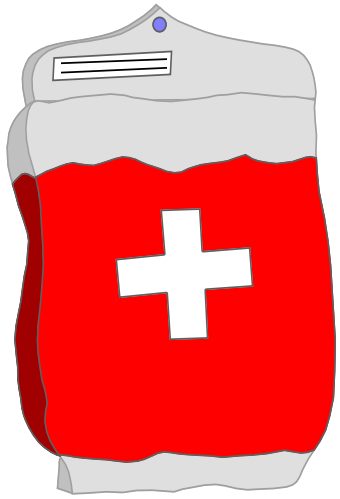
    Thrombocytopenia, Hemophilia & DIC
- Diseases of white blood cells and lymphatic system
  - Lymphoproliferative disorders: Leukemia / Lymphoma
  - Myeloproliferative disorders: CML

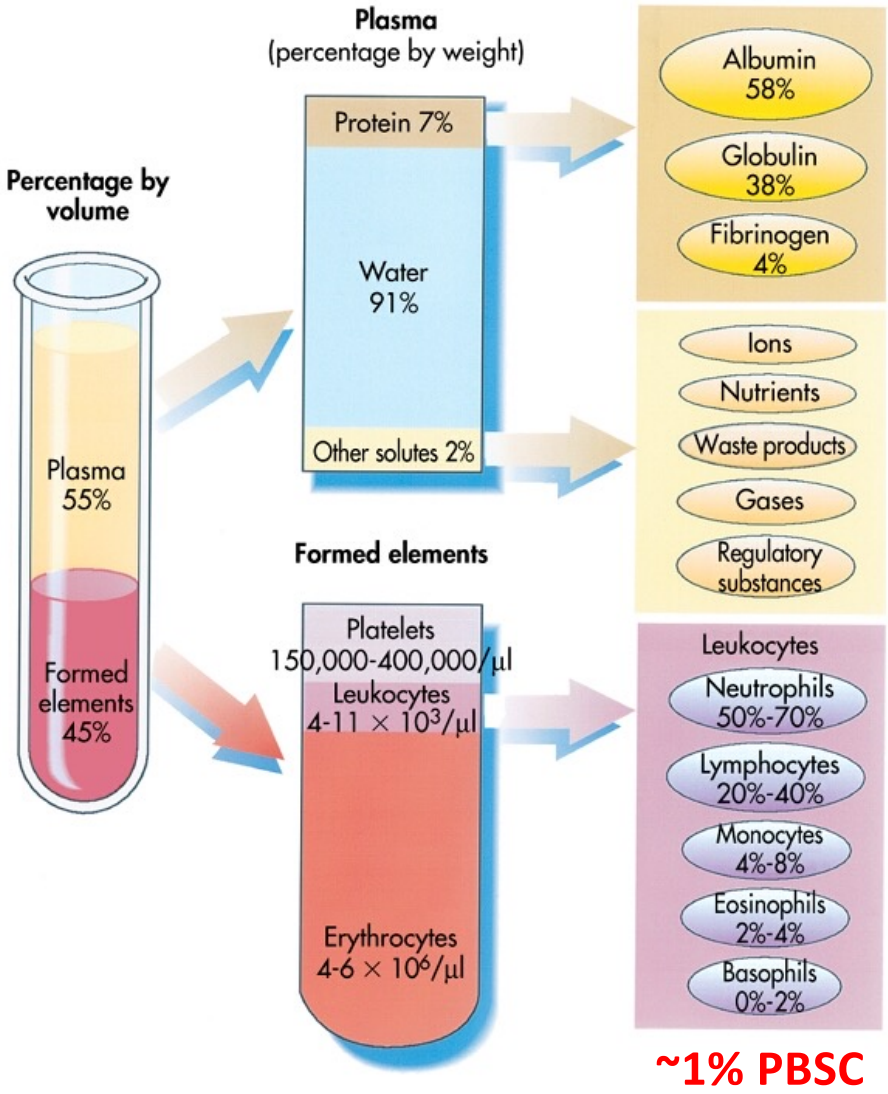
Part I

- Composition & Functions of Blood cells
- Anemias
- Bleeding disorders

Blood

- Hem/o and Hemat/o
- Plasma - 55%
- Formed elements - 45%
- Serum
  - plasma without clotting proteins

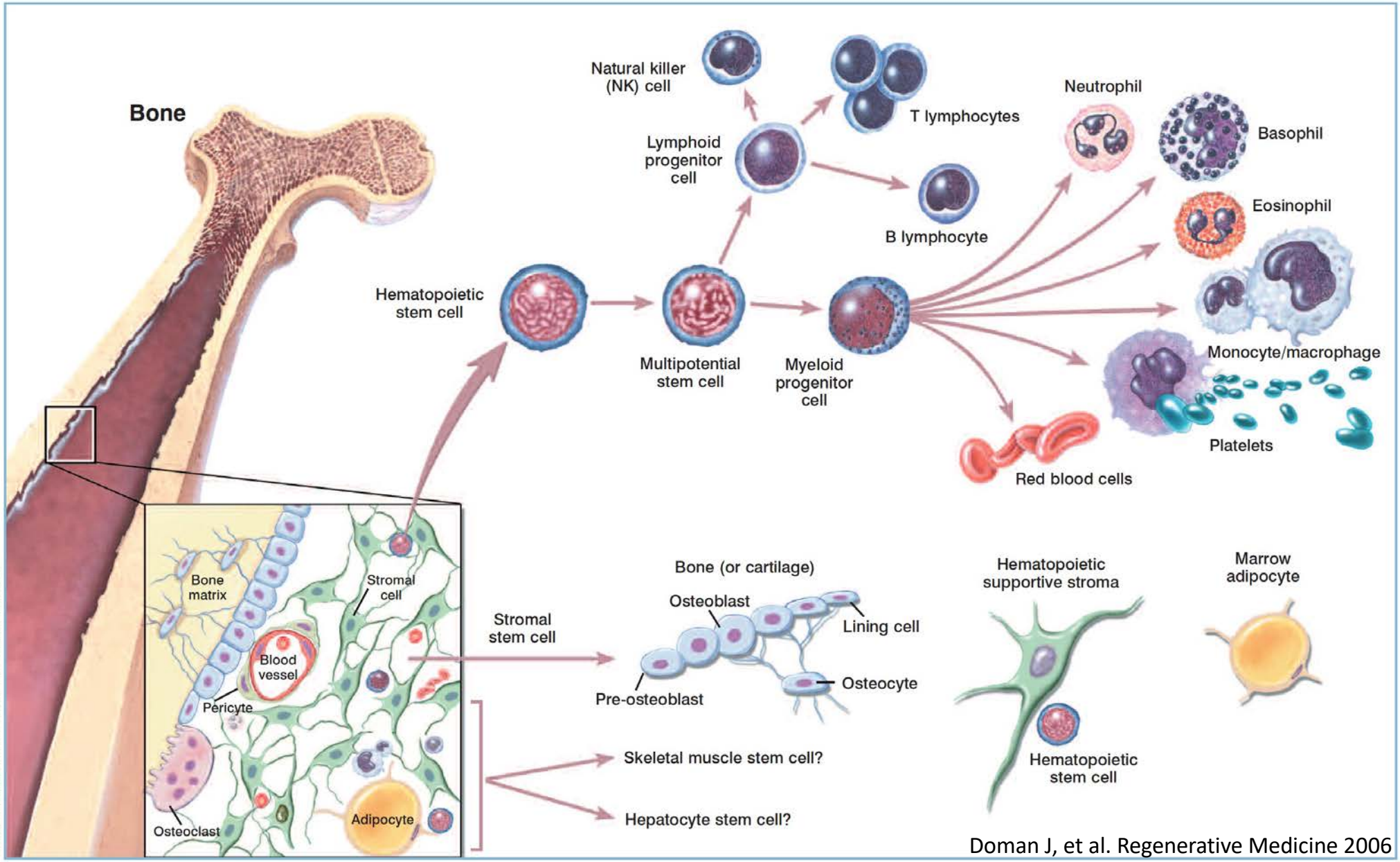




~1% PBSC

From Thibodeau GA, Patton KT: *The human body in health and disease*, ed 3, St. Louis, 2002, Mosby.

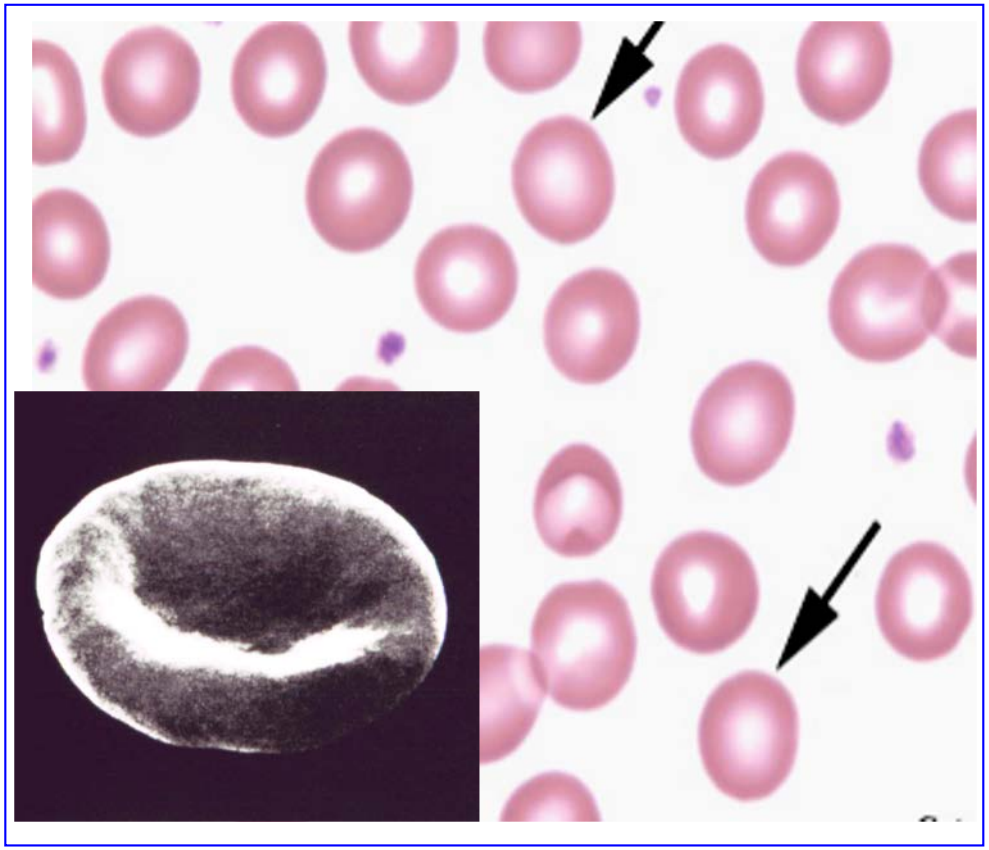
Hematopoietic Cells



Doman J, et al. Regenerative Medicine 2006

Mature red blood cells / Erythrocytes

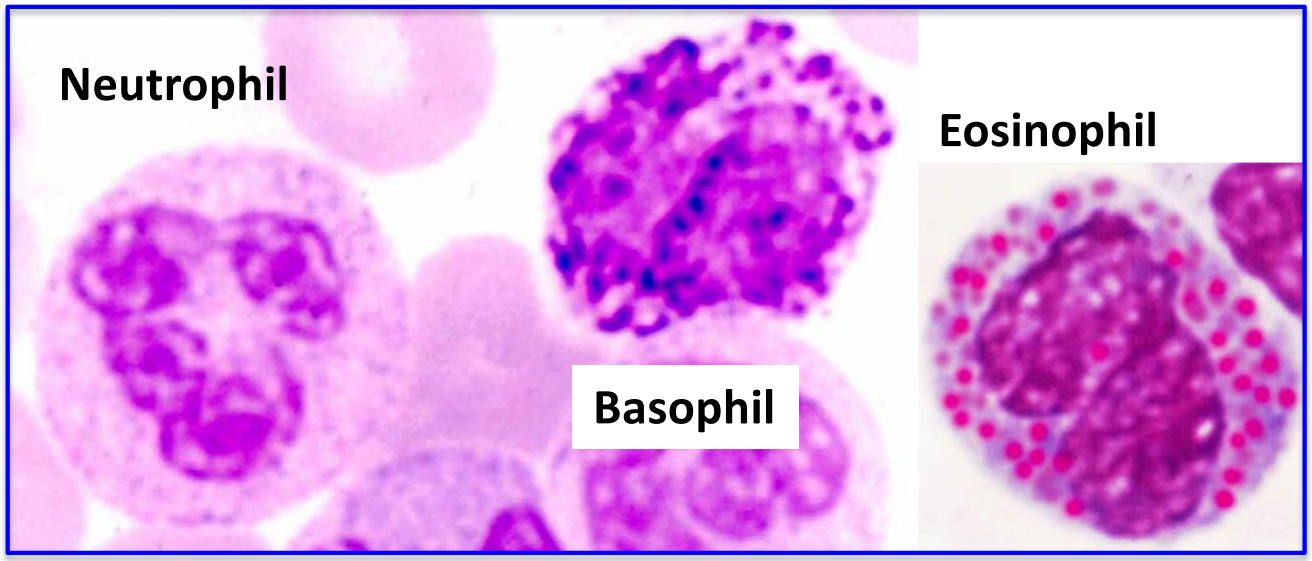
- Erythroblast: precursor cell in bone marrow
- Most numerous cells (4.5 M cells/μl)
- Survive 120 days
- Contain Hemoglobin: oxygen-carrying protein formed by the developing red cell
- Main function: transport of oxygen



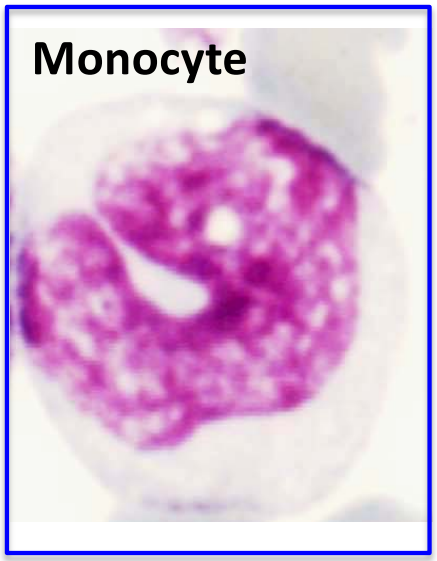
Assist. Prof. Prathom Prathomthanapongs.Blood cell morphology.CMU

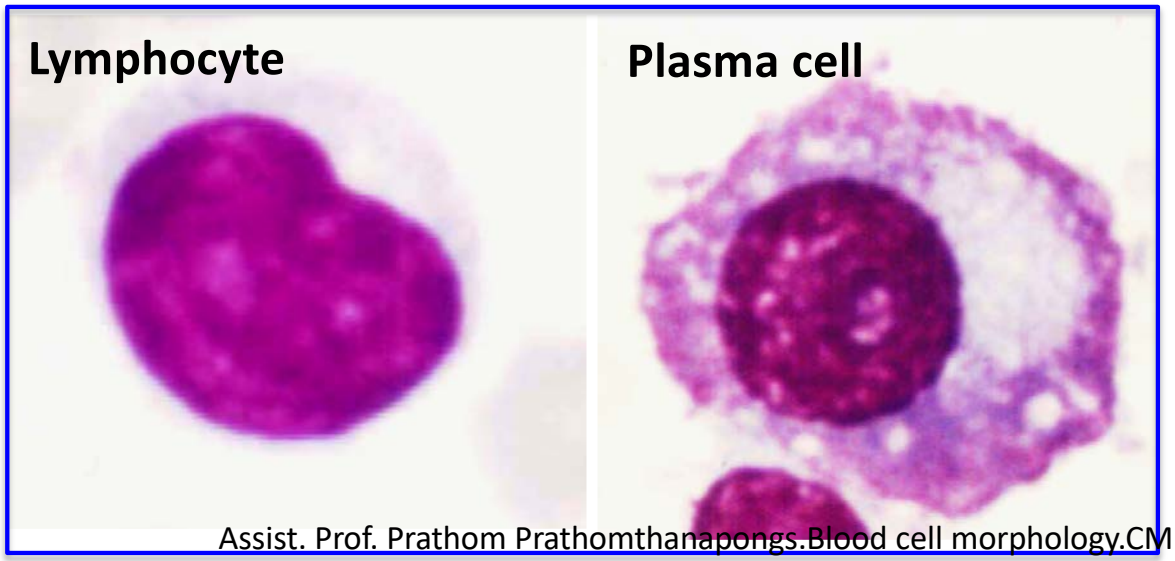
White blood cells / Leukocytes

Polymorphonuclear cells



Monomorphonuclear cells





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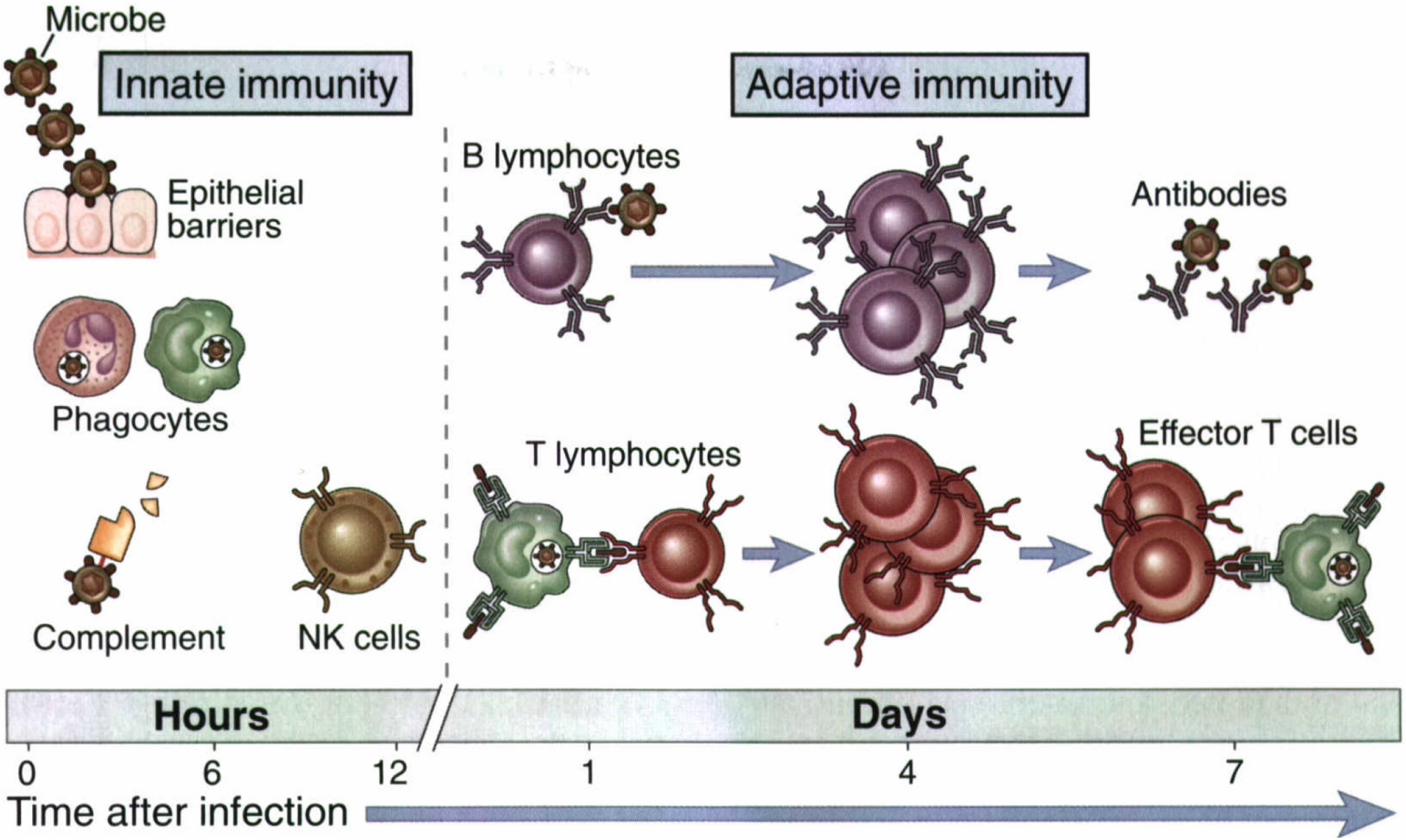
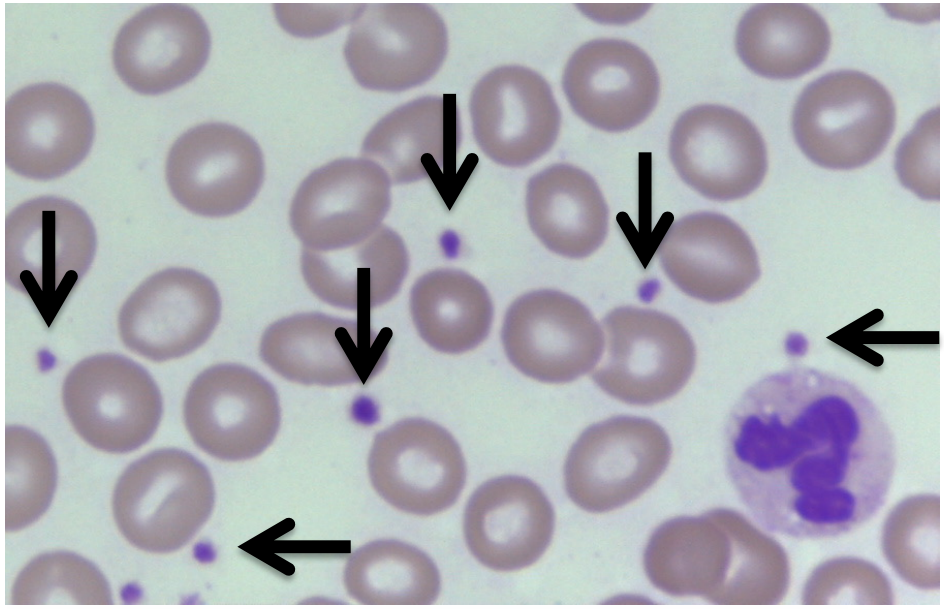
White blood cells / Leukocytes

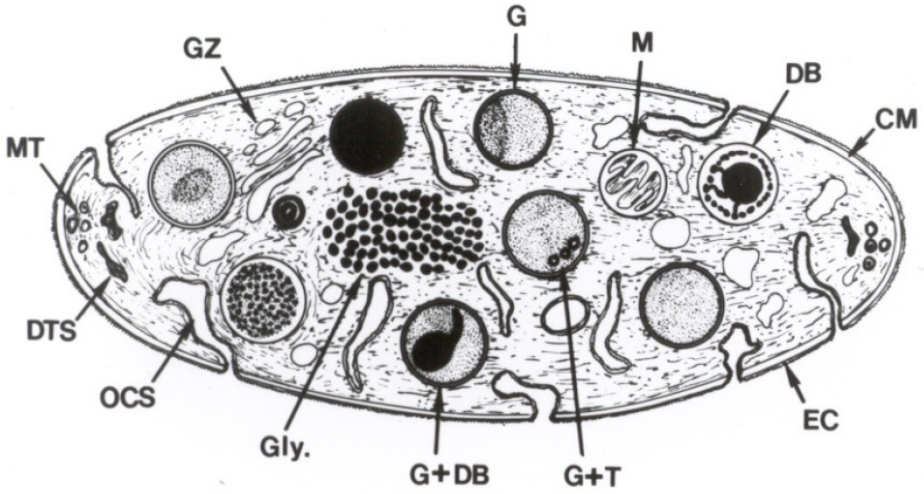


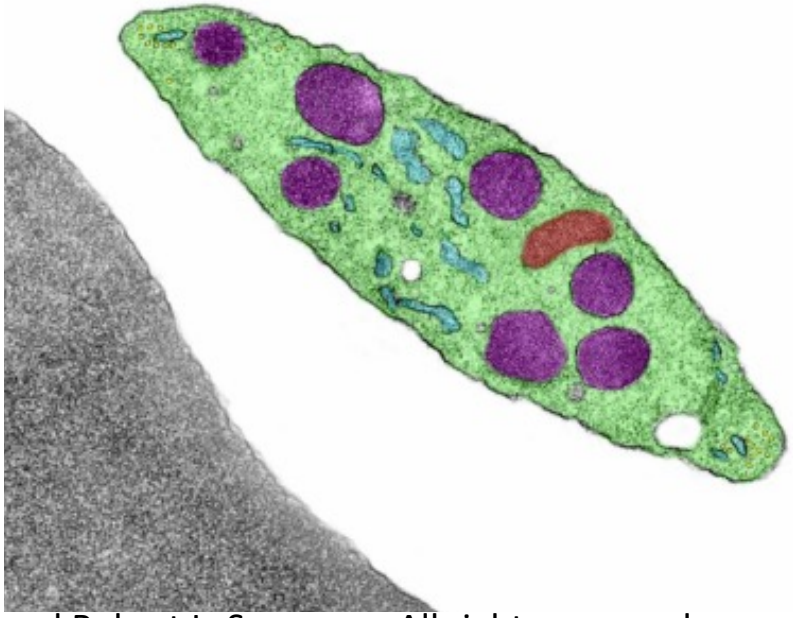
Abbas, et al. Cellular and molecular immunology.Saunders.2007

Platelet

- Essential for blood coagulation
- Represent bits of the cytoplasm of megakaryocytes, largest precursor cells in the bone marrow
- Short survival, about 10 days





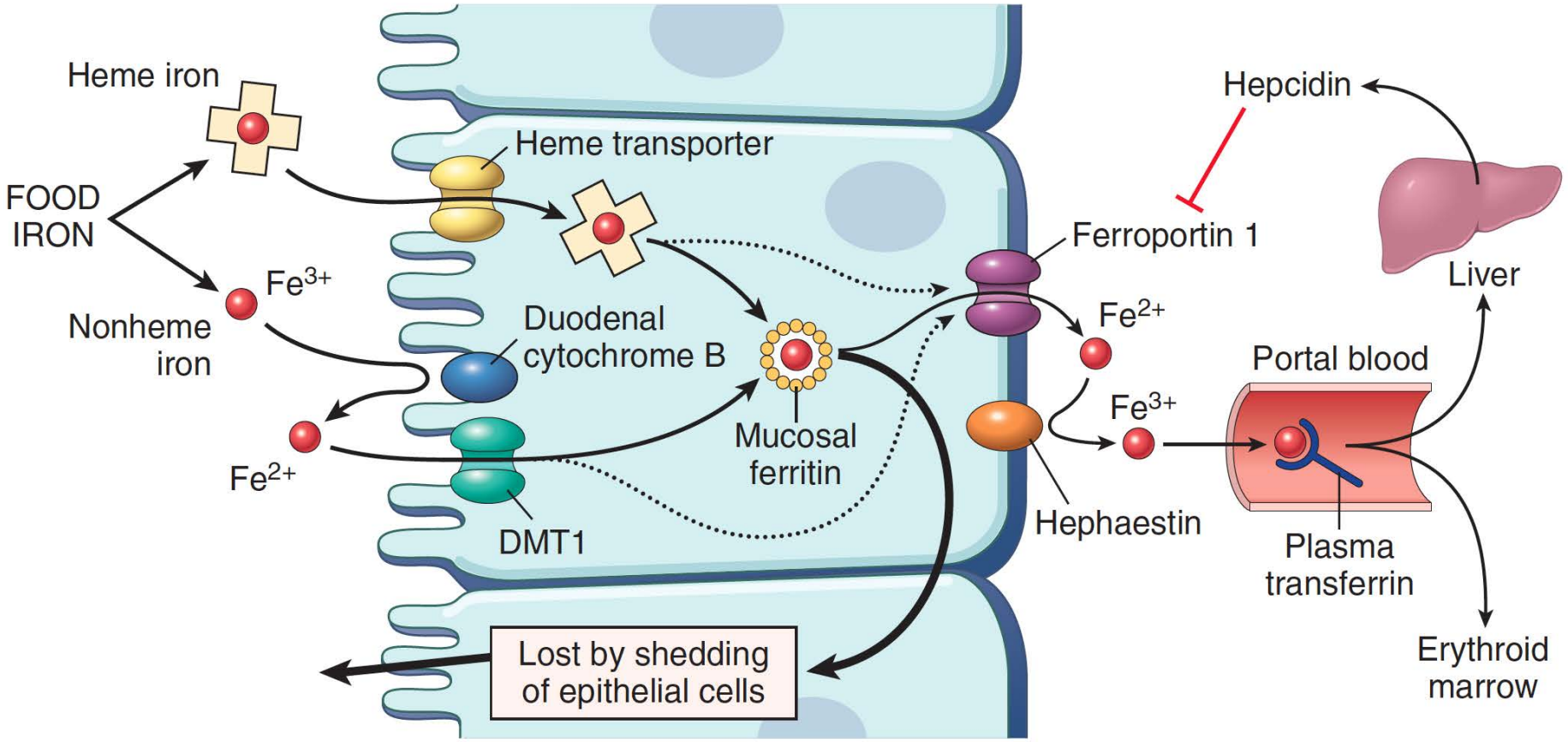


HEMATOPOIESIS

Hematopoiesis

- Formation and development of blood cells
- Bone marrow replenishes the blood cells
- Substances necessary for hematopoiesis
  - Protein
  - Vitamin B_{12}
  - Folic acid (one of the vitamin B group)
  - Iron
  - Hormones
  - Cytokines

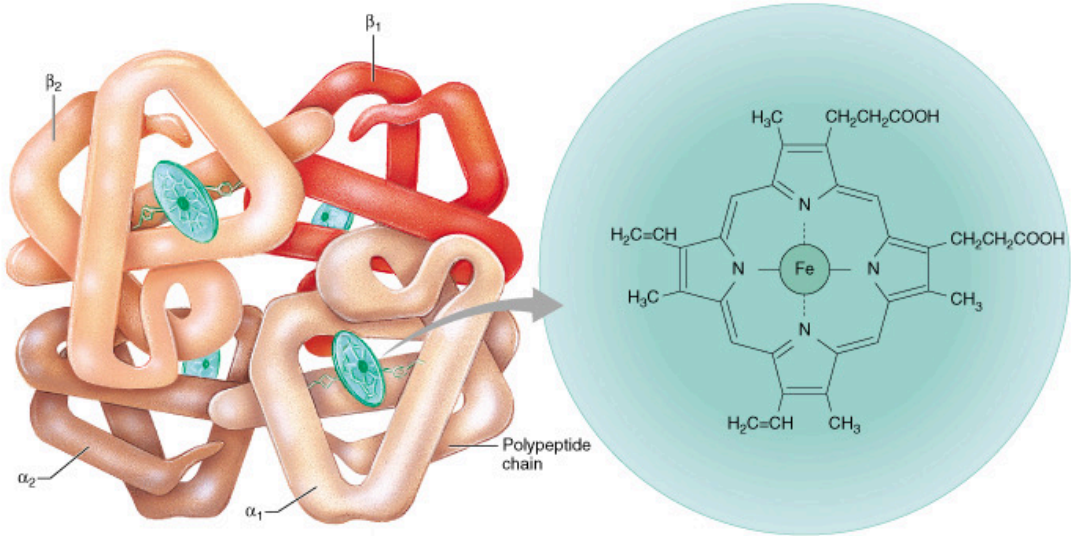
Iron metabolism

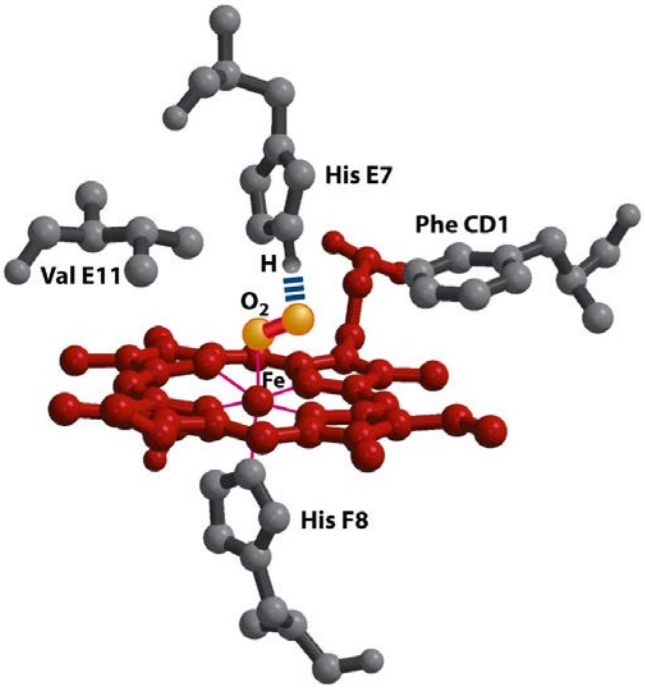


DMT1; divalent metal transporter-1

Kumar, et al.Basic Pathology. Saunders.2013

Hemoglobin A





Lehninger Principles of Biochemistry, 6th Ed, 2013. W.H. Freeman and company

The Bohr effect

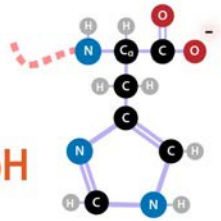
water + carbon dioxide —carbonic anhydrase→ carbonic acid (H_2CO_3) ⇌ bicarbonate (HCO_3^-)

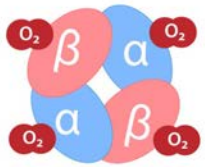
The Bohr effect explains how high CO_2 helps hemoglobin release oxygen in tissues that need it

oxygen-loving R form

His 146 unprotonated - T-stabling salt bridges can't form

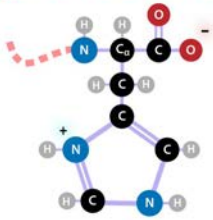
high O_2
low CO_2
higher pH





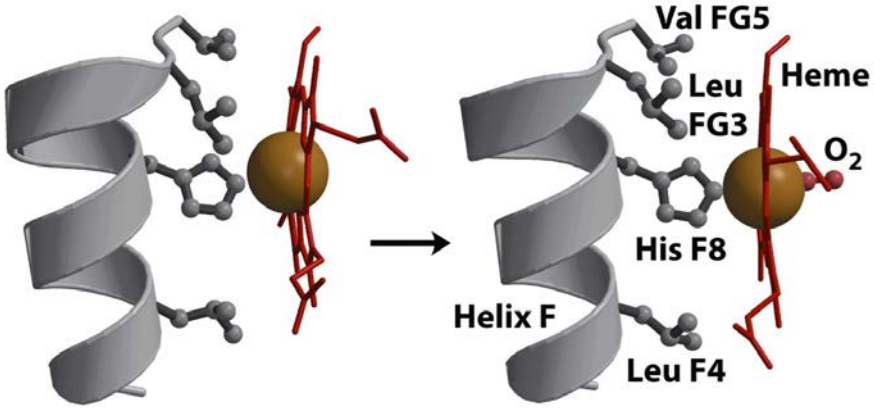
oxygen-not-so-loving T form

low O_2
high CO_2
lower pH



His 146 protonated - salt bridges stabilize T state

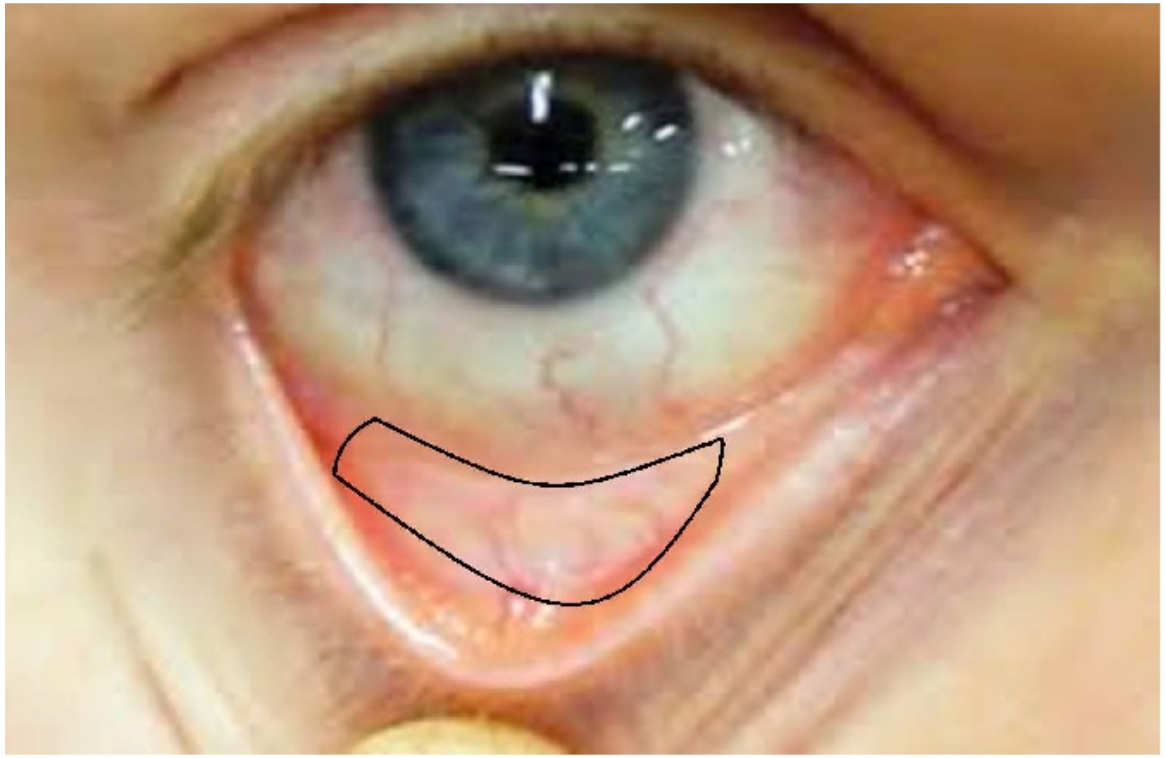
T (Tense) state R (Relex) state



Lehninger Principles of Biochemistry, 6th Ed, 2013. W.H. Freeman and company

ANEMIA

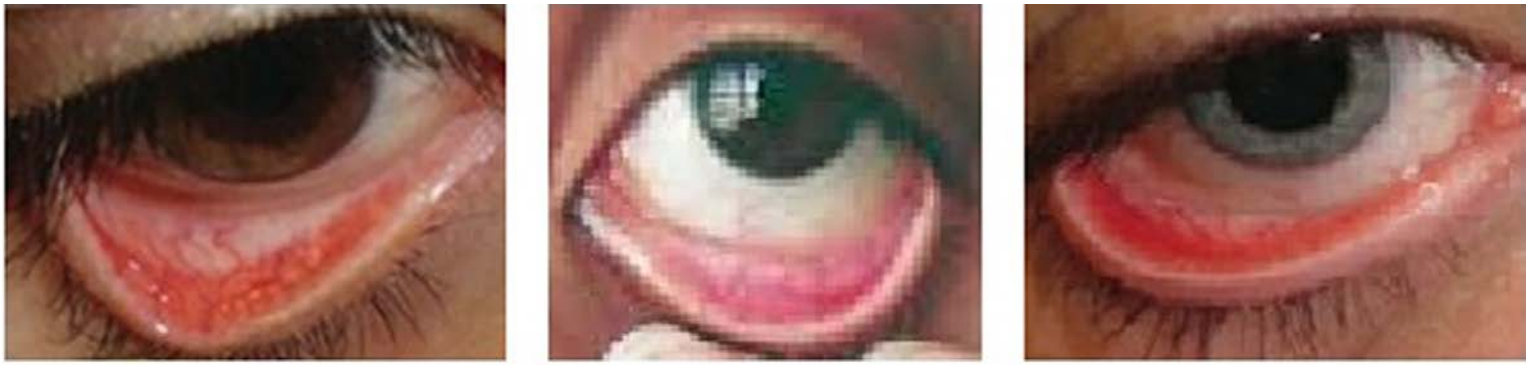
The anterior conjunctival pallor of the eye



Anemia

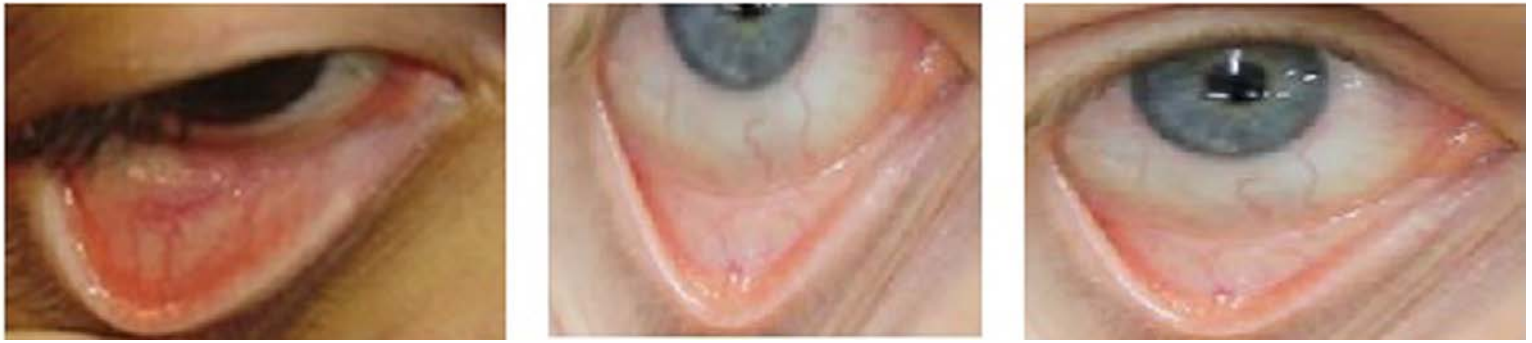
Non-anemic patients

(A)



Anemic patients

(B)



Int J Imaging Syst Technol. 2020;30:112–125.

Anemia

- Reduction in RBCs or subnormal level of hemoglobin
- Inadequate production of RBCs
- Insufficient raw materials
  - Iron deficiency
  - Vitamin B_{12} deficiency
  - Folic acid deficiency
- Inability to deliver adequate red cells into circulation due to marrow damage or destruction (aplastic anemia), replacement of marrow by foreign or abnormal cells

Anemia

- Excessive loss of RBCs
  - External blood loss (hemorrhage)
  - Shortened survival of RBCs in circulation
  - Defective RBCs: hereditary hemolytic anemia
  - Accelerated destruction of cells from antibodies to RBC or by mechanical trauma to circulating RBCs

DeLong, et al. Dental Hygienist.2nd edition.Lippincott Williams&Wilkins.2013

Morphological Classification of Anemia

Size (abnormal in size = Anisocytosis)

- Normocytic anemia: normal size and appearance
- Macrocytic anemia: cells larger than normal
  - Folic acid deficiency
  - Vitamin B_{12} deficiency
- Microcytic anemia: cells smaller than normal

Color

- Normochromia
- Hypochromia
- Hyperchromia
- Polychromasia

Shape

- Abnormal in shape = Poikilocytosis

RED BLOOD CELL MORPHOLOGY

Size variation

- Normal
- Microcyte
- Macrocyte
- Oval macrocyte
- Hypochromic macrocyte

Hemoglobin distribution

- Hypochromia
  - 1+
  - 2+
  - 3+
  - 4+
- Polychromasia (Reticulocyte)

Shape variation

- Target cell
- Acanthocyte
- Spherocyte
- Helmet cell (fragmented cell)
- Ovalocyte
- Schistocyte (fragmented cell)
- Stomatocyte
- Tear drop
- Sickle cell
- Burr cell

Inclusions

- Pappenheimer bodies (siderotic granules)
- Cabot's ring
- Basophilic stippling (coarse)
- Howell-Jolly

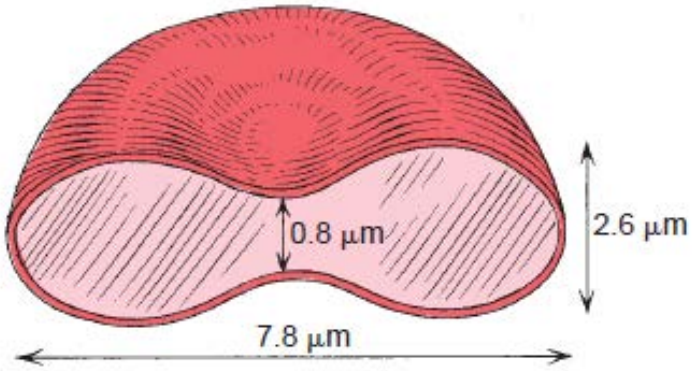
Red cell distribution

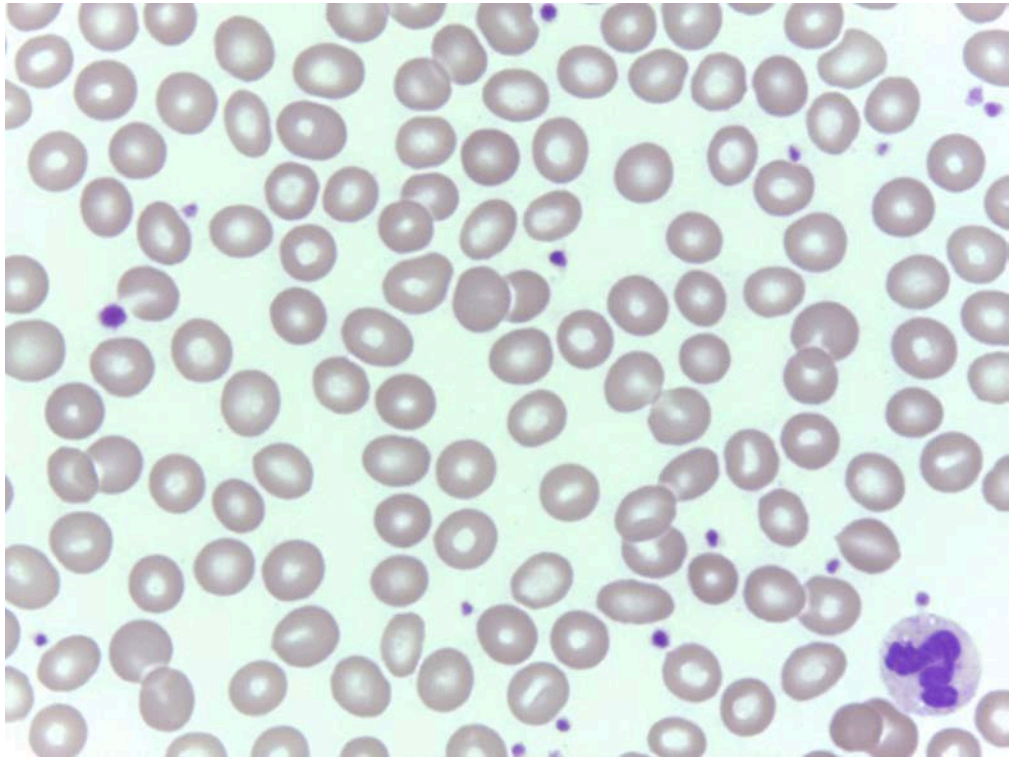
- Agglutination
- Rouleaux

Crystal formation

- HbSC
- HbC

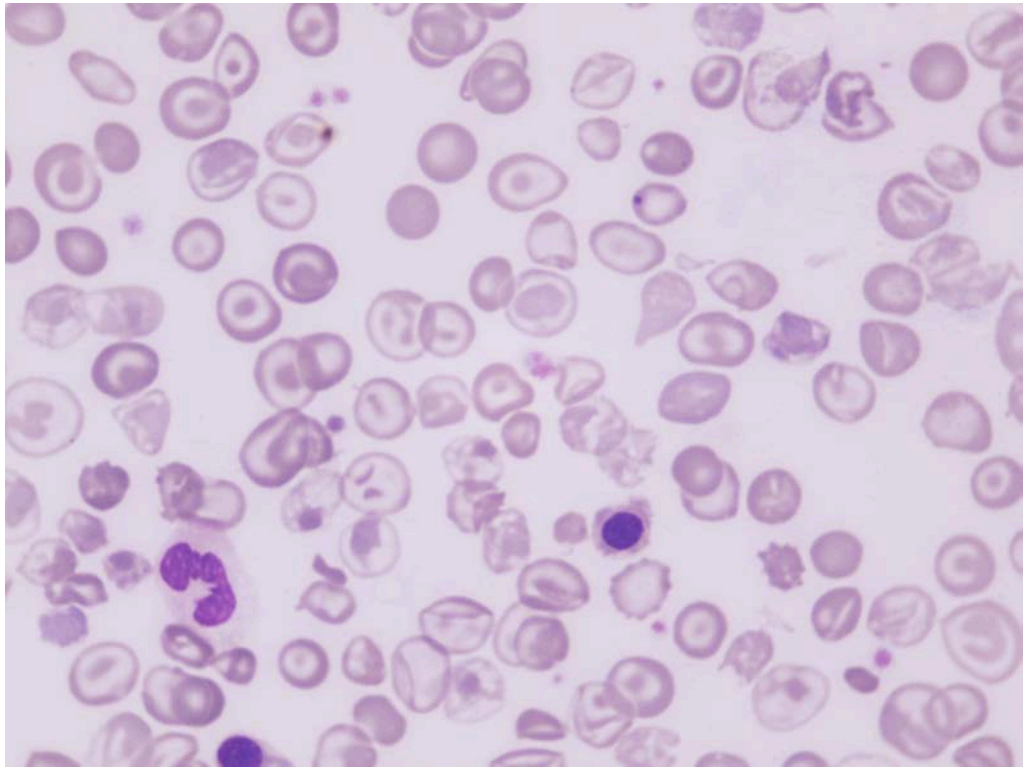
Normocytic Normochromia





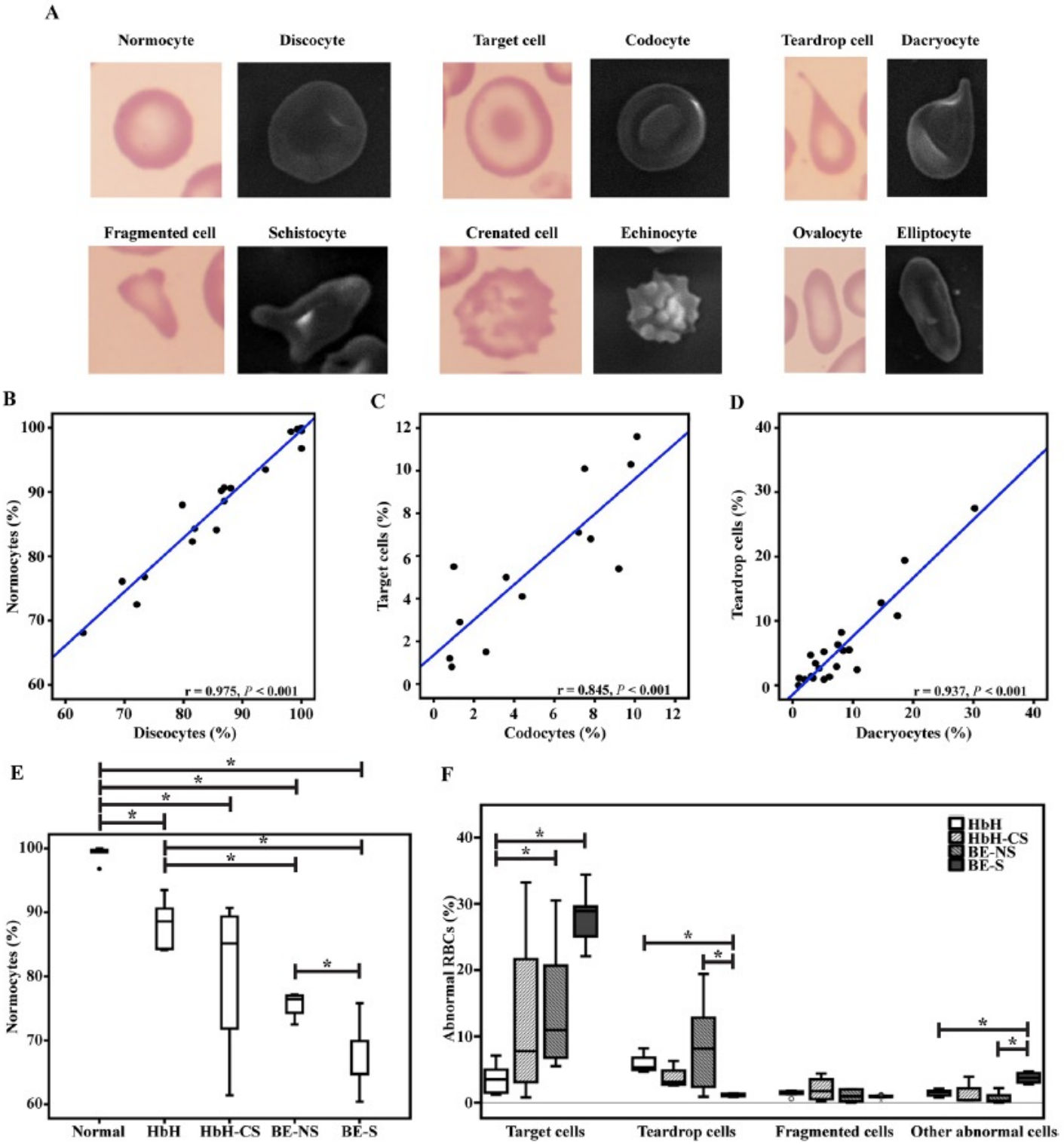
Microcytic Hypochromic anemia

- Anisopoikilocytosis



Ariz's Thesis

Quantitative analysis of abnormal red cells in thalassaemia



Chaichompoo P, *et al.*
J Clin Pathol.2019;72:520–524.

Iron deficiency anemia

- Most common type of anemia
- Hypochromic microcytic anemia
- Iron absorbed from duodenum, transferred via transferrin, stored as ferritin
- Etiology
  1. Inadequate dietary intake
     - Found in 30% of the world's population
  2. Malabsorption
     - Absorbed in duodenum
     - GI surgery
  3. Blood loss
     - 2 ml blood contain 1mg iron
     - GI, GU losses
  4. Hemolysis

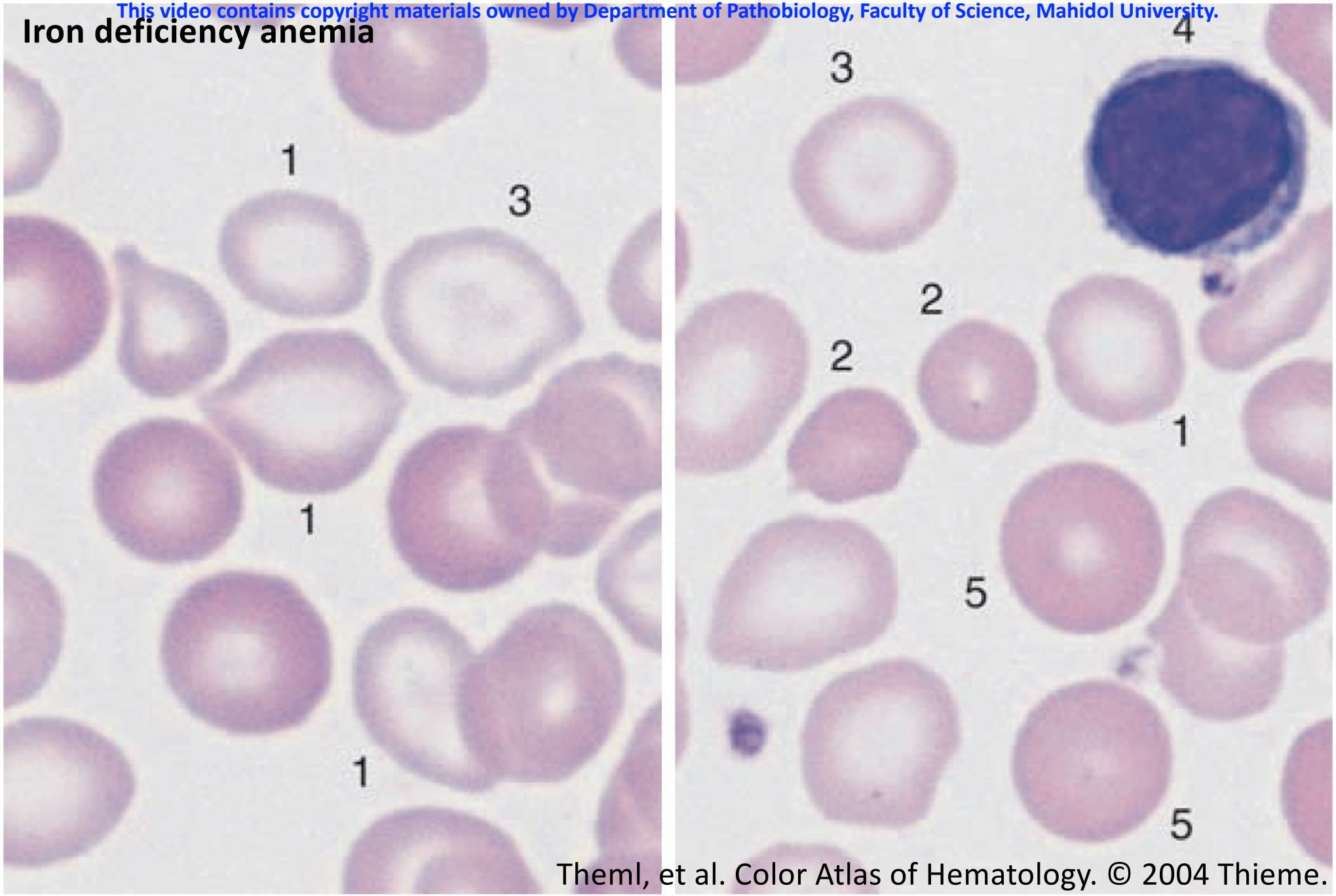
Iron deficiency anemia

- Clinical Manifestations
  - Most common: pallor
  - Second most common: inflammation of the tongue (glossistis)
  - Cheilitis=inflammation/fissures of lips
  - Sensitivity to cold
  - Weakness and fatigue
- Diagnostic Studies
  - CBC
  - Iron studies Diagnostics:
  - Iron levels: Total iron-binding capacity (TIBC), Serum Ferritin.
  - Endoscopy/Colonscopy

Iron deficiency anemia

- Characteristic laboratory profile
  - Low serum ferritin and serum iron
  - Higher than normal serum iron-binding protein
  - Lower than normal percent iron saturation
- Treatment
  - Primary focus: learn cause of anemia
  - Direct treatment towards cause than symptoms
  - Administer supplementary iron
- Examples
  - Infant with a history of poor diet
  - Adults: common cause is chronic blood loss from GIT (bleeding ulcer or ulcerated colon carcinoma)
  - Women: excessive menstrual blood loss
  - Too-frequent blood donations

Iron deficiency anemia

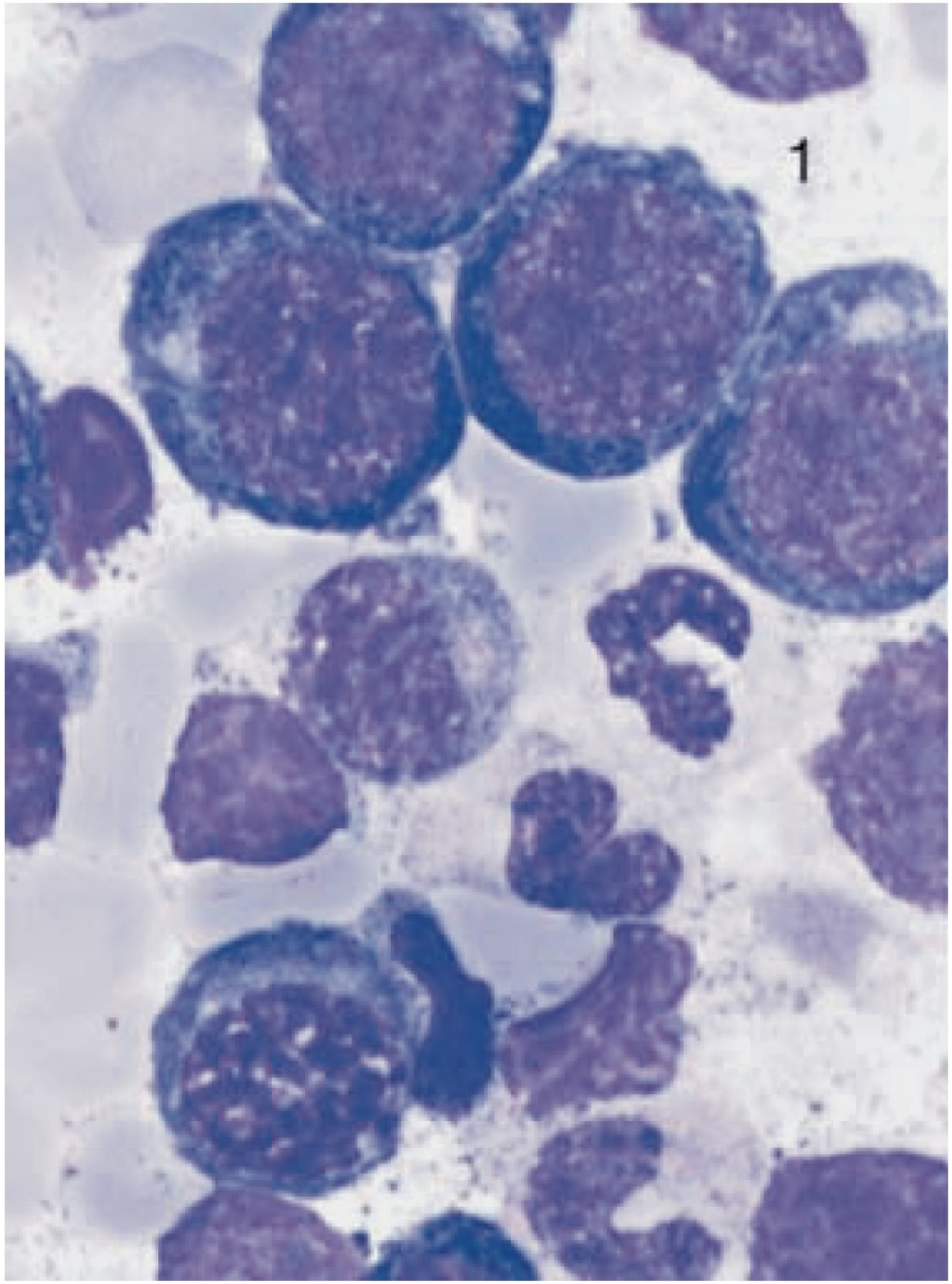


Theml, et al. Color Atlas of Hematology. © 2004 Thieme.

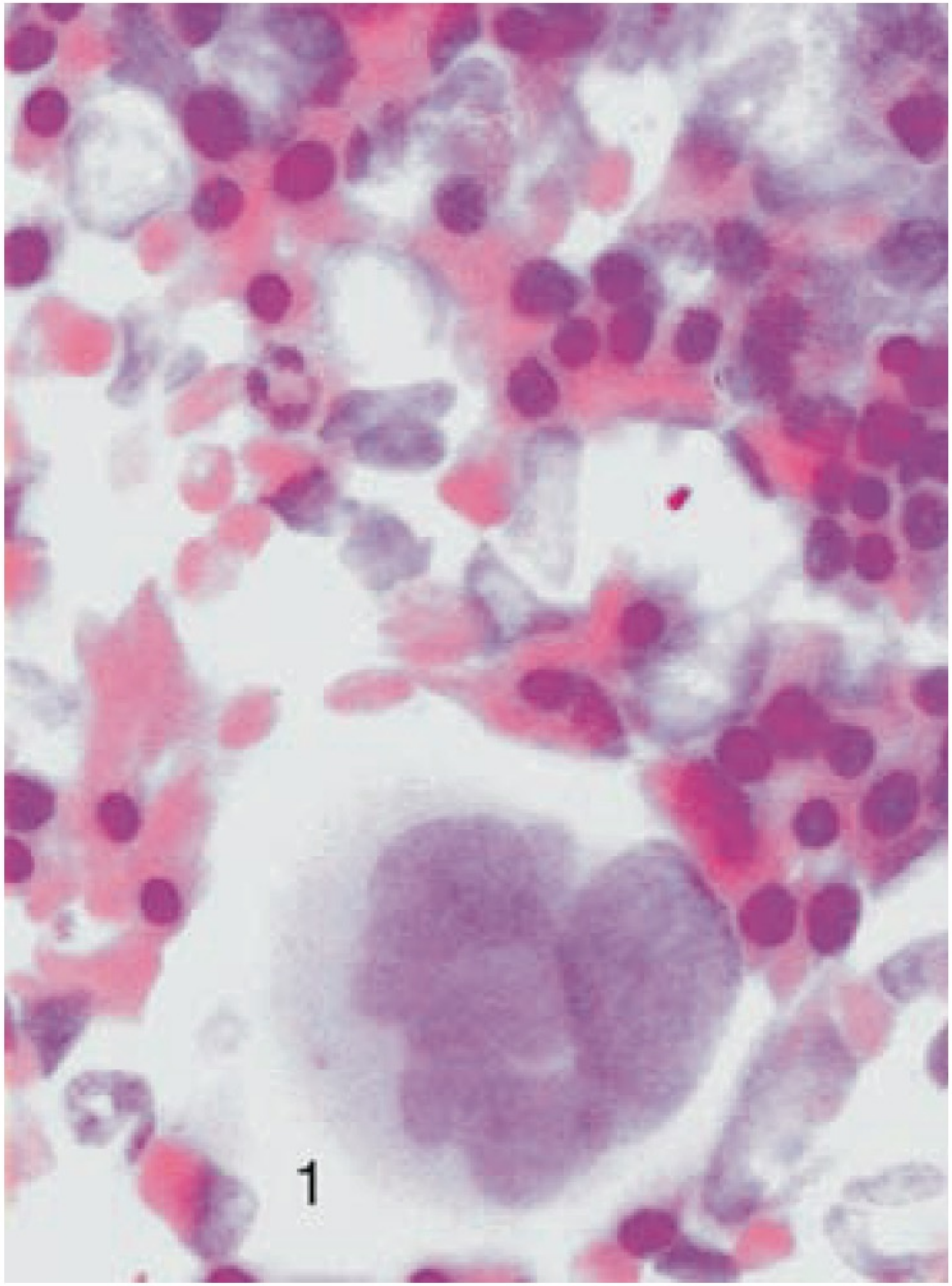
1. Ring-shaped erythrocytes; 2. Microcytes; 3. Faintly visible target cells; 4. Small lymphocyte;
5. Normal-sized erythrocytes after blood transfusion

Iron deficiency anemia – Bone marrow

Wright-Giemsa staining



Prussian blue staining



Theml, et al. Color Atlas of Hematology. © 2004 Thieme.

Vitamin B_{12} deficiency anemia

- Vitamin B_{12}: meat, liver, and foods rich in animal protein
- Folic acid: green leafy vegetables and animal protein foods
  - Both required for normal hematopoiesis and normal maturation of many other types of cells
  - Vitamin B_{12}: for structural and functional integrity of nervous system; deficiency may lead to neurologic disturbances

Vitamin B_{12} deficiency anemia

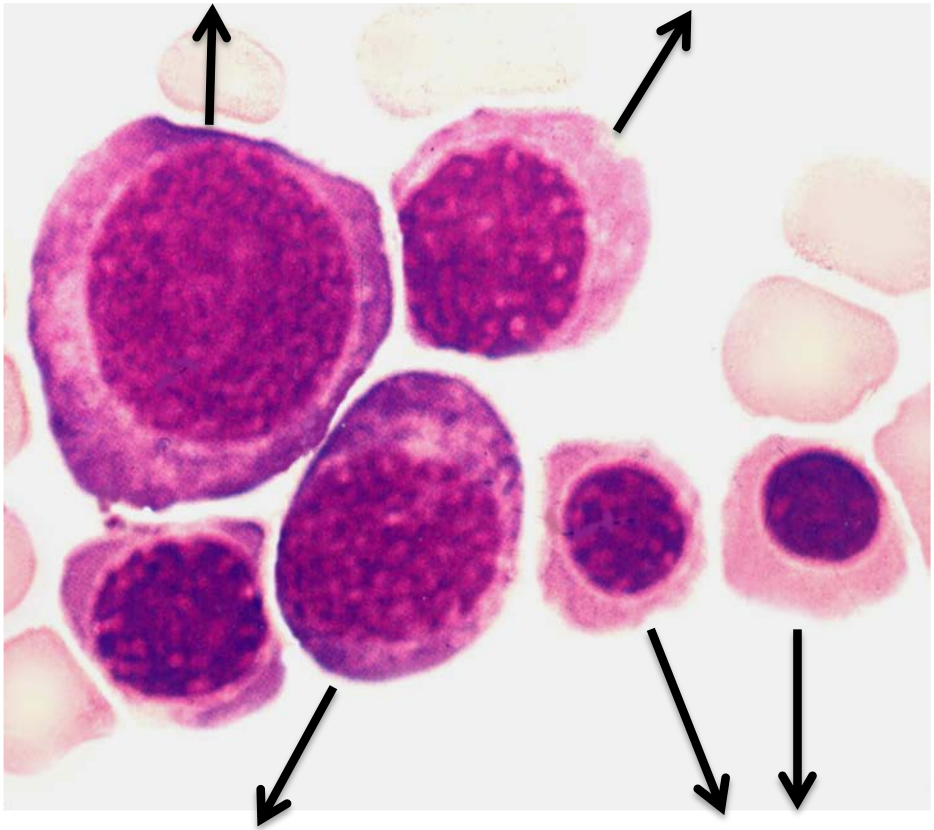
- Absence or deficiency of vitamin B_{12} or folic acid
  - Abnormal red cell maturation or megaloblastic erythropoiesis with formation of large cells called megaloblasts
  - Mature red cells formed are larger than normal or macrocytes; corresponding anemia is called macrocytic anemia
  - Abnormal development of white cell precursors and megakaryocytes: leukopenia, thrombocytopenia

Megaloblastic Series

- Delay development of nucleus in erythroblasts

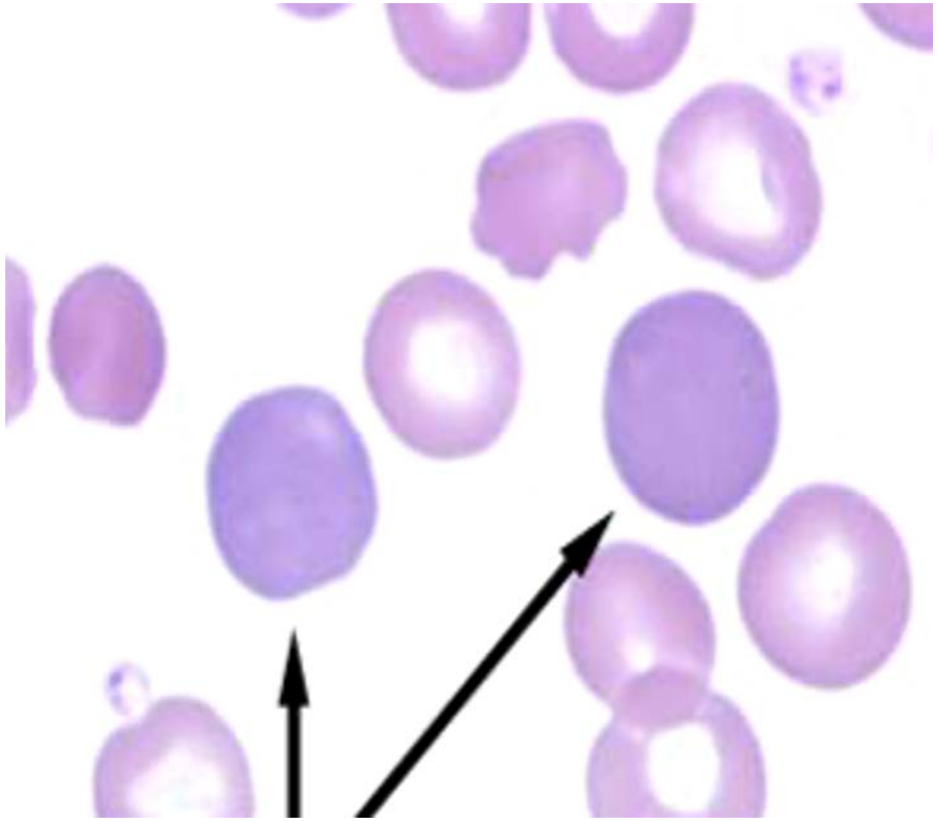
Promegaloblast

Polychromatic megaloblast



Basophilic megaloblast

Orthochromatic megaloblast



Polychromasia

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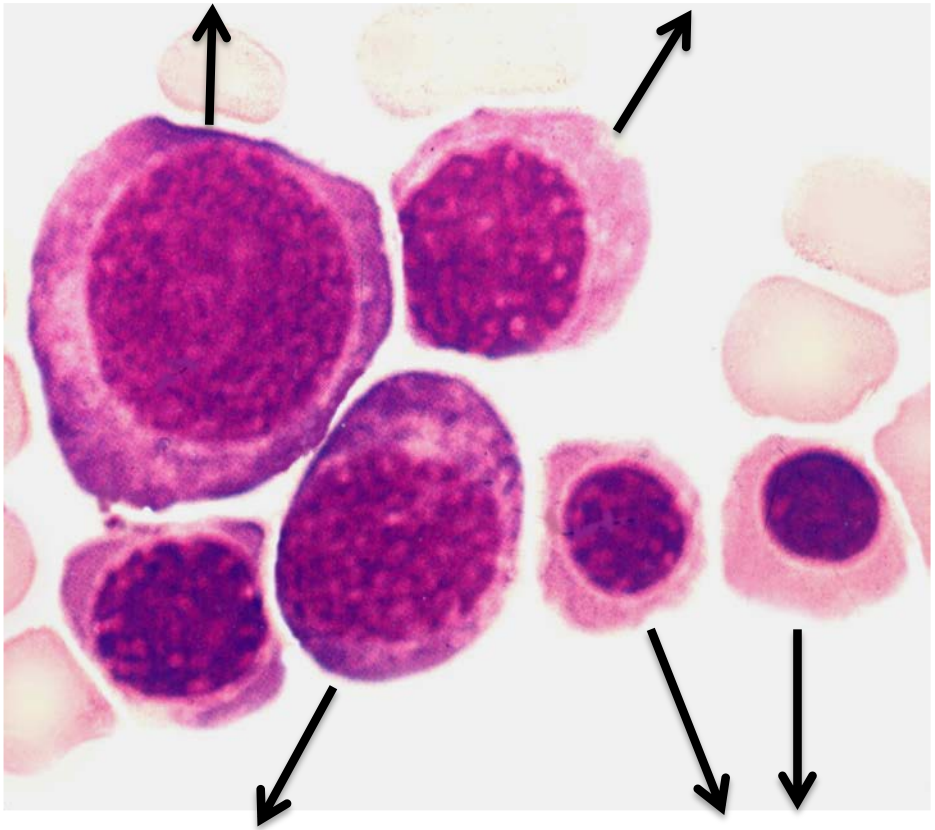
Megaloblastic Series

Promegaloblast

Polychromatic megaloblast



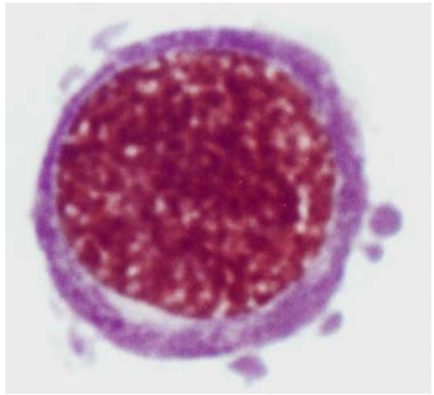
Basophilic megaloblast

Orthochromatic megaloblast

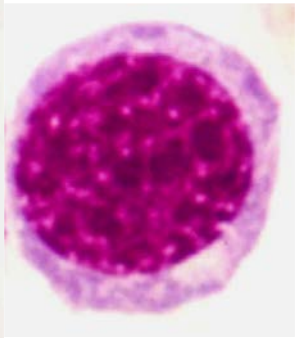
Erythroid series (Normal)

1.Pronormoblast

2.Basophilic normoblast

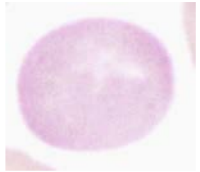


3.Polychromatophilic normoblast



4.Orthochromatic normoblast

5.Polychromasia



6.Mature RBC

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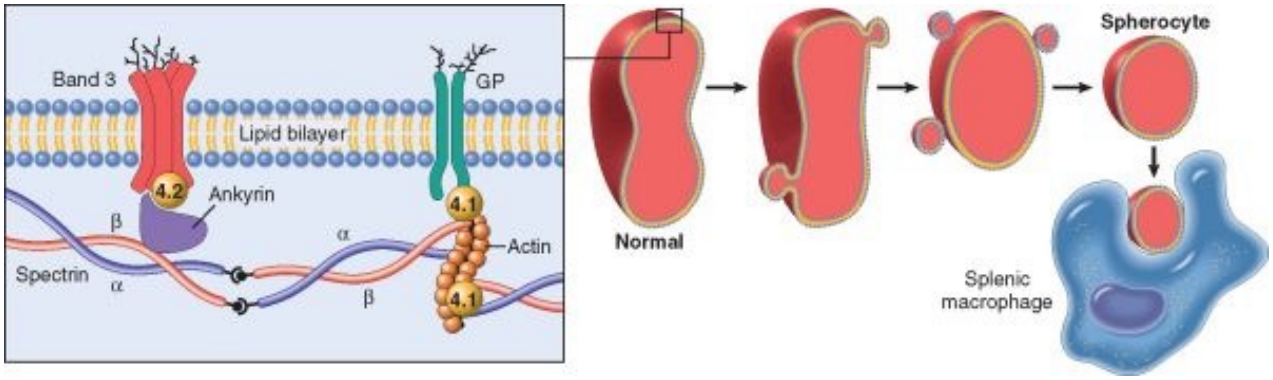
Hemolytic Anemia

Hereditary hemolytic anemia

- Genetic abnormality prevent normal survival

1. Abnormal shape:
   - Hereditary spherocytosis, Hereditary elliptocytosis
2. Abnormal hemoglobin (Hemoglobinapathy):
   - Sickle cell disease
3. Defective hemoglobin synthesis:
   - Thalassemia
4. Enzyme defects:
   - Glucose-6-phosphatase dehydrogenase deficiency

Hereditary Spherocytosis



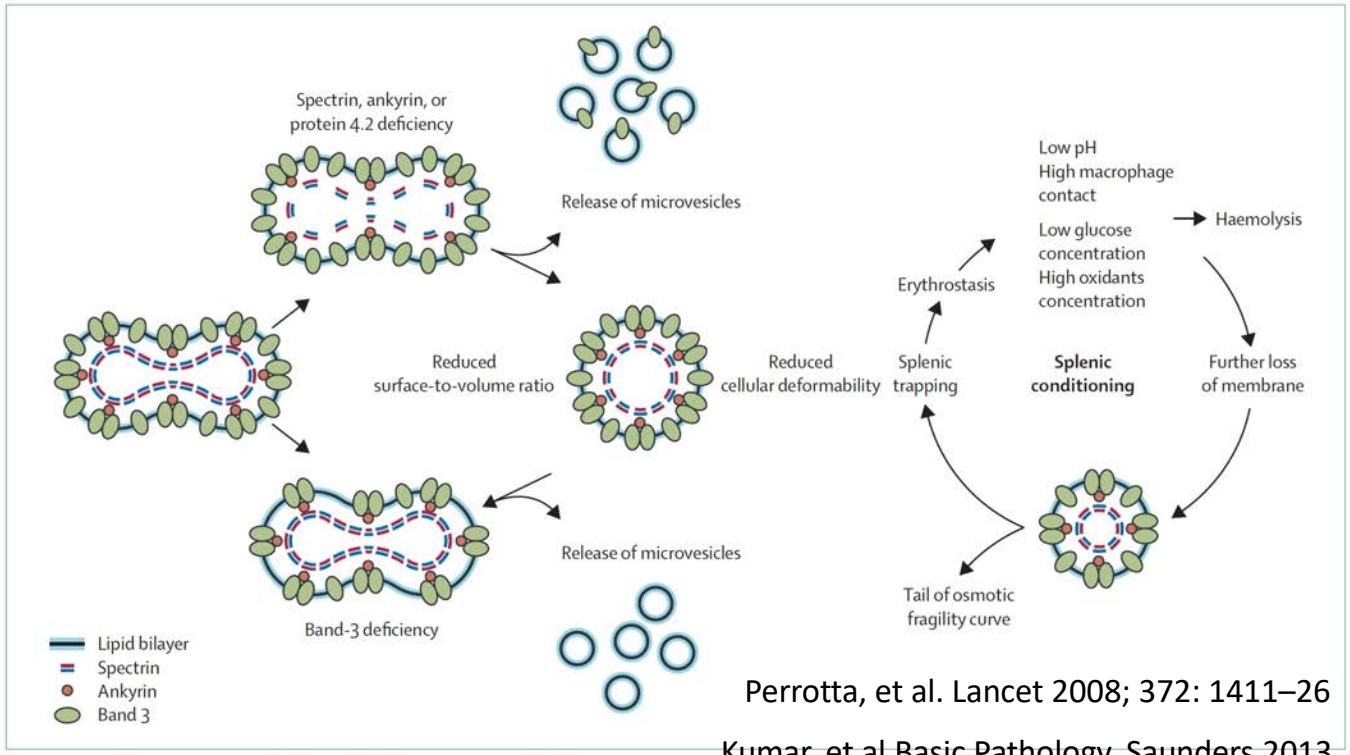
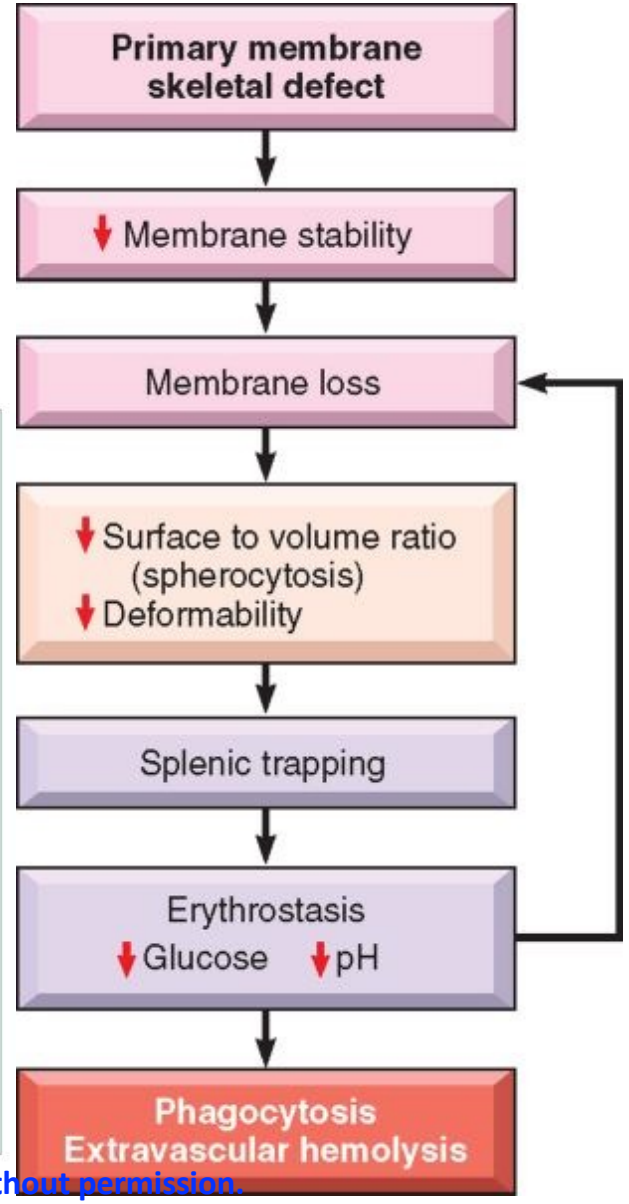


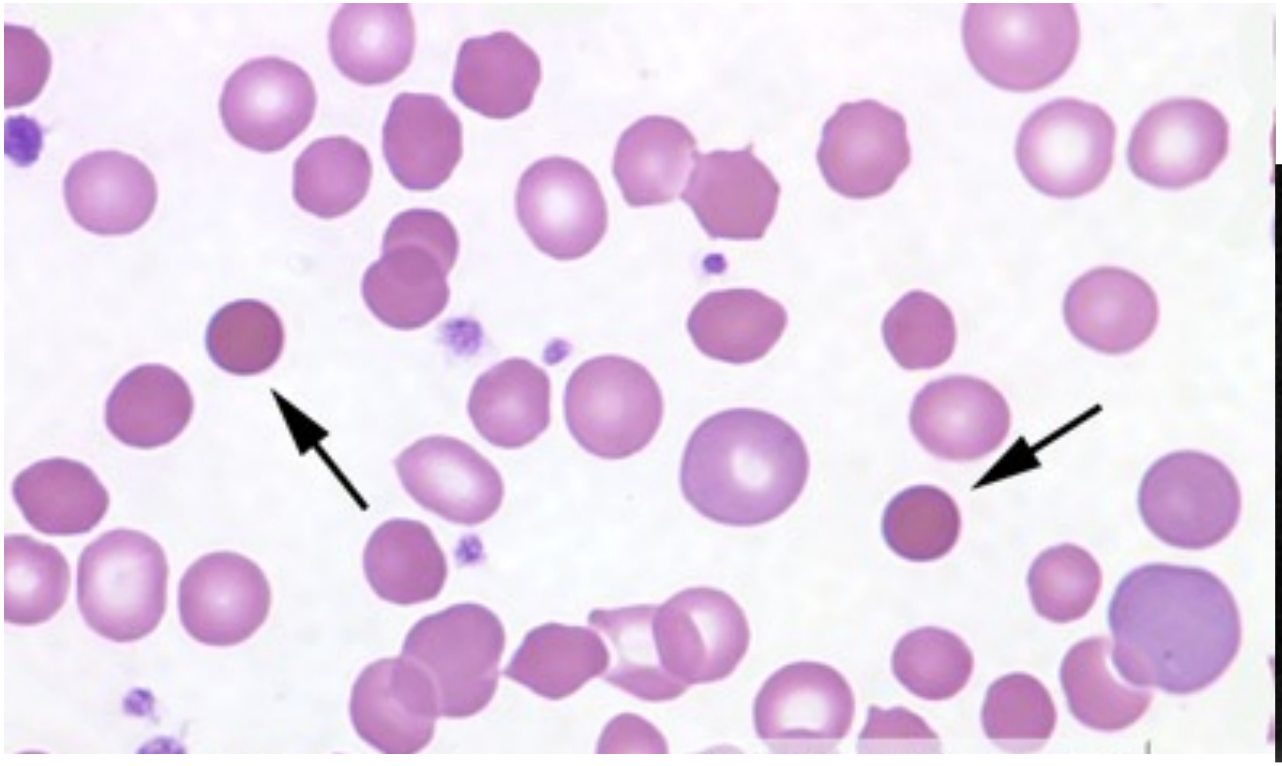
Figure 2: Pathophysiological effects of hereditary spherocytosis

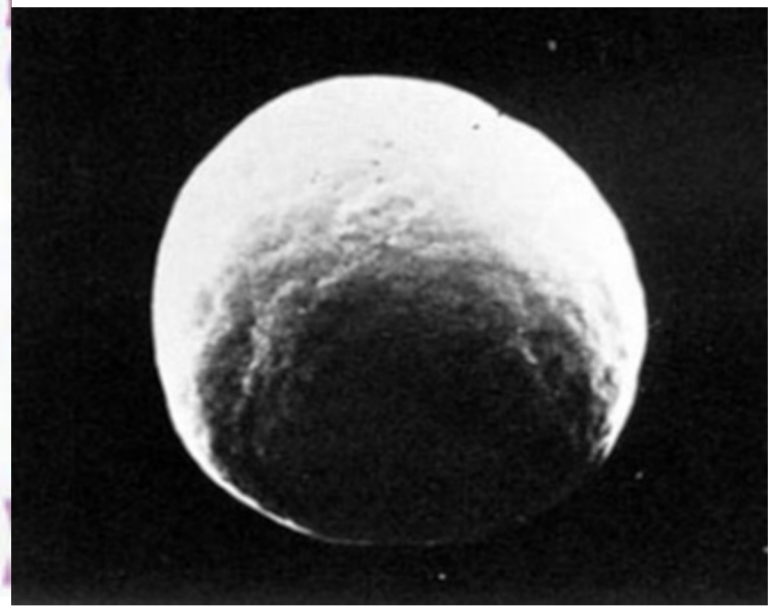


Perrotta, et al. Lancet 2008; 372: 1411–26

Kumar, et al.Basic Pathology. Saunders.2013

Hereditary Spherocytosis





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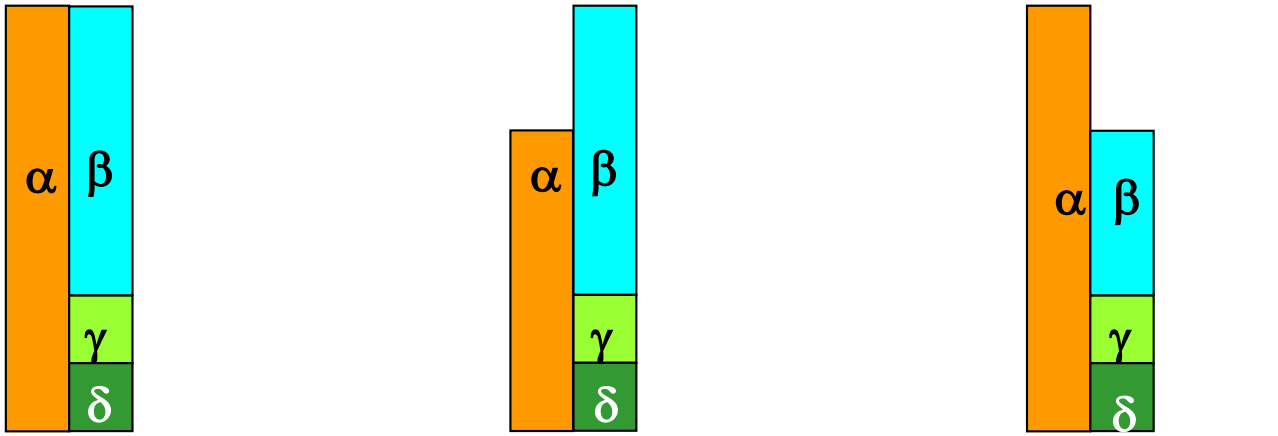
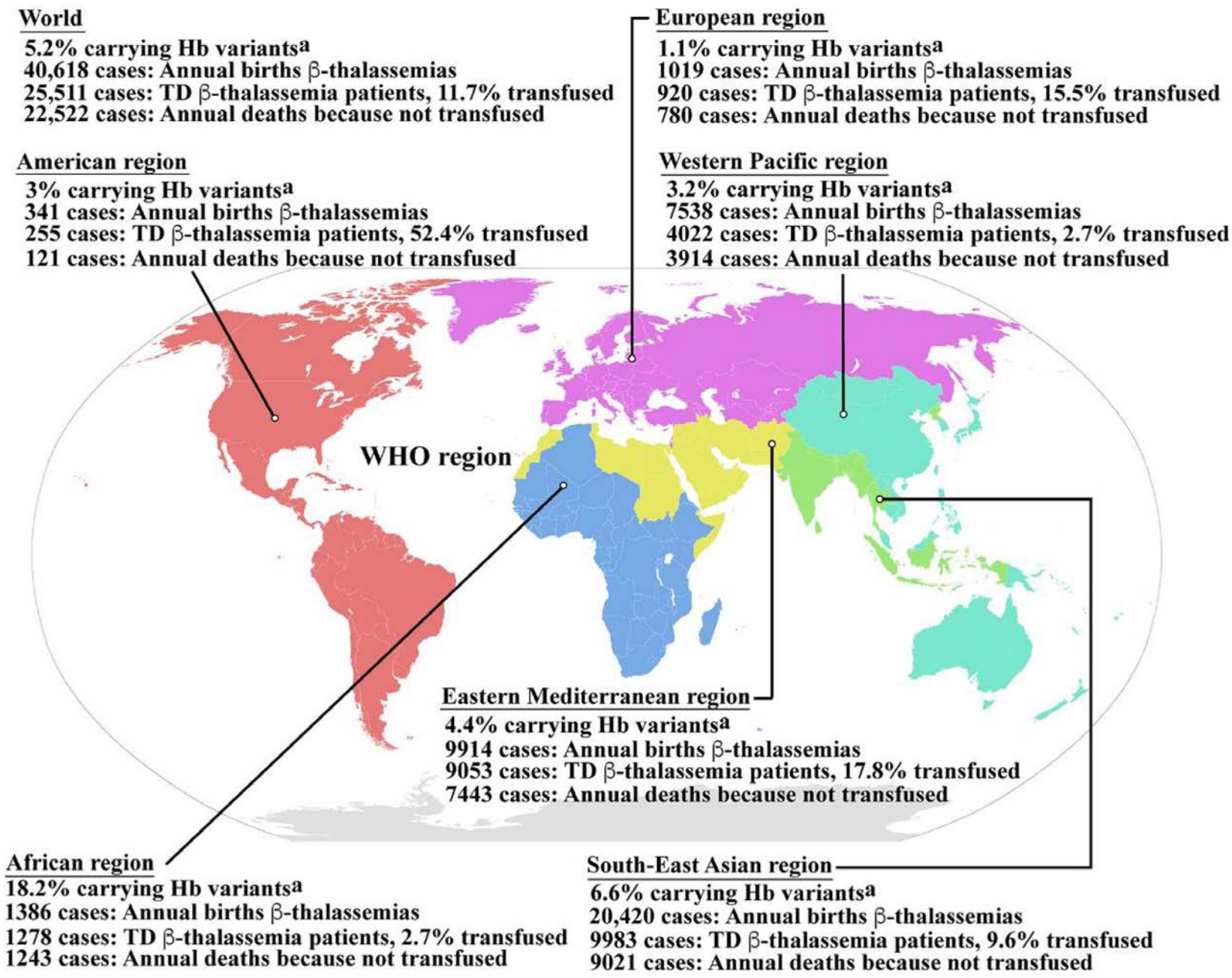
Thalassemia



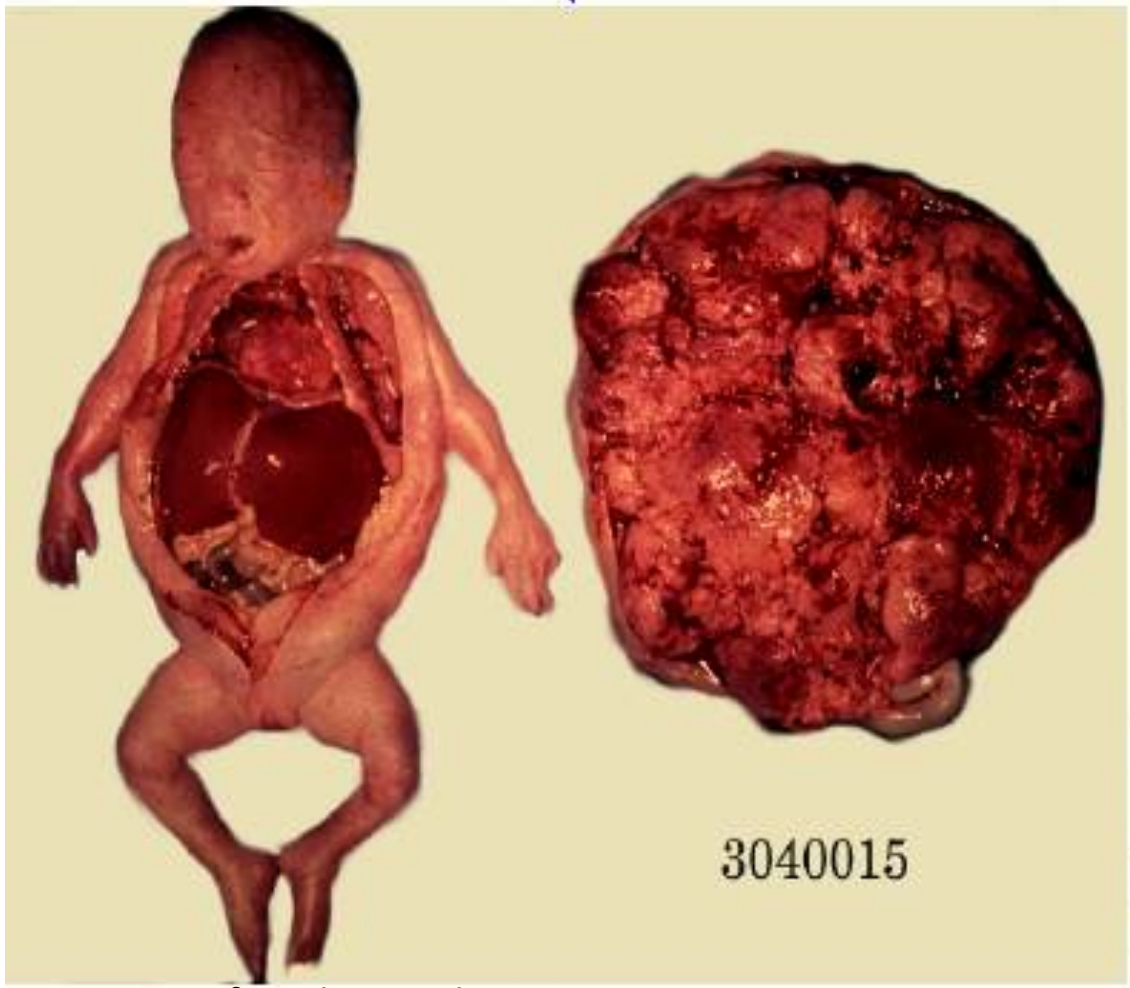
Thalassemia



Chaichompoo P, *et al.* Int. J. Mol. Sci. 2022, 23, 10811.

Hb H Disease

Hb Bart's Hydrops Fetalis



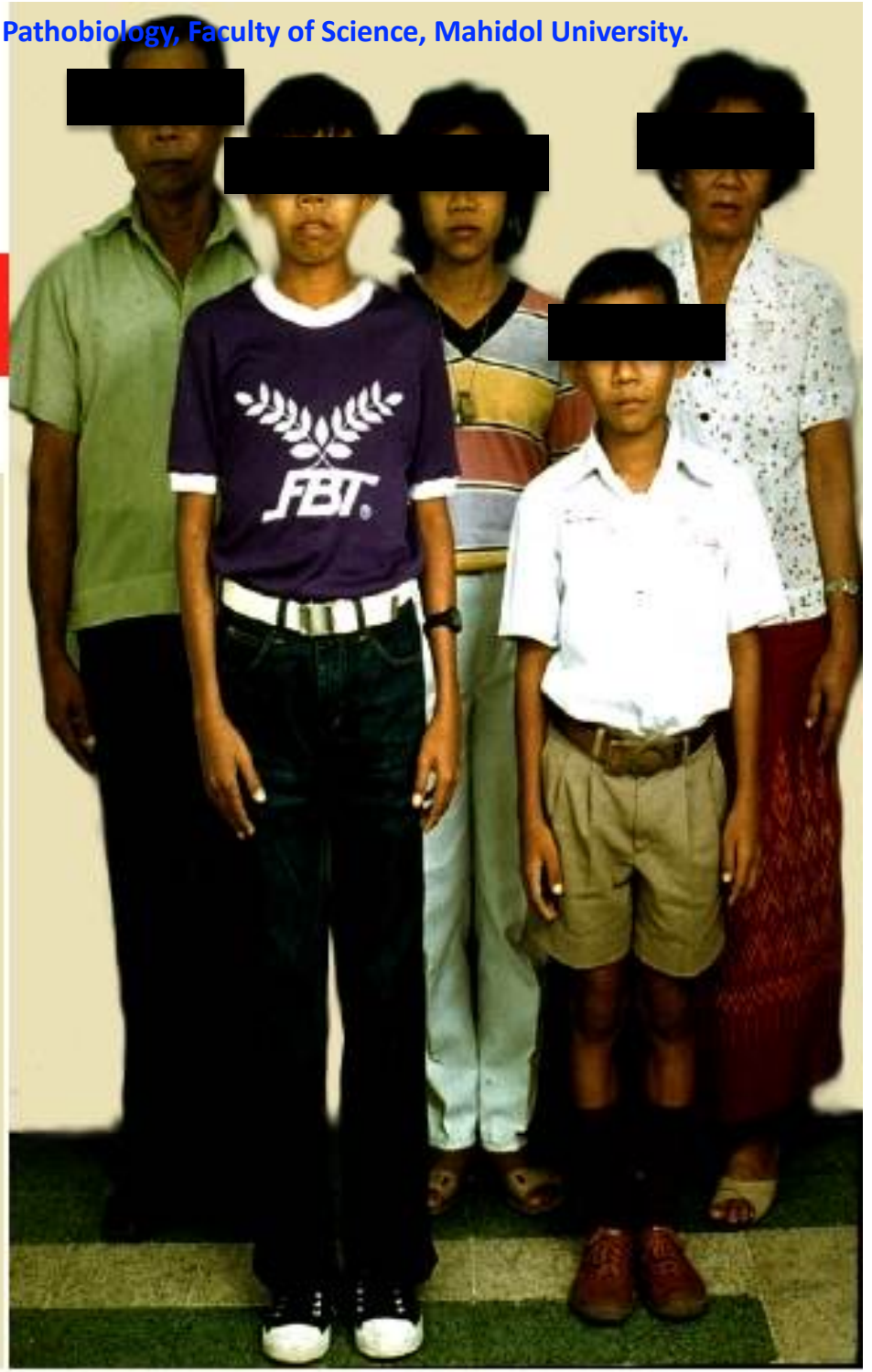
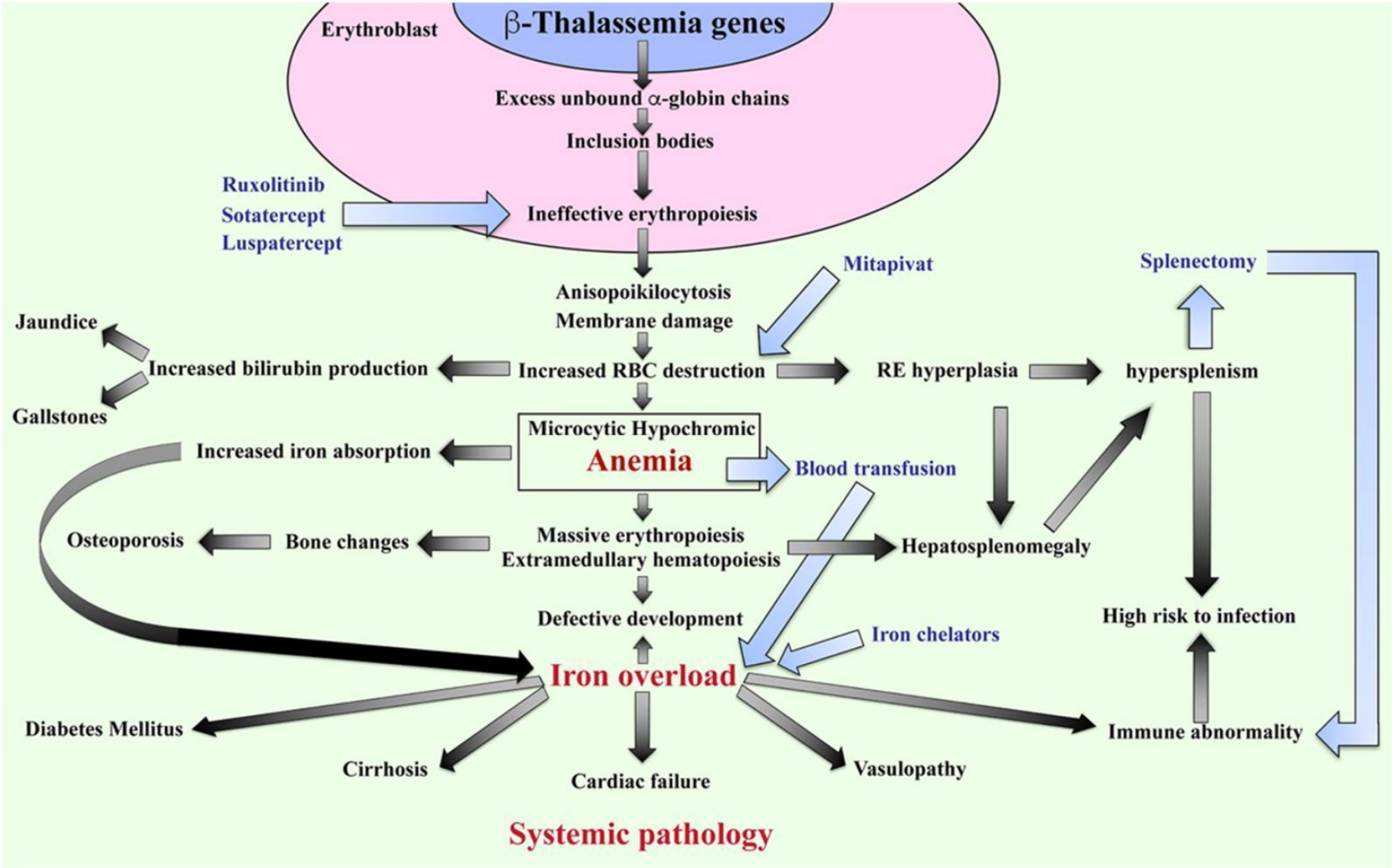


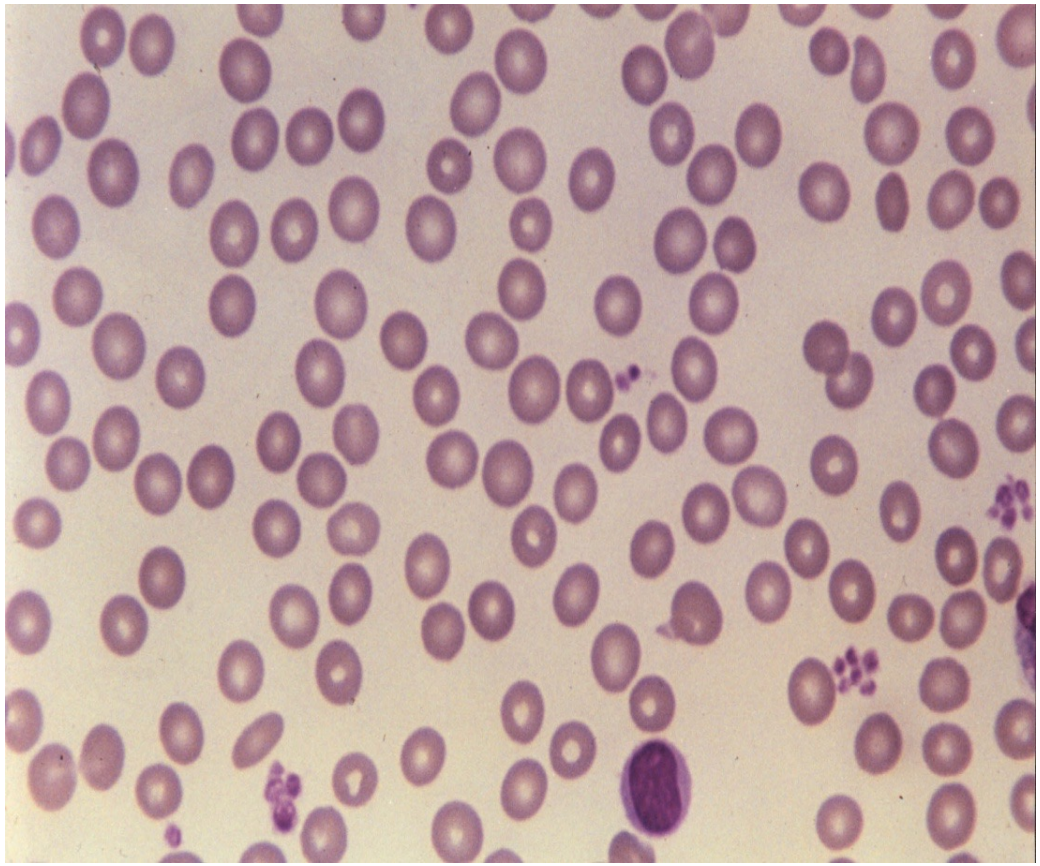
Image: Prof. Suthat Fucharoen

Pathophysiology of β-Thalassemia Disease



Chaichompoo P, *et al.* Int. J. Mol. Sci. 2022, 23, 10811.

Normal



Thalassemia

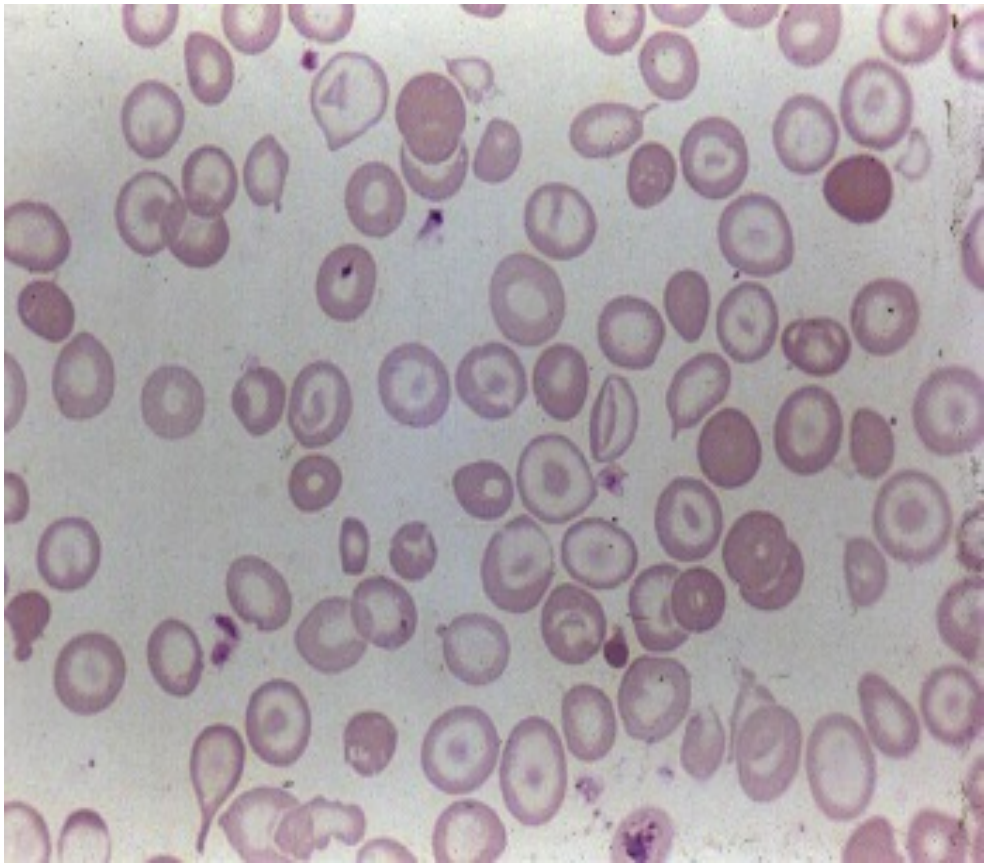
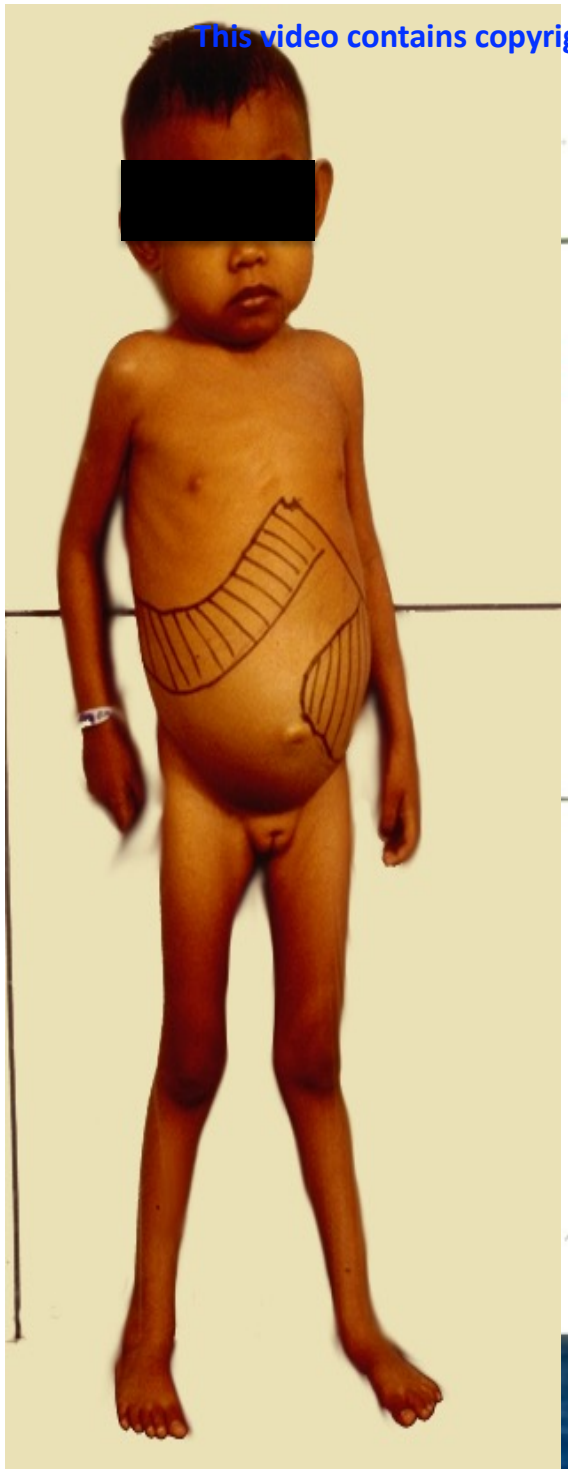
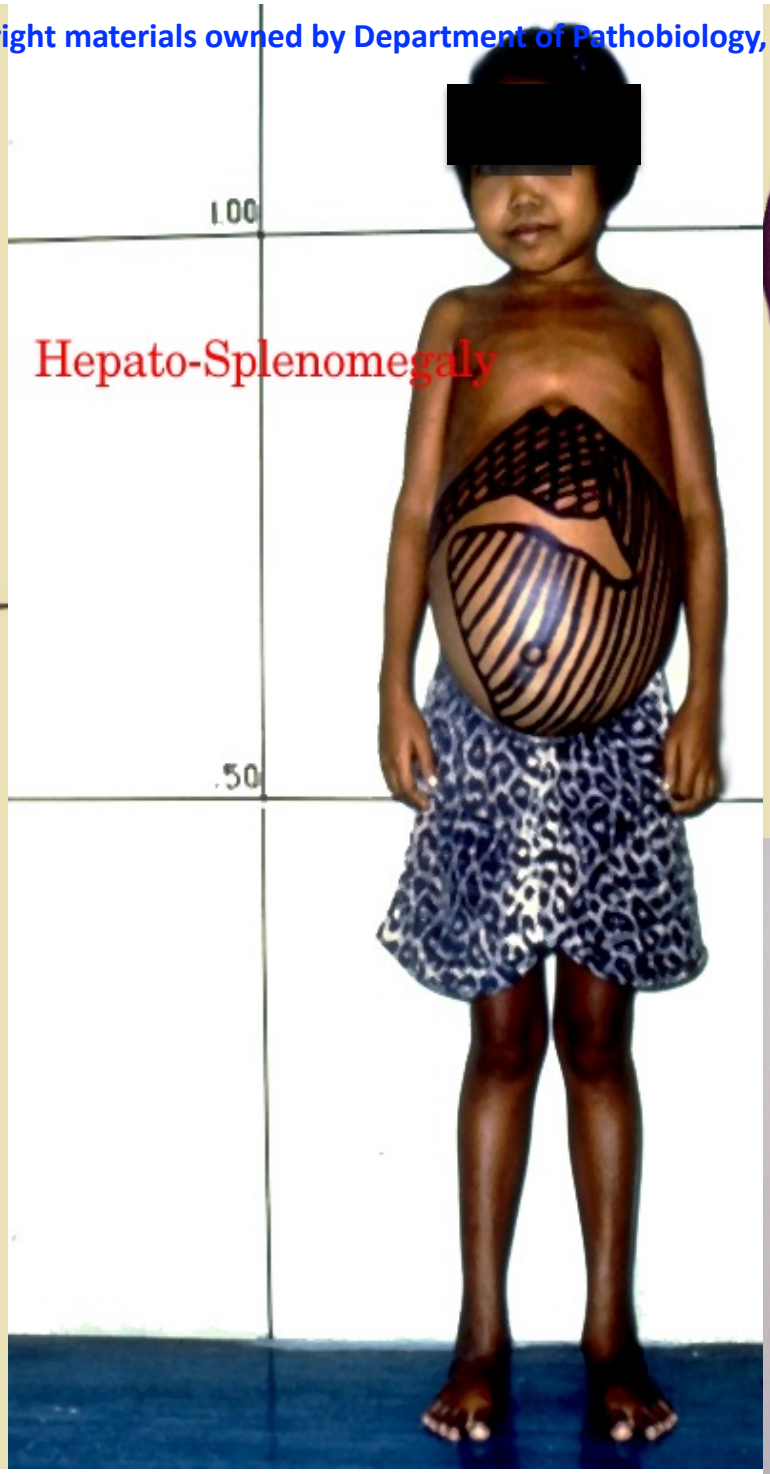


Image: Prof. Suthat Fucharoen





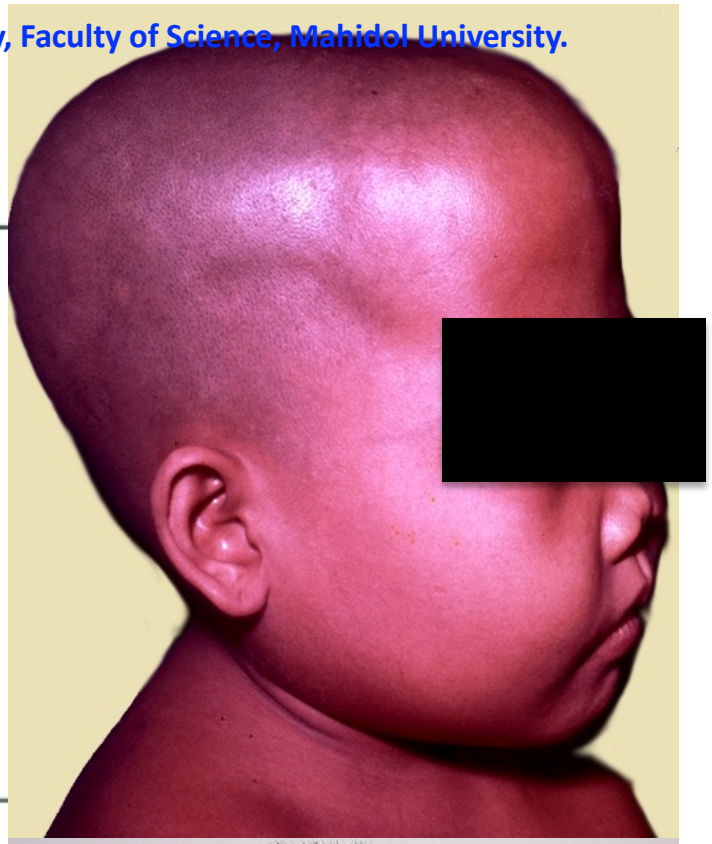
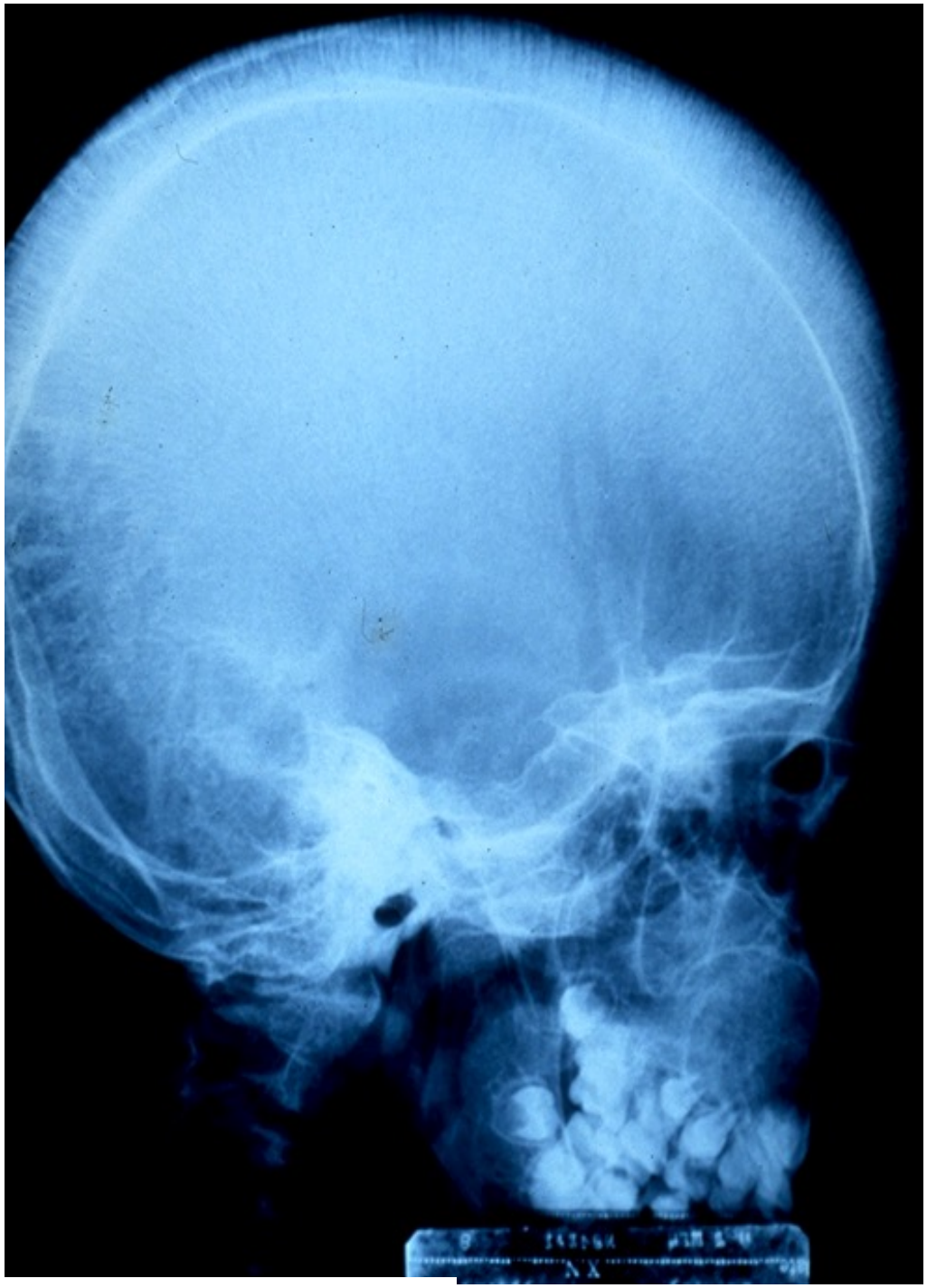


Image: Prof. Suthat Fucharoen



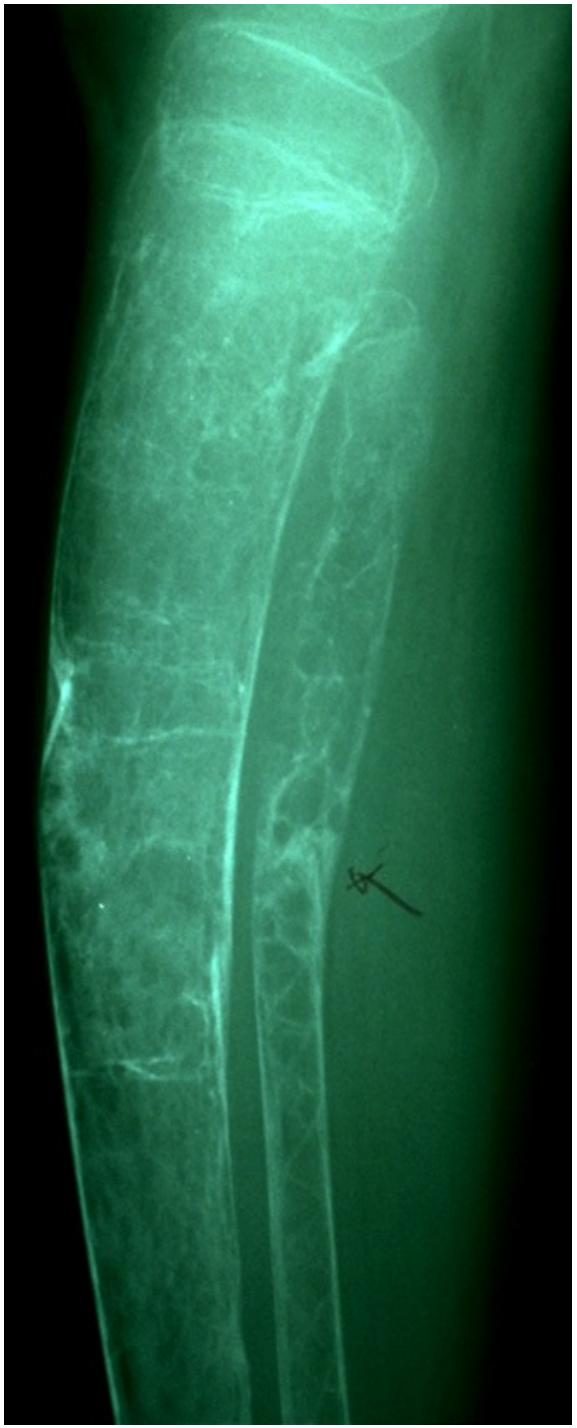
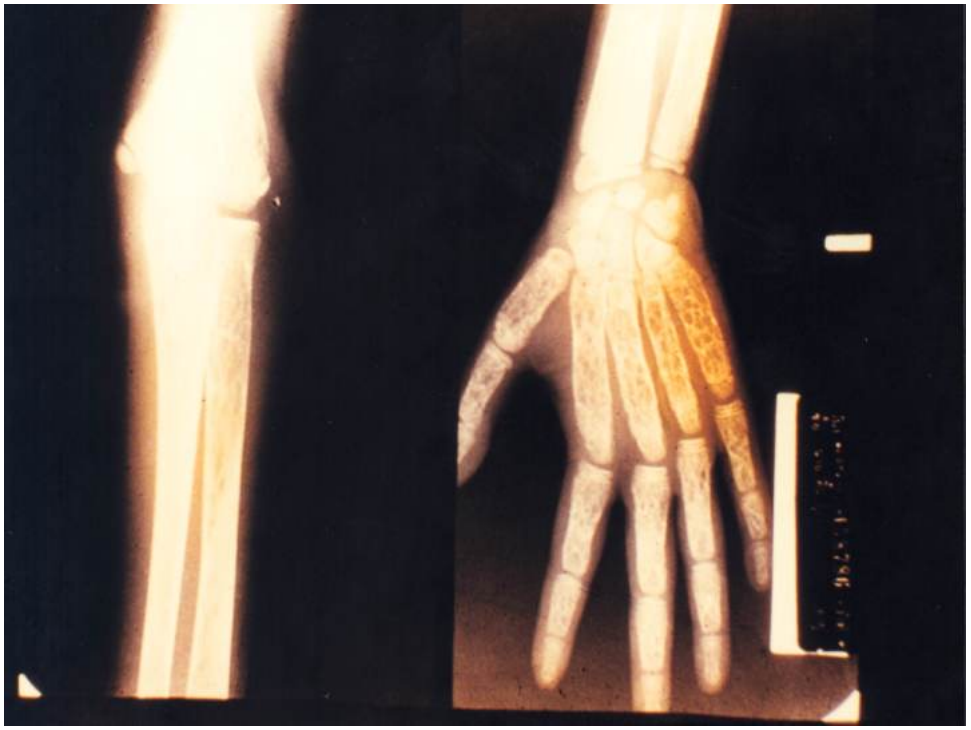
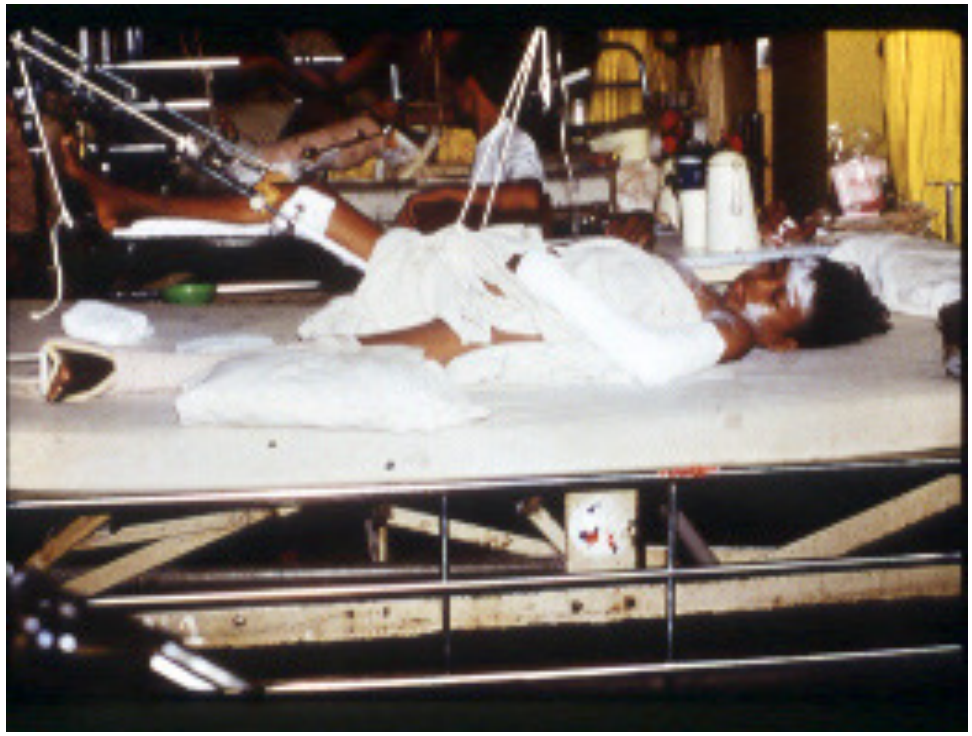


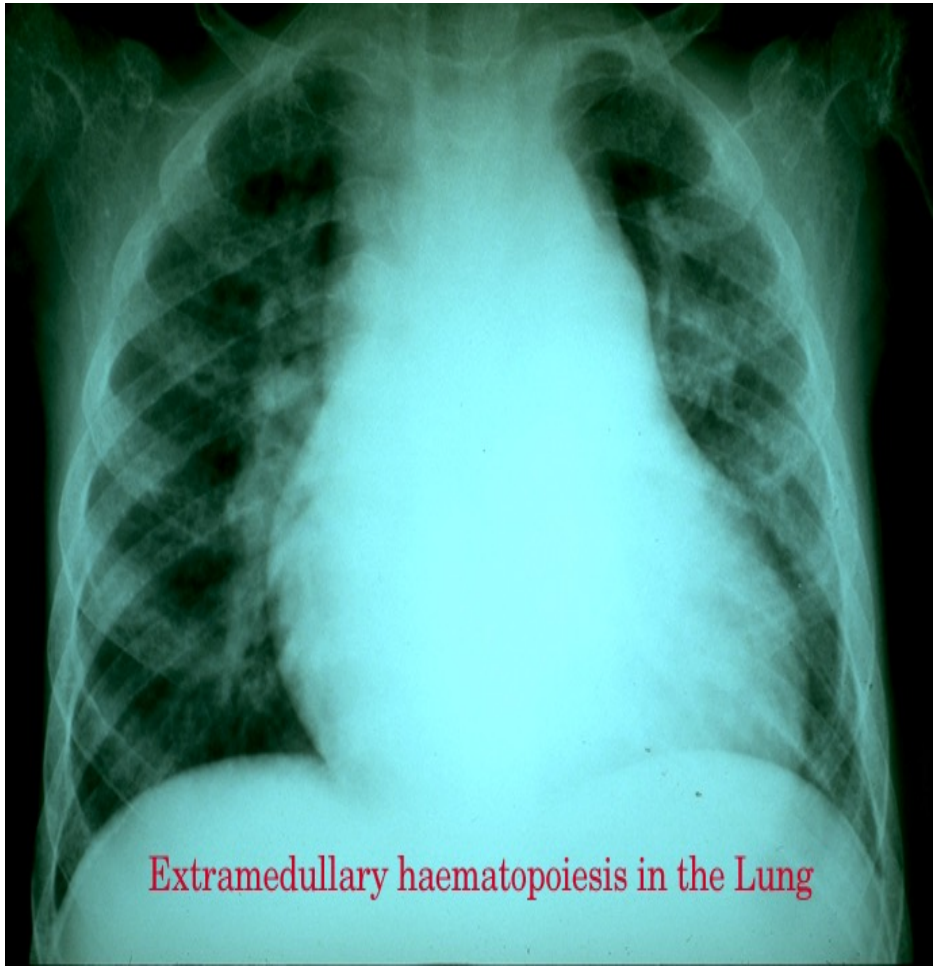
Image: Prof. Suthat Fucharoen

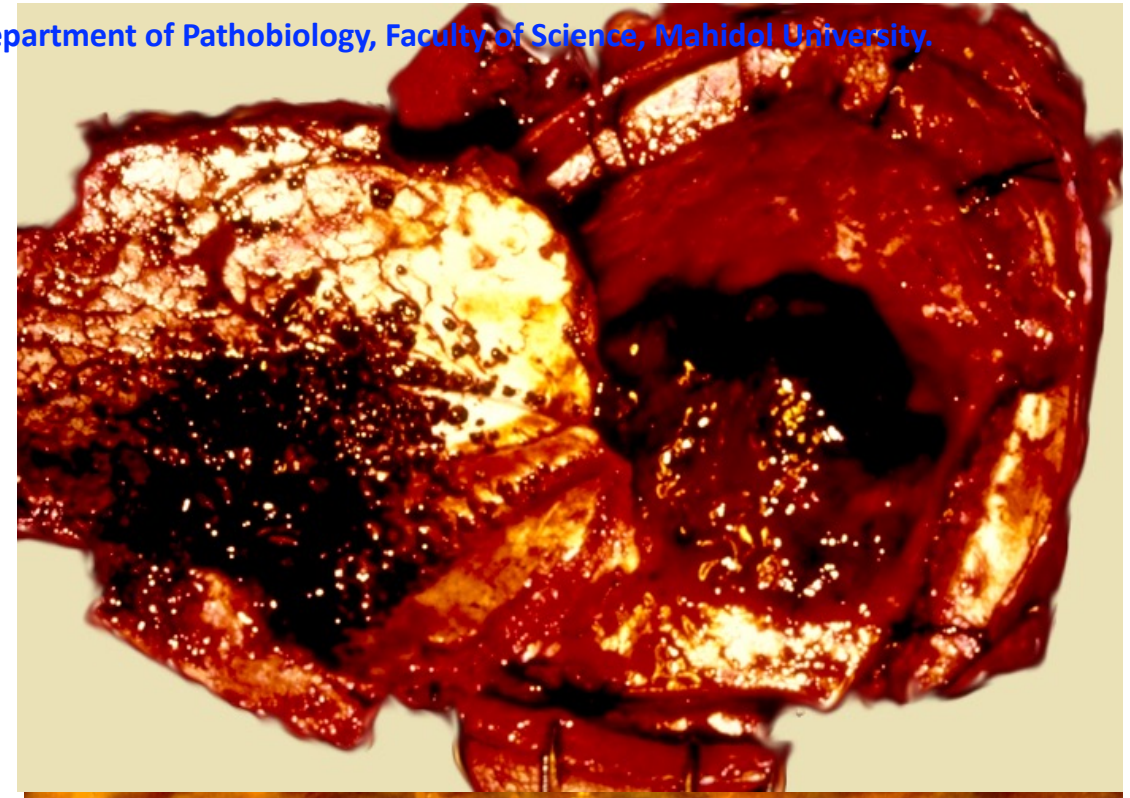




OSTEOPOROSIS AND MULTIPLE FRACTURE

Image: Prof. Suthat Fucharoen





EXTRAMEDULLARY HEMATOPOIETIC MASS

Image: Prof. Suthat Fucharoen

BLEEDING DISORDERS

Bleeding

- Skin - Purpura
- Nose - Epistaxis
- Joint - Hemarthrosis
- Brain - Intracranial hemorrhage
- GI (Gastrointestinal) tract
- GU (Genitourinary) tract

Purpura

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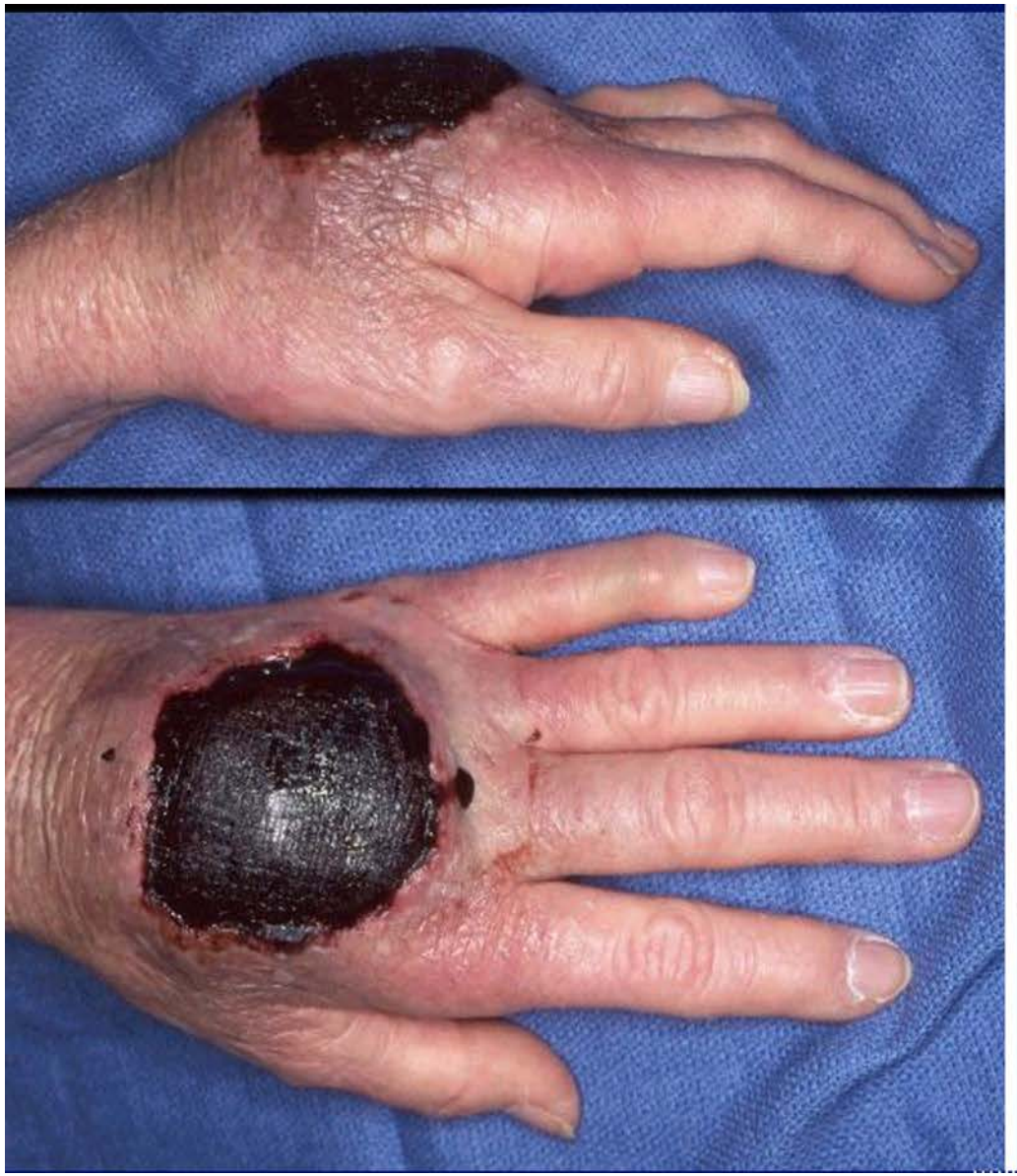
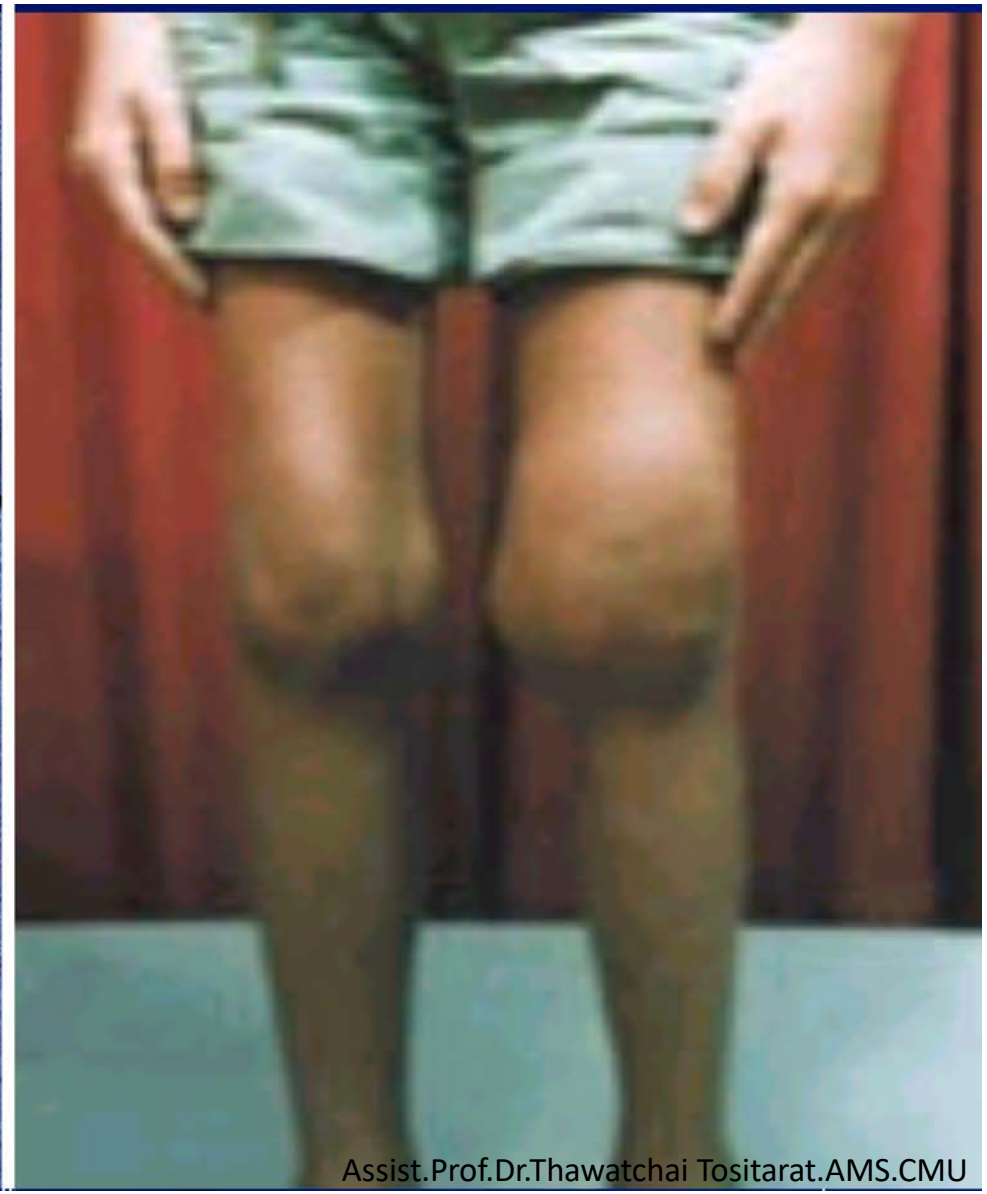
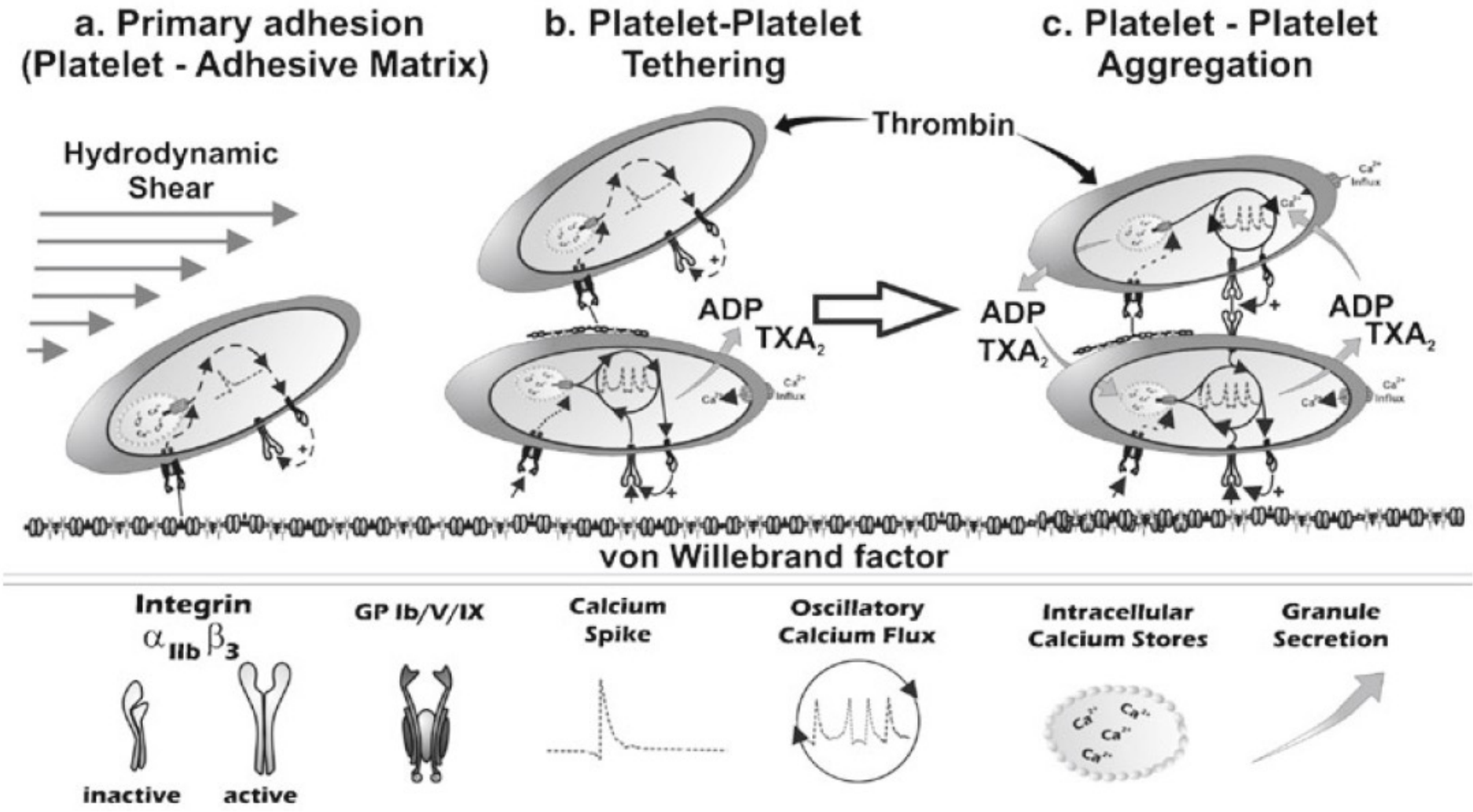
Hematoma



Hemarthrosis

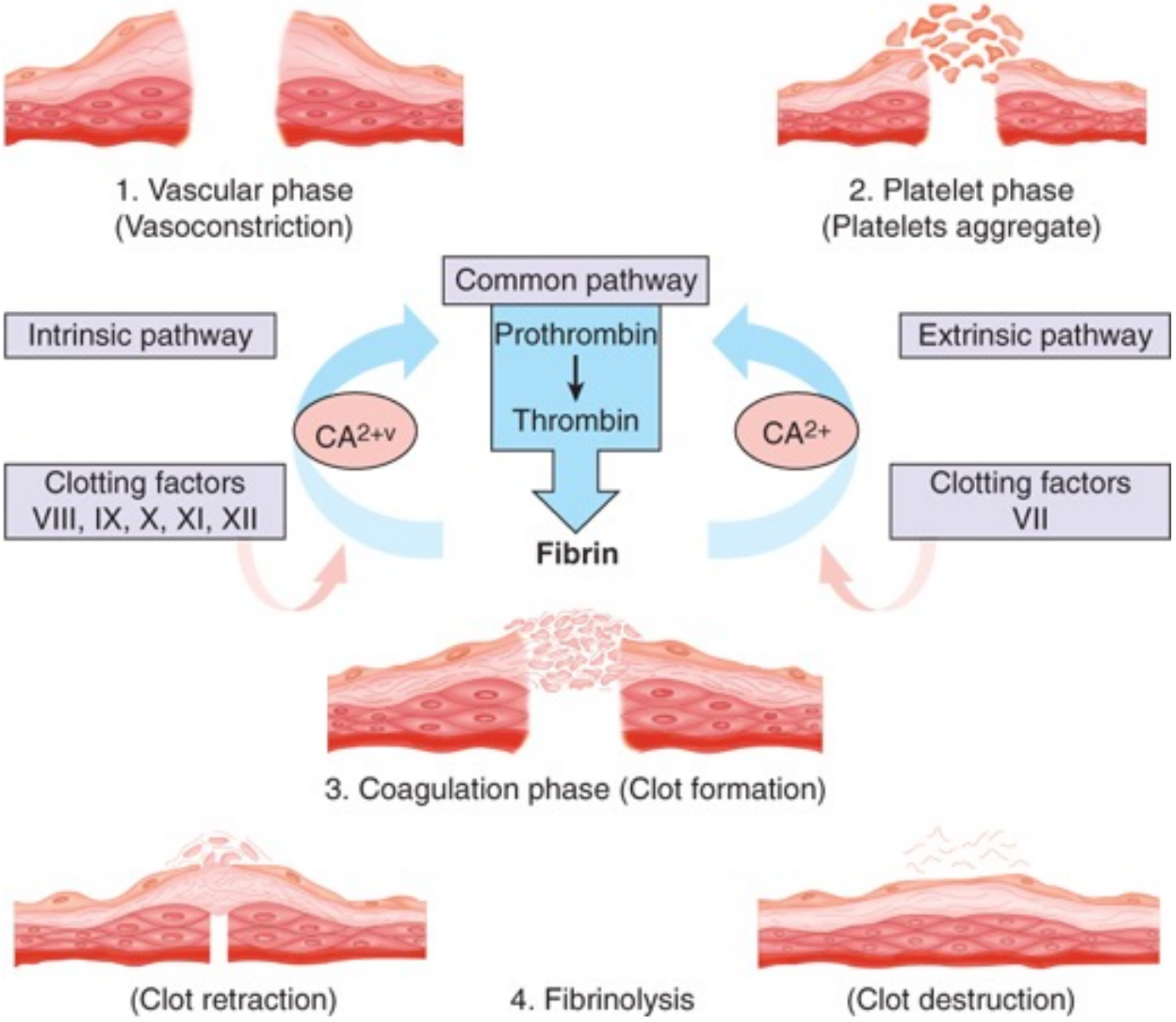


Platelet function



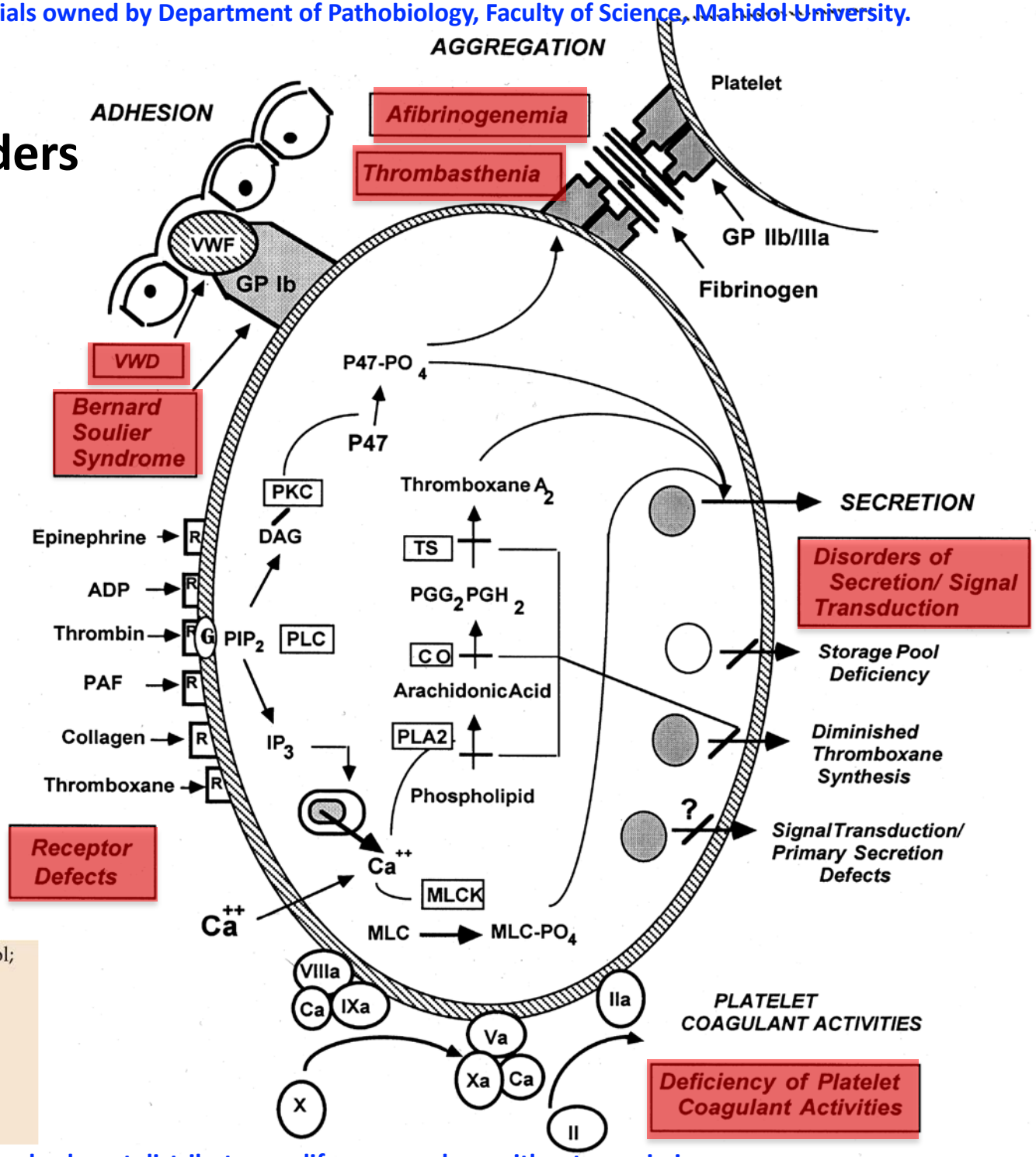
W.S. Nesbitt et al. Springer Science+Business Media, LLC 2012

Hemostasis



basicmedicalkey.com (accesed on Sep 18, 2022)

Platelets & Platelet function disorders



Sharathkumar, et al.Hemophilia.2008

Abbreviations: CO = cyclooxygenase; DAG = diacylglycerol;
IP3 = inositoltriphosphate; MLC = myosin light chain;
MLCK = myosin light chain kinase;
PIP2 = phosphatidylinositol bisphosphate;
PKC = protein kinase C; PLC = phospholipase C;
PLA2 = phospholipase A2;
VWF = von Willebrand factor;
VWD = von Willebrand disorder.

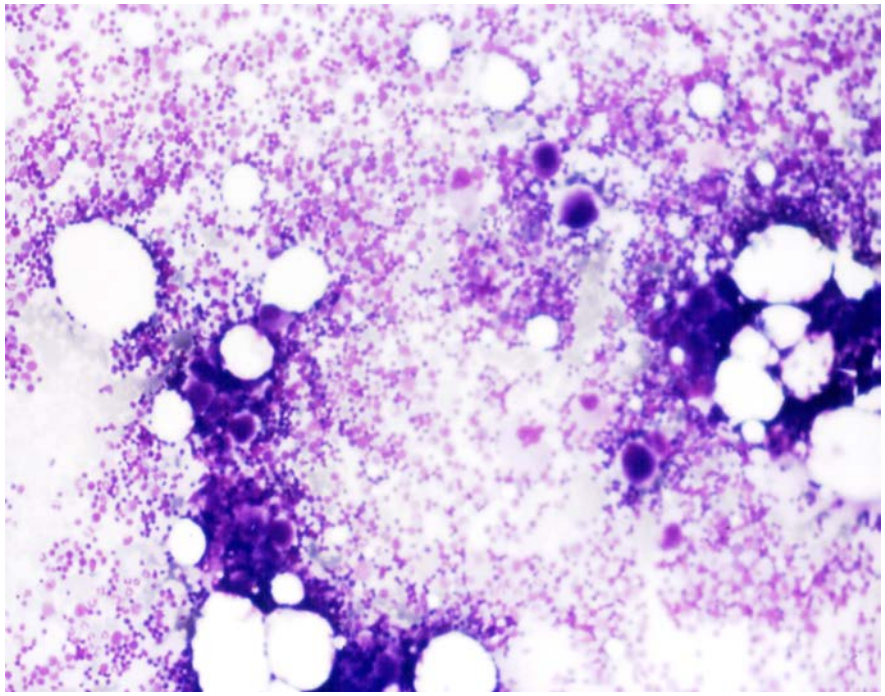
Thrombocytopenia

- Disorder of decreased platelets
- Platelet count below 150,000 cells/µl
- Causes
  - Low production of platelets
  - Increased breakdown of platelets

- Symptoms
  - Bruising
  - Nosebleeds
  - Petechiae (pinpoint microhemorrhages)

Thrombocytopenia

- Types of Thrombocytopenia
  - Immune Thrombocytopenic Purpura (ITP)
    - Abnormal destruction of circulating platelets
    - Autoimmune disorder
    - Destroyed in hosts' spleen by macrophages
  - Thrombotic Thrombocytopenic Purpura (TTP)
    - ↑ agglutination of platelets that from microthrombi



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Thrombocytopenia

- Diagnostic Studies
  - Platelet count
  - Prothrombin Time (PT)
  - Activated Partial Thromboplastin Time (aPTT)
  - Hgb/Hct
- Treatment
  - Based on cause
  - Corticosteroids
  - Plasmaphoresis
  - Splenectomy
  - Platelet transfusion

Hemophilia

- Hereditary blood clotting disorder
- Prolonged bleeding times
- Sex-linked, usually in men
- Hemophilia A
  - Also called classic hemophilia
  - Result of a deficiency or absence of antihemophilic factor VIII (coagulation factor VIII)
    - Deficiency results in traumatic or spontaneous bleeding
  - Characterized by bleeding in joints, gums, or mouth
  - Hematuria is a common characteristic

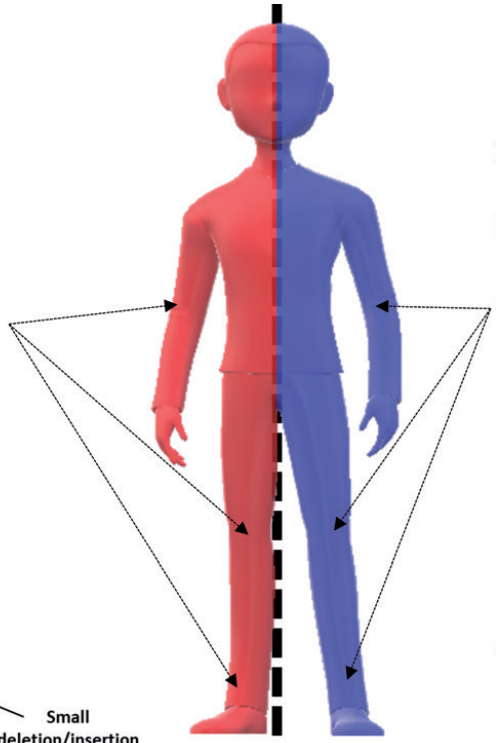
Hemophilia

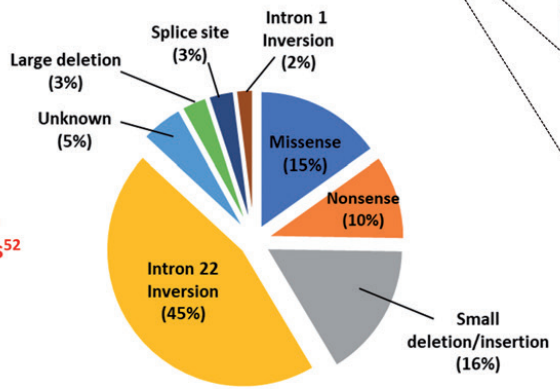
Hemophilia A

Prevalence: 1:5,000 males

Mode of inheritance: X-linked recessive

Clinical symptoms: Joint bleeding, muscle hematoma, soft tissue bleeding





F8 gene defects reported in severe Hemophilia A patients[52]

Characteristics of missing clotting factor (FVIII):

Function: Co-factor

Molecular Weight: 280 kDa[53]

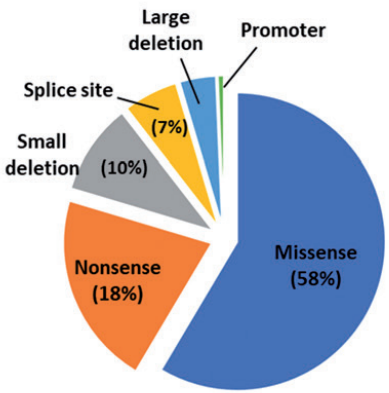
Normal concentration in plasma: 0.1-0.25 µg/mL

Hemophilia B

Prevalence 1:30,000 males

Mode of inheritance: X-linked recessive

Clinical symptoms: Joint bleeding, muscle hematoma, soft tissue bleeding



F9 gene defects reported in severe Hemophilia B patients[7]

Characteristics of missing clotting factor (FIX):

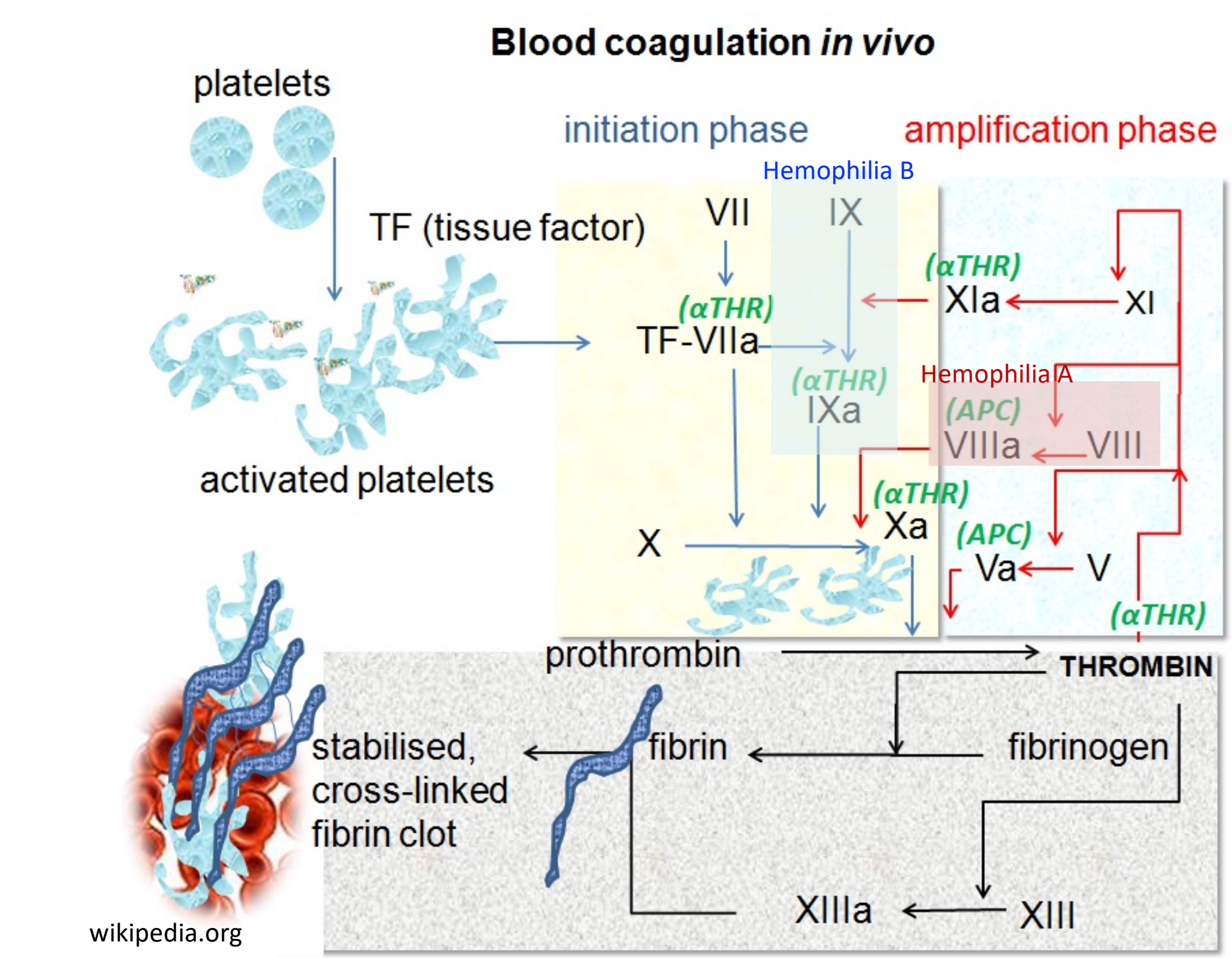
Function: Enzyme

Molecular Weight: 55 kDa[54]

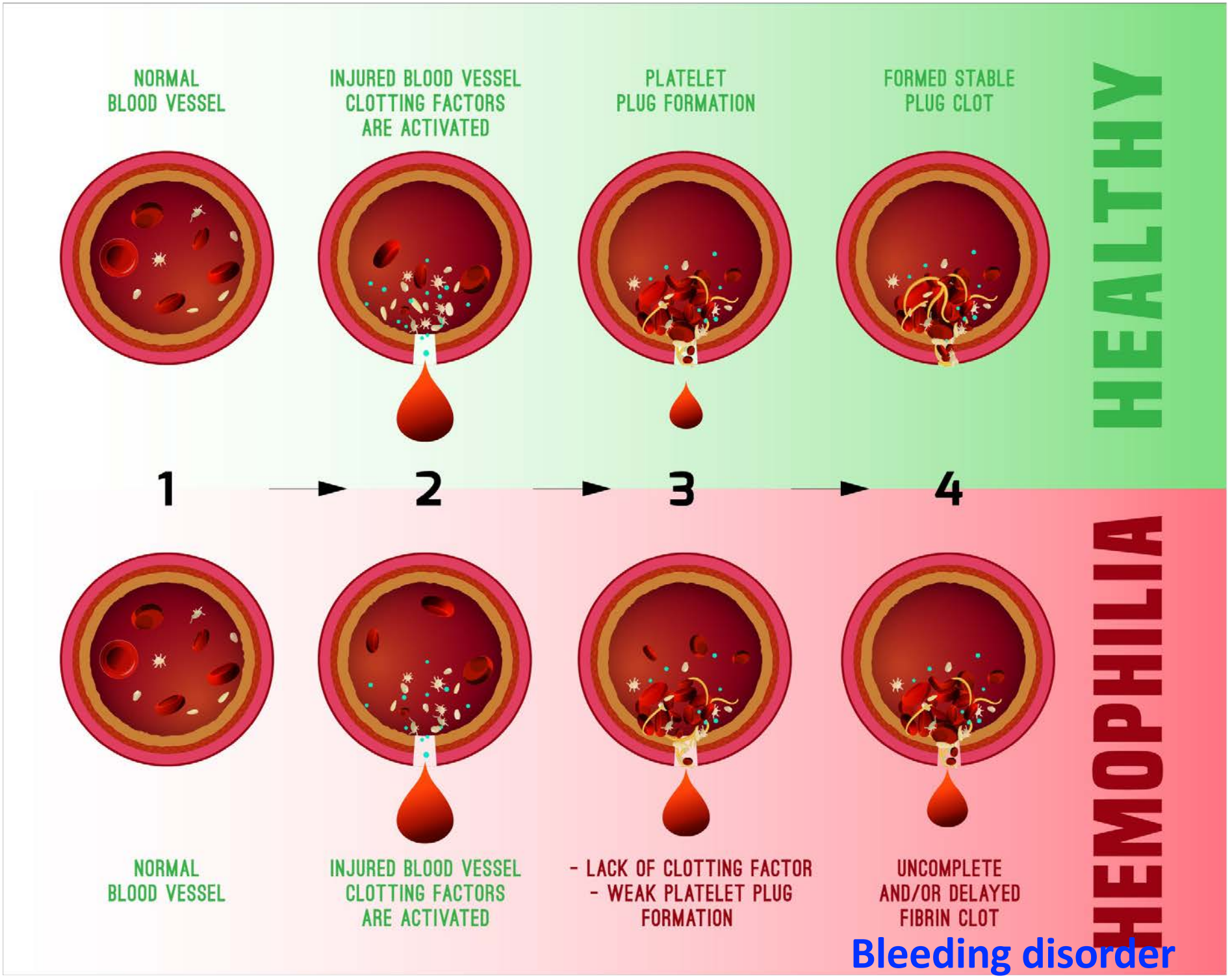
Normal concentration in plasma: 3-5 µg/mL

Castaman G & Matino D. Haematologica.2019.

Blood coagulation *in vivo*



wikipedia.org



Bleeding disorder

Bleeds & Bruises in Children with hemophilia

MUSCLE AND/OR JOINT BLEEDS

Call the parent/guardian

P.R.I.C.E.

P : Protection

Lower Limb: Take weight off the joint or muscle
Upper Limb: No carrying using affected arm

R : Rest

- Rest means rest!
- Try not to allow use of the joint or muscle where possible.

I : Ice

- Regular ice packs can help with pain & reduce swelling.
- Put an ice pack over the affected area for 20 minutes. Repeat every two hours.

DO NOT leave the ice pack on for more than 20 minutes
DO NOT place ice pack directly on skin (Use a tea towel/cold pack cover)

C : Compression

- Use an elasticated bandage to compress the affected area to reduce swelling.

E : Elevation

- Elevate the affected limb to help reduce swelling.
- Keep the affected joint or muscle above the level of the heart.

FIRST AID

Mouth & Gum Bleeds

These can be hard to control because clots that form are washed away by saliva or knocked off by the tongue or food. Try giving the child an ice cube or ice pop to suck. These bleeds may need treatment by parents or the treatment centre.

Nosebleeds

Tilt head forward and pinch the bridge of the nose below the bone for 10 - 20 minutes and / or put an ice-pack on the bridge of the nose for **not more than 5 minutes.**

Cuts and Grazes

Cover with a plaster and bandage. Apply pressure for a few minutes. Deep cuts may need stitching, if so contact parents and/or haemophilia treatment centre.

Bruises

Children with haemophilia bruise more easily than children without haemophilia and their bruises will be bigger. Bruises only need treatment if they are very painful.

SIGNS OF A SERIOUS HEAD BLEED

* Headache.
* Drowsiness.
* Nausea.
* Vomiting.
* Unsteady Balance.
* Irritability.
* Confusion.
* Seizures.
* Loss of consciousness.

SIGNS OF A SOFT TISSUE BLEED

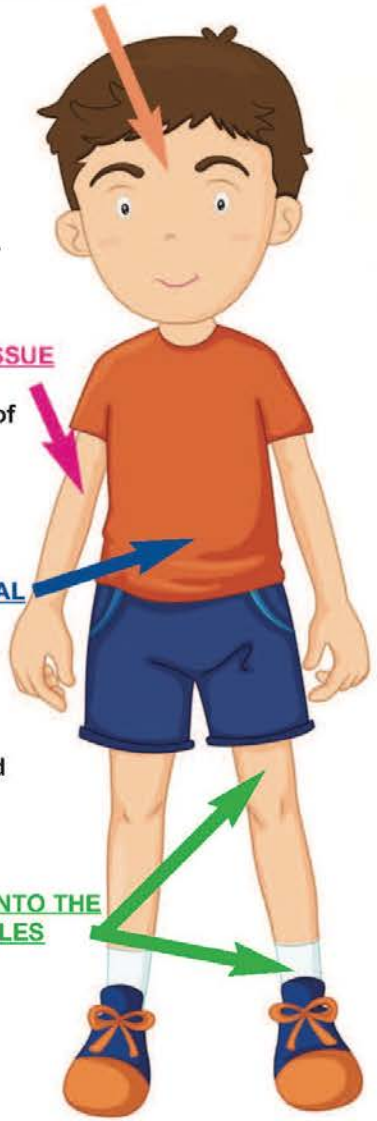
* Bruising, discolouring of skin.
* Mild swelling.

SIGNS OF AN ABDOMINAL BLEED

* Bloody, black or tar-like bowel motions.
* Red or brown urine.
* Pain.
* Vomiting of blood (blood may be red or black).

SIGNS OF BLEEDING INTO THE JOINTS OR MUSCLES

* Tingling / Tightness.
* Pain.
* Redness.
* Swelling.
* Warmth.
* Tenderness.
* Reluctance to move the affected limb / joint.



Bleeds in the following areas are especially serious and require immediate attention:

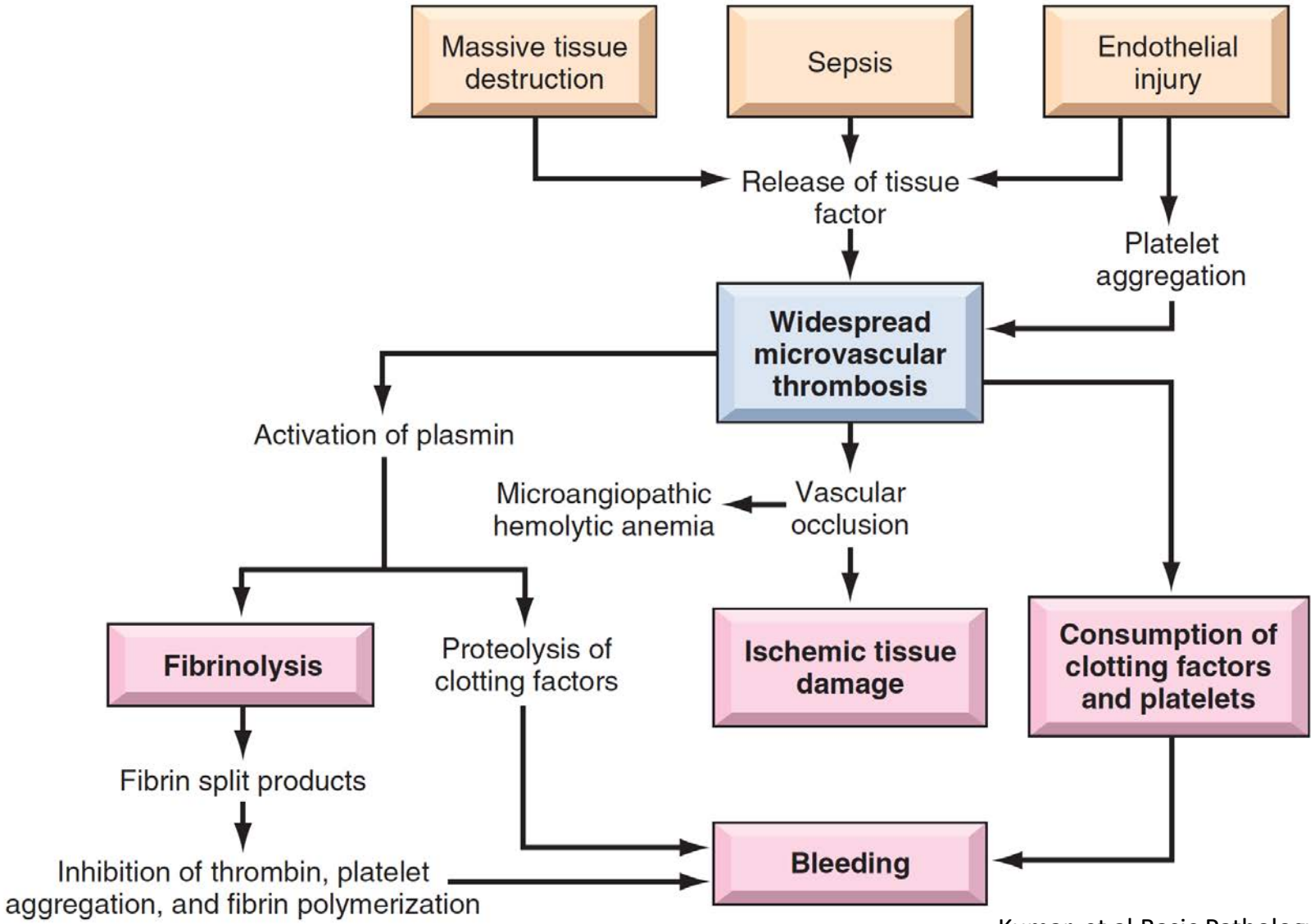
*** HEAD * EYE * NECK * ABDOMEN * GROIN * HIP**

Call parents and Haemophilia Treatment Centre immediately.

Disseminated Intravascular Coagulation (DIC)

- Blood clotting
  - Soft tissue (tissue thromboplastin) or endothelial damage (coagulation factor XII)
- Causes:
  - Release of clotting factors
    - Amniotic fluid embolization
    - Cytoplasmic granules
    - Promyelocytic leukemia
    - Mucus
    - Calcium
    - Gram-negative bacteria infection (sepsis)
  - Extensive endothelial damage, burns, SLE

DIC



Kumar, et al.Basic Pathology. Saunders.2013

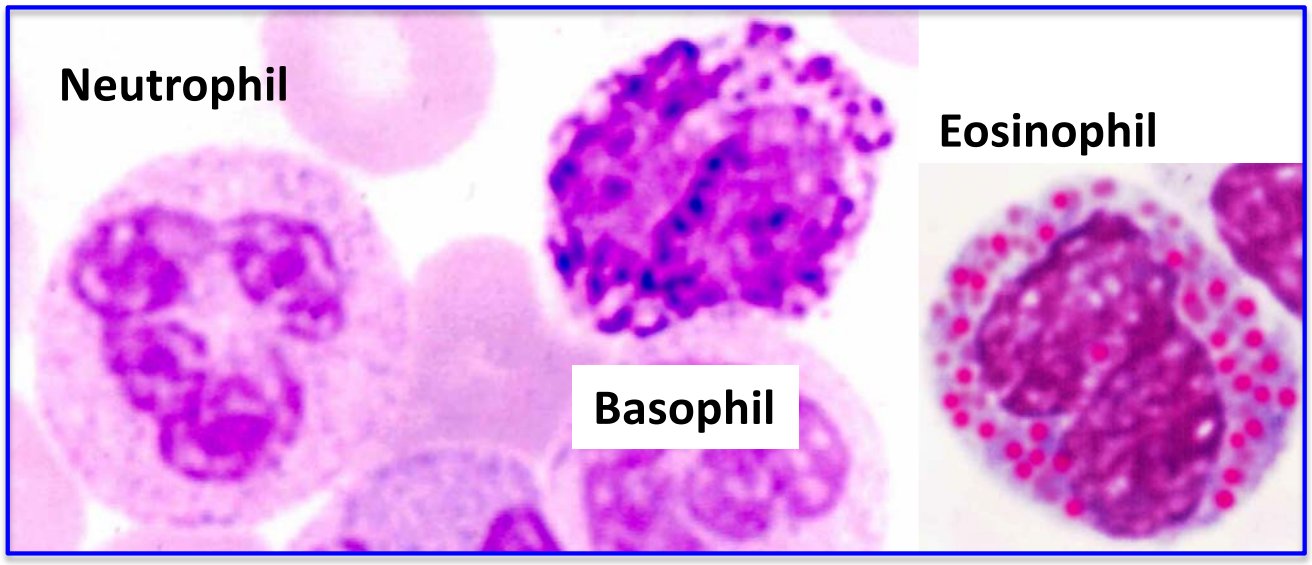

15
MINUTE
BREAK

Part II

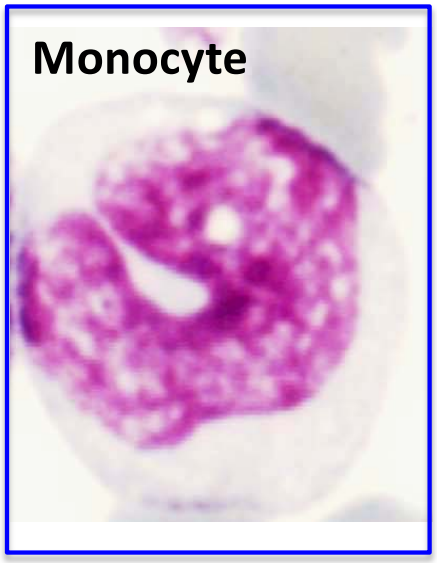
- Composition & Functions of Lymphatic system
- Lymphoproliferative disorders
  - Leukemia
  - Lymphoma

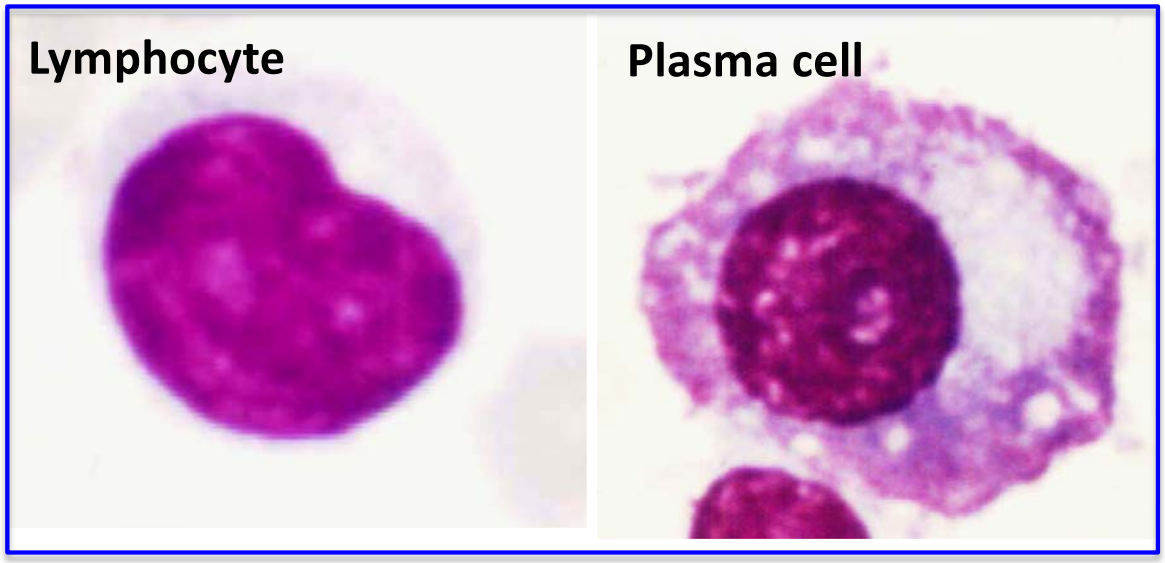
White blood cells / Leukocytes

Polymorphonuclear cells

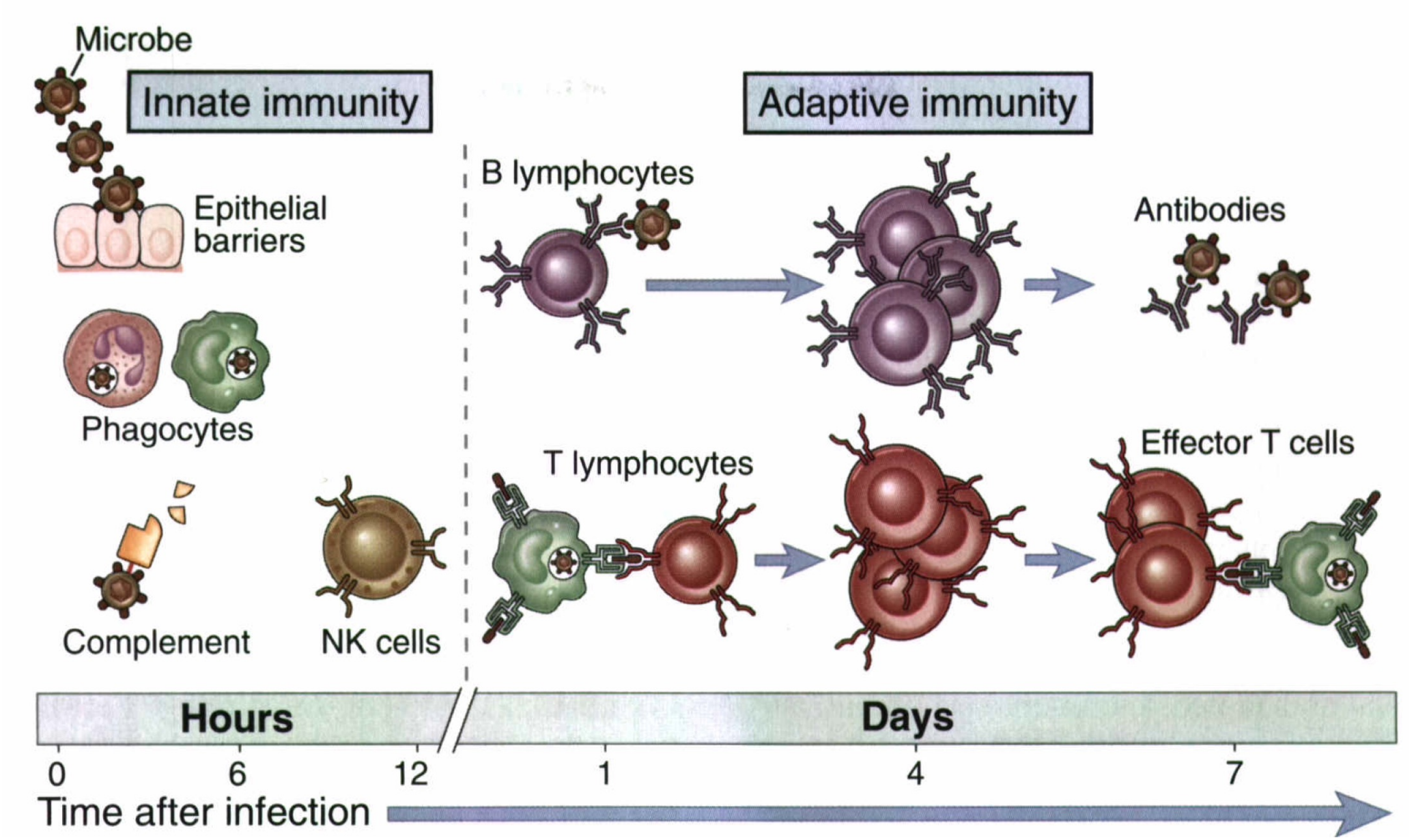


Monomorphonuclear cells



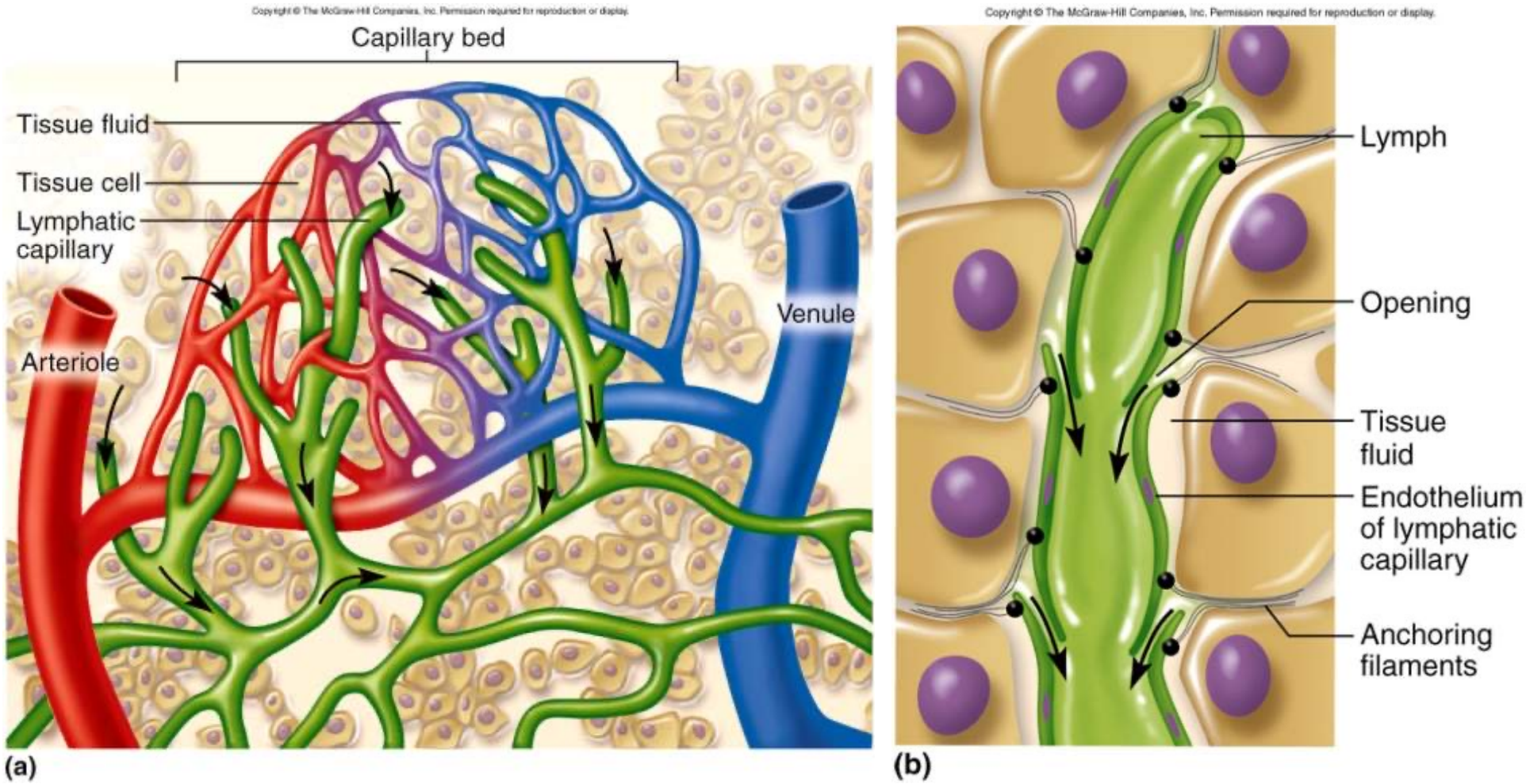


White blood cells / Leukocytes



Abbas, et al. Cellular and molecular immunology.Saunders.2007

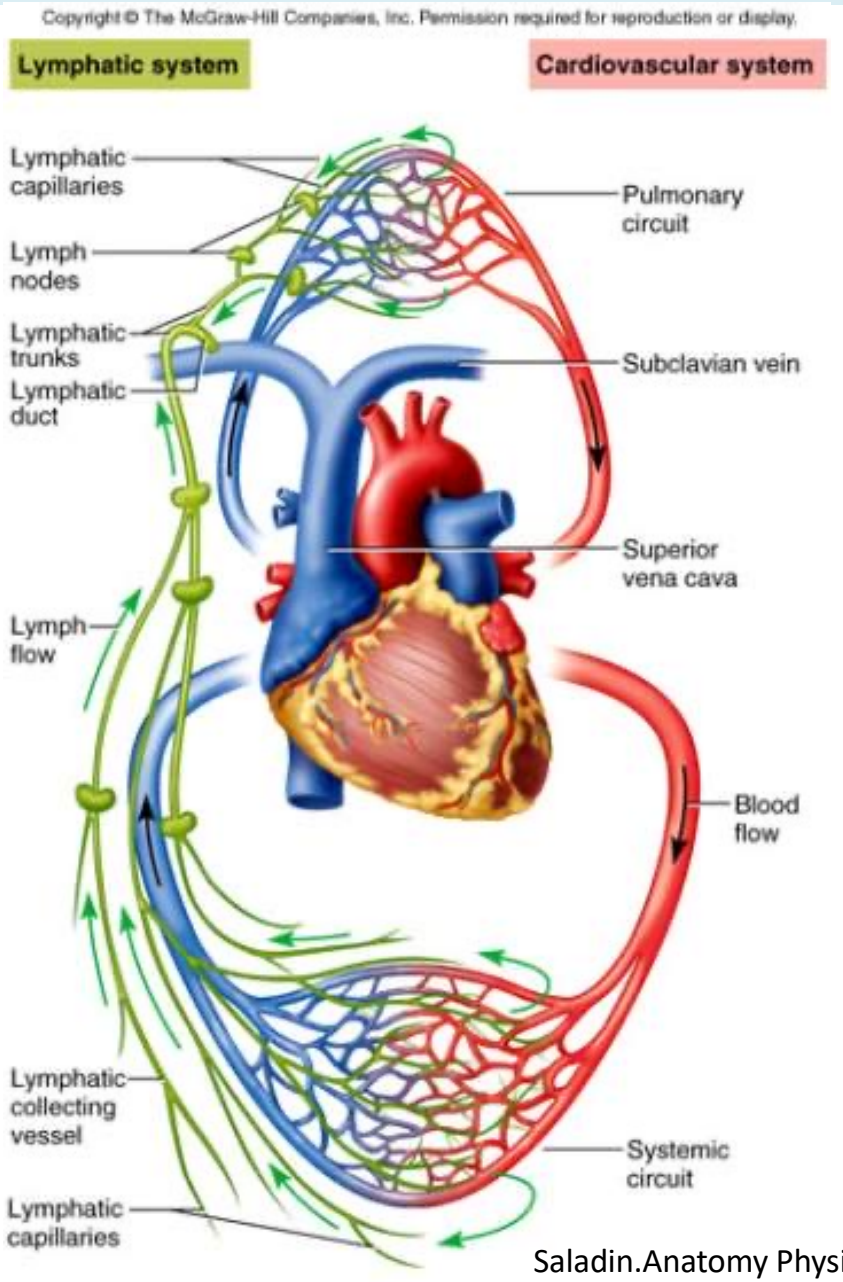
Lymphatic and Immune Systems

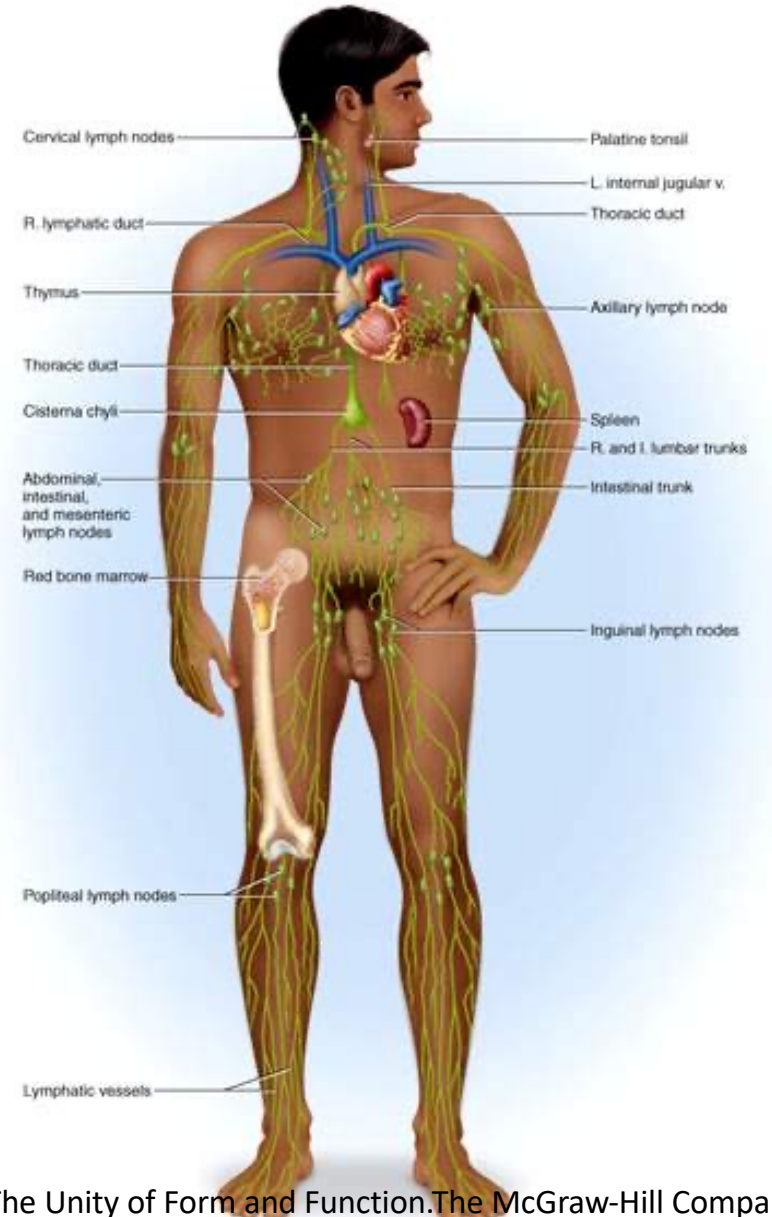


- Maintain fluid balance
- Protect body from infection and disease

Saladin.Anatomy Physiology:The Unity of Form and Function.The McGraw-Hill Companies.2006

The Fluid Cycle





Saladin.Anatomy Physiology:The Unity of Form and Function.The McGraw-Hill Companies.2006

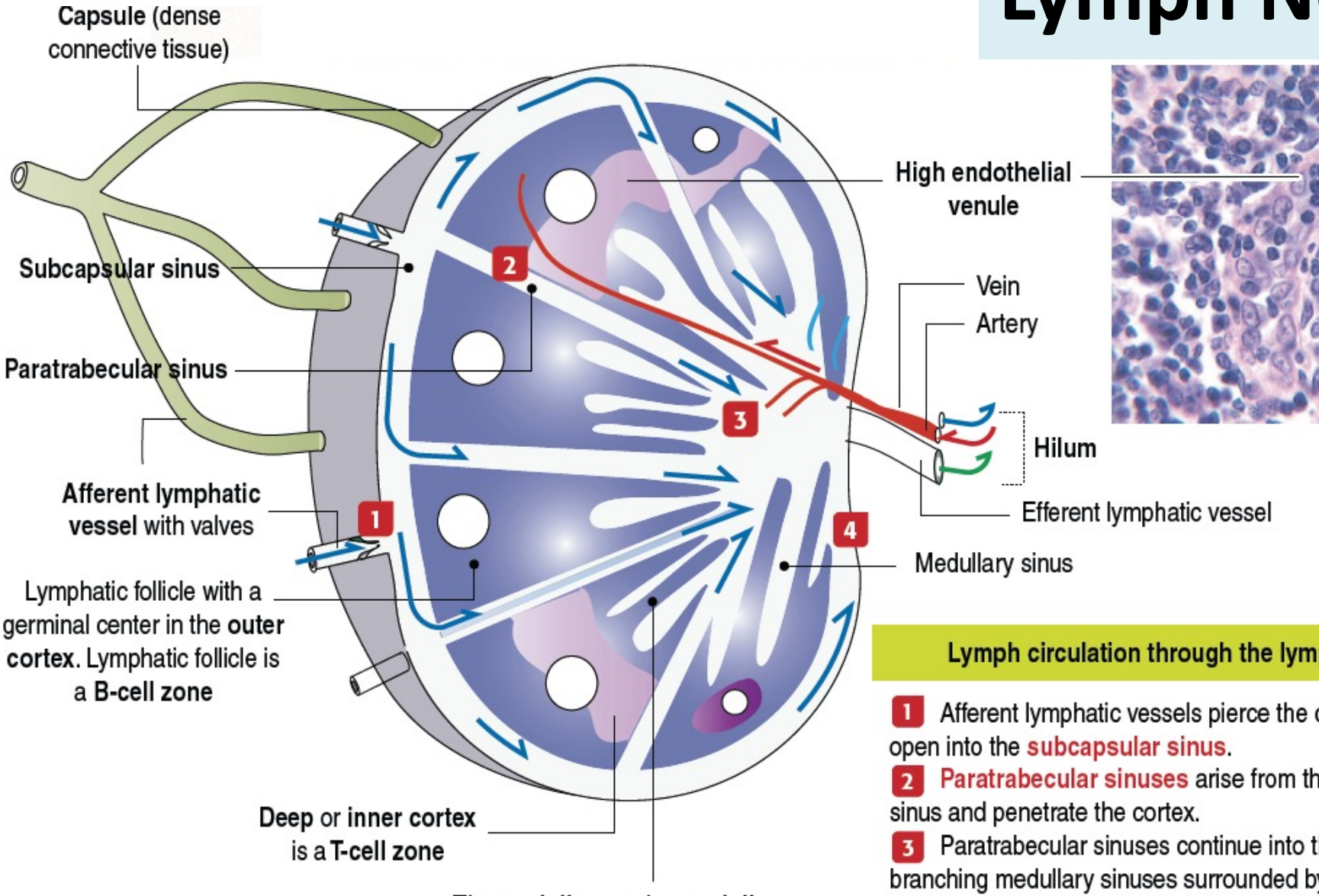
Functions of the Lymphatic System

- Drain fluid from tissue spaces and return to it to the blood
- Transport materials (nutrients, hormones and oxygen) to body cells
- Carry away waste products to the blood
- Transport lipids away from digestive system
- Control of infection

Lymphatic System

- Lymph originates in blood plasma
- Interstitial fluid
- Cleans and nourishes body tissues
- Collects cellular debris, bacteria, etc.
- Return to blood or lymphatic capillaries

Lymph Nodes



Lymph circulation through the lymph node

1 Afferent lymphatic vessels pierce the capsule and open into the subcapsular sinus.

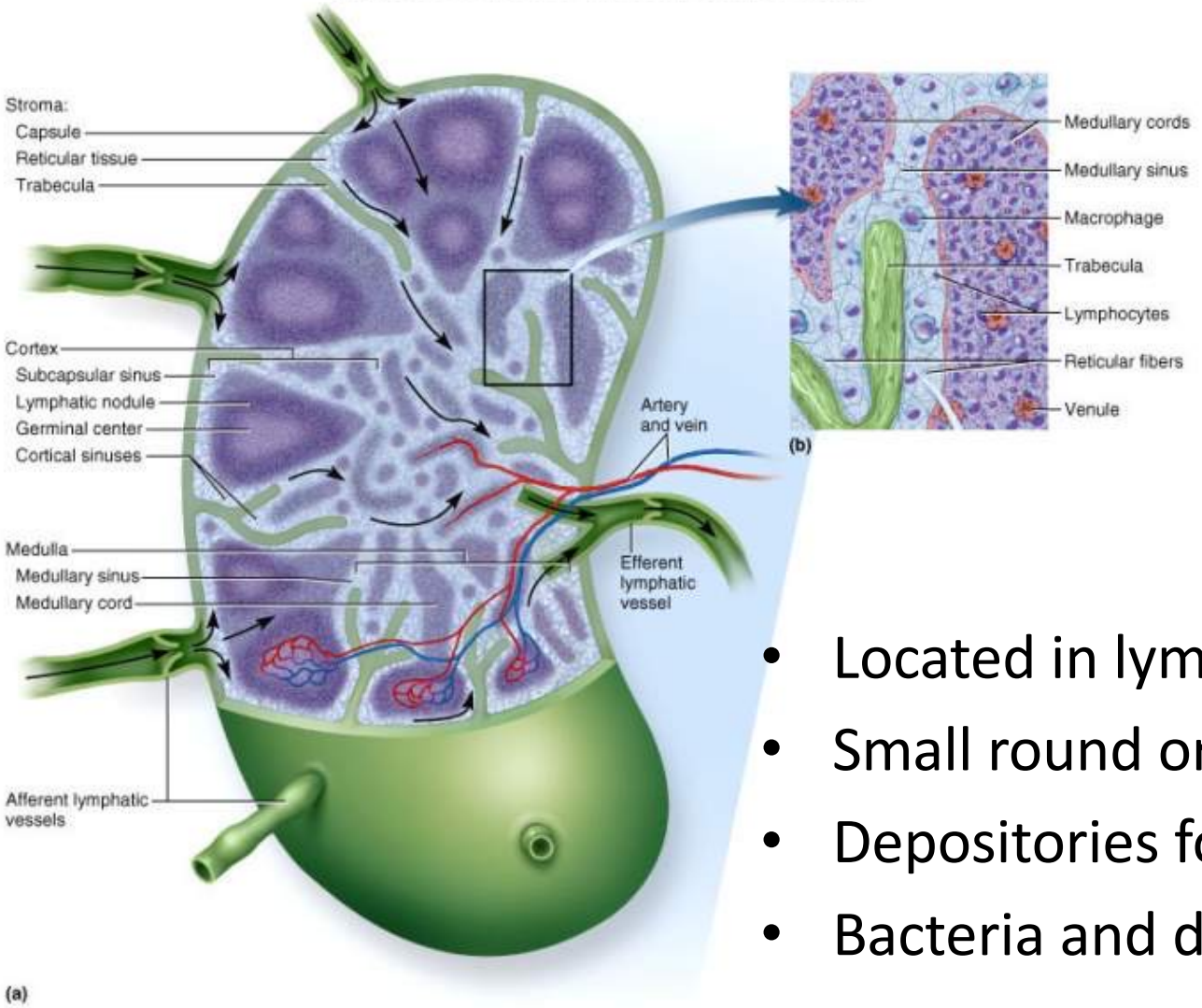
2 Paratrabecular sinuses arise from the subcapsular sinus and penetrate the cortex.

3 Paratrabecular sinuses continue into the medulla as branching medullary sinuses surrounded by medullary cords.

4 The subcapsular/paratrabecular sinuses are confluent with the medullary sinuses at the hilum and penetrate the capsule to join the efferent lymphatic vessel.

Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

Lymph Nodes

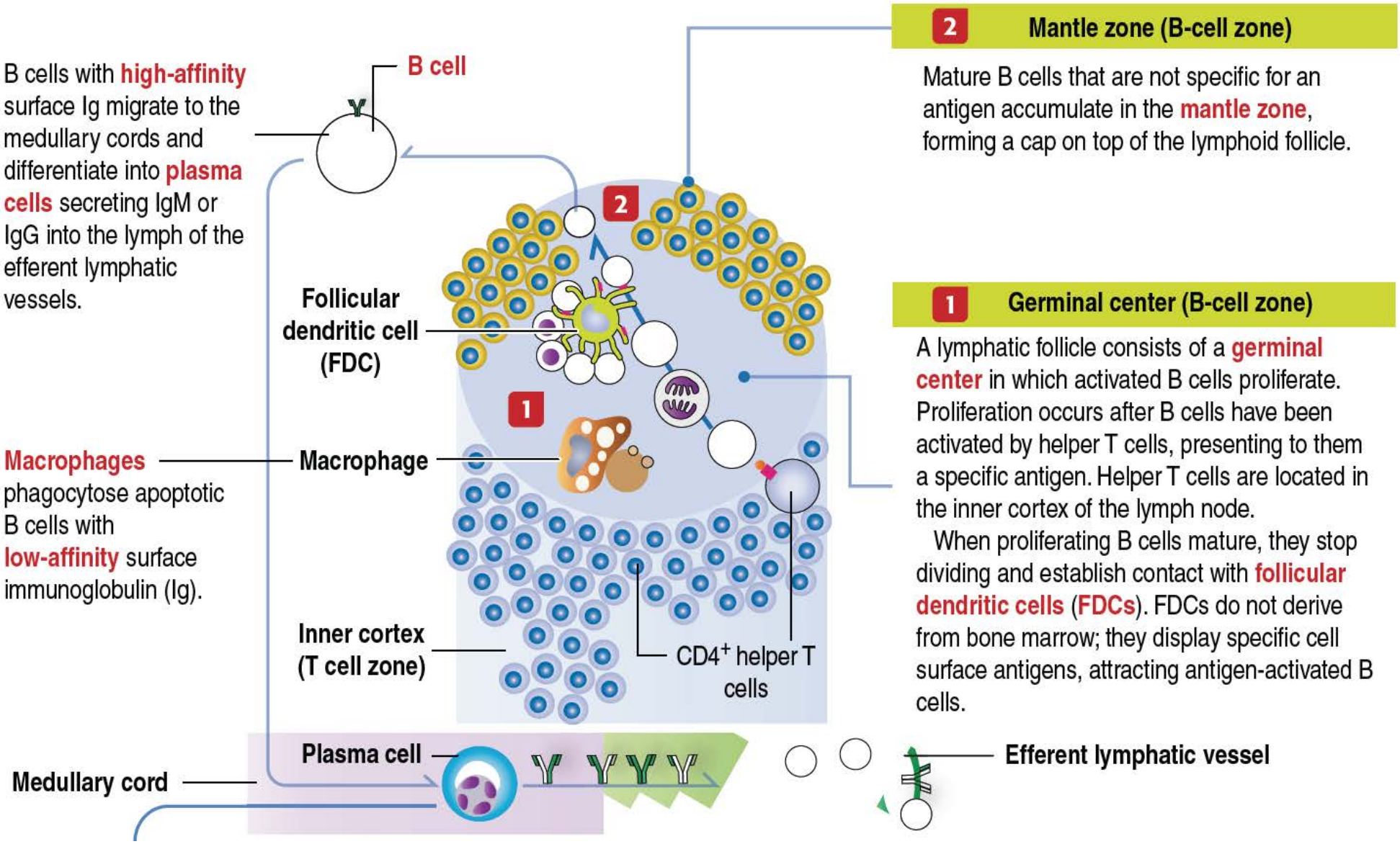


- Located in lymphatic vessels
- Small round or oval structures (filters)
- Depositories for cellular debris
- Bacteria and debris phagocytized

- Inside are masses of tissue which contain WBCs
- Invading cells destroyed in lymph nodes that cause of lymph node swelling used as an indicator of the disease process

Saladin.Anatomy Physiology:The Unity of Form and Function.The McGraw-Hill Companies.2006

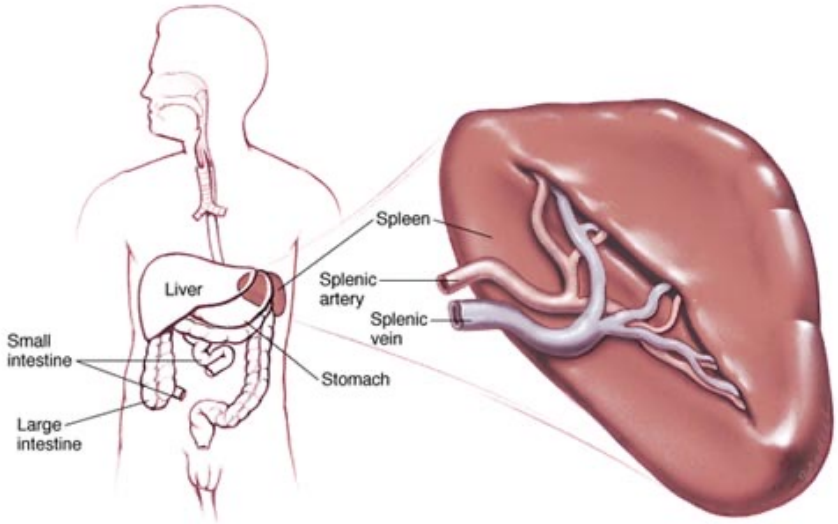
Lymphatic follicle



Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

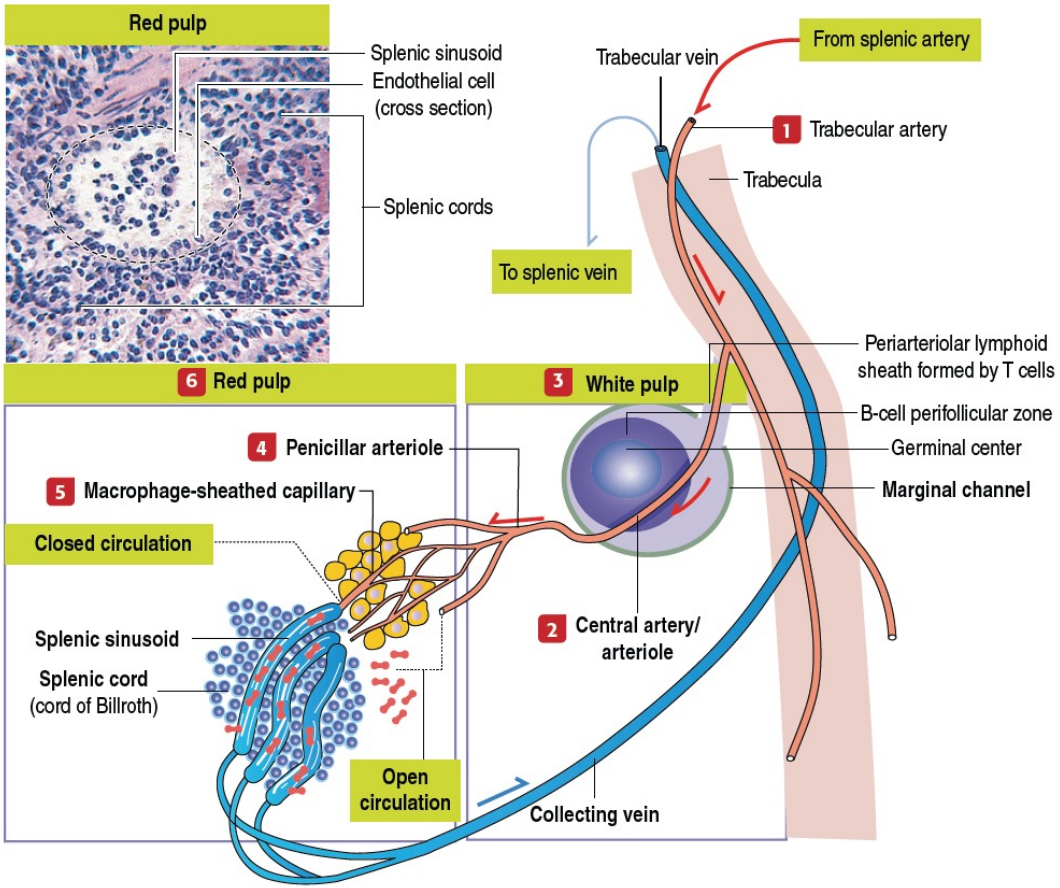
Spleen

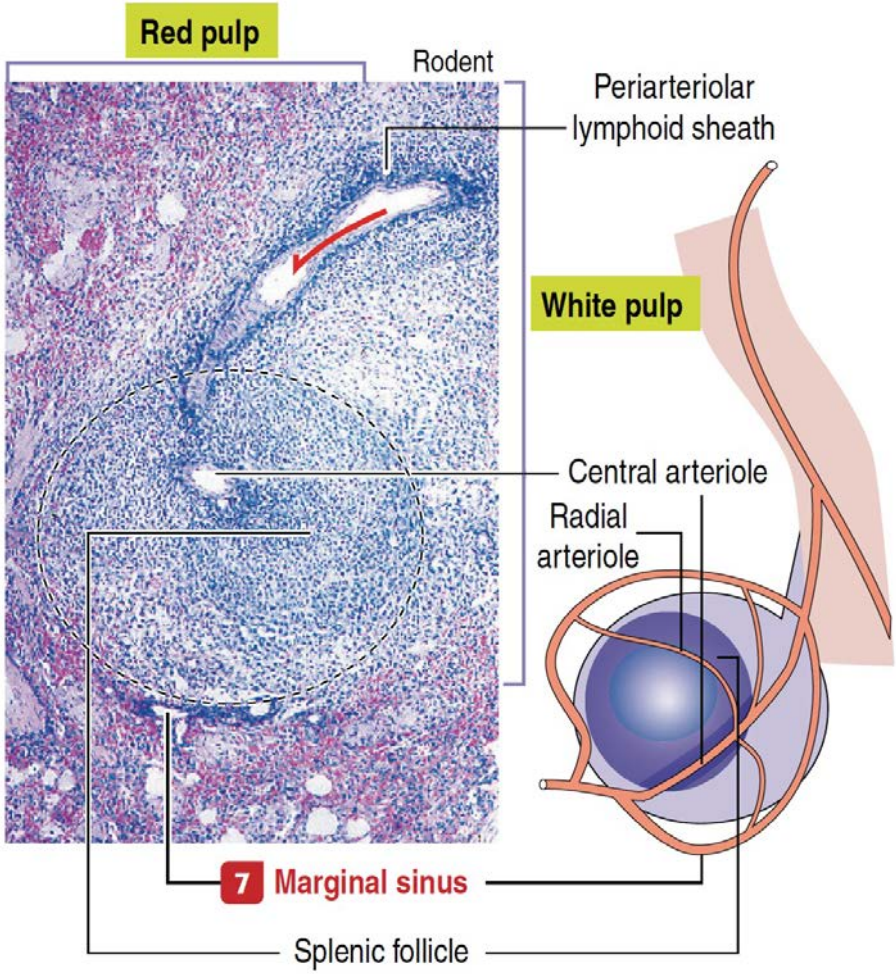
- Reticuloendothelial system
- Functions
  - Hematopoietic function
    - Produces fetal RBCs
  - Filter function
    - Filter and reuse certain cells
  - Immune function
    - Lymphocytes, monocytes
  - Storage function
    - 30% platelets stored in spleen



Saladin.Anatomy Physiology:The Unity of Form and Function.The McGraw-Hill Companies.2006

Spleen

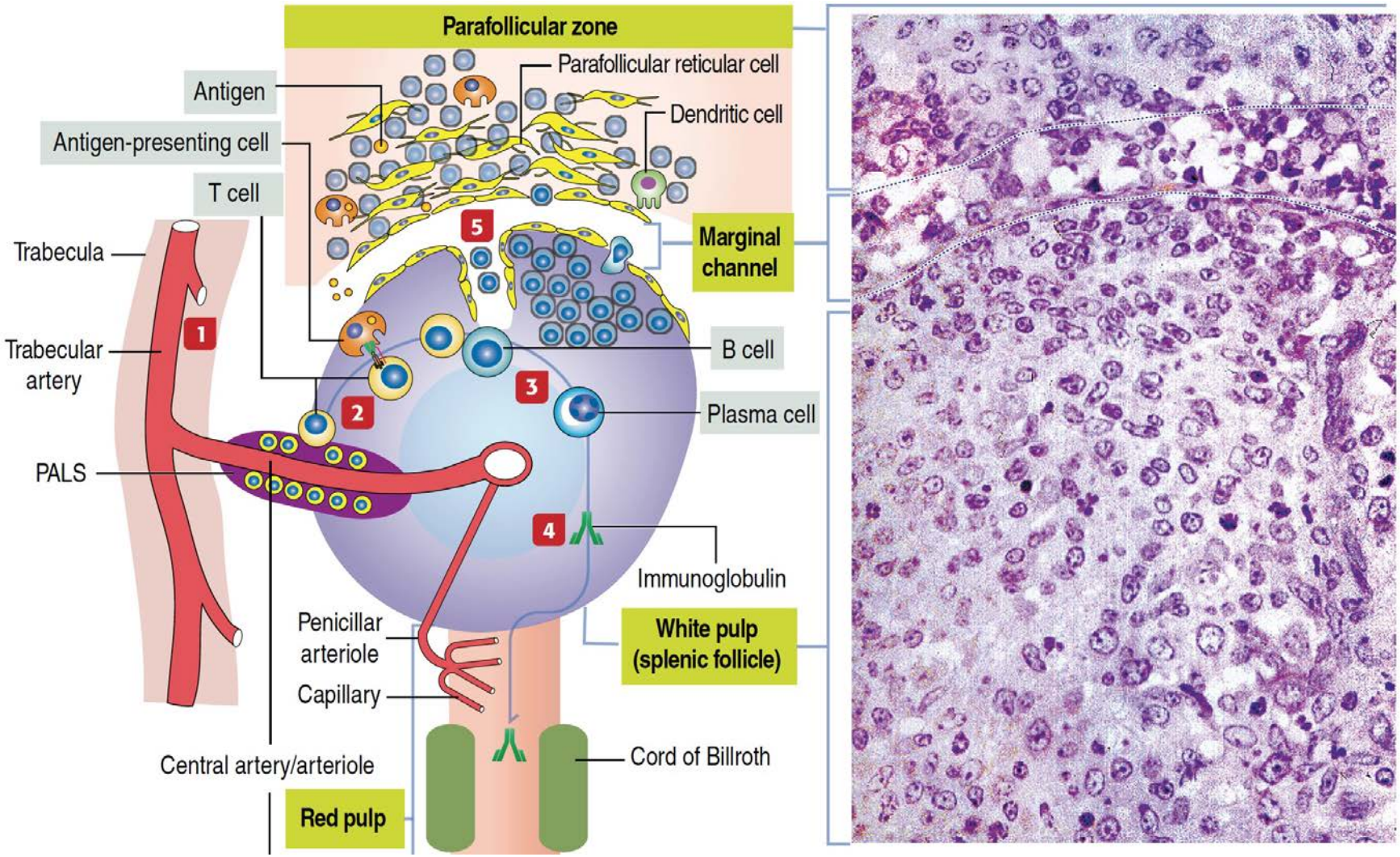




Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

Spleen

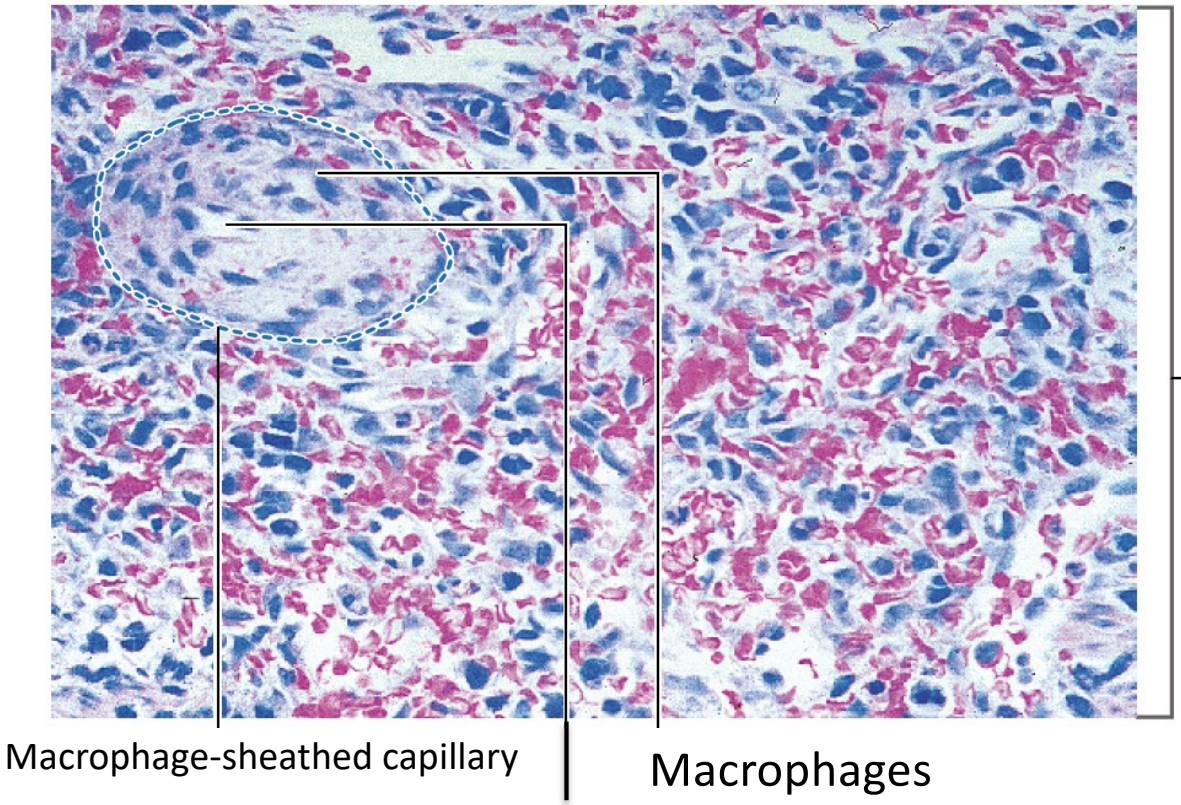
White pulp is a lymphoid follicle-like structure

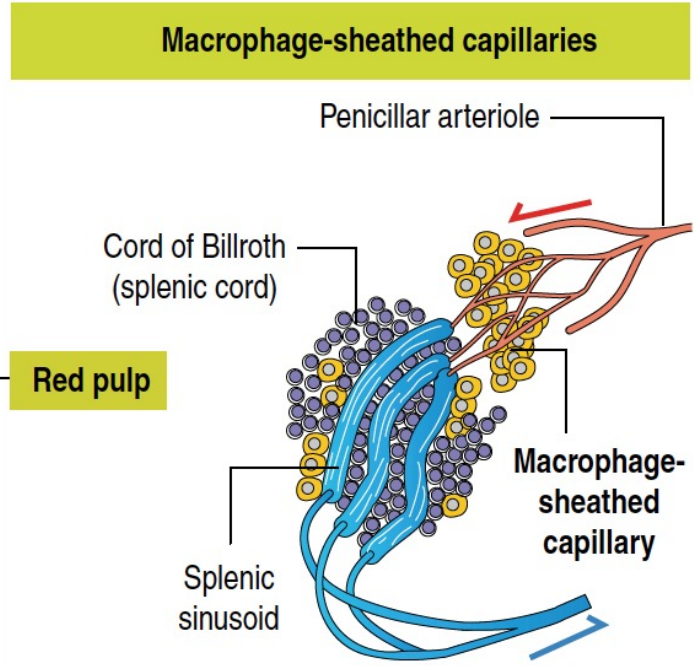


Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

Spleen

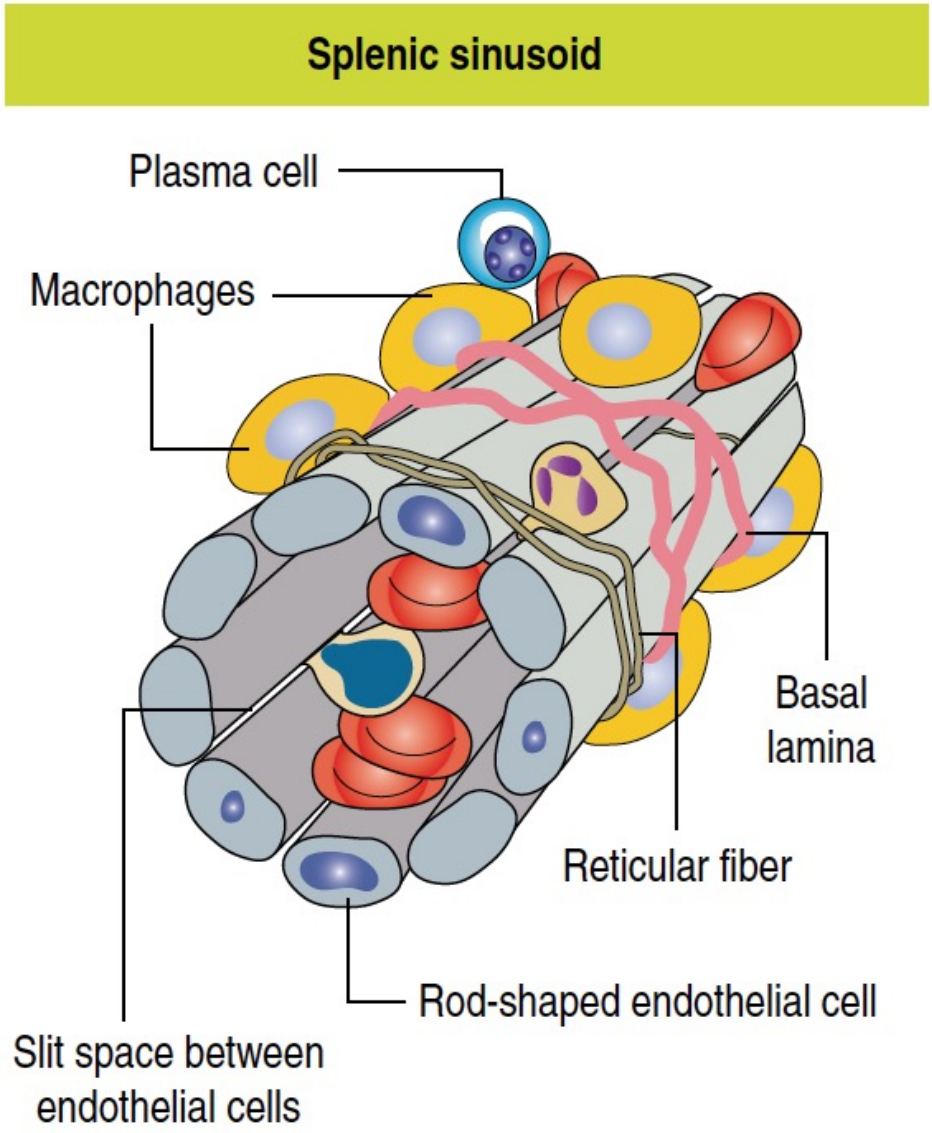
Red pulp





Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

Spleen

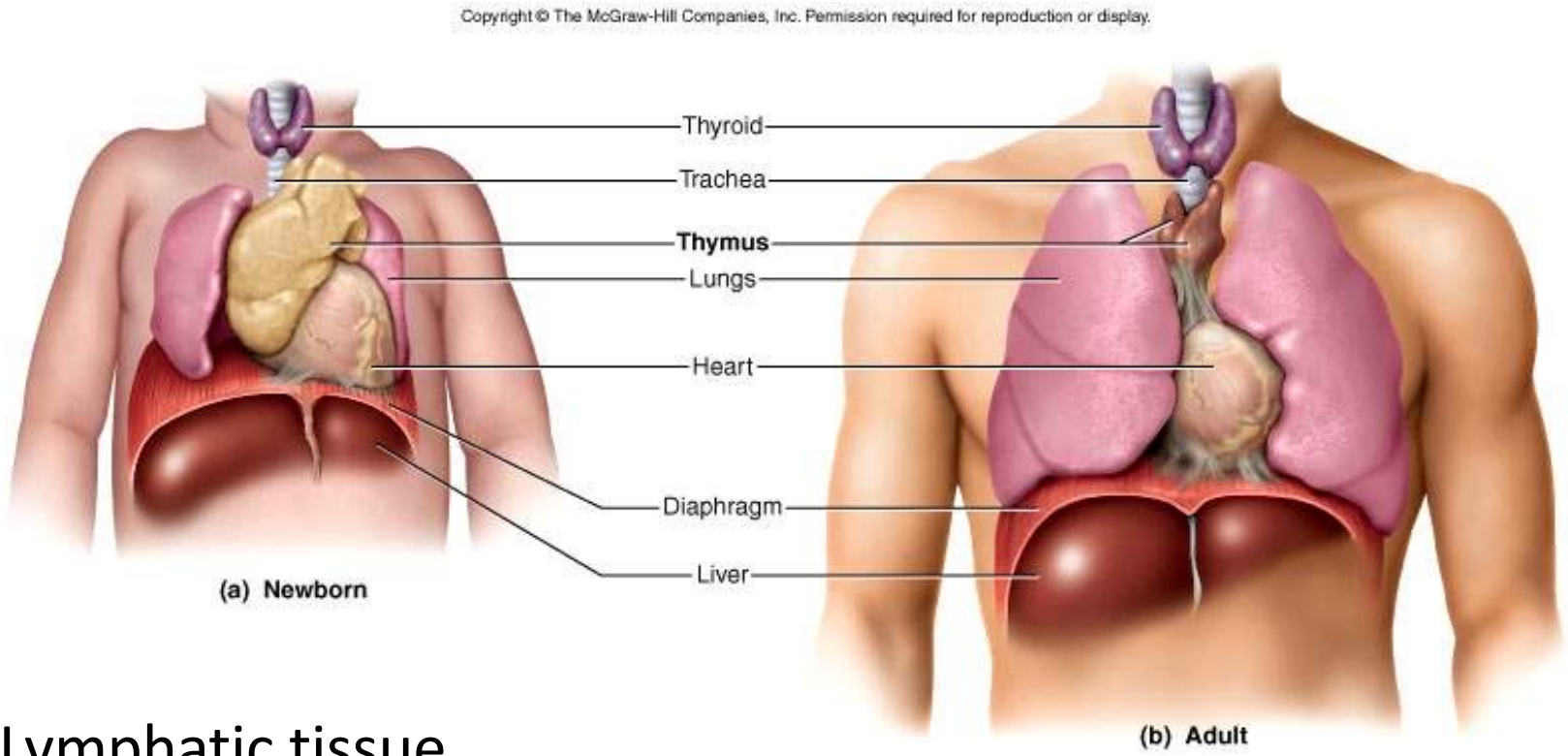


Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

Splenectomy

- Reasons for splenectomy
  - Traumatic injury: to prevent fatal hemorrhage
  - Blood diseases: excessive destruction of blood cells in the spleen (hereditary hemolytic anemia)
  - Patients with Hodgkin's disease prior to treatment
  - Standard treatment for patients with hypersplenism
- Effects
  - Increase risk to infection
  - Increased risk to thromboembolic events
  - Impaired production of antibodies
- Treatment:
  - Antibacterial vaccines
  - Antibiotic prophylaxis
  - Baby aspirin or anti-platelet

Thymus

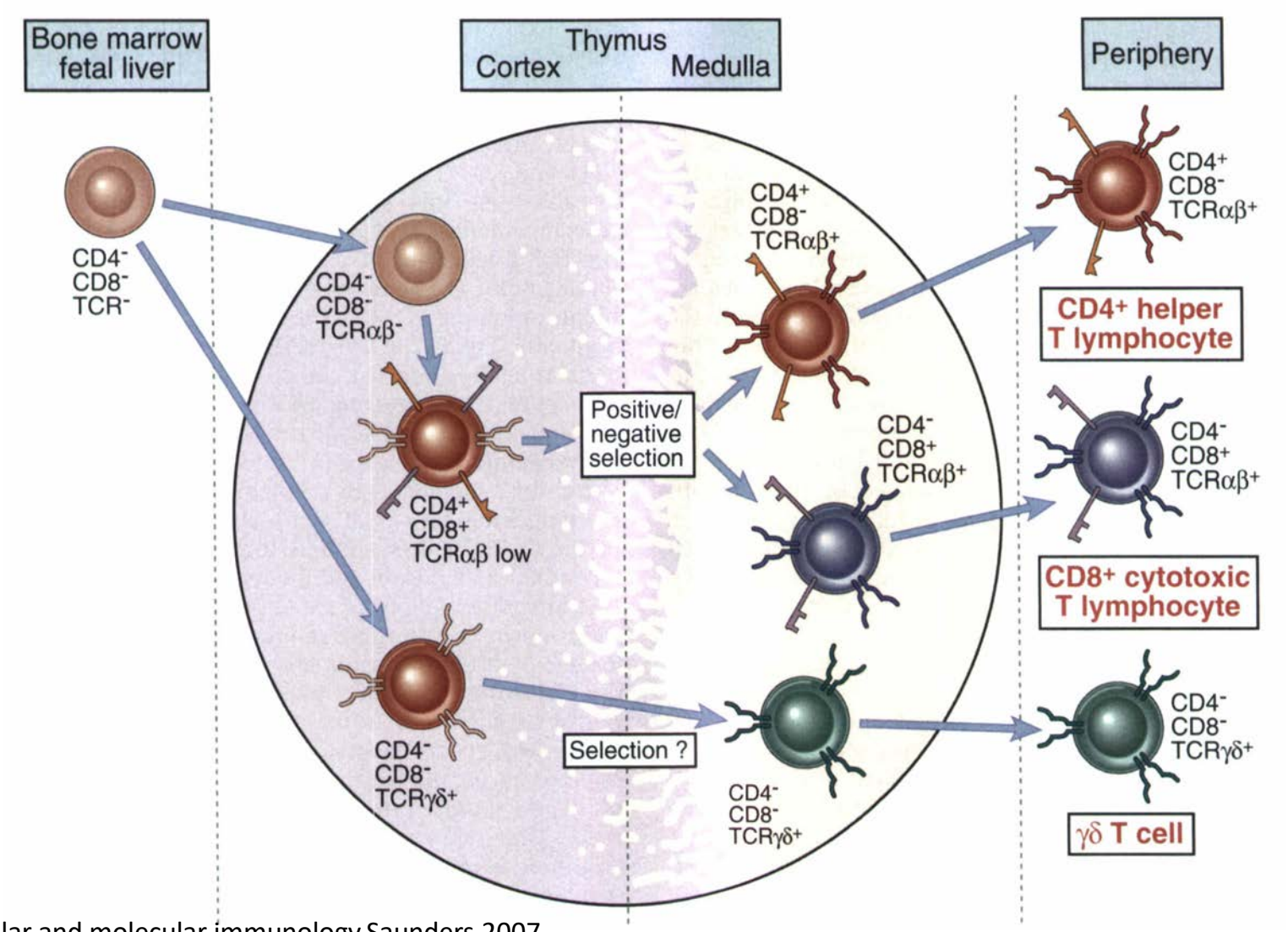


- Lymphatic tissue
- Mediastinum
- Primary role: changes lymphocytes to T cells for cellular immunity

Saladin.Anatomy Physiology:The Unity of Form and Function.The McGraw-Hill Companies.2006

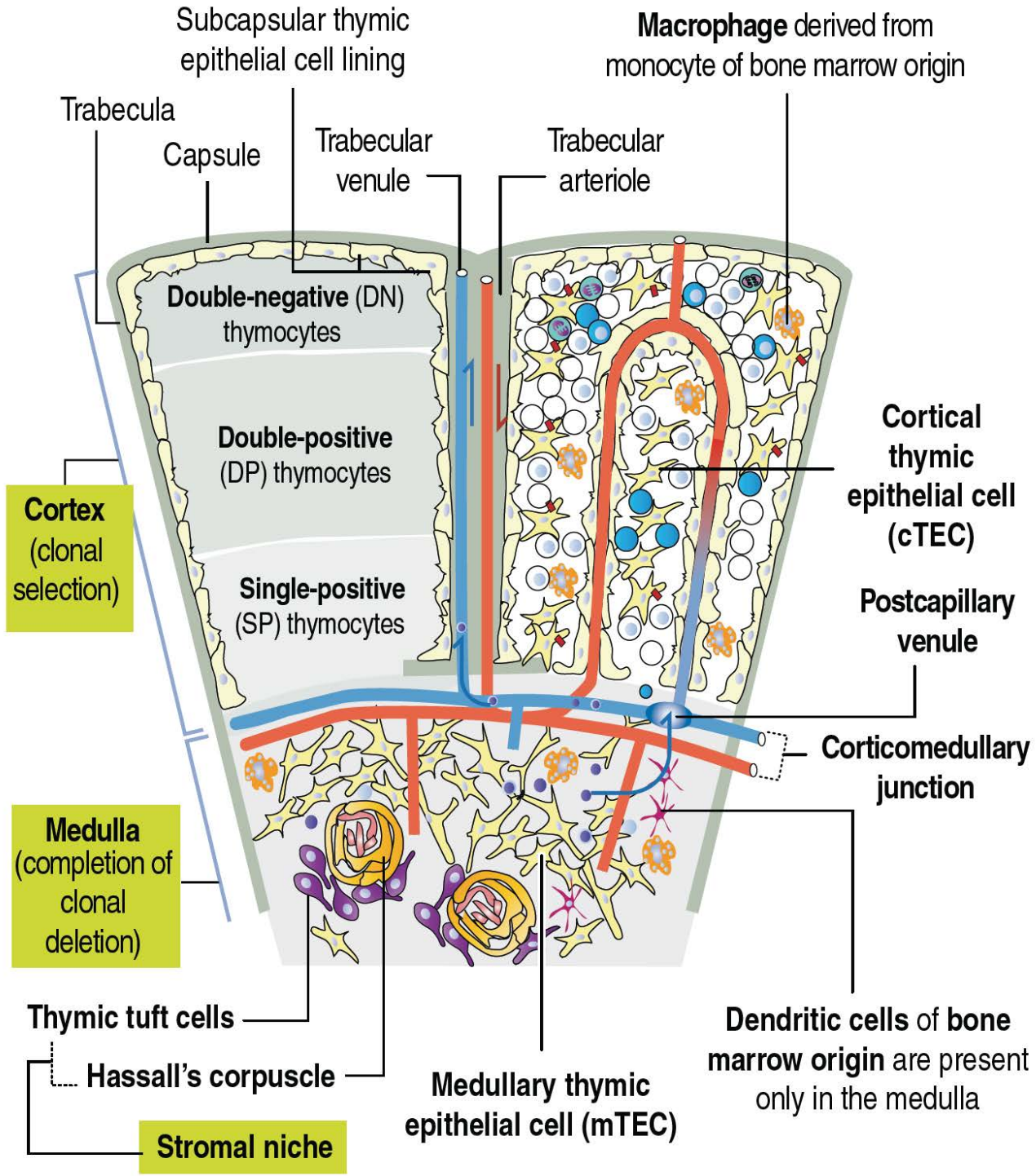
Thymus

T cell development



Abbas, et al. Cellular and molecular immunology.Saunders.2007

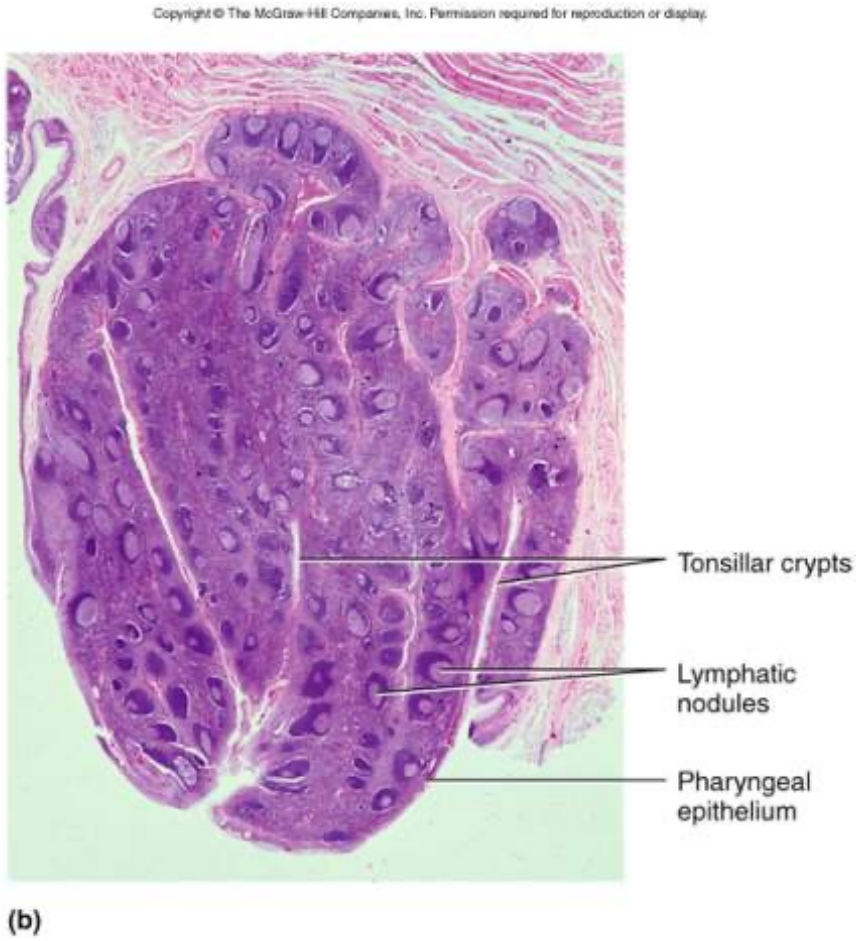
Thymus



Kierszenbaum AL & Tres LL. Histology & cell biology: An Introduction to pathology, 5th Ed, 2020. Elsevier.

Tonsils

- Masses of lymph tissue designed to filter tissue fluid, not lymph
- Located beneath certain areas of moist epithelium exposed to outside and hence to contamination
- Any or All may become so loaded with bacteria that the pathogens gain dominance
- Should not be removed unless absolutely necessary



Saladin.Anatomy Physiology:The Unity of Form and Function.The McGraw-Hill Companies.2006

LYMPHOPROLIFERATIVE DISORDERS

Lymphoproliferative disorders

- Abnormal proliferation of lymphocytes in peripheral blood, bone marrow, lymph nodes or lymphoid tissues
- Malignant lymphoproliferative disorders
  - Leukemia: Neoplastic cells in hematopoietic system (Hematopoietic disorders)
  - Lymphoma: Neoplastic cells in lymphoreticular system (Lymphatic disorders)
- Non-malignant lymphoproliferative disorders

Leukemia

- Major oncological disorder of blood-forming organs
- Malignant cells replace health bone marrow cells
- Acute myelogenous leukemia
- Acute lymphocytic leukemia

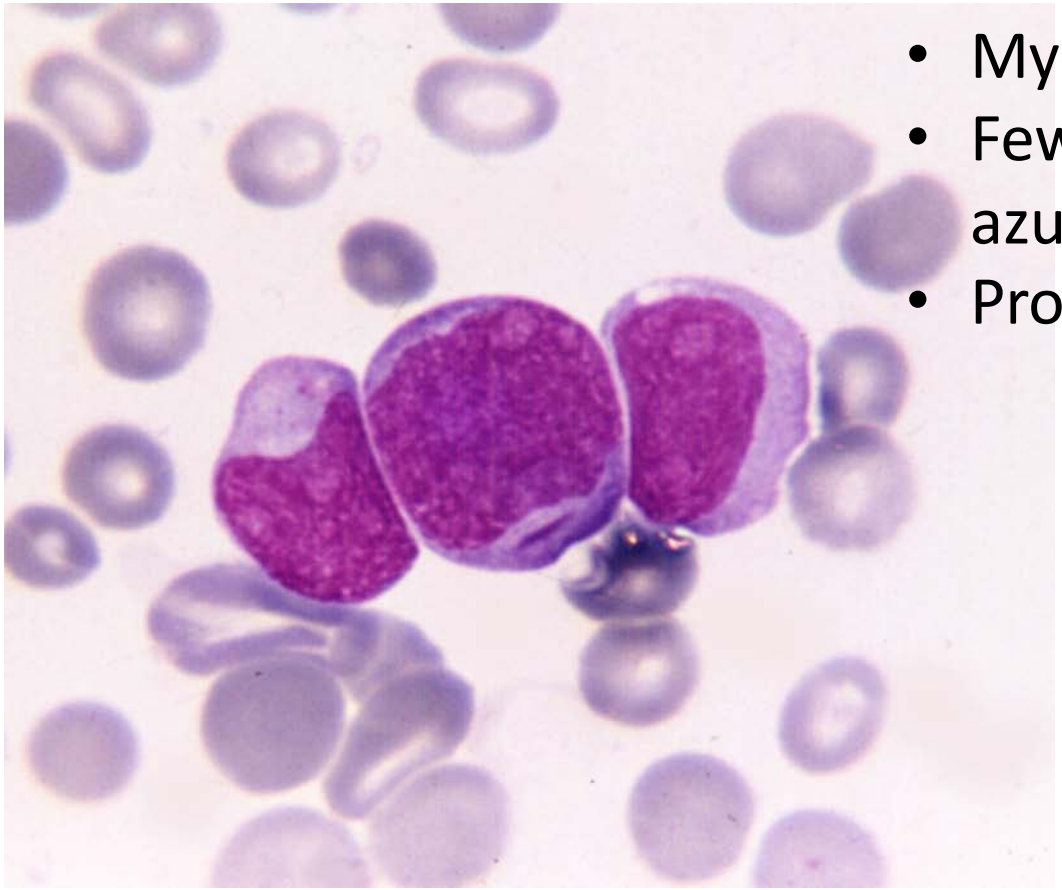
FAB Classification of Leukemia

- French-American-British Classification System

AML: Acute myeloblastic leukemia

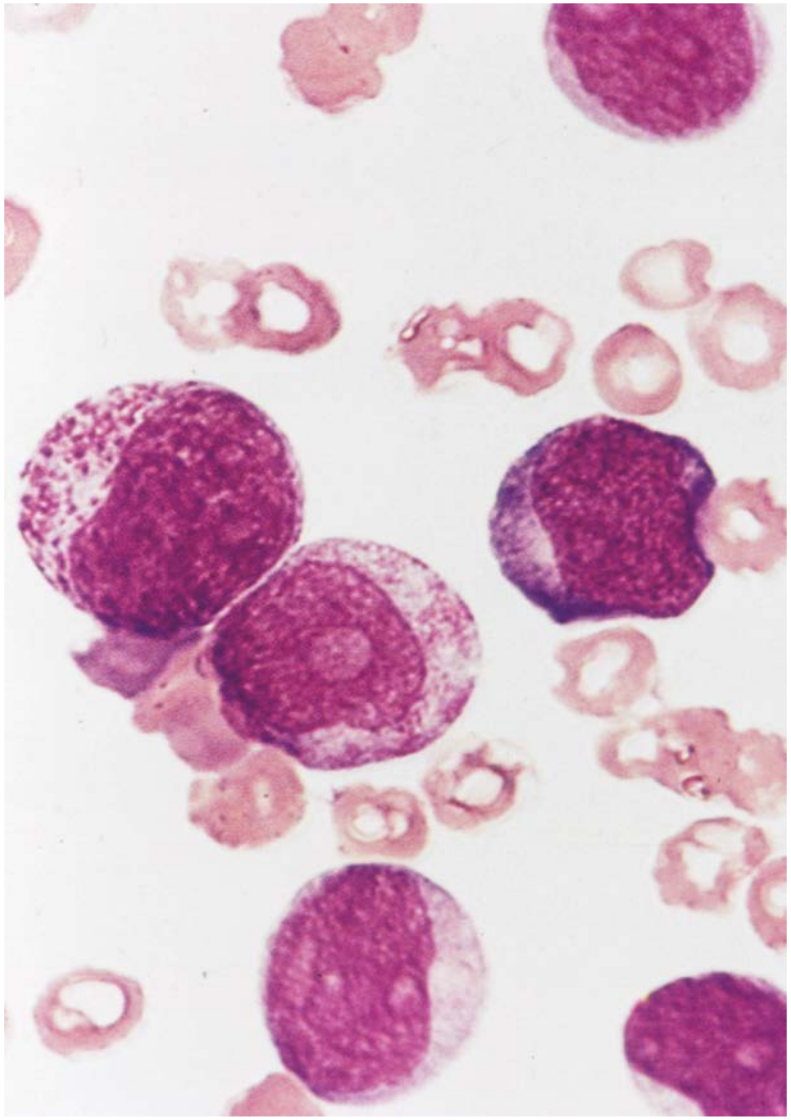
FAB subtype	Name	Adult AML patients (%)
M0	Undifferentiated acute myeloblastic leukemia	5%
M1	Acute myeloblastic leukemia with minimal maturation	15%
M2	Acute myeloblastic leukemia with maturation	25%
M3	Acute promyelocytic leukemia	10%
M4	Acute myelomonocytic leukemia	20%
M4eos	Acute myelomonocytic leukemia with eosinophilia	5%
M5	Acute monocytic leukemia	10%
M6	Acute erythroid leukemia	5%
M7	Acute megakaryocytic leukemia	5%

M_1 Acute Myeloblastic Leukemia (with Minimal Maturation)



- Myeloblast > 90 %
- Few Myeloblast with auer rod & azurophilic granules
- Promyelocyte < 10 %

M_2 Acute Myeloblastic Leukemia (with Maturation)



- Myeloblast with azurophilic granules
- Myeloblast 30-89 %
- Promyelocytes > 10%
- Monocytic presursor cells > 20% (May be found)
- Auer rods
- Pseudo Pelger-Huet anomaly
- Eosinophilic precursors with translocation of chromosome 8 & 21(t(b;21))

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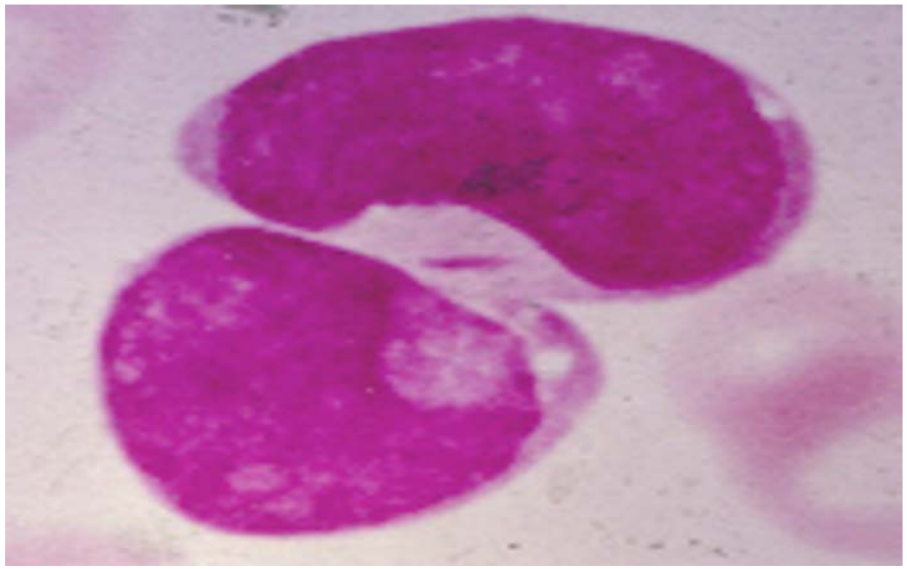
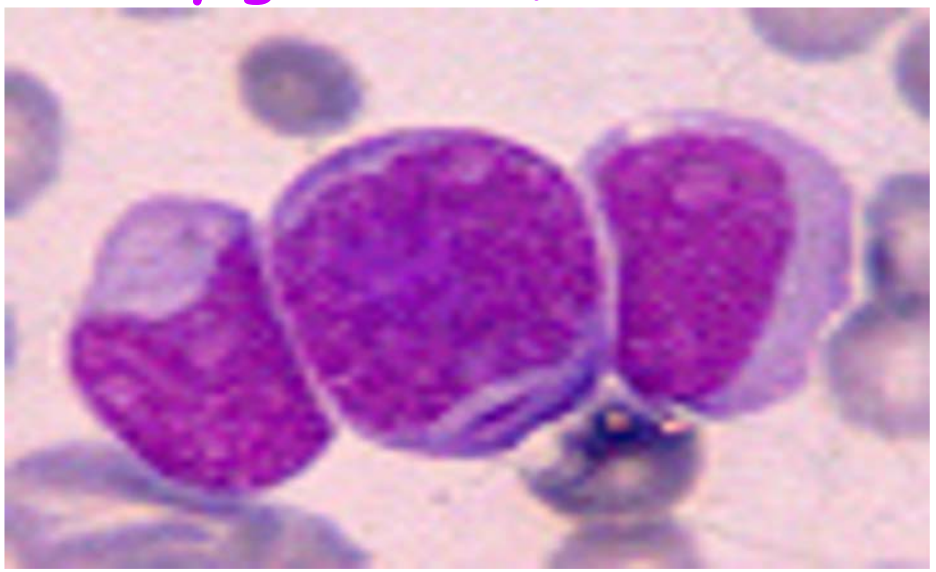
Auer rods

(Abnormal development of Primary granules)





Found in Leukemic Blood cells:-

Myelocytic series..

-Myeloblast,Promyelocyte..

Found in Monoblast called :

"Auer rod like structure"

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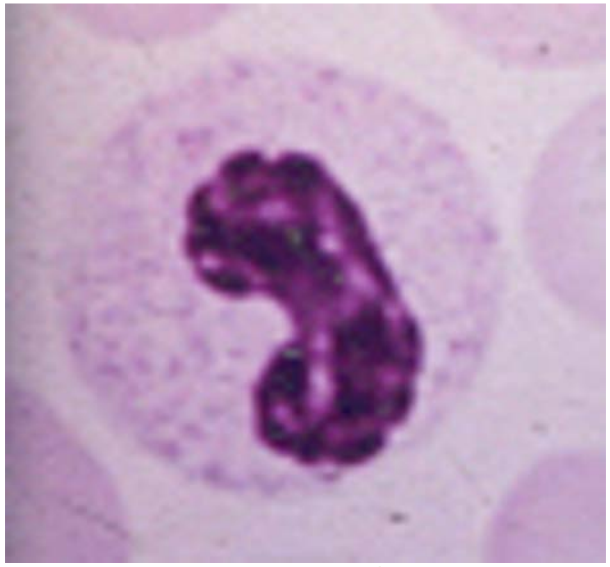
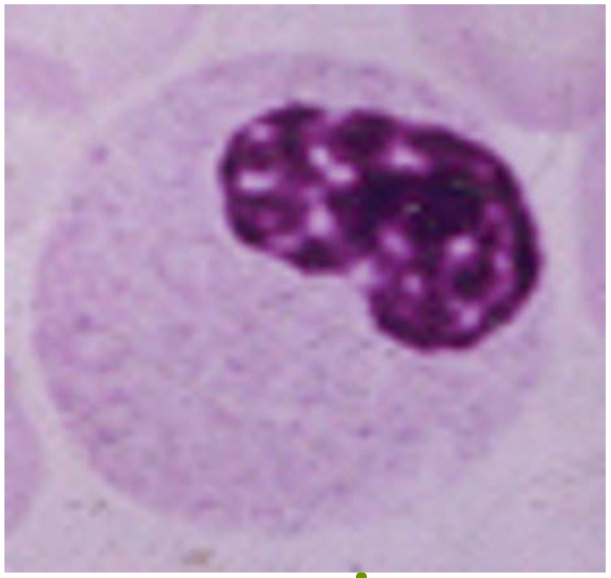
Pelger-Huet anomaly

2 lobes

Congenital anomaly (autosomal dominant)





Pseudo Pelger-Huet anomly:

- Chronic myelocytic leukemia
- Acute leukemia
- Myeloprolifertive disorders
- Malaria ,Others.....

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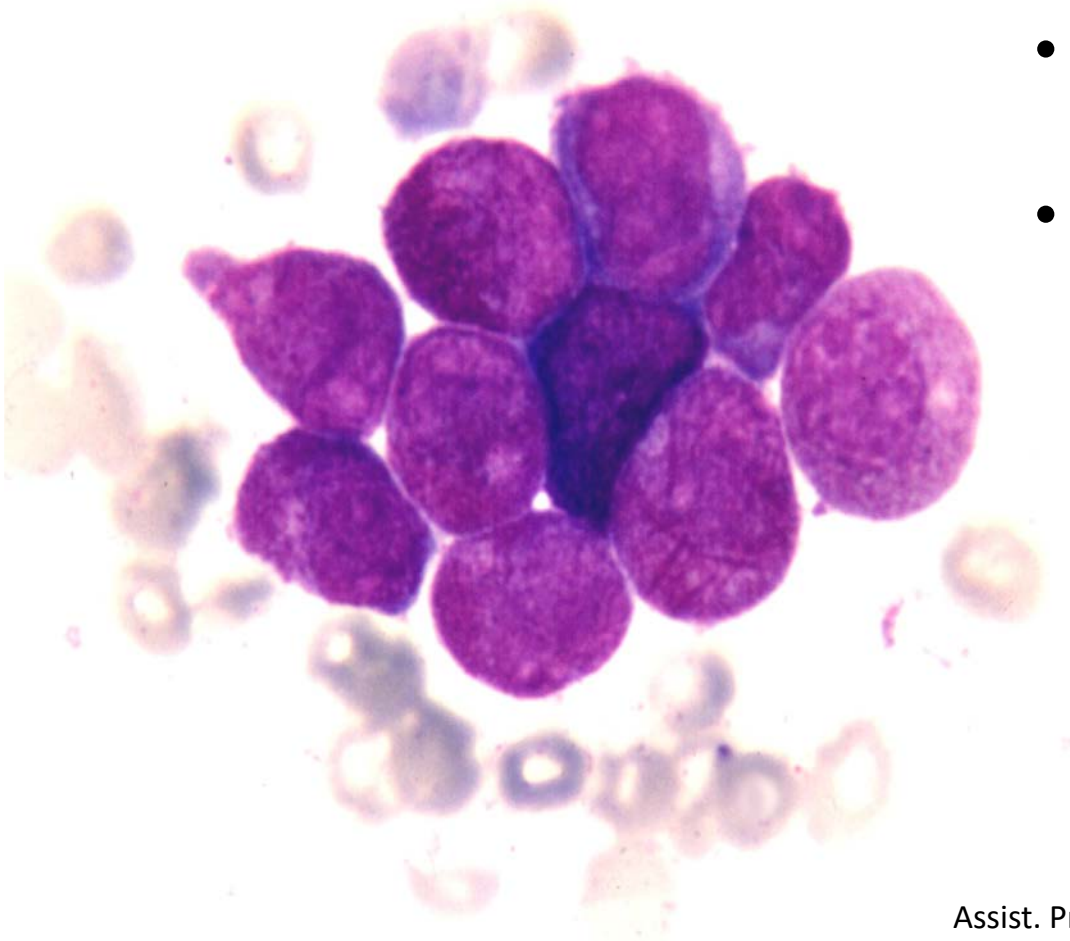
M_3 Acute Promyeloblastic Leukemia



- Promyelocytes with hypergranules and auer rods
- Promyelocytes > 50%

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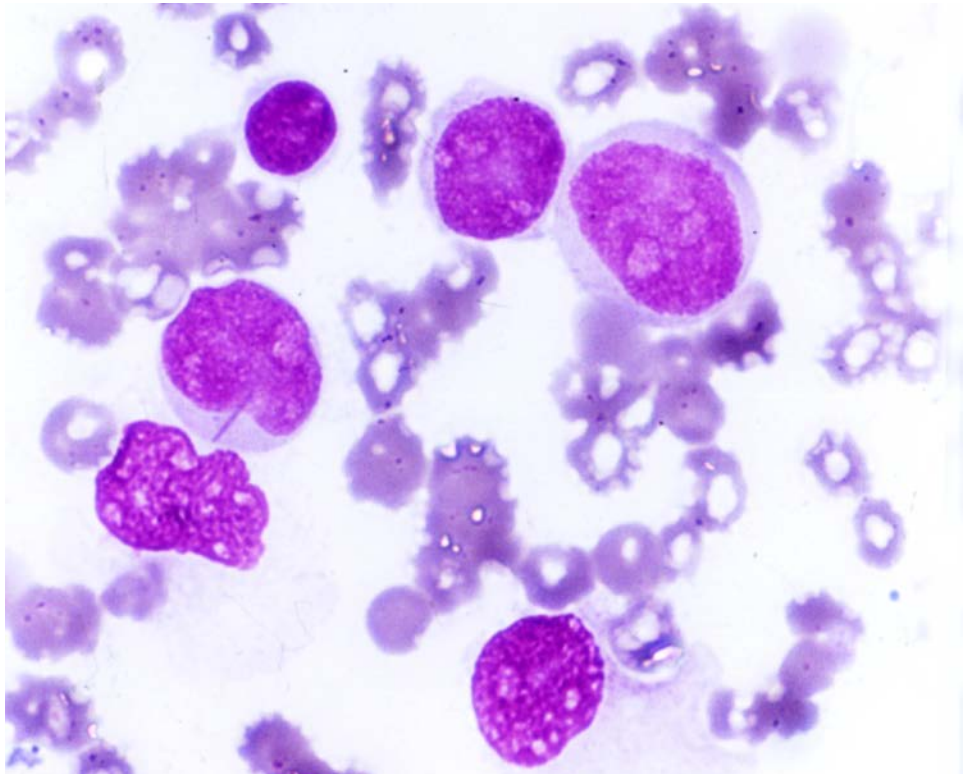
M_4 Acute Myelomonocytic Leukemia

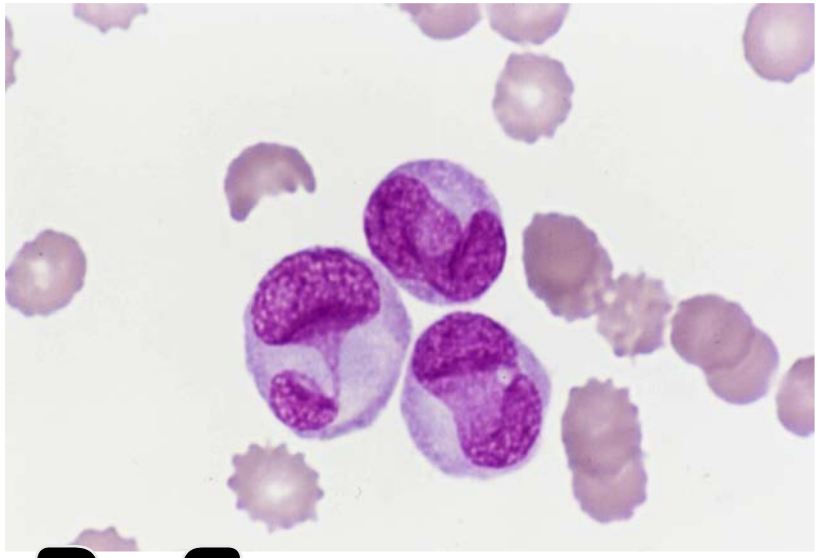


- Myeloblasts 30-80%
- Monocytes > 20%
- May be found auer rods
- Blast cell morphology like **"Myelo-Monoblast"**

M_{4eos} Varient of M4

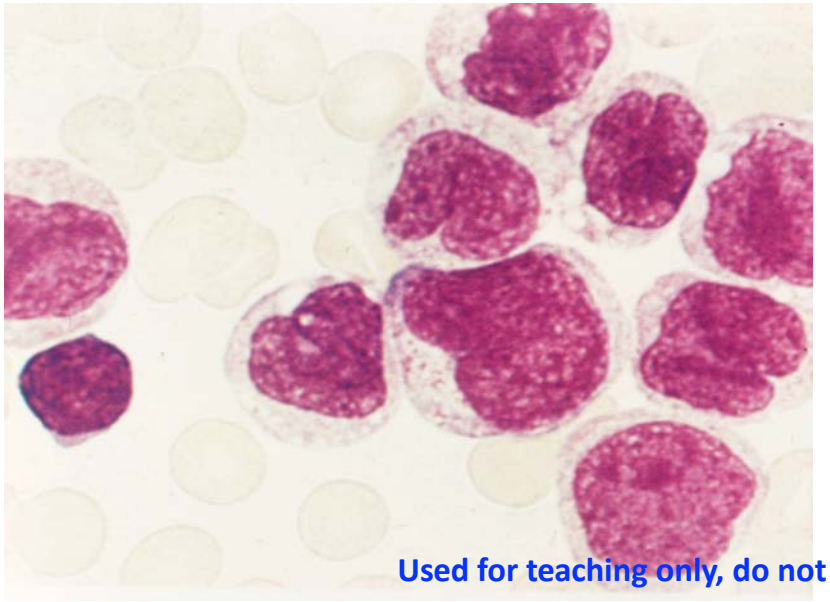
- Found eosinophils ~10% in BM

M5a Acute Monoblastic Leukemia (without maturation)



- Monoblasts > 80%
- May be found pseudopods & granules

M5b Acute Monoblastic Leukemia (with maturation)



- Monocytes < 20%
- Folded nucleus
- Gray-blue cytoplasm
- Azurophilic granules

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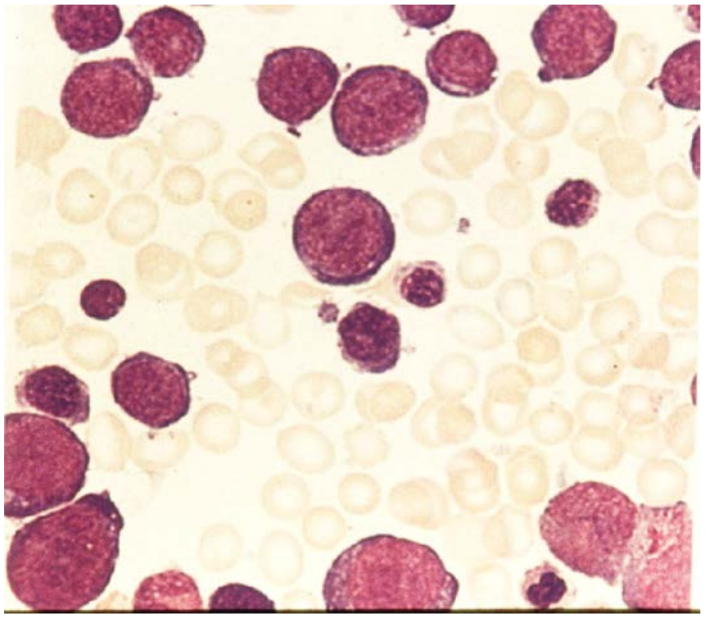
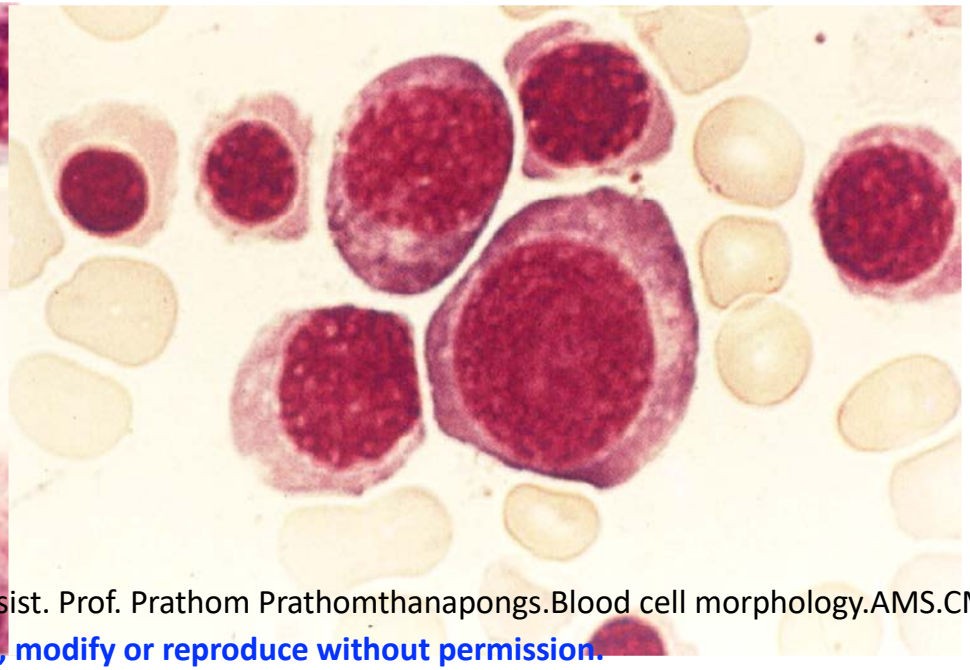
M_6 Erythroleukemia

- Megaloblastic erythroid precursors > 50%
- Multinucleaus giant cells
- Myeloblasts > 30%





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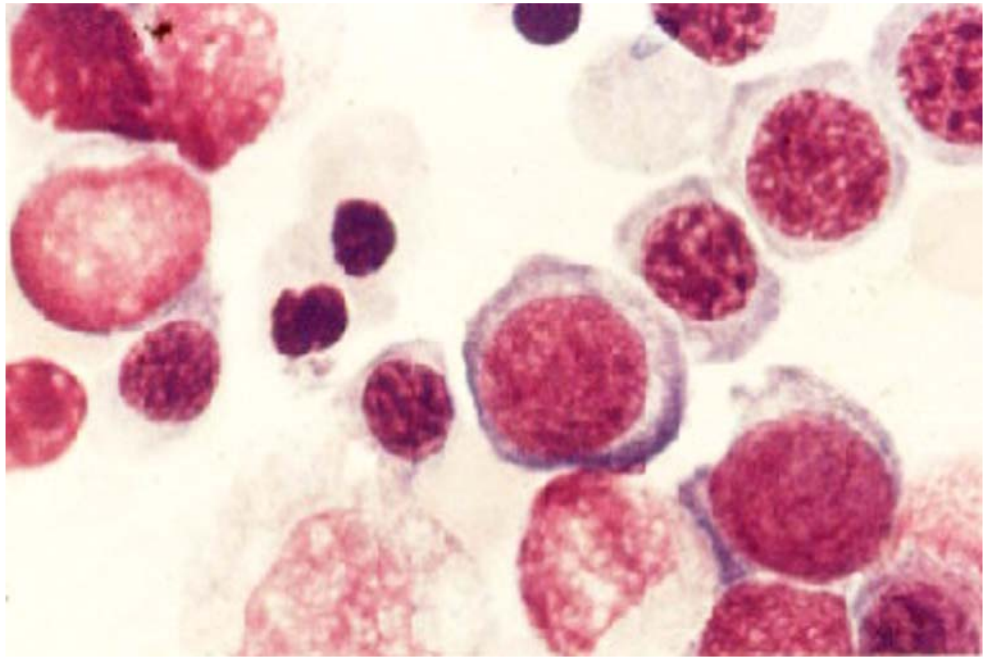
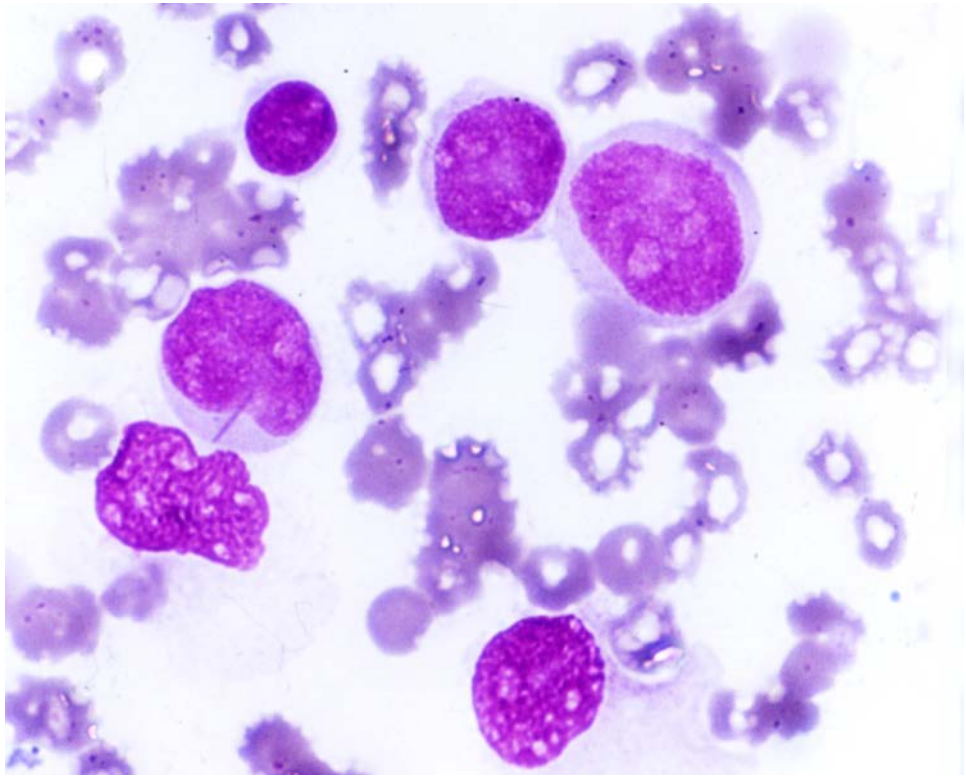
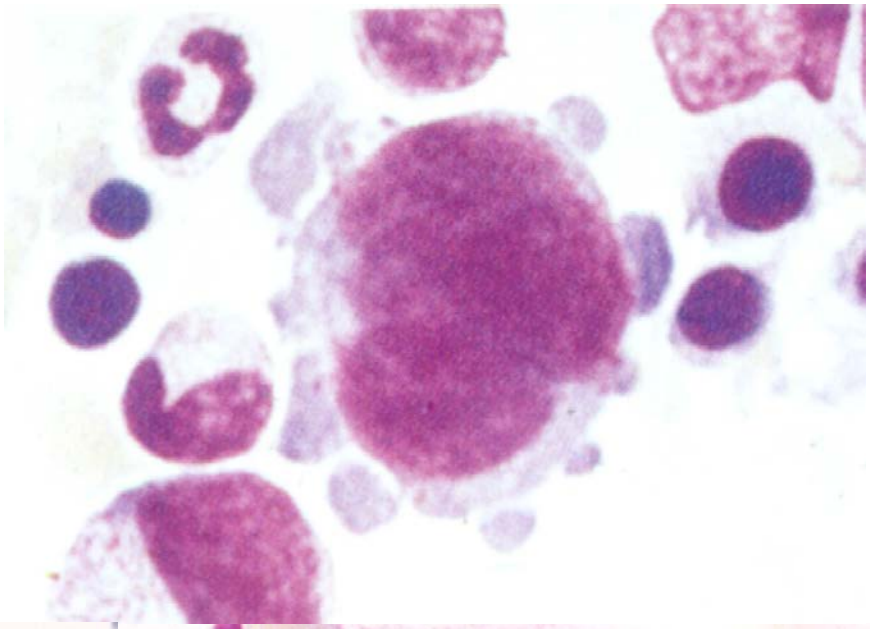
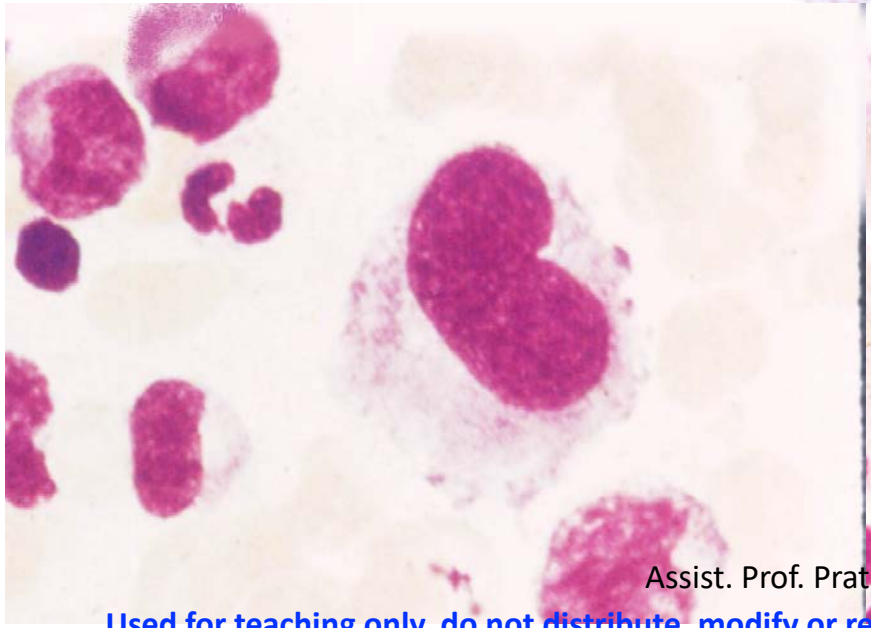


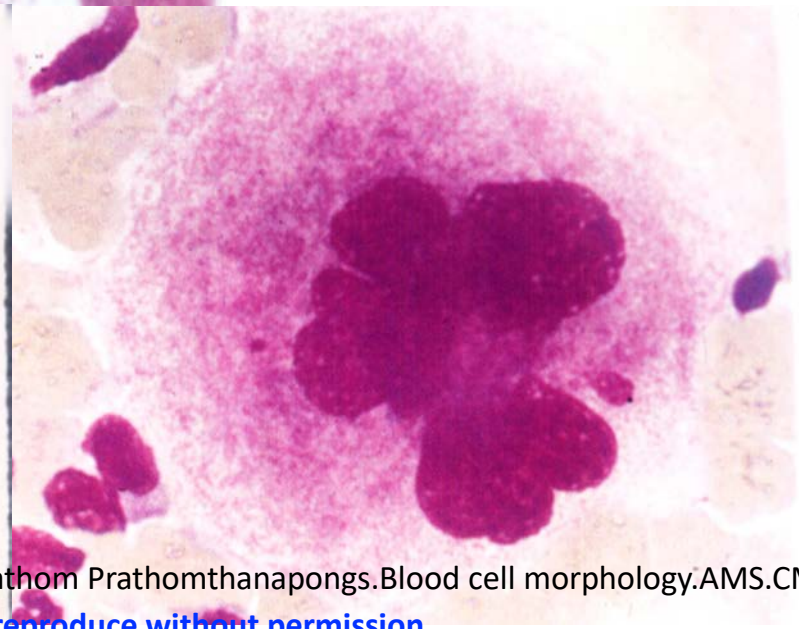


M_7 Acute Megakaryoblastic Leukemia

- Megakaryoblasts 20-30%
- Megakaryocytic fragments
- Fibrosis in BM







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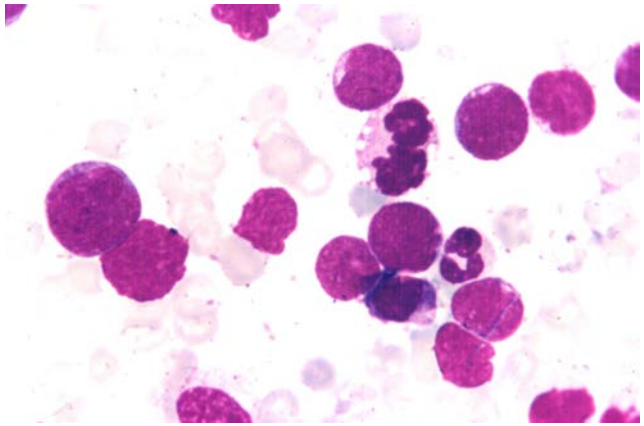
M0 Acute Myeloid Leukemia with Minimal Evidence of Myeloid Differentiation

- Myeloperoxidase (MPO) activity or Sudan black positive <3%
- Found CD13+CD33+ clusters
- Basophiloblast positive by cytochemical reaction or ultrastructural cytochemistry

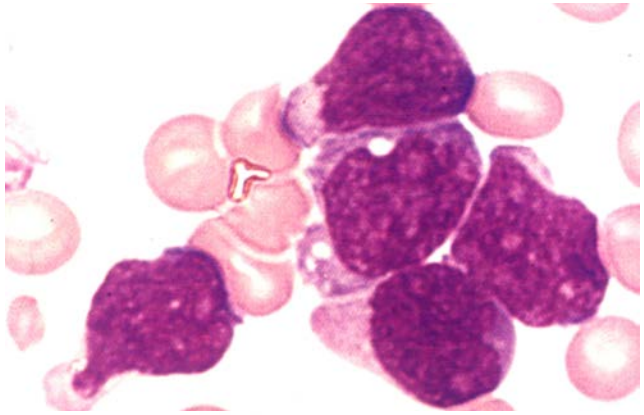
FAB Classification of Leukemia

ALL: Acute lymphoblastic leukemia



L1

- Small lymphoblast
- Homogeneously Nucleus
- Nucleoli not clear



L2

- Medium to Large lymphoblast
- Irregular Nucleus

L3

- Large lymphoblast
- Basophilic cytoplasm with vacuoles

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MYELOIDPROLIFERATIVE DISORDERS

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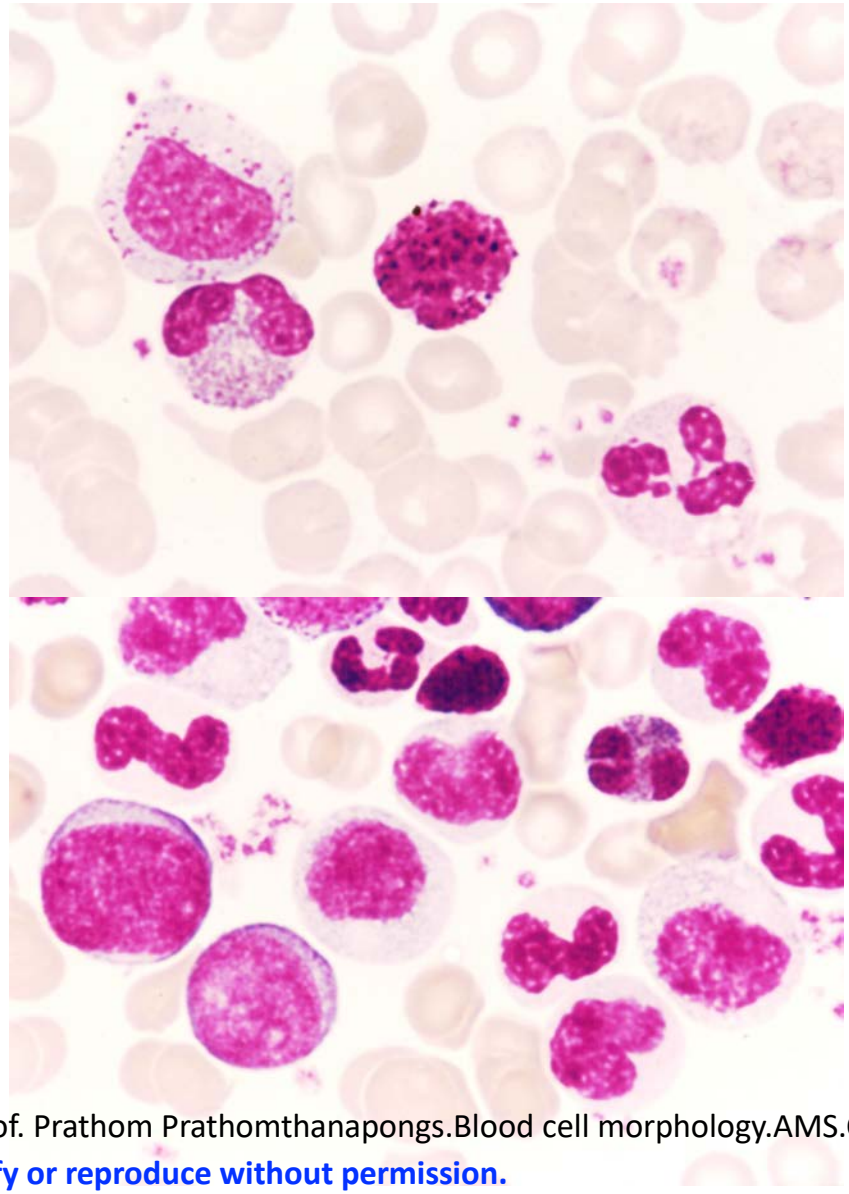
Chronic Myelocytic Leukemia (CML)

- Hyperleukocytosis ($1\text{-}4x10^5$ cells/µl)
- Myeloblast to PMN
- Eosinophils & Basophils
- Few NRBC
- Thrombocytosis



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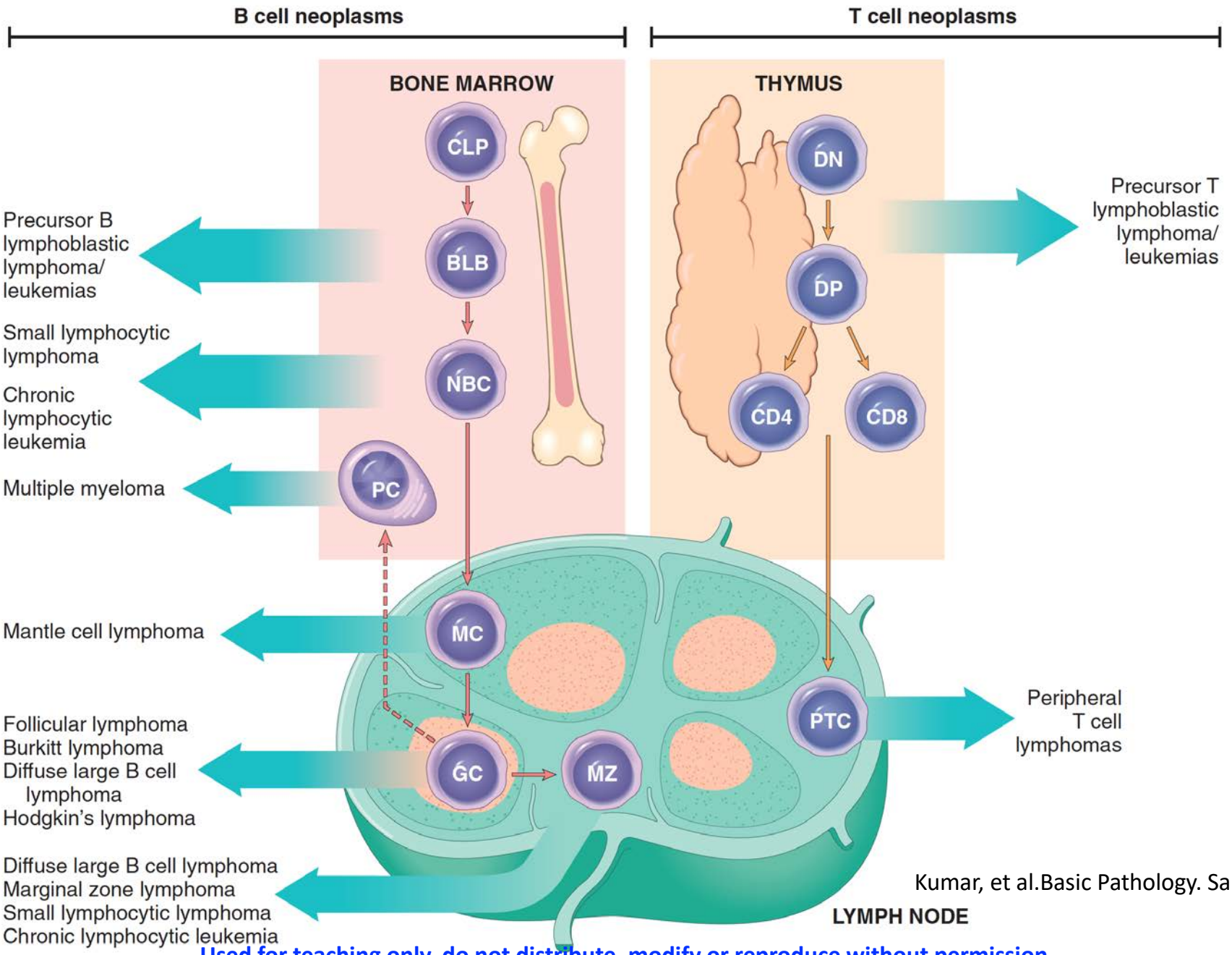
Lymphoma

- Hodgkin's disease
  - Lymphocyte predominance
  - Nodular sclerosing
  - Mixed cellularity
  - Lymphocyte depleted
- Non-Hodgkin's disease
  - B-cell lymphoma: Burkitt's lymphoma
  - T-cell lymphoma
- Other lymphatic malignancies
  - Chronic lymphocytic leukemia (CLL)
  - Multiple myeloma

B- & T-cell lymphoma



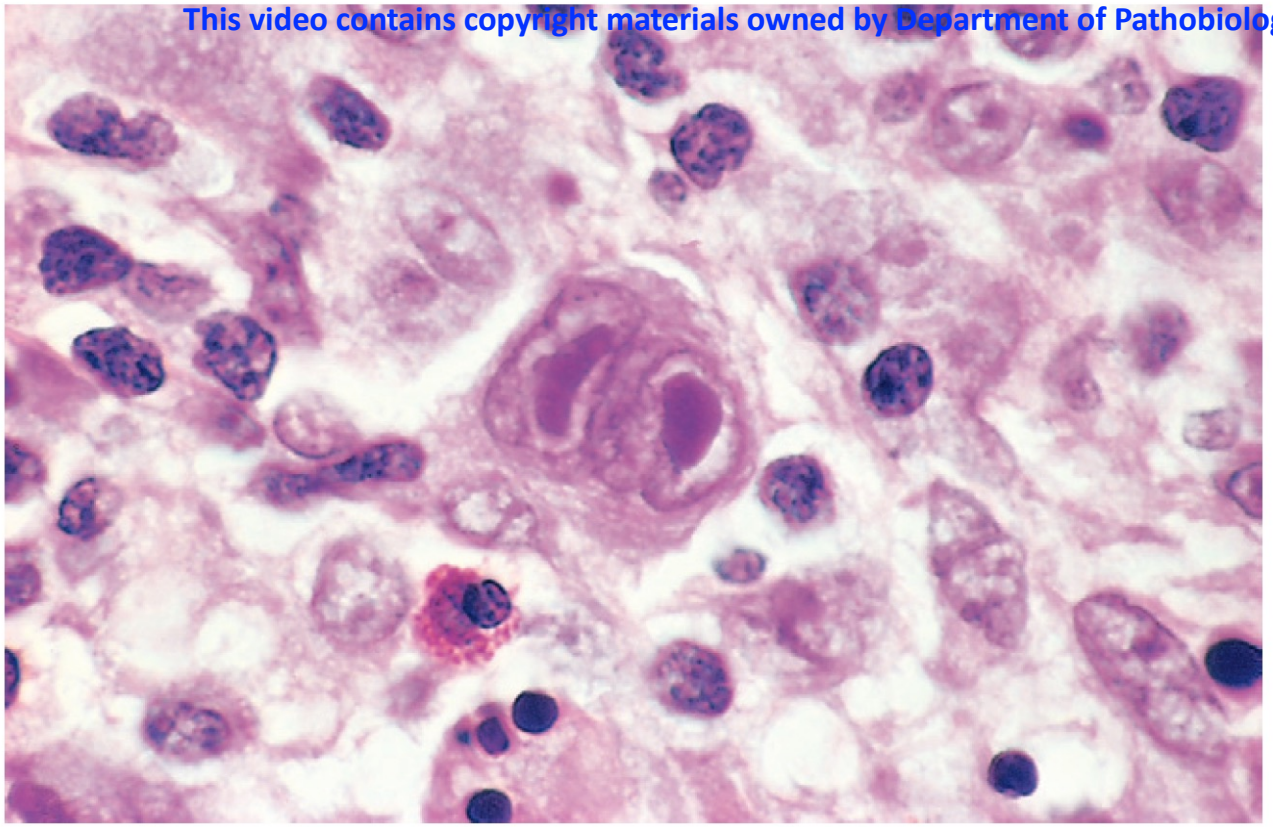
Kumar, et al.Basic Pathology. Saunders.2013

Hodgkin's Disease

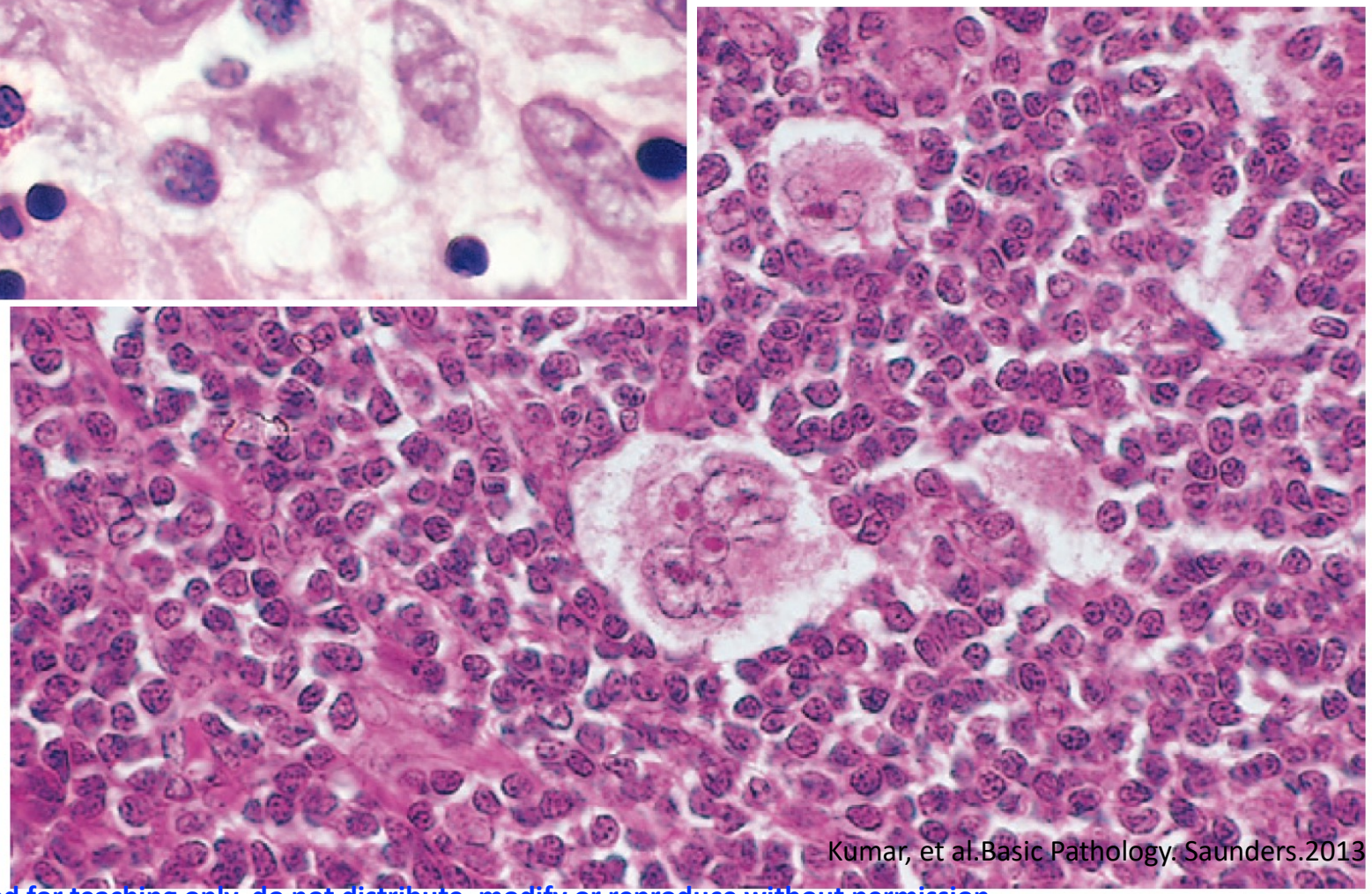
- Malignant disorder
- Painless, progressive enlargement of lymphoid tissue first evident in cervical lymph nodes; splenomegaly
- Anorexia, weight loss, pruritus, anemia, leukocytosis

Cause of Hodgkin's Disease

- Most cases: unknown – what is the cause of disease – but related to mutation in some genes that regulate hematopoietic differentiation
- Other cause:
  - Infection with Epstein-Barr virus (EBV) or HIV
  - Immunosuppression: an inherited immune deficiency disease, HIV infection or rejection of a transplanted organ



A binucleate **Reed-Sternberg cell** with large, inclusion-like nucleoli and abundant cytoplasm is surrounded by lymphocytes, macrophages, and an eosinophil.



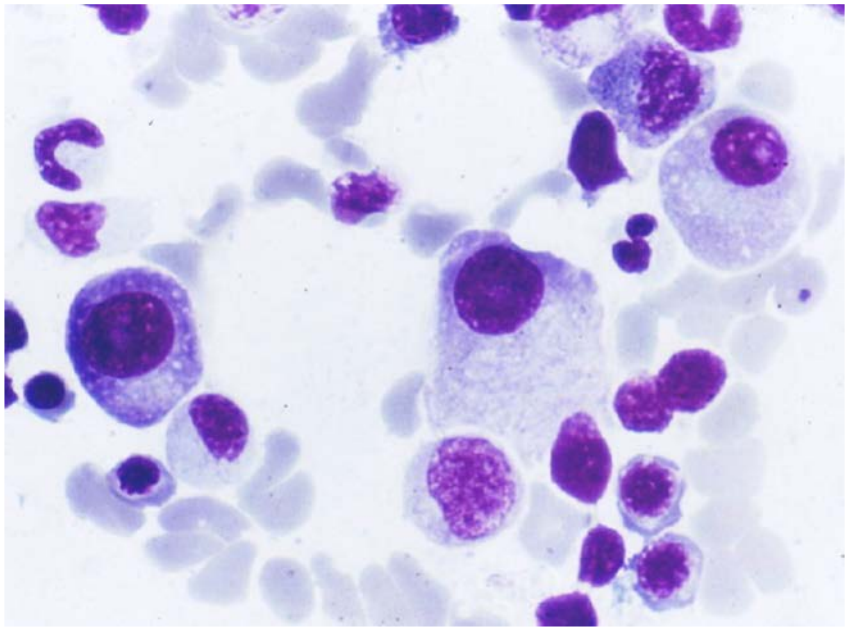
Kumar, et al.Basic Pathology. Saunders.2013

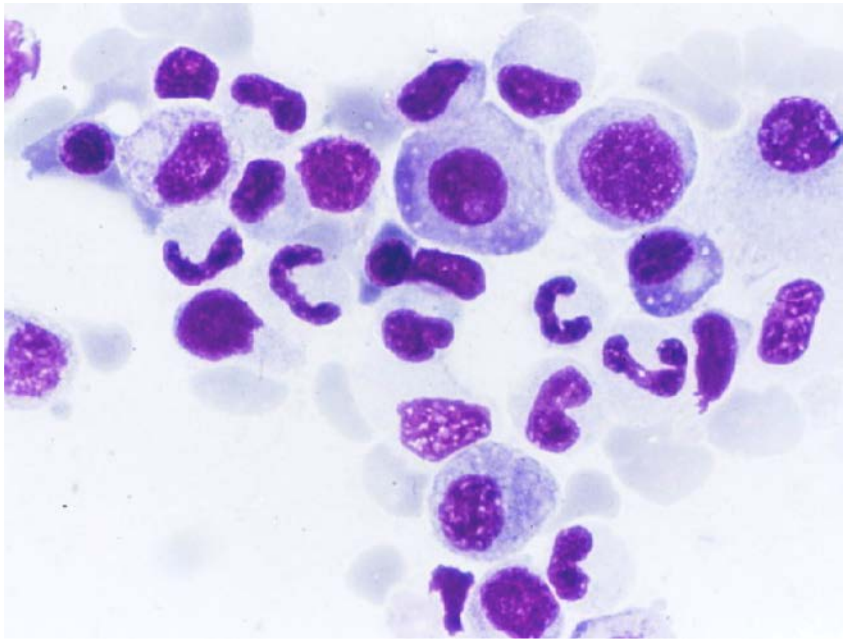
Non-Hodgkin's Disease

- B- & T- cell lymphomas: cancers of lymphatic system
- Lymphomas arise when developing B and T-lymphocytes undergo a malignant change and multiply in an uncontrolled way.
- These abnormal lymphocytes (lymphoma cells) form tumours in lymph nodes and other parts of the body
- In most cases the exact cause of lymphomas remains unknown
- Related to genetic, Infection (EBV, HIV, bacteria *helicobacter pylor* - MALT lymphoma)

Multiple Myeloma

- Plasma cells > 10 % in BM
- Osteolytic bone lesions & Osteoporosis
- Immunoglobulins in urine





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