Chapter 10

Blood and Circulatory System Disorders

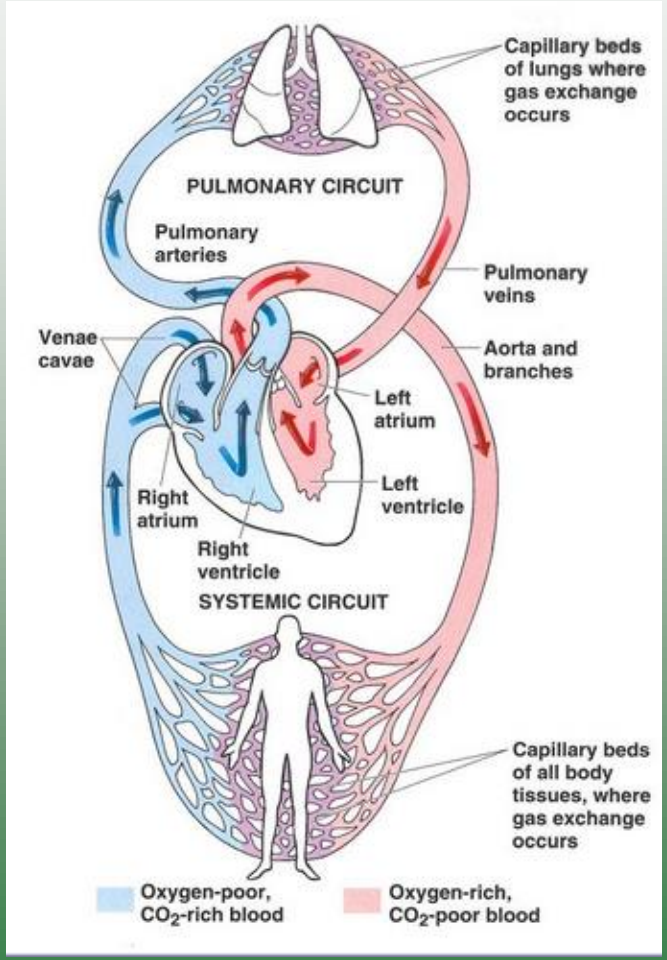
Review of the Circulatory System

- The circulatory system consists of the cardiovascular system and lymphatic system
- This chapter will cover the blood vessels, the blood, and associated disorders.

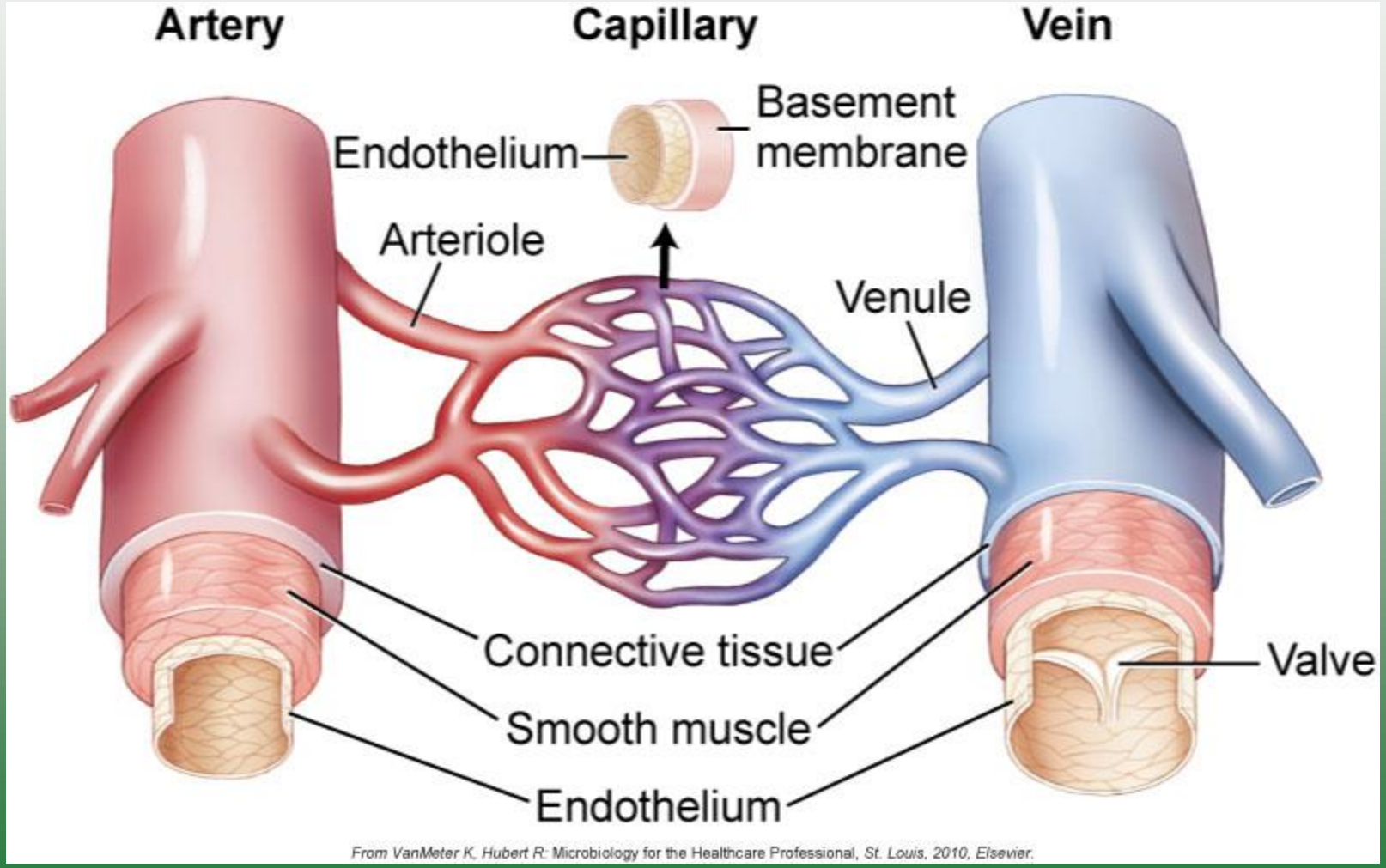
- Blood vessels – “Circulatory System”
- Blood – “Hematopoietic System”

Blood Vessels

- Arteries—arterioles
  - Transport blood away from heart
- Veins—venules
  - Return blood back to the heart
- Capillaries
  - Microcirculation within tissues
- Systemic circulation
  - Exchange of gases, nutrients, and wastes in tissues
- Pulmonary circulation
  - Gas exchange in lungs



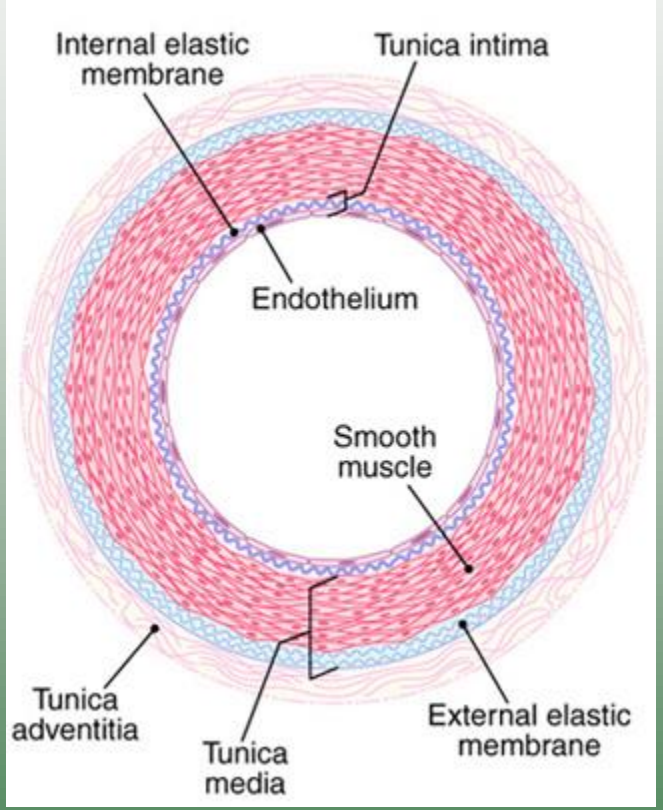
Blood Vessels (Cont.)

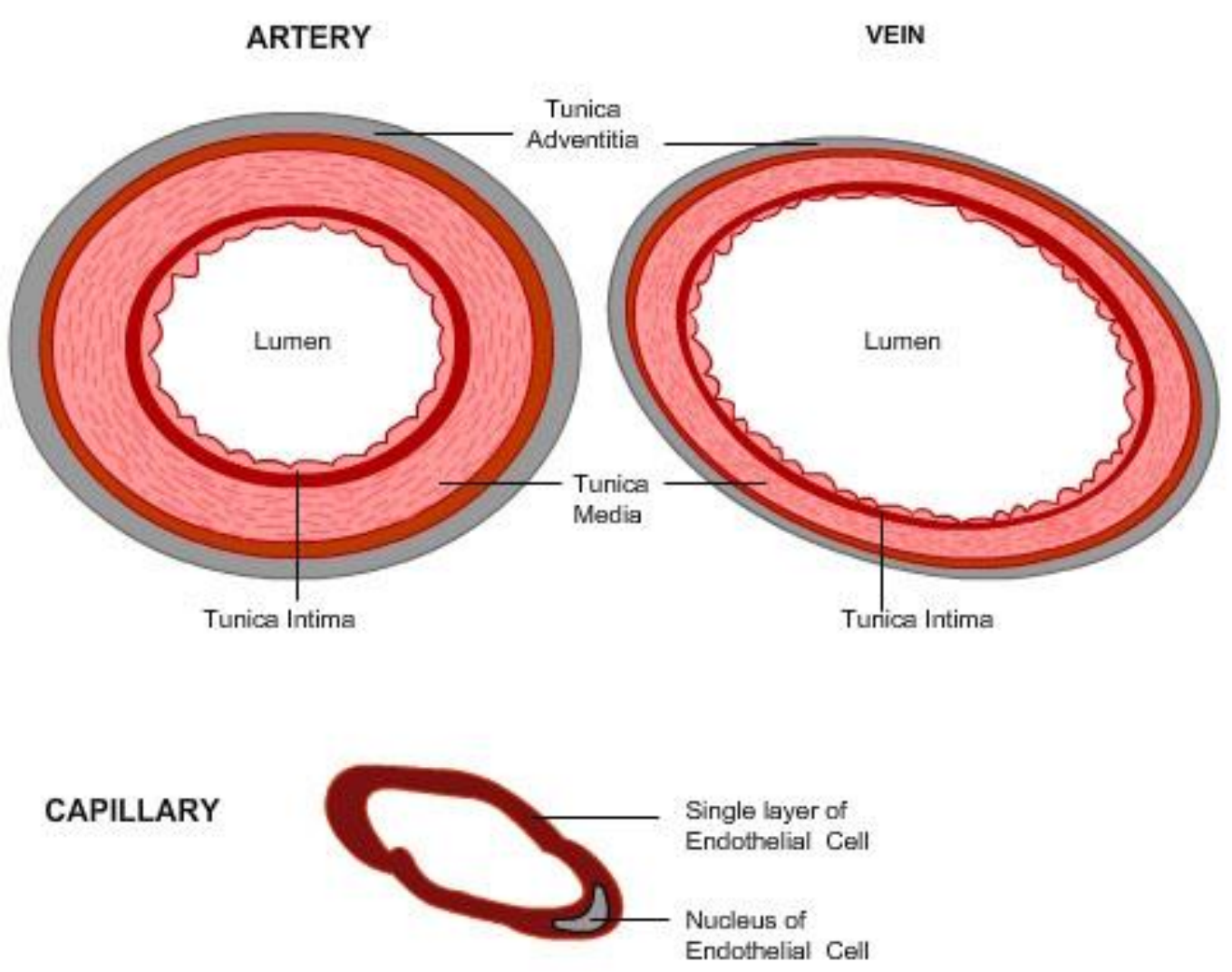


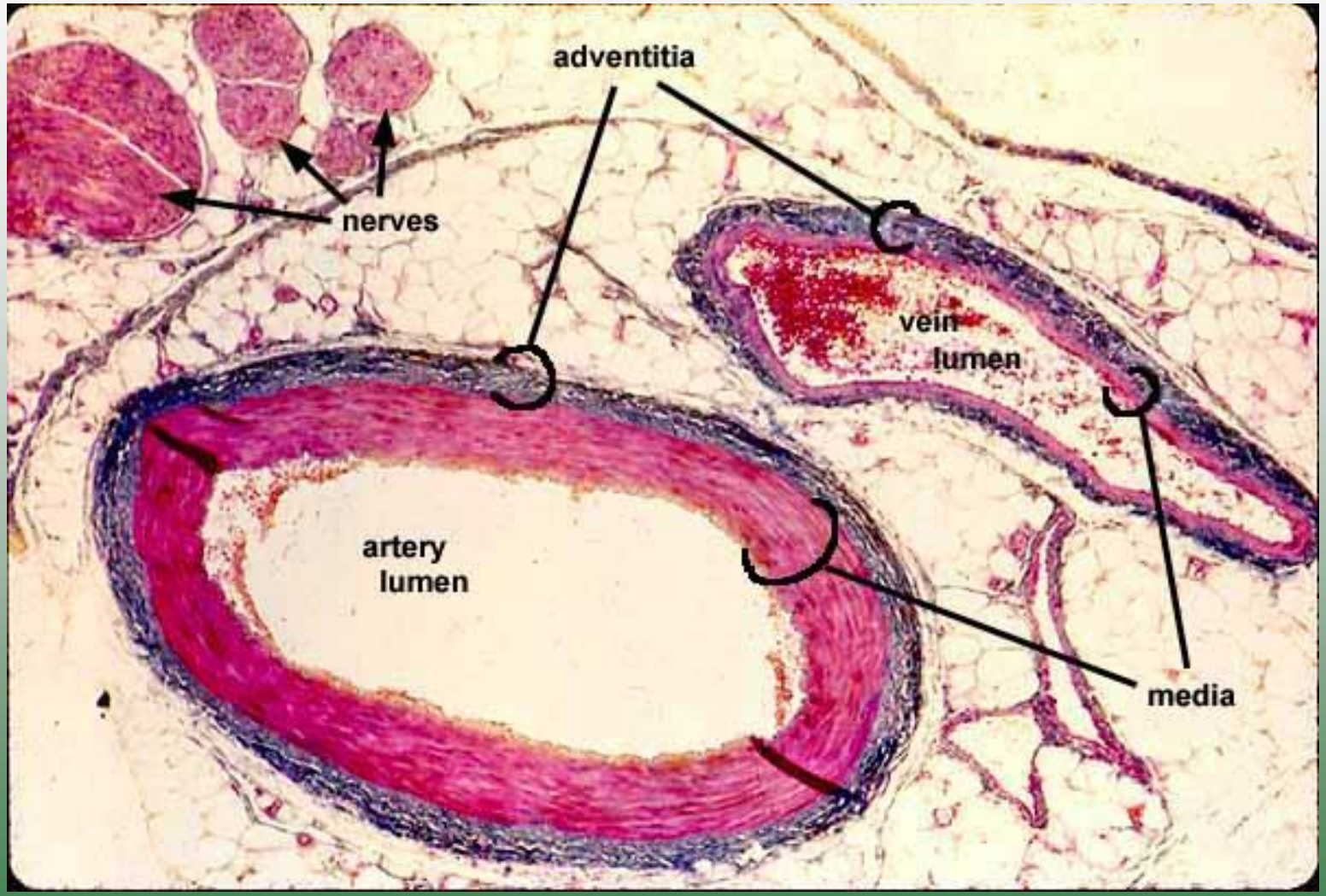
From VanMeter K, Hubert R: Microbiology for the Healthcare Professional, St. Louis, 2010, Elsevier.

Histology of Arteries and Veins

- Tunica intima—endothelium (simple squamous epithelium)
- Tunica media—middle layer, mostly smooth muscle
- Tunica adventitia (externa)—connective tissue with fibrocytes, collagen (type I), and elastic fibers







Blood

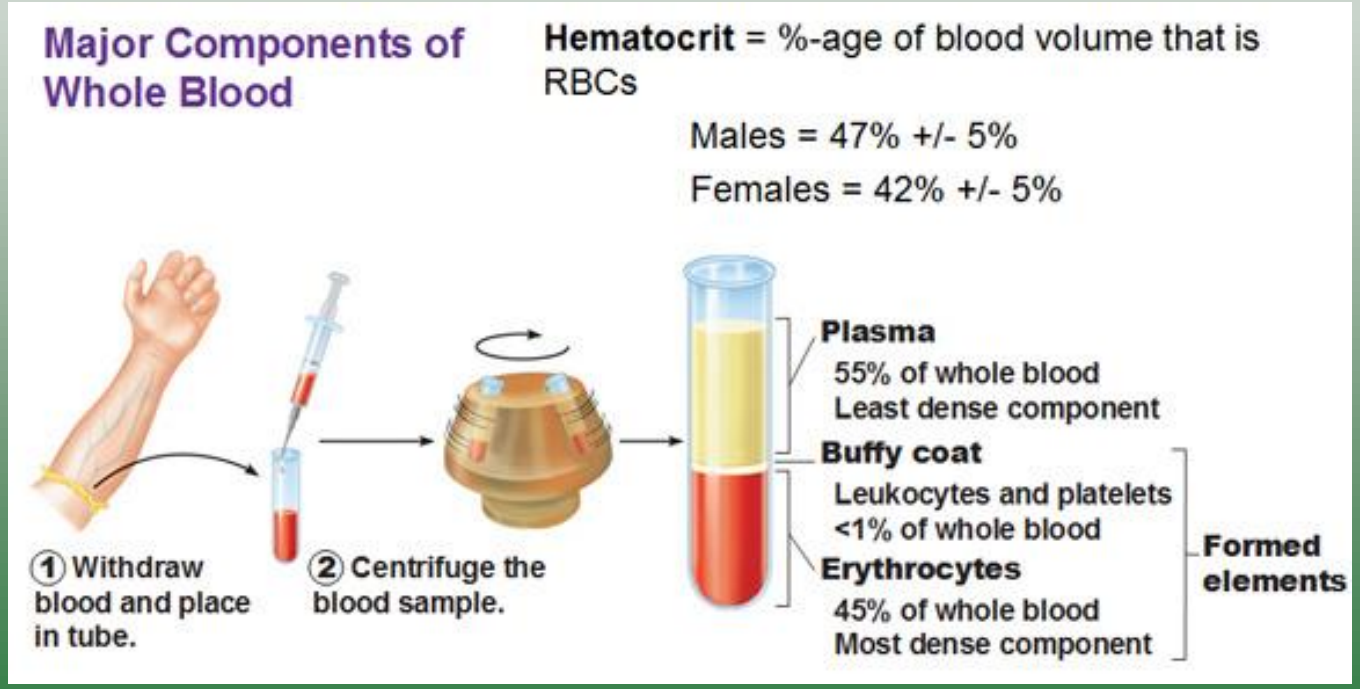
Hematopoietic

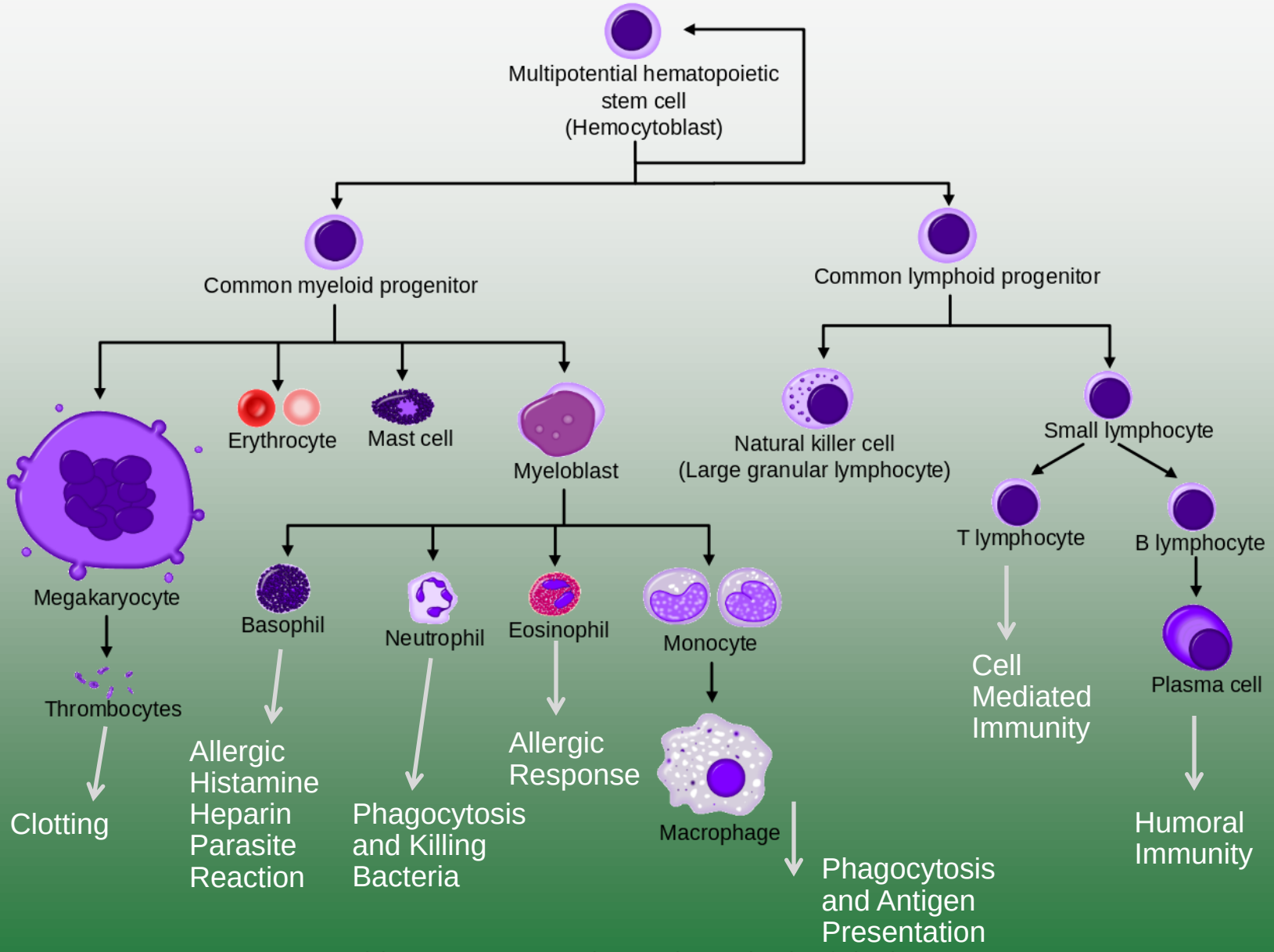
Haematopoiesis

(from Greek αἷμα, "blood" and ποιεῖν "to make)

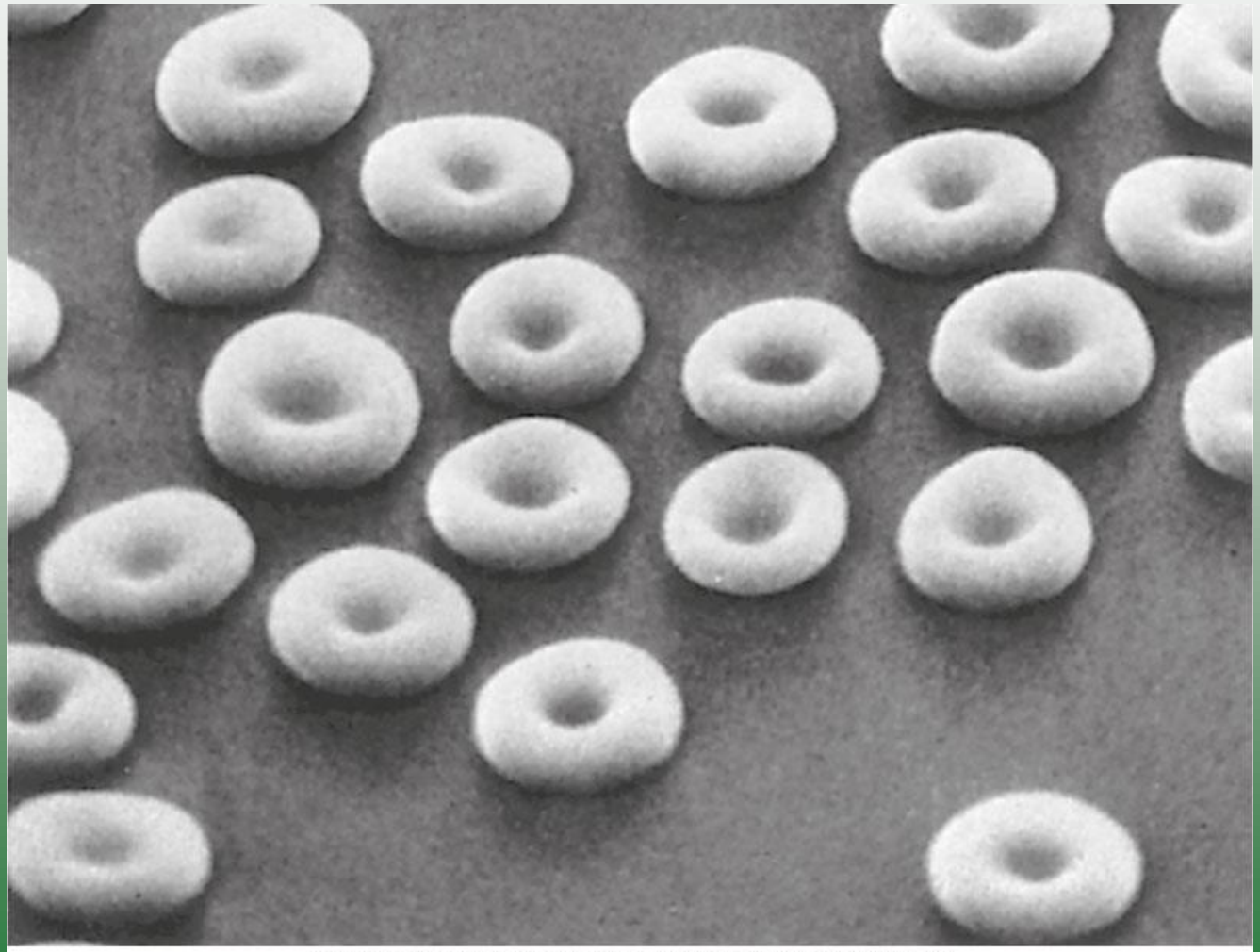
Composition of Blood

- Cellular component
  - Erythrocytes
  - Leukocytes
  - Thrombocytes (platelets)
- Plasma
  - Albumin (oncotic / osmotic pressure)
  - Globulins (immunoglobulins)
  - Fibrinogen (clotting)
  - Biomolecules, nutrients, electrolytes.





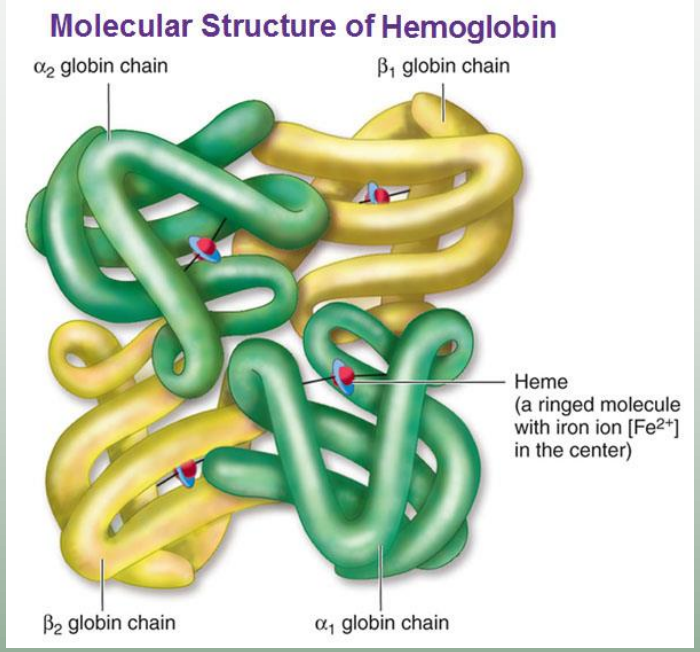
Normal Red Blood Cells

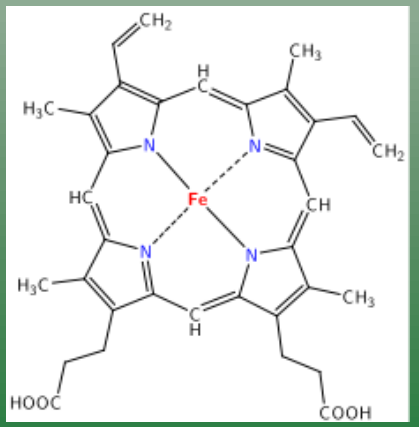


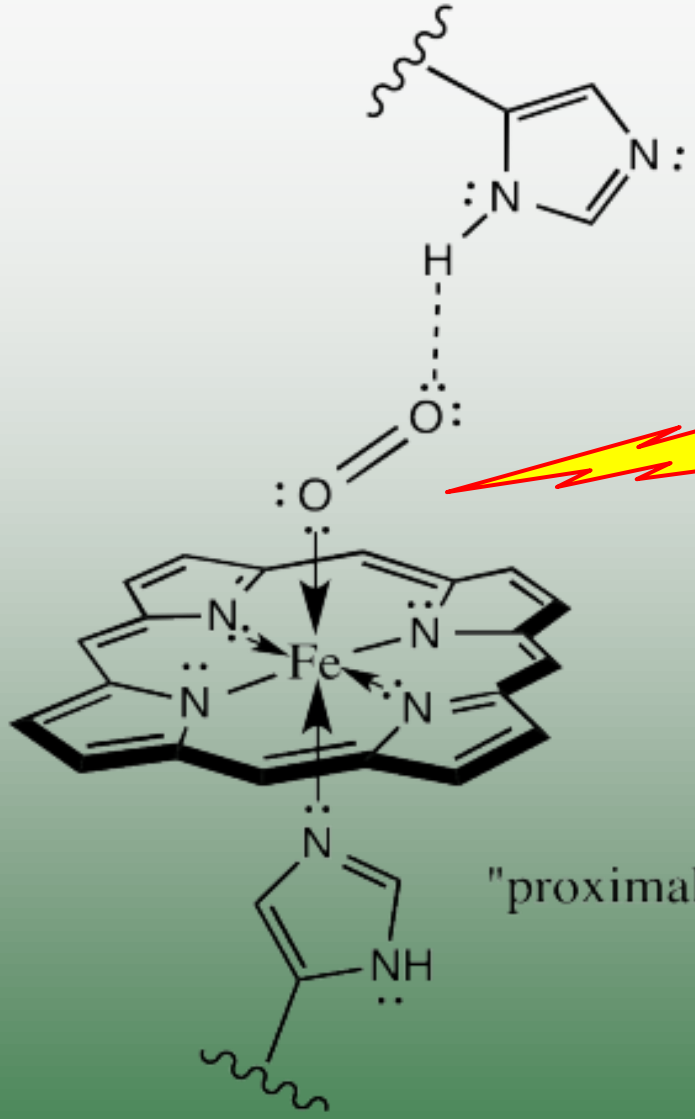
From Rodak BR: Hematology: Clinical Principles and Applications, *ed 2, Philadelphia, 2002, Saunders.*

Erythrocytes (Red Blood Cells)

- Biconcave flexible discs
- No nucleus in mature state
- Contains hemoglobin
  - Globin portion
  - Heme group
- Life span—≈120 days
- Erythropoietin produced in the kidney stimulates erythrocyte production.



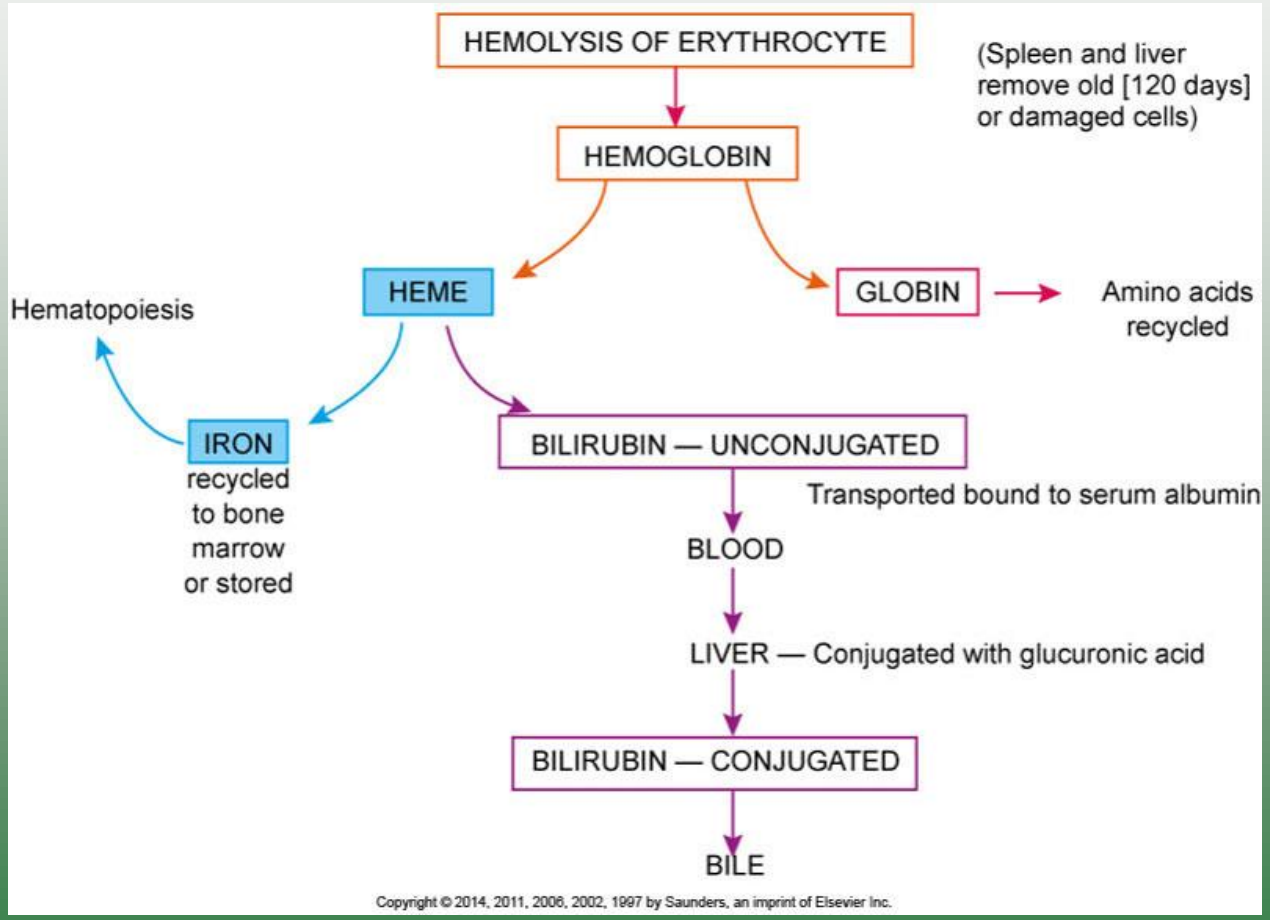


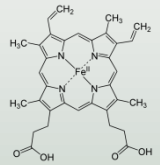


:C≡O:

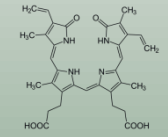
Carbon Monoxide

Breakdown of Hemoglobin

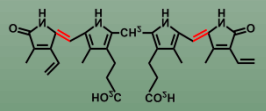




heme



biliverdin



bilirubin

Blood Typing

Blood typing is based on antigens in the plasma membrane of the erythrocytes.

- ABO system
  - Based on the presence or absence of specific antigens
  - Antibodies in the blood plasma
- Rh system
  - Antigen D in plasma membrane: Rh+
  - Absence of antigen D: Rh–

ABO Blood Groups

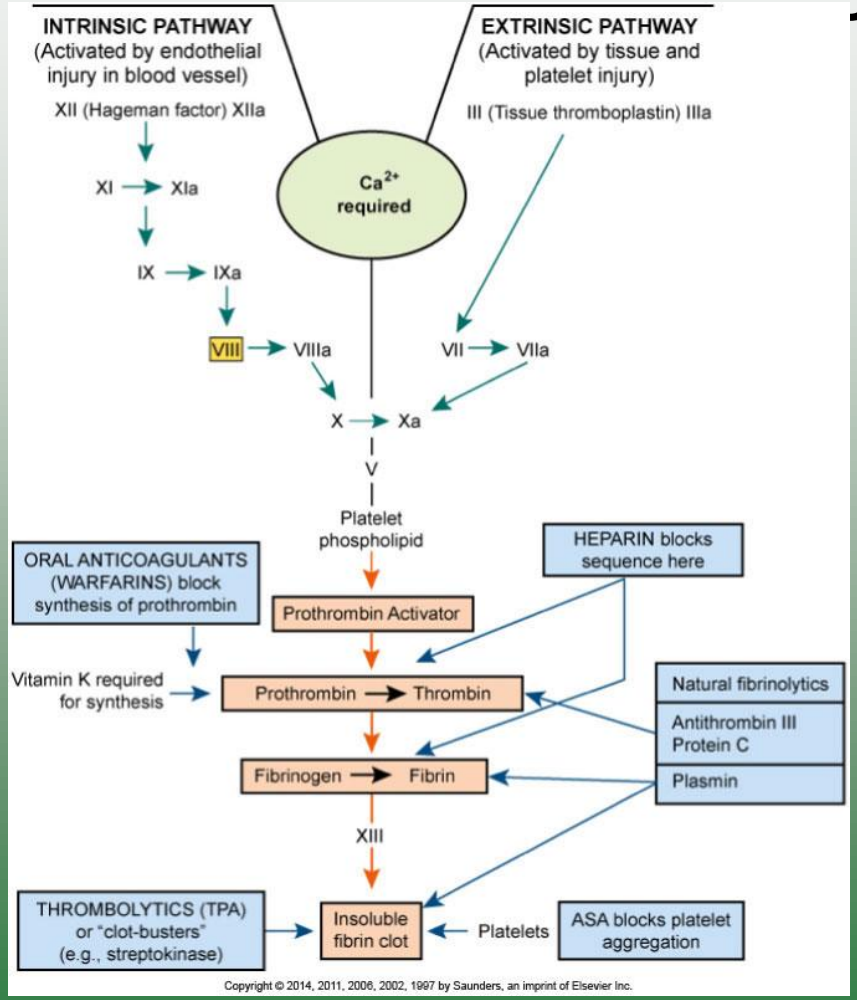
TABLE 10-1 ABO Blood Groups and Transfusion Compatibilities

Blood Group	RBC Antigens	Antibodies in Plasma	For Transfusion, Can Receive Donor Blood Group
O	None	Anti-A and anti-B	O
A	A	Anti-B	O or A
B	B	Anti-A	O or B
AB	A and B	None	O, A, B, or AB

Blood Clotting—Hemostasis

- Three steps:
  - Vasoconstriction or vascular spasm after injury
  - Platelet clot
  - Coagulation mechanism
- Plasmin will eventually break down the blood clot.

Hemostasis and Anticoagulant Drugs



Anticoagulants:

- Inerfere with enzymes in clotting cascade.
- Chelate calcium.
- Inhibit platelet adhesion.

Diagnostic Tests

- Complete blood count (CBC)
  - Includes total red blood cells (RBCs), white blood cells (WBCs), and platelets
  - Leukocytosis (increased WBCs)
    - Associated with inflammation or infection
  - Leukopenia (decreased WBCs)
    - Associated with some viral infections, radiation, chemotherapy
  - Increased eosinophils
    - Common in allergic responses
- Differential count for WBCs

Diagnostic Tests (Cont.)

- Morphology
  - Observed with blood smears
  - Shows size, shape, uniformity, maturity of cells
    - Different types of anemia can be distinguished.
- Hematocrit
  - Percent by volume of cellular elements in blood
- Hemoglobin
  - Amount of hemoglobin per unit volume of blood
  - Mean corpuscular volume (MCV)
    - Indicates the oxygen-carrying capacity of blood

Diagnostic Tests (Cont.)

- Reticulocyte (immature RBC) count
  - Assessment of bone marrow function
- Chemical analysis
  - Determines serum levels of components, such as iron, vitamin B_{12}, folic acid, cholesterol, urea, glucose
- Bleeding time
  - Measures platelet function
- Prothrombin time (PT) and partial thromboplastin time (PTT)
  - Measure function of various factors in coagulation process
  - International normalized ratio (INR) is a standardized version.

Blood Therapies

- Whole blood, packed red blood cells, packed platelets
  - For severe anemia or thrombocytopenia
- Plasma or colloid volume-expanding solutions
  - To maintain blood volume
- Artificial blood products
  - Compatible with all blood types
  - None of them can perform all the complex functions of normal whole blood.

Blood Therapies (Cont.)

- Epoetin alfa
  - Artificial form of erythropoietin
    - Before certain surgical procedures
    - Anemia related to cancer
    - Chronic renal failure
- Bone marrow or stem cell transplantation
  - Close tissue match necessary
    - Treatment of some cancers
    - Severe immunodeficiency
    - Severe blood cell diseases
- Drug treatment
  - Aids in the clotting process

Blood Dyscrasias

Ancient Use

"bad mixture"

blood, black bile, yellow bile, water

Modern Use

abnormal state

The Anemias

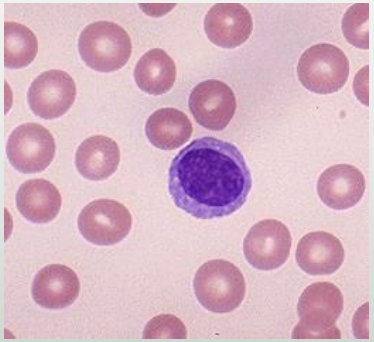
- Anemia (rbc too few or too small) causes a reduction in oxygen transport.
- Basic problem is hemoglobin deficit
- Oxygen deficit leads to:
  - Less energy production in all cells
    - Cell metabolism and reproduction diminished
  - Compensation mechanisms
    - Tachycardia and peripheral vasoconstriction
  - General signs of anemia
    - **Fatigue, pallor (pale face), dyspnea, tachycardia**

The Anemias (Cont.)

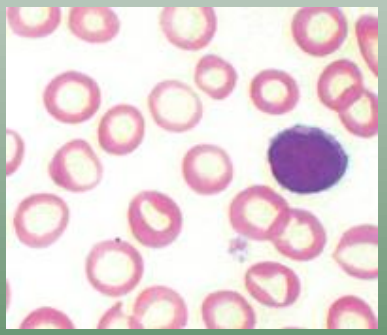
- Oxygen deficit leads to:
  - Decreased regeneration of epithelial cells
    - Digestive tract becomes inflamed and ulcerated, leading to stomatitis
    - Inflamed and cracked lips
    - Dysphasia
    - Hair and skin may show degenerative changes.
  - Severe anemia may lead to angina or congestive heart failure (CHF).

Iron Deficiency Anemia

- Insufficient iron impairs hemoglobin synthesis.
  - Microcytic, hypochromic RBCs
    - Result of low hemoglobin concentration in cells
- Very common
  - Ranges from mild to severe
  - Occurs in all age groups, but more common in women of childbearing age
  - Estimated that one in five women is affected
    - Proportion increases for pregnant women
- Frequently sign of an underlying problem



Normal



Microcytic
Hypochromic

Iron Deficiency Anemia: Causes

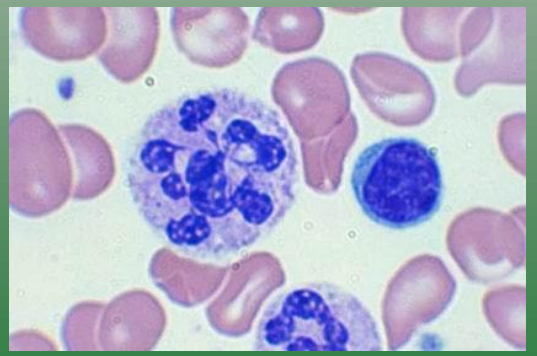
- Dietary intake of iron below minimum requirement
- Chronic blood loss
  - As from bleeding, ulcer, hemorrhoids, cancer
- Impaired duodenal absorption of iron
  - In many disorders, malabsorption syndromes
- Severe liver disease
  - May affect iron absorption as well as storage

Iron Deficiency Anemia: Signs and Symptoms

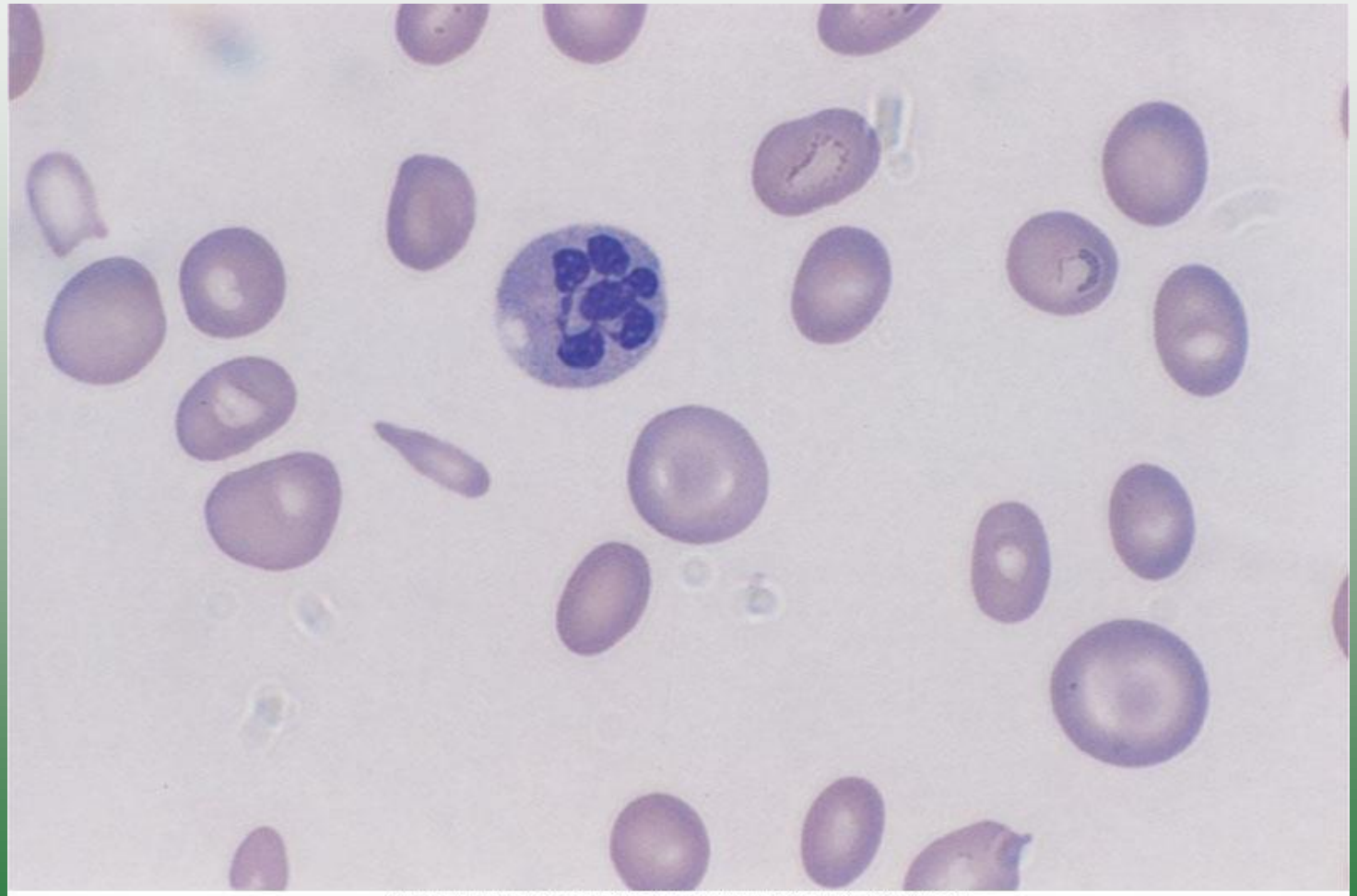
- Pallor of skin and mucous membranes
- Fatigue, lethargy, cold intolerance
- Irritability
- Degenerative changes
- Stomatitis and glossitis
- Menstrual irregularities
- Delayed healing
- Tachycardia, heart palpitations, dyspnea, syncope

Pernicious Anemia: Vitamin B_{12} Deficiency

- Basic problem is lack of absorption of vitamin B_{12} because of lack of intrinsic factor
  - Intrinsic factor secreted by gastric mucosa
  - Required for intestinal absorption of vitamin B_{12}
- Characterized by very large, immature, erythrocytes and hyperlobated neutrophils.
  - Carry less hemoglobin
  - Shorter life span



Vitamin B_{12} Deficiency



From Stevens ML: Fundamentals of Clinical Hematology, *Philadelphia, 1997, Saunders.*

Pernicious Anemia: Vitamin B_{12} Deficiency

- Dietary insufficiency is very rarely a cause.
- Genetic factors have been implicated.
  - More common in light-skinned women of northern European ancestry
- Often accompanies chronic gastritis
- May also be an outcome of gastric surgery

Vitamin B_{12} and Nerve Cells

- Vitamin B_{12} is needed for the function and maintenance of neurons.
- Significant deficit of the vitamin will cause symptoms in the peripheral nerves.
- These may be reversible.

Pernicious Anemia: Vitamin B_{12} Deficiency (Cont.)

- Manifestations in addition to those typical for anemias
  - Tongue is typically enlarged, red, sore, and shiny.
  - Digestive discomfort, often with nausea and diarrhea
  - Feeling of pins and needles, tingling in limbs
- Diagnostic tests {CBC – macrocytic}
  - Microscopic examination (erythrocytes)
  - Bone marrow examination (hyperactive)
  - Vitamin B_{12} serum levels below normal
  - Presence of hypochlorhydria or achlorhydria (decreased or absent acid in stomach) due to gastric atrophy.

Aplastic Anemia

- Impairment or failure of bone marrow
- May be temporary or permanent
- Often idiopathic but possible causes include:
  - Myelotoxins
    - Radiation, industrial chemicals, drugs
  - Viruses
    - Particularly hepatitis C
  - Genetic abnormalities
    - Myelodysplastic syndrome
    - Fanconi's anemia

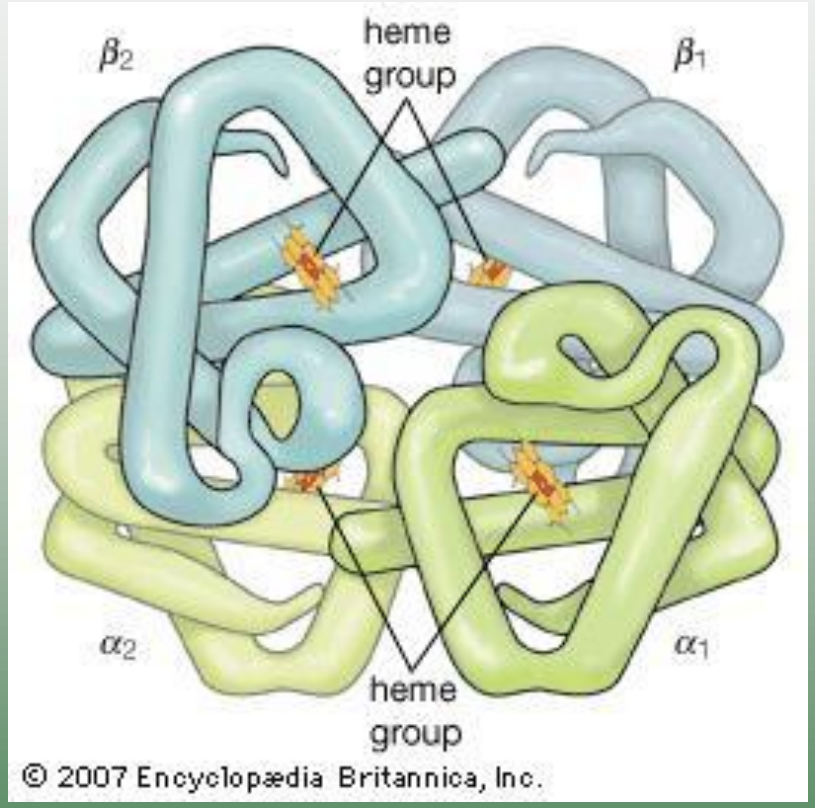
Aplastic Anemia (Cont.)

- Blood counts indicate pancytopenia.
  - Anemia, leukopenia, thrombocytopenia
  - Bone marrow biopsy may be required.
  - Erythrocytes often appear normal.
- Identification of cause and prompt treatment needed for bone marrow recovery
  - Removal of any bone marrow suppressants
  - Failure to identify cause and treat effectively is **life-threatening!**

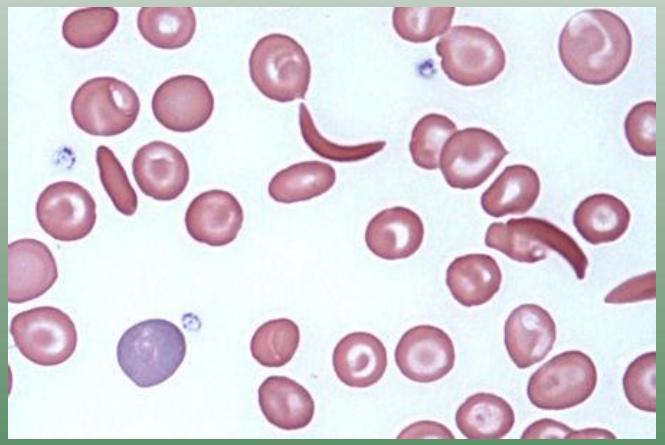
Hemolytic Anemia

- Results from excessive destruction of RBCs
- Causes
  - Genetic defects
  - Immune reactions
  - Changes in blood chemistry
  - Infections such as malaria
  - Toxins in the blood
  - Antigen-antibody reactions
    - Incompatible blood transfusion
    - Erythroblastosis fetalis

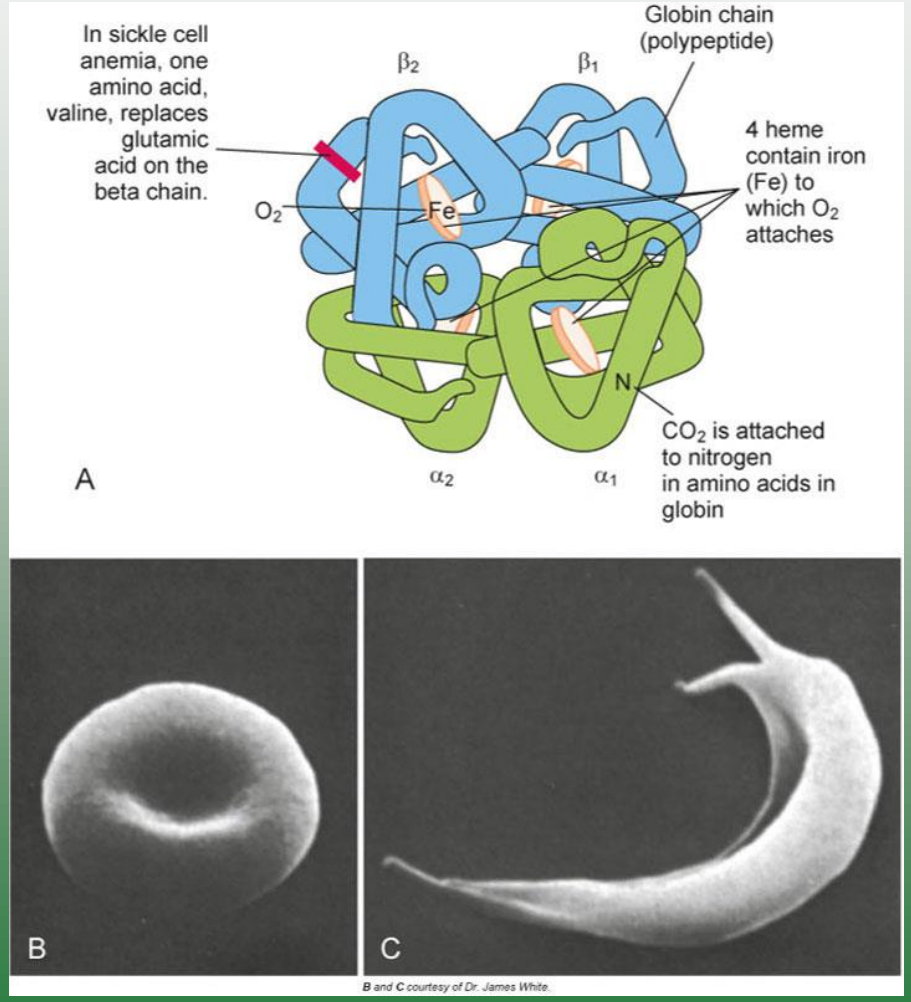
Sickle Cell Anemia



Single amino acid substitution in beta chain.



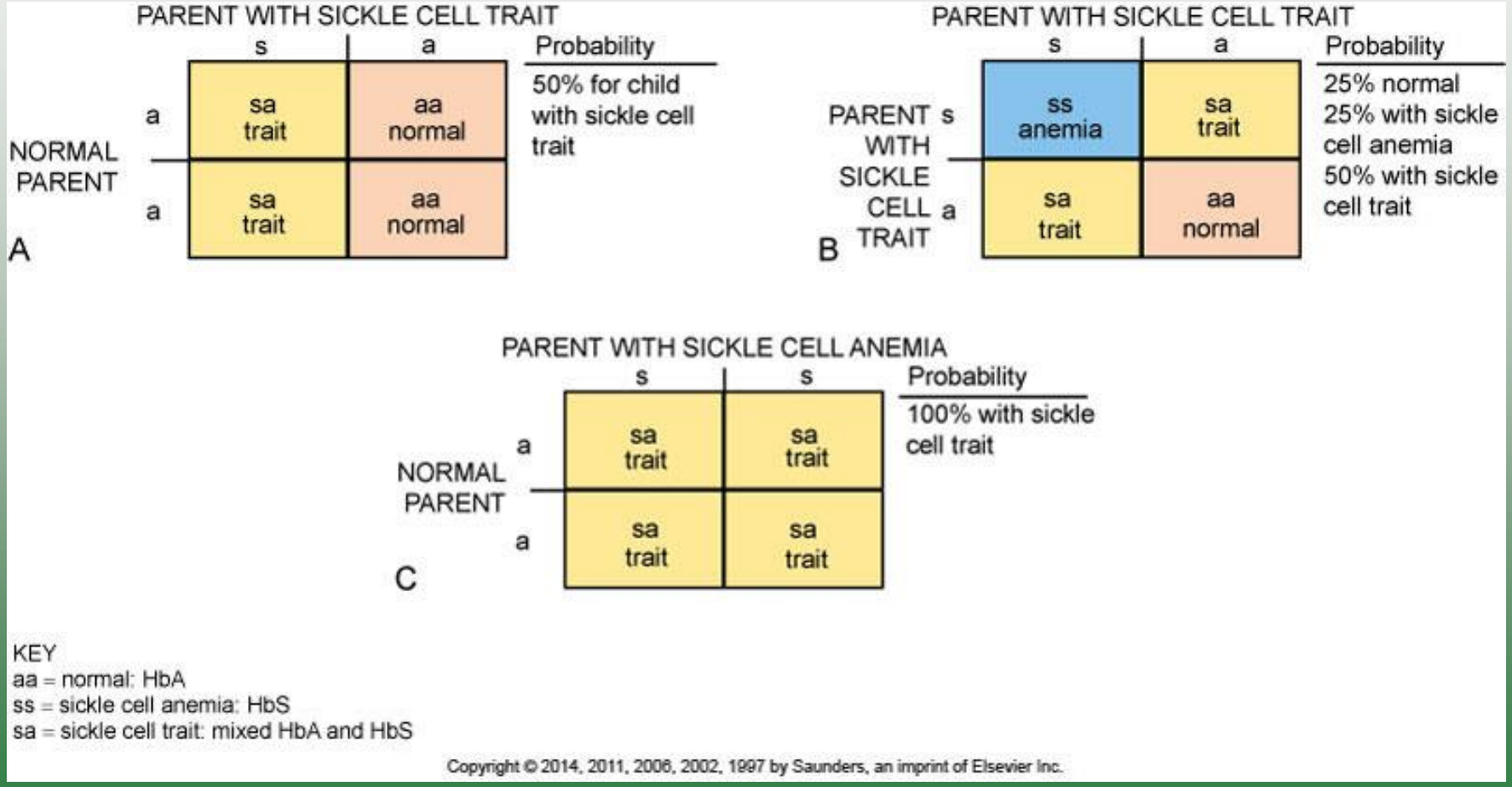
Sickle Cell Anemia (Cont.)



Sickle Cell Anemia

- Genetic condition
  - Autosomal
  - Incomplete dominance
  - Anemia occurs in homozygous recessive.
  - Diagnostic testing is available.
  - More common in individuals of African ancestry
    - Heterozygous condition is somewhat protective against malaria.
    - One in ten African Americans is heterozygous for the trait.

Sickle Cell Anemia (Cont.)



Sickle Cell Anemia (Cont.)

- Abnormal hemoglobin (HbS)
- Sickle cell crisis occurs whenever oxygen levels are lowered.
- Altered hemoglobin is unstable and changes shape in hypoxemia.
- Sickle-shaped cells are too large to pass through the microcirculation.
- Obstruction leads to multiple infarctions and areas of necrosis.

Sickle Cell Anemia (Cont.)

- Multiple infarctions affect brain, bones, organs
- In addition to basic anemia:
  - Hyperbilirubinemia, jaundice, gallstones
    - Caused by high rate of hemolysis
- Clinical signs
  - Do not usually appear until the child is about 12 months old

Sickle Cell Anemia: Signs and Symptoms

- Severe pain because of ischemia of tissues and infarction
- Pallor, weakness, tachycardia, dyspnea
- Hyperbilirubinemia—jaundice
- Splenomegaly
- Vascular occlusions and infarctions
  - In lungs
    - Acute chest syndrome
  - Smaller blood vessels
    - Hand-foot syndrome
- Delay of growth and development
- Congestive heart failure

Sickle Cell Anemia (Cont.)

- Diagnostic tests
  - Blood test
    - Hemoglobin electrophoresis
  - Prenatal DNA analysis
- Treatment
  - Hydroxyurea has reduced the frequency of this crisis.
  - Dietary supplementation with folic acid
  - Bone marrow transplantation
  - Immunization in children
    - Against pneumonia, influenza, meningitis

Polycythemia

- Primary polycythemia—polycythemia vera
  - Increased production of erythrocytes and other cells in the bone marrow
  - Neoplastic disorder
  - Serum erythropoietin levels are low.
- Secondary polycythemia—erythrocytosis
  - Increase in RBCs in response to prolonged hypoxia
  - Increased erythropoietin secretion
  - Compensation mechanism to provide increased oxygen transport

Polycythemia: Signs and Symptoms

- Distended blood vessels, sluggish blood flow
- Increased blood pressure
- Hypertrophied heart
- Hepatomegaly
- Splenomegaly
- Dyspnea
- Headaches
- Visual disturbances
- Thromboses and infarctions

Polycythemia (Cont.)

- Diagnostic tests
  - Increased cell counts
  - Increased hemoglobin and hematocrit values
  - Hypercellular bone marrow
  - Hyperuricemia
- Treatment
  - Identify cause
  - Drugs or radiation
    - Suppression of bone marrow activity
  - Periodic phlebotomy

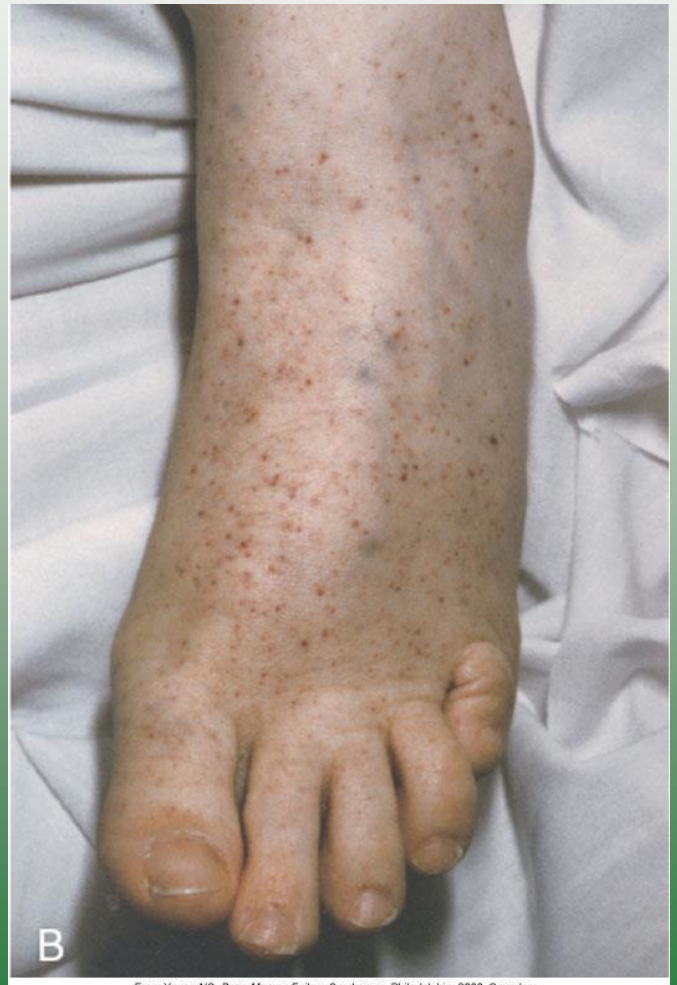
Indications of Blood-Clotting Disorders

- Persistent bleeding from gums
- Repeated epistaxis (nose bleed).
- Petechiae
  - Pinpoint, flat, red spots on skin and mucous membrane
- Frequent purpura and ecchymosis (bruising).
- More than normal bleeding in trauma
- Bleeding into joint—hemarthroses
  - Swollen, red, painful
- Hemoptysis

Blood-Clotting Disorders

- Hematemesis
  - Coarse brown particles (coffee ground emesis)
- Blood in feces
  - Black or occult (melena)
- Anemia
- Feeling faint and anxious
- Low blood pressure
- Rapid pulse

Petechiae



From Young NS: *Bone Marrow Failure Syndromes*, Philadelphia, 2000, Saunders.

Hemophilia A

- Classic hemophilia
  - Deficit or abnormality of factor VIII
- Most common inherited clotting disorder
  - X-linked recessive trait
  - Manifested in men, carried by women
- Varying degrees of severity
- Prolonged bleeding after minor tissue trauma
- Spontaneous bleeding into joints
- Possible hematuria or blood in feces

Hemophilia A (Cont.)

- Diagnostic tests
  - Bleeding time and PT normal
  - PTT, activated PTT (aPTT), coagulation time prolonged
  - Serum levels of factor VIII are low.
- Treatment
  - Desmopressin (DDAVP)
  - Replacement therapy for factor VIII

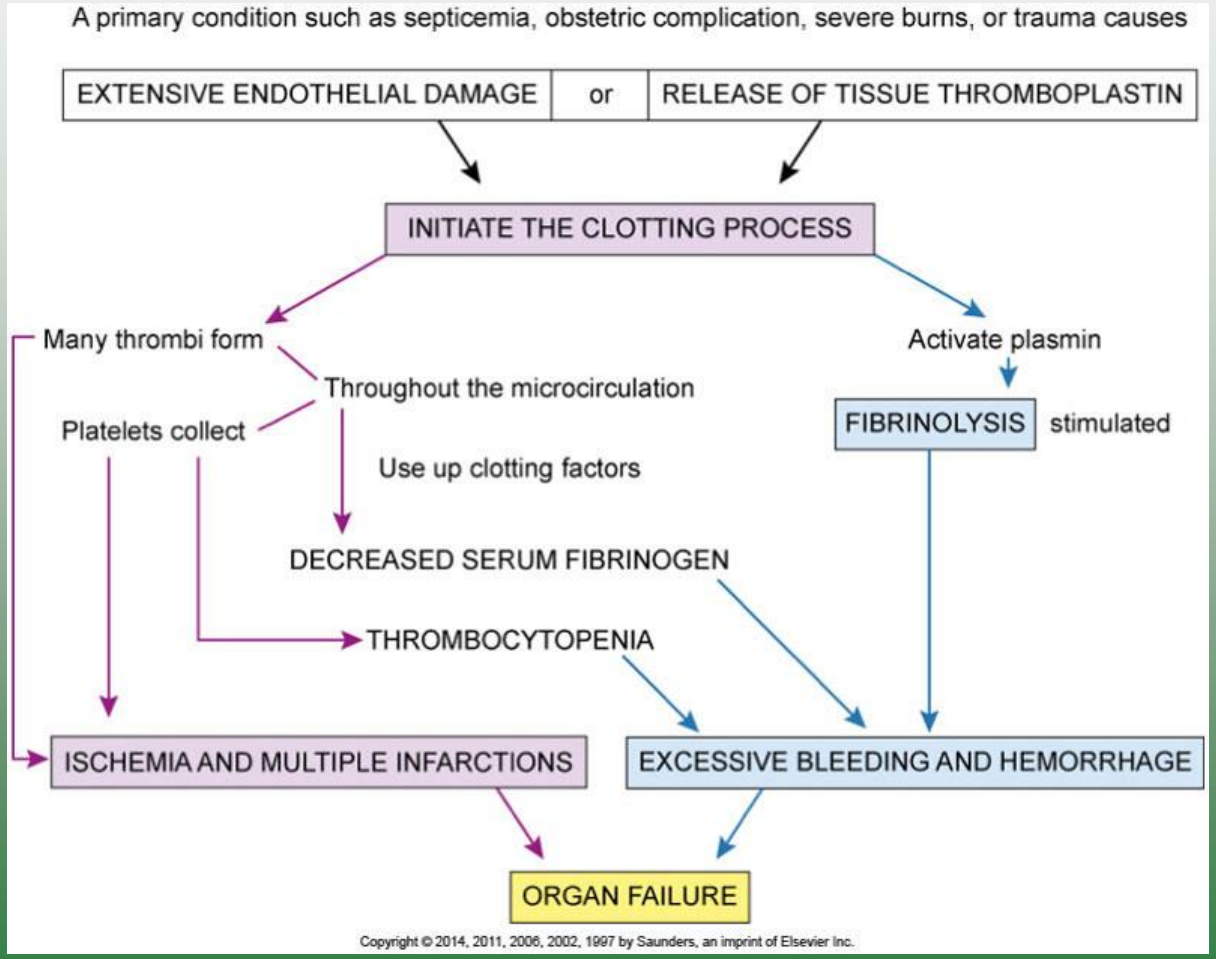
Von Willebrand's Disease

- Most common hereditary clotting disorder
- Three major types
- Signs and symptoms include:
  - Skin rashes
  - Frequent nosebleeds
  - Easy bruising
  - Bleeding of gums
  - Abnormal menstrual bleeding
- Treatment based on type and severity

Disseminated Intravascular Coagulation (DIC, consumpive coagulopathy)

- Involves both excessive bleeding and clotting
- Excessive clotting in circulation
  - Thrombi and infarcts occur.
- Clotting factors are reduced to a dangerous level.
- Widespread, uncontrollable hemorrhage results.
- Very poor prognosis, with high fatality rate
- Complication of many primary problems
  - Obstetrical complications, such as abruptio placentae
  - Infections
  - Carcinomas
  - Major trauma

Disseminated Intravascular Coagulation (Cont.)



Big thrombogenic stimulus.

↓

Wide spread clotting (thrombi).

↓

Small vessel occlusion

↓

Infarcts

↓

Organ Failure

Thrombophilia

"prone to clotting"

- Group of inherited or acquired disorders
- Risk of abnormal clots in veins or arteries
- Blood testing for clotting factor levels and abnormal antibody levels
- Causative condition should be treated.

Myelodysplastic Syndromes

- Diseases that involve inadequate production of cells by the bone marrow
- Signs and symptoms include anemia; dependent on type of deficiencies that occur
- May be idiopathic or occur after chemotherapy or radiation treatment
- Treatment measures depend on deficiency type.
  - Transfusion replacement
  - Chelation therapy to reduce iron overload
  - Bone marrow transplantation

The Leukemias

- Group of neoplastic disorders involving white blood cells
- Uncontrolled WBC production in bone or lymph nodes
- Other hemopoietic tissues are reduced.
- One or more types of leukocytes are undifferentiated, immature, and nonfunctional.
- Large numbers released into general circulation
- Infiltrate lymph nodes, spleen, liver, brain, other organs

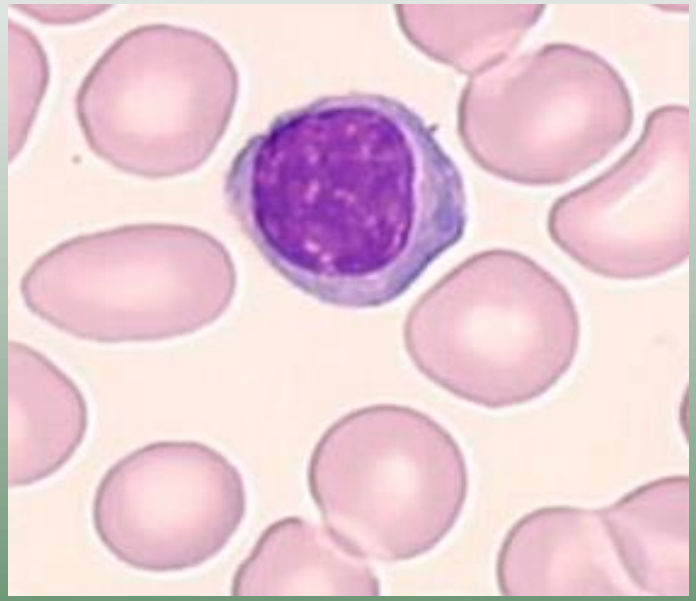
TABLE 10-3 Types of Leukemias

Type	Malignant Cell	Primary Age Group
Acute lymphocytic leukemia (ALL)	B-lymphocytes	Young children
Acute myelogenous (or myelocytic) leukemia (AML)	Granulocytic stem cells	Adults
Chronic lymphocytic leukemia	B-lymphocytes	Adults greater than 50 years
Chronic myelogenous leukemia (CML)	Granulocytic stem cells	Adults 30-50
Acute monocytic leukemia	Monocytes	Adults
Hairy cell leukemia	B-lymphocytes	Males greater than 50 years

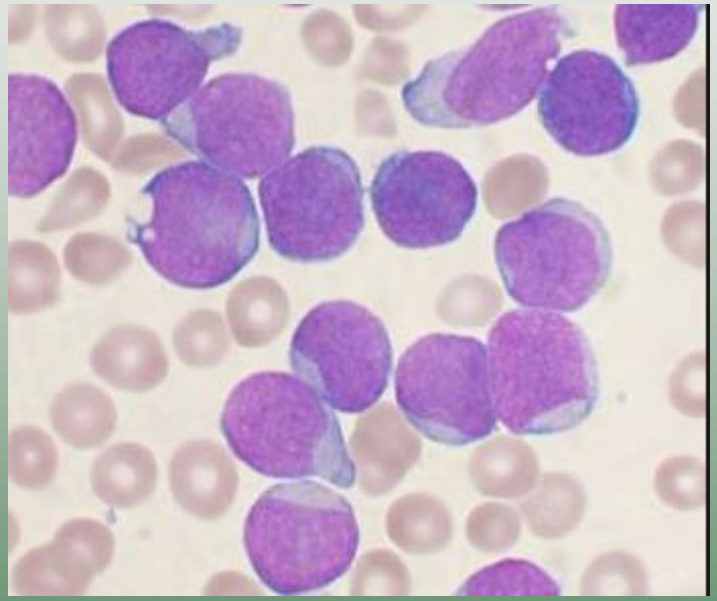
The Leukemias (Cont.)

- Acute leukemias (ALL and AML)
  - High proportion of immature nonfunctional cells in bone marrow and peripheral circulation
  - Onset usually abrupt , marked signs of complications
    - Occurs primarily in children and younger adults
- Chronic leukemias (CLL and CML)
  - Higher proportion of mature cells
  - Insidious onset
  - Mild signs and better prognosis
    - Common in older adults

Acute Leukemia



Normal lymphocyte



Leukemic Blasts

Signs and Symptoms of Acute Leukemia

- Usual signs at onset (from bone marrow supression)
  - Frequent or uncontrolled infections
  - Petechiae and purpura
  - Signs of anemia
- Severe and steady bone pain
- Weight loss, fatigue, possible fever
- Enlarged lymph nodes, spleen, liver
- Headache, visual disturbances, drowsiness, vomiting

The Leukemias (Cont.)

- Diagnostic tests
  - Peripheral blood smears
    - Immature leukocytes and altered numbers of WBCs
    - Numbers of RBCs and platelets decreased
    - Bone marrow biopsy for confirmation
- Treatment
  - Chemotherapy
  - ALL in young children responds well to drugs
  - Biological therapy (interferon)
    - May be used to stimulate the immune system

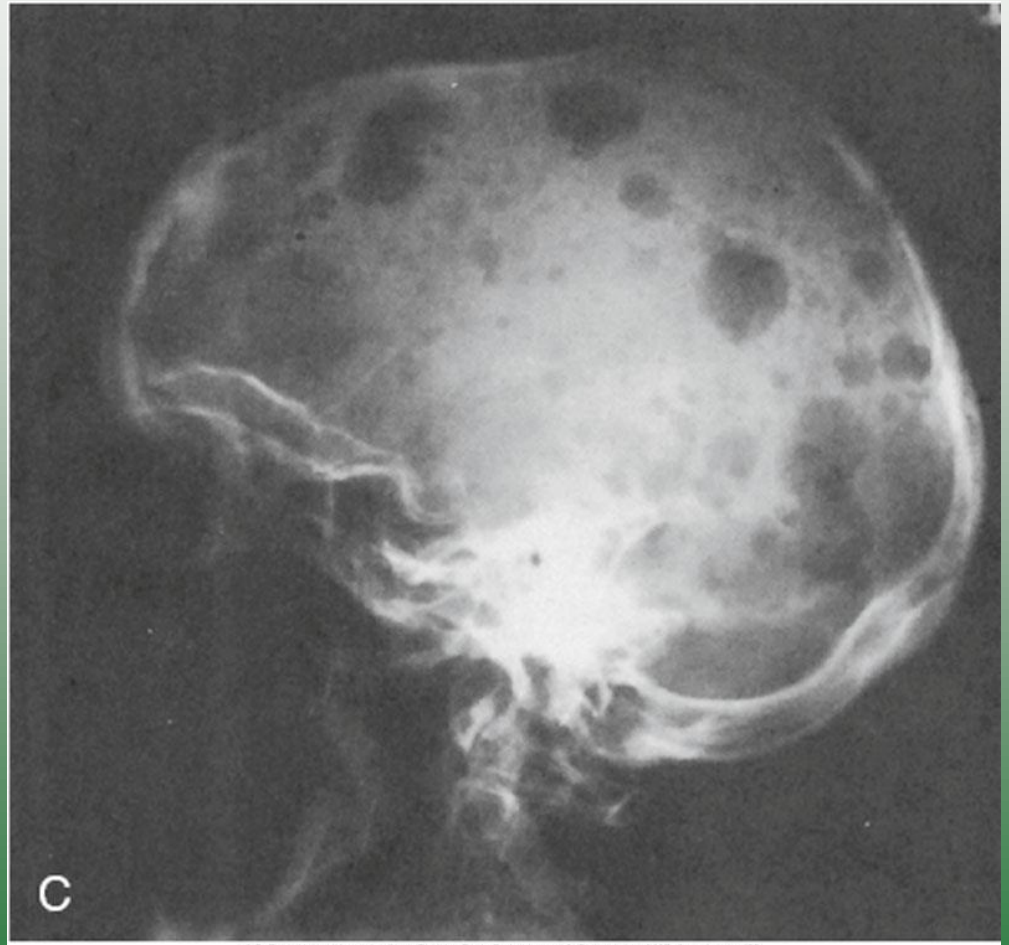
Complications of Leukemia

- Opportunistic infections, including pneumonia
- Sepsis
- Congestive heart failure
- Hemorrhage
- Liver failure
- Renal failure
- CNS depression and coma

Multiple Myeloma

- Neoplastic disease that involves increased production of plasma cells in bone marrow
- Unknown cause
- Occurs in older adults
- Production of other blood cells is impaired
- Multiple tumors in bone
  - Loss of bone
  - Severe bone pain
- Prognosis poor, with short life expectancy

Multiple Myeloma of the Skull



A,B. From Kumar V, et al, editors: Robbins Basic Pathology, ed 8, Philadelphia, 2007, Saunders, p 455.
C. Courtesy Marvin J. Stone, MD, Sammons Cancer Center, Baylor University Medical Center, Dallas. From Copstead LE, Banasik J: *Pathophysiology*, ed 5, St. Louis, 2013, Mosby.