Chapter 15

Topics

- Defense Mechanisms
- Systems
- Non-specific immunity

Defense Mechanisms

- Inate and nonspecific
  - Firstline of defense
  - Secondline of defense
- Acquired and specific
  - Thirdline of defense

Summary of the major components of the host defenses.

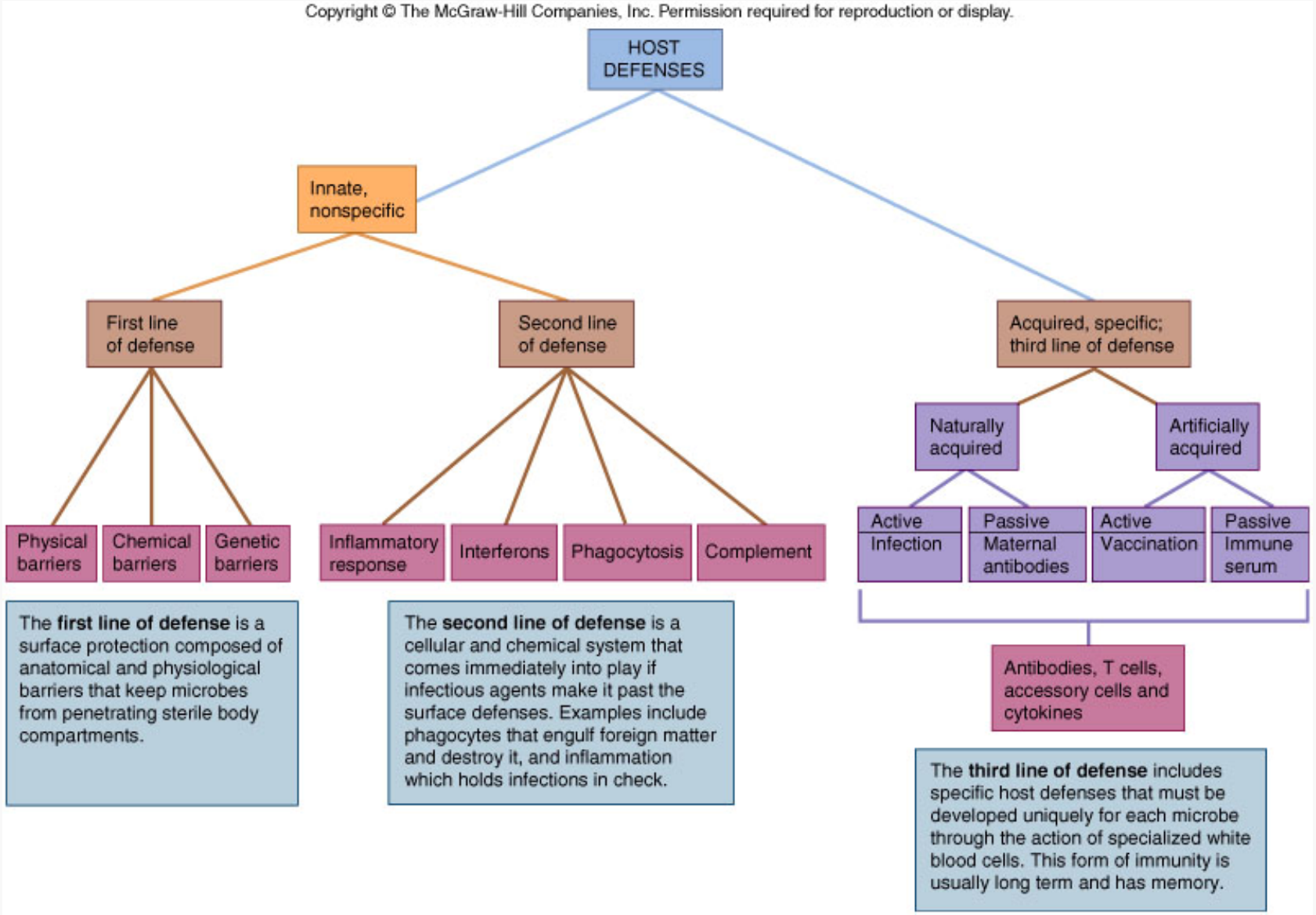


Fig. 14.1 Flowchart summarizing the major components of the host defenses.

Firstline of defense

- Barriers
  - Anatomical
  - Chemical
  - Genetic

Anatomical barriers

- Skin
  - Outermost layer
  - Hair follicles
  - Skin glands
- Mucous membrane
  - Digestive
  - Urinary
  - Respiratory
  - Eye

The trachea contain cilia that entrap and propel particles out of the respiratory tract.

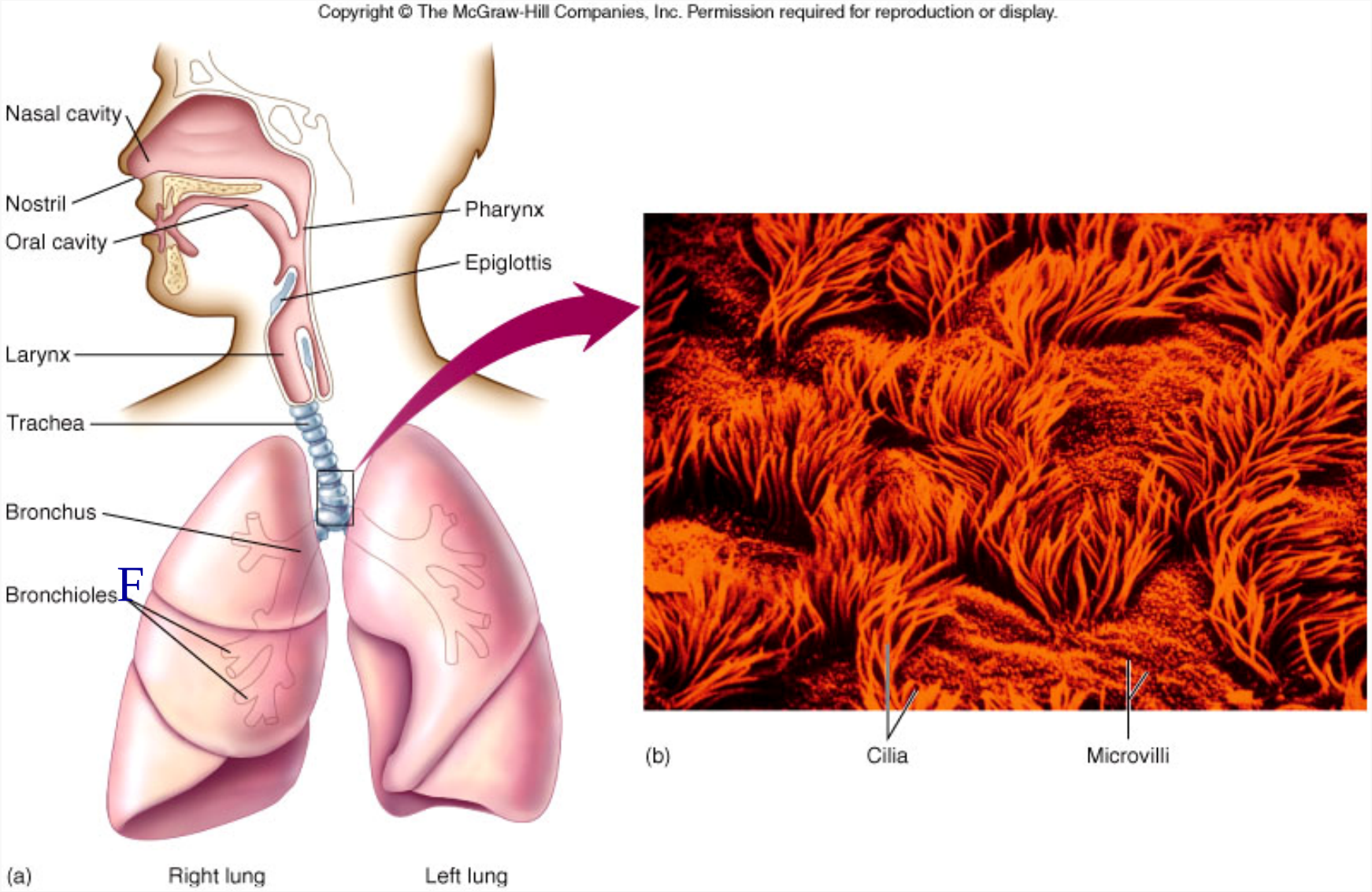


Fig. 14.3 The ciliary defense of the respiratory tree.

Chemical barriers

- Sebaceous secretions
- Eyelid glands – meibomian gland
- Tears and saliva – lysozyme
- Acidic pH
  - Sweat
  - Stomach
  - Skin
  - Semen
  - Vagina

Representation of the primary anatomical and chemical defense barriers.

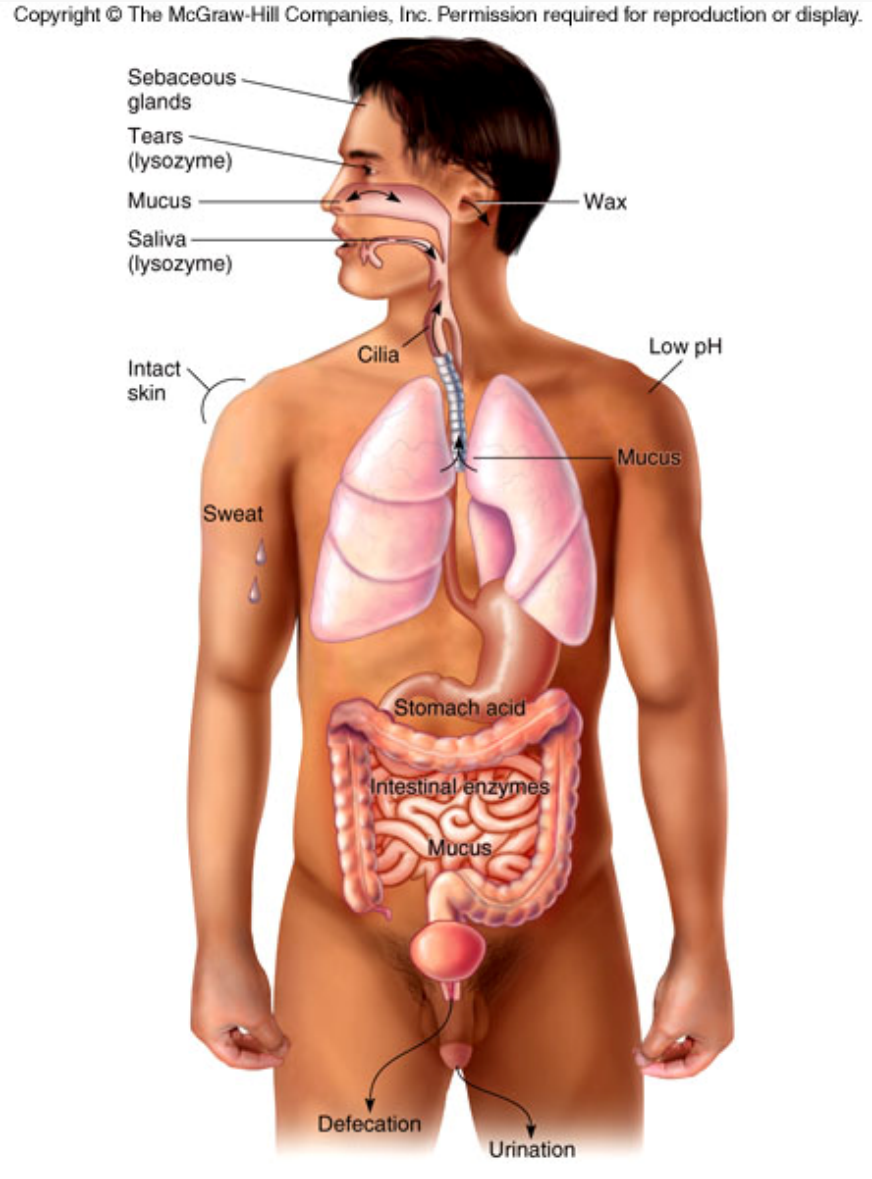


Fig. 14.2 The primary physical and chemical defense barriers.

Genetic barriers

- Different level of sensitivity and resistance to infectious agents
  - Malaria
  - Tuberculosis
  - Leprosy
  - Fungal infections

Secondline and Thirdline of defense

- Defines immunology
- Protective cells

Immunology

- Study of the development of resistance to infectious agents by the body
  - Surveillance of the body
  - Recognition of foreign material
  - Destruction of foreign material or agent
- Involve nonspecific and specific immune defense systems
- White blood cells (wbc) or leukocytes are involved

WBC

- WBC recognize self markers on the host cell
  - Do not attack or do not respond to host cell
- WBC recognize nonself markers on the invading microbe
  - Attack or respond to microbe

WBC do not destroy self cells, while nonself cells are recognized and destroyed.

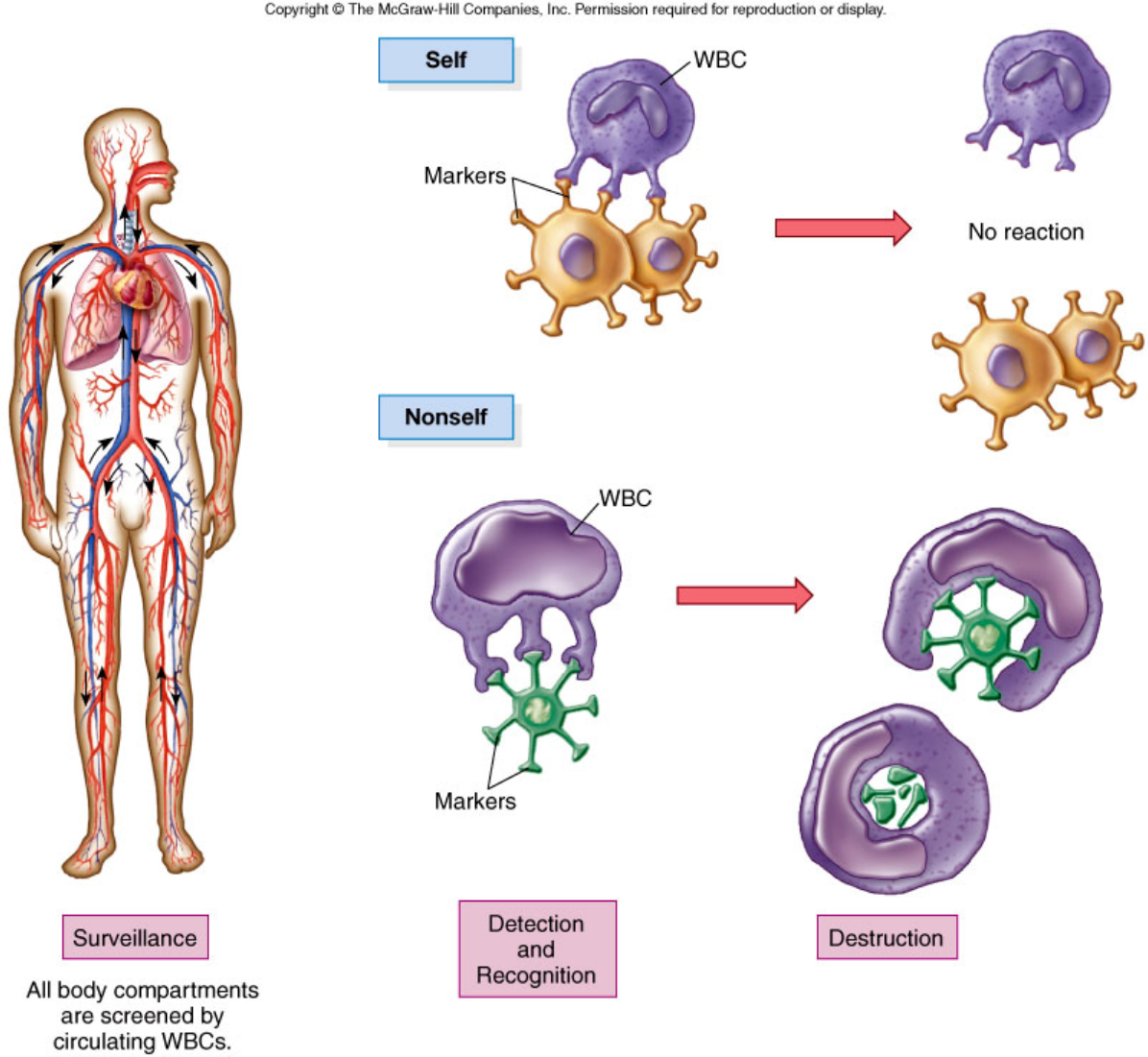


Fig. 14.4 Search, recognize,and destroy is the mandate of the immune system.

Systems

- All systems are integrated
  - Recticuloendothelial system (RES)
  - Extracellular fluids system (ECF)
  - Blood or circulatory
  - Lymphatic

The integration of the systems enable the recognition and destruction of foreign particles in the human body.

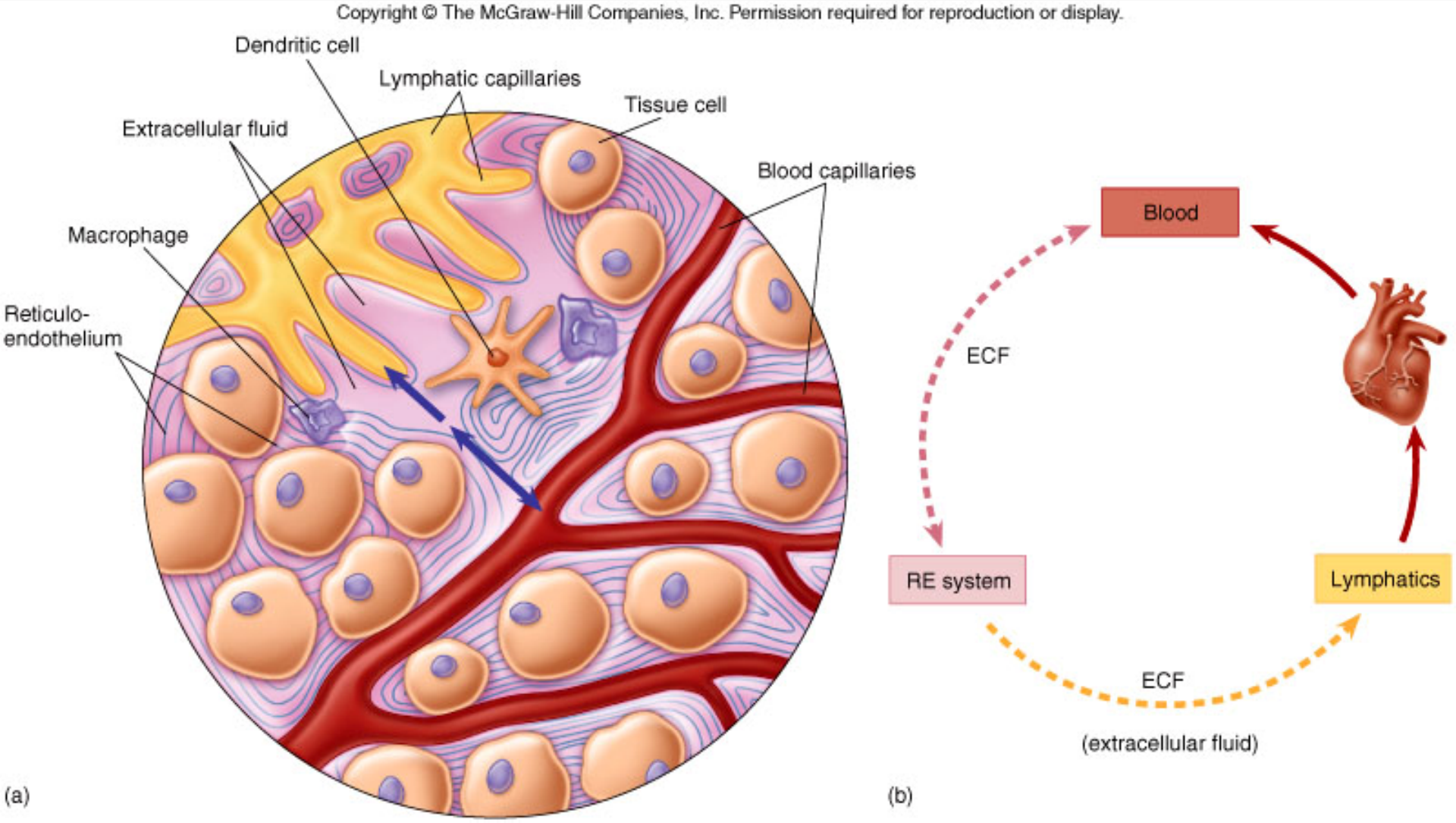


Fig. 14.5 Connection between the body compartments.

Reticuloendothelial (RES)

- Network of connective tissue fibers (Reticulum)
- Interconnects cells
- Allows immune cells to bind and move outside the blood and lymphatic system

Extracellular fluid (ECF)

- The spaces surrounding tissue cells and RES
- Enable immune cells to move

Representation of the RES and the ECF, which surrounds the cells.

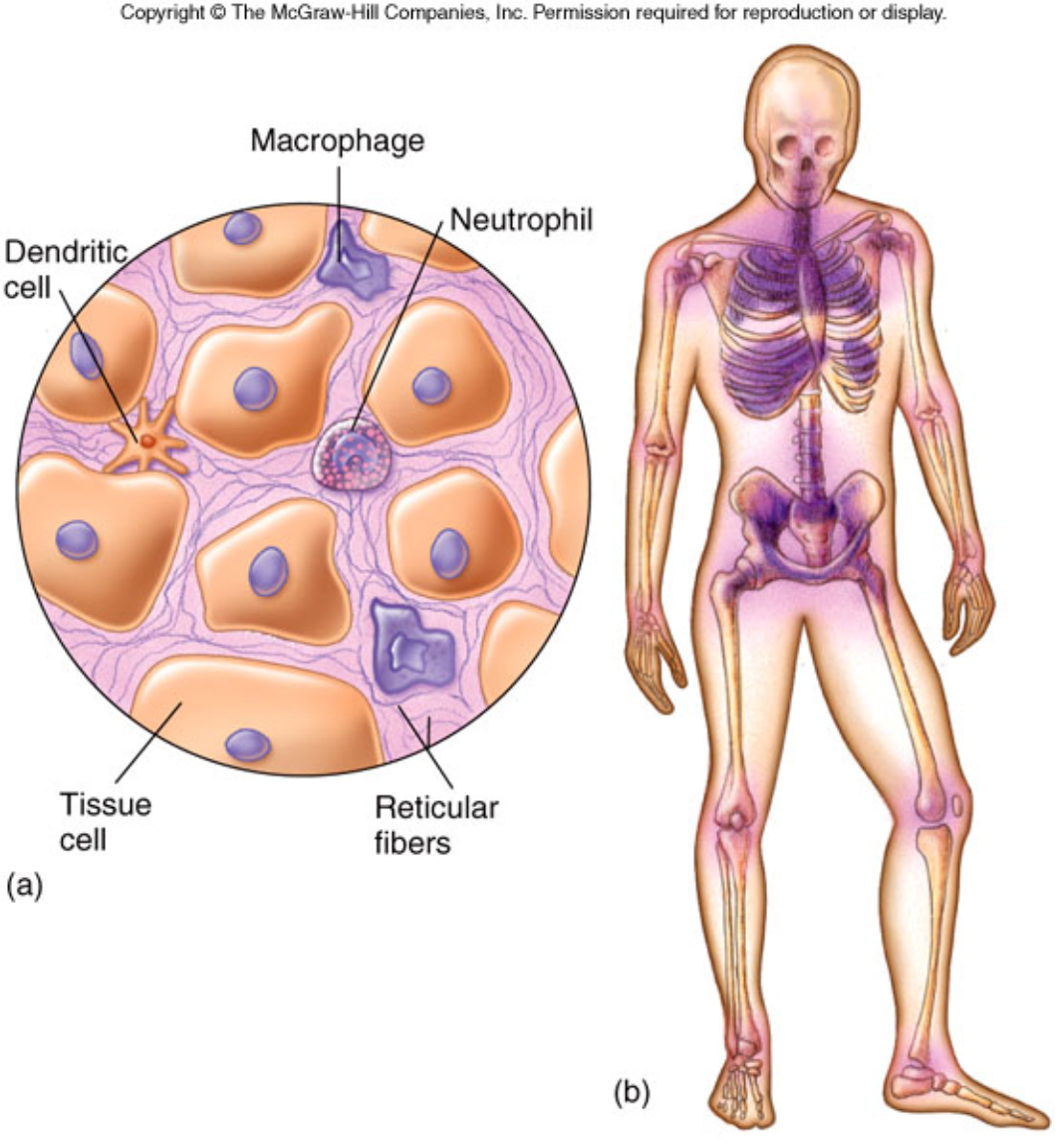


Fig. 14.6 The reticuloendothelial system

Blood

- Stem cells precursors
- Hemopoiesis
- Components

Stem cells

- From blood cells
  - Rbc
  - platelets
- Hematopoietic stem cells in bone marrow
  - Neutraphils, basophils, eosinophils, monocytes
- Lymphoid stem cells
  - T cells
  - B cells

Hemopoiesis

- Production of blood
  - Starts at the embryonic stage
    - Yolk sac and liver
  - Continues during adult stage
    - Bone marrow

Components of blood

- White blood cells (WBC) or leukocytes
- Red blood cells (RBC)
- Platelets

The different stages of hemopoiesis in humans.

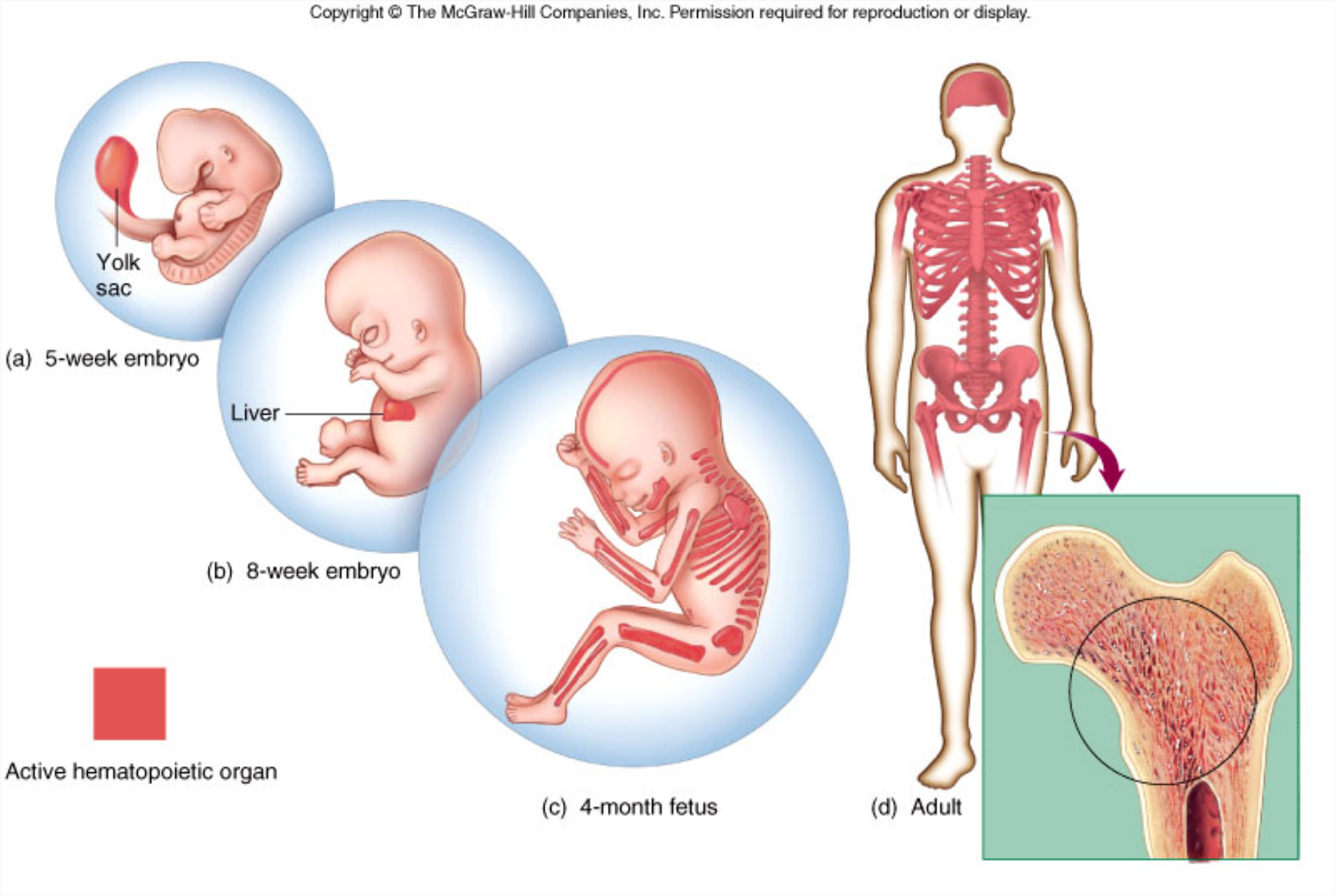


Fig. 14.8 Stages in hemopoiesis

The three types of stem cells differentiate into blood, platelets, granulocytes, and agranulocytes.

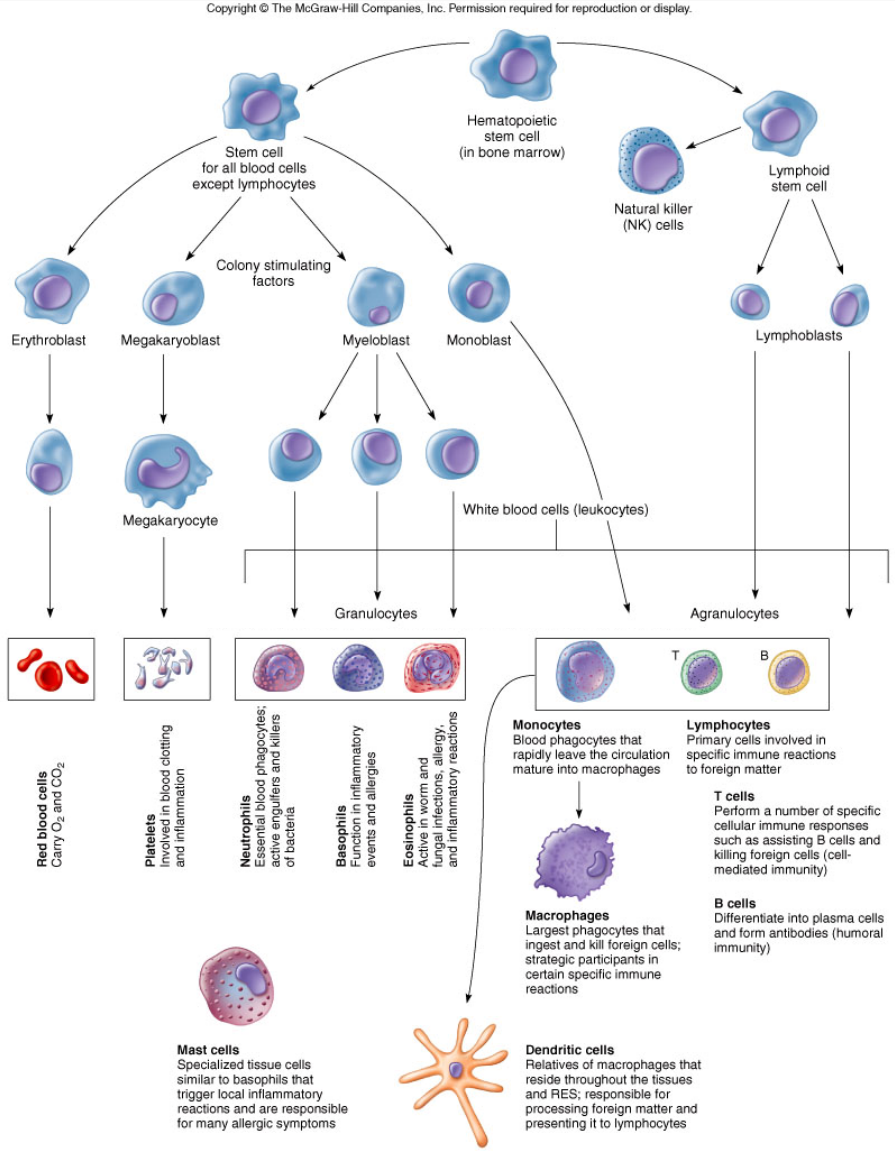


Fig. 14.9 The development of blood cells and platelets.

White blood cell

- Leukocytes
  - Granulocytes (large cytoplasmic granules)
    - Neutrophils
    - Basophils
    - Eosinophils
  - Agranulocytes (very small granules)
    - T cells
    - B cells
    - Monocytes

The buffy coat layer from unclotted blood contains WBCs.

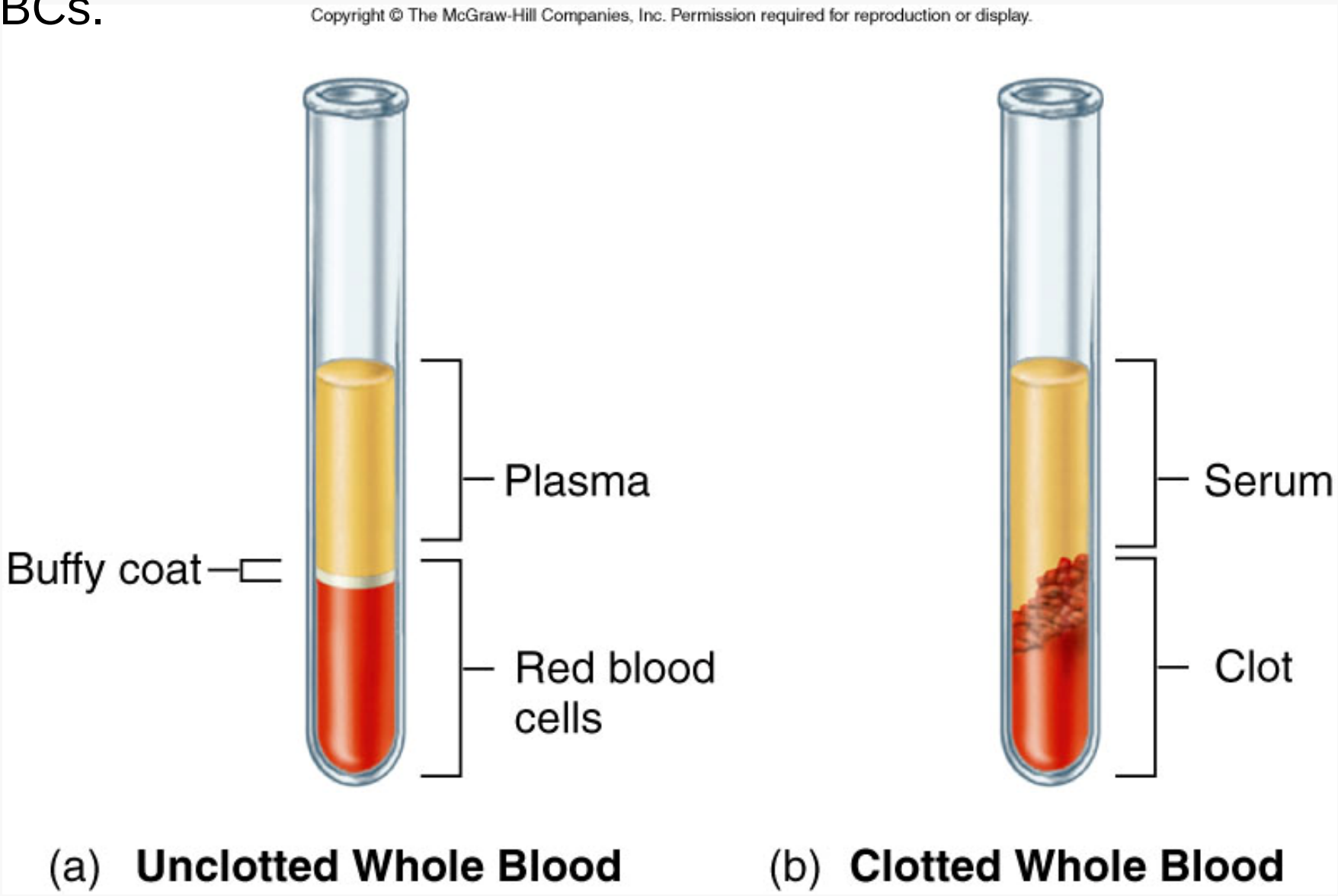


Fig. 14.7 The macroscopic composition of whole blood.

Neutrophils

- Nuclei - horse shoe or polymorphic nuclei
- Present in high numbers in blood and tissue
- Phagocytizes bacteria – granules are digestive enzymes
- First to arrive during an immune response (inflammation)

Eosinophils

- Nuclei – bilobed
- Present in the bone marrow and spleen
- Attach and destroy eucaryotic pathogens
- Associated with inflammation and allergies

Basophils

- Nuclei – constricted
- Present in low in number in the body
- Function is similar to eosinophils
- Localized basophils are called mast cells

Lymphocytes

- Specific immunity
  - T cells
  - B cells
- Present throughout the body

Monocytes

- Agranulocyte
- Differentiate into macrophages (circulation and lymphatics) and dendritic cells (tissue associated)
- Phagocytosis

Lymphatic system

- Network of vessels that extend to most body areas
- Connected to the blood system
- Provides an auxiliary route for the return of extracellular fluid to the circulatory system
- “Drain off” system for inflammatory response
- Contains lymphocytes, phagocytes and antibodies

Representation of the lymphatic system.

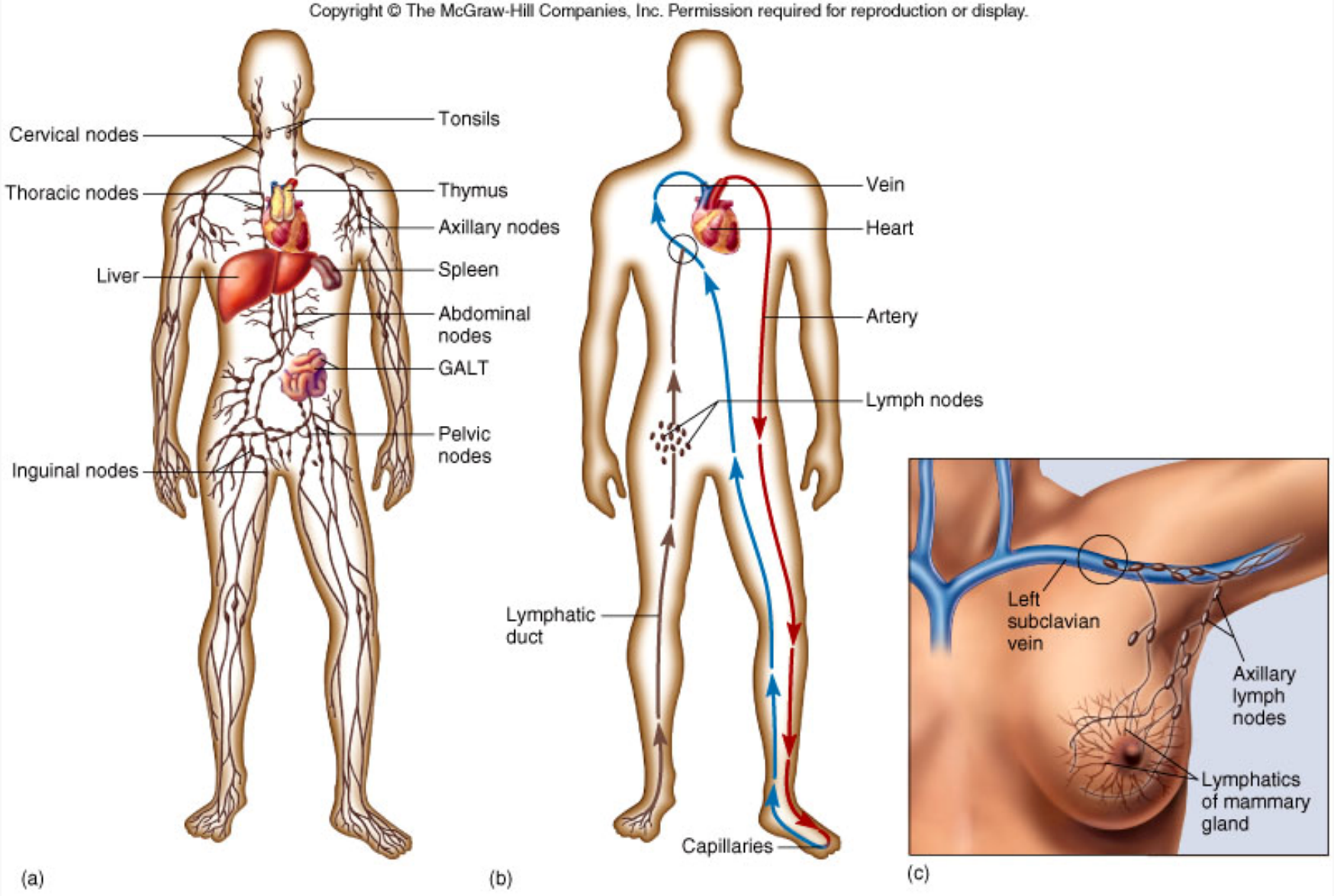


Fig. 14.11 General components of the lymphatic system.

Lymphatic system

- Fluids
- Vessels
- Nodes
- Spleen
- Thymus
- Miscellaneous

Fluids

- Plasma-like fluid (lymph)
  - Water
  - Dissolved salts
  - Proteins (antibodies, albumin)
  - White blood cells
  - No red blood cells
- Formed from blood components
  - Diffuse into the lymphatic capillaries

Vessels

- Parallels the blood system
- Returns lymph to the blood system
- Movement of lymph depends on muscle contractions
- Permeate all parts of the body except the central nervous system, bone, placenta, and thymus.

Lymph nodes

- Exist in clusters
- Located
  - along the lymphatic channels and blood vessels
  - in the thoracic and abdominal cavity regions, armpit, groin and neck
- Filter for the lymph
- Provide environment for immune reactions

Spleen

- Located in the upper left portion of the abdominal cavity
- Filter for blood
  - traps pathogens and phagocytizes pathogens
- Adults can survive without spleen
- Asplenic children are severely immunocompromised

Thymus

- Embryo
  - two lobes in the pharyngeal region
  - High activity (releases mature T cells) until puberty
- Adult
  - Gradually shrinks
  - Lymph node and spleen supply mature T cells

Infants rely on the thymus to differentiate immature T cells into mature T cells.

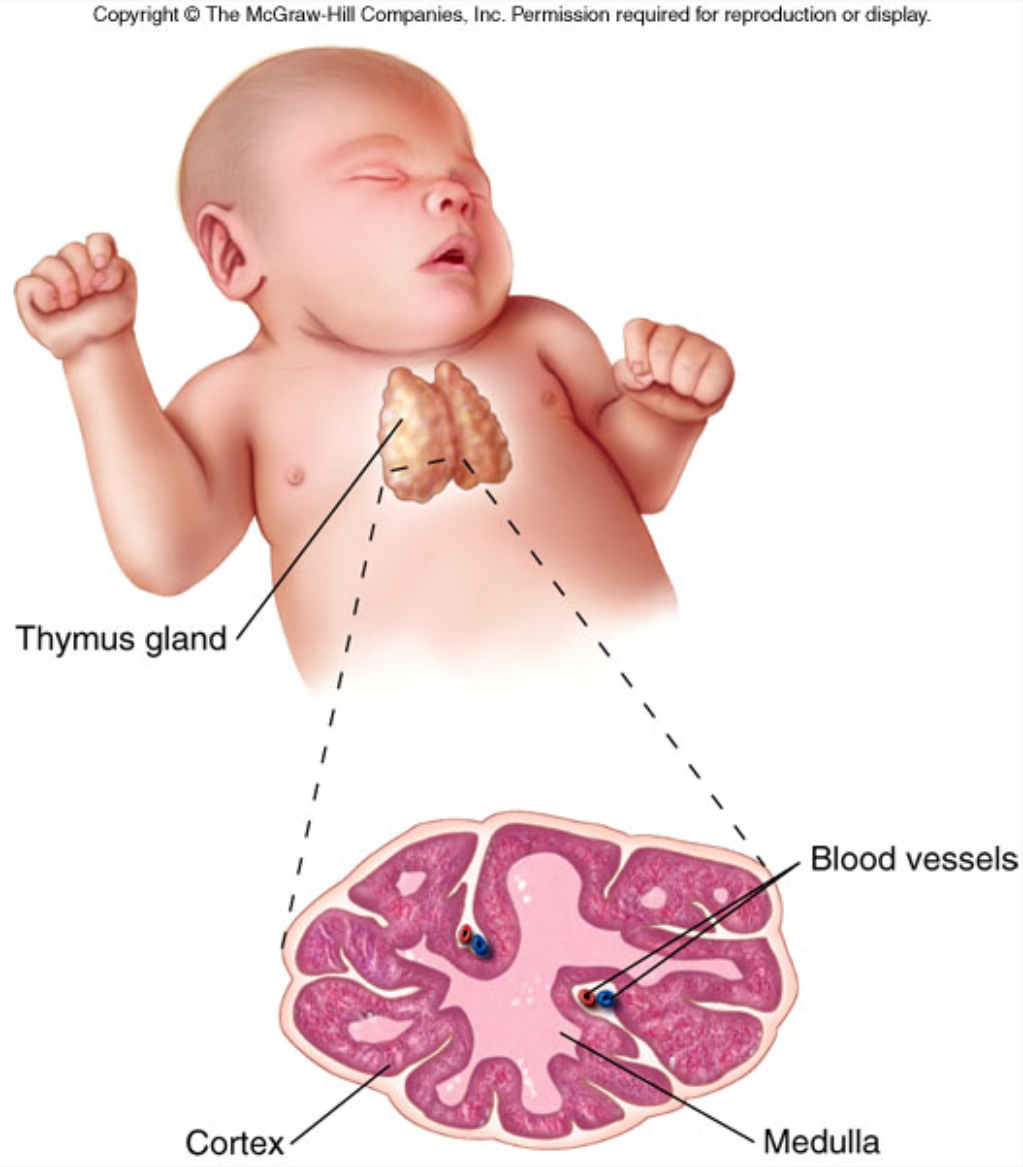


Fig. 14.12 The thymus gland

Gut-associated lymphoid tissue (GALT)

- Recognized incoming microbes from food
- Supply lymphocytes for antibody response
- Ex. Appendix, lacteals, Peyer’s patches

***Non-specific Immunity

- Inflammation
- Phagocytosis
- Interferon
- Complement

Inflammation

- Five major symptoms
  - Redness
  - Warmth
  - Swelling
  - Pain
  - Loss of function

The typical symptoms that occur after injury.

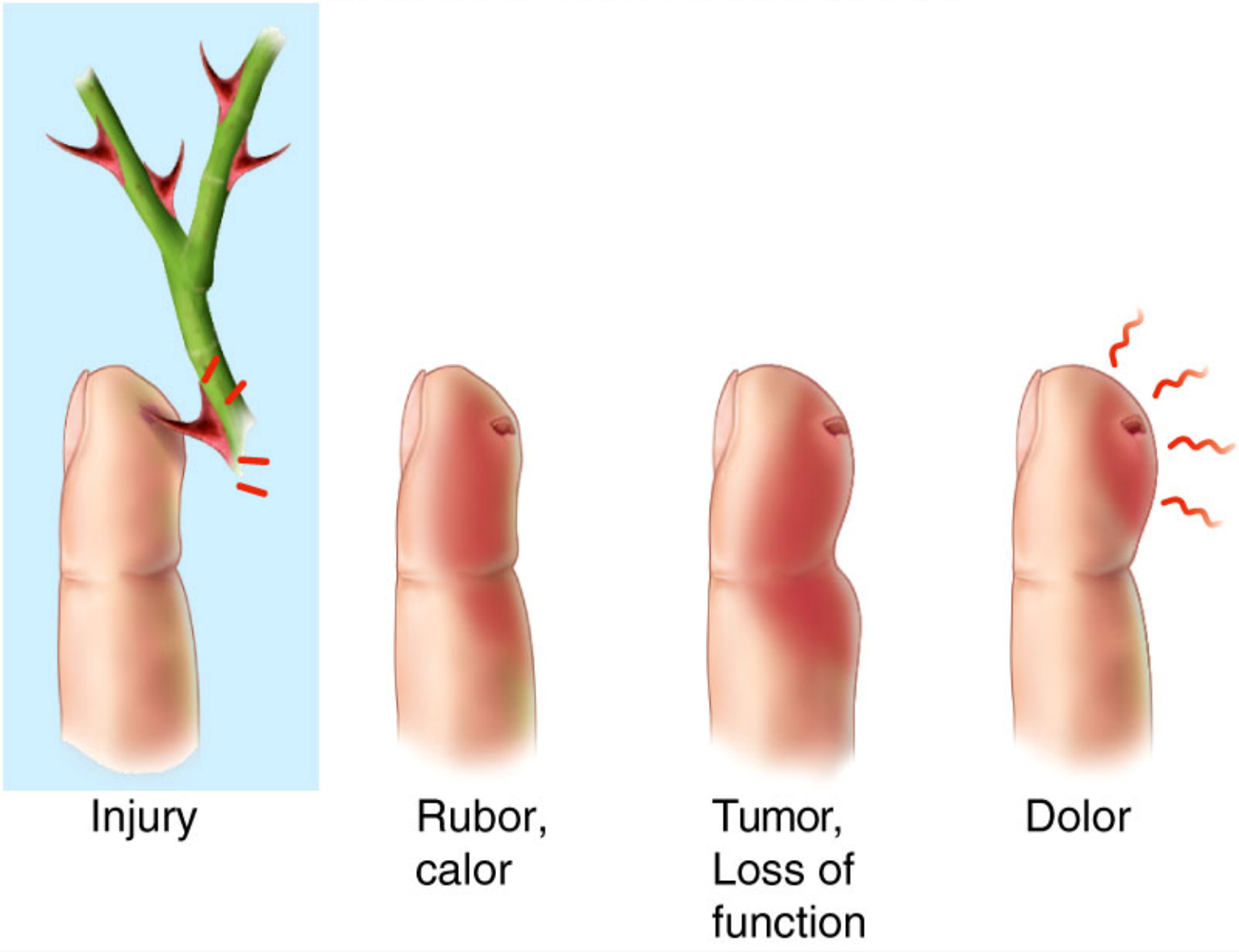


Fig. 14.13 The response to injury

Inflammation

- Causes
- Function
- Stages

Causes

- Trauma
- Tissue injury due to physical or chemical agents
- Specific immune reactions

Function

- Mobilize and attract immune components to the site of injury
- Aid in the repair of tissue damage
- Localized and remove harmful substances
- Destroy microbes and block their invasion

The major events in inflammation are injury, vascular reactions, edema, and resolution.

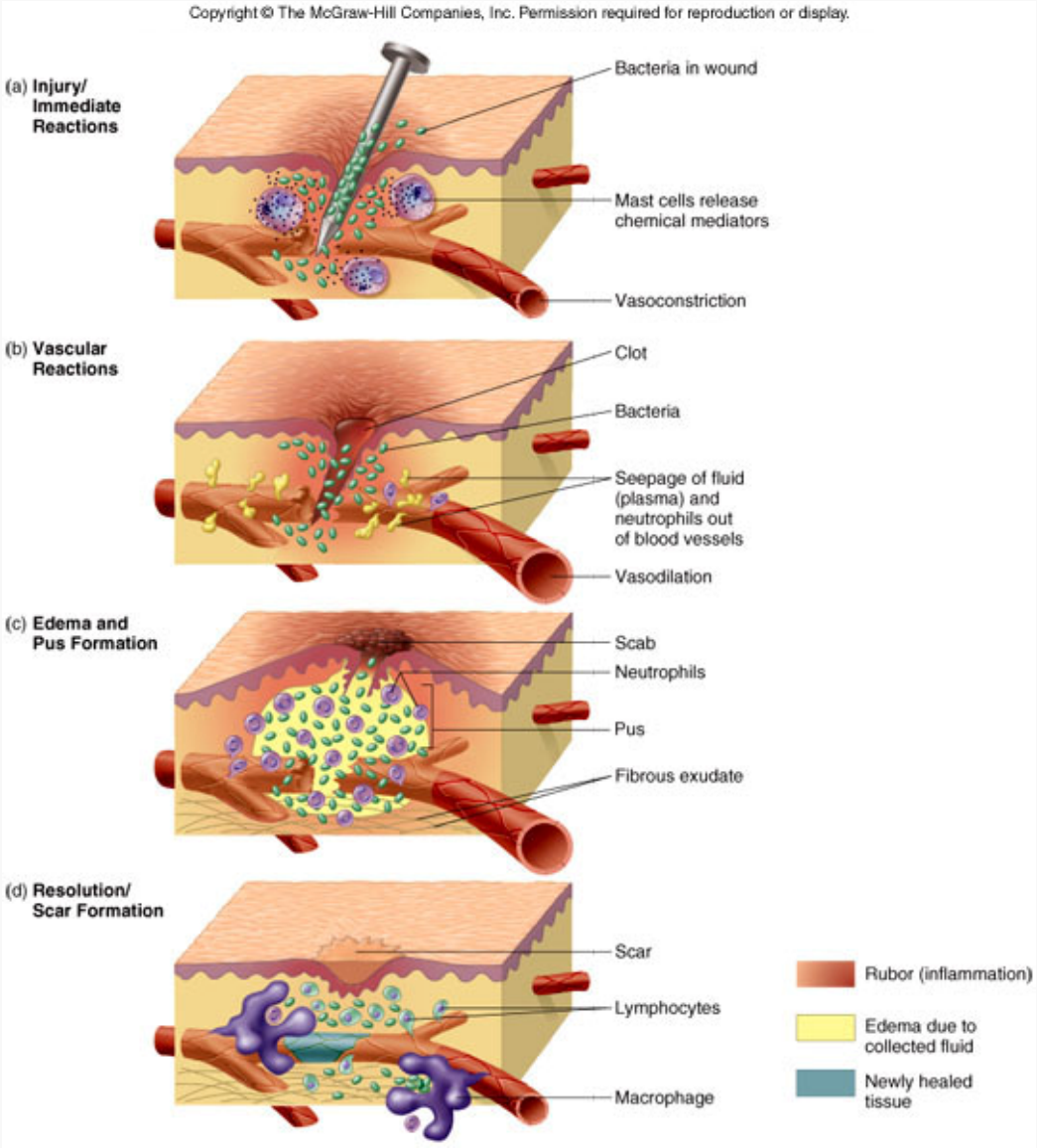


Fig. 14.14 The major events in inflammation

Stages

- Vascular changes
- Edema
- Fever

Vascular changes

- Blood cells, tissue cells, and platelets release chemical mediators and cytokines
- Chemical mediators
  - Vasoactive
    - Affect endothelial cells, smooth muscles of blood vessels
  - Chemotactic (chemokines)
    - Affect WBC

Chemical mediators

- Cause fever, stimulate lymphocytes, prevent virus spread, cause allergic reactions
  - Vasoactive mediators
    - Affect endothelial cells, smooth muscles of blood vessels
  - Chemotactic (chemokines) mediators
    - Affect WBC

Representation of the effects of chemical mediators during inflammation.

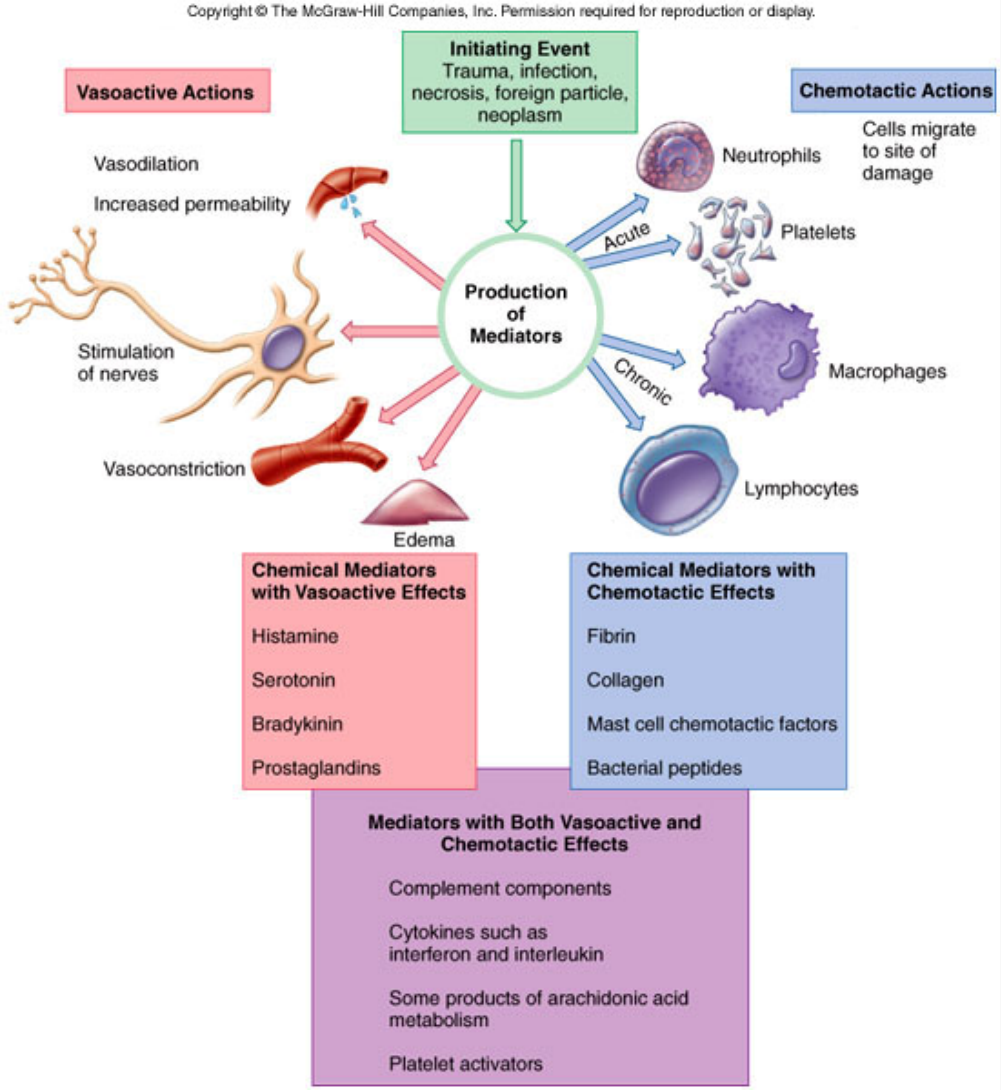


Fig. 14.15 Chemical mediators of the inflammatory response and their effects.

Edema

- Leakage of vascular fluid (exudate) into tissue
- Exudate - plasma proteins, blood cells (wbc), debris, and pus
- Migration of wbc is called diapedesis or transmigration
  - Chemotaxis

The transmigration of WBCs is followed by chemotaxis.

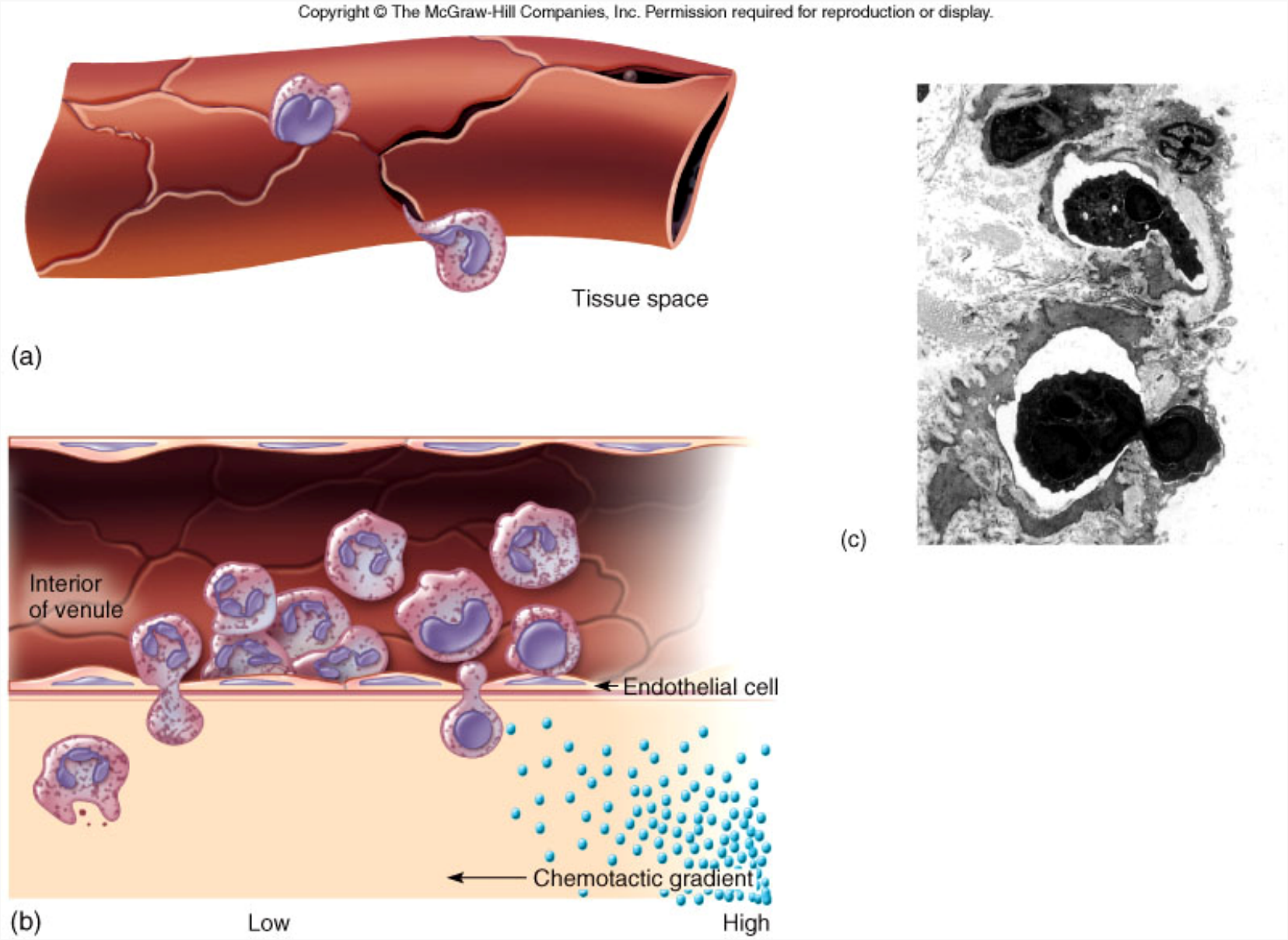


Fig. 14.16 Diapedesis and chemotaxis of leukocytes.

Fever

- Caused by pyrogens
  - reset the hypothalamic thermostat (increase temperature)
  - Vasoconstriction
- Pyrogens
  - Microbes and their products (ex. LPS)
  - Leukocyte products (ex. Interleukins)
- Inhibits microbe and viral multiplication, reduces nutrient availability, increases immune reactions

Phagocytosis

- Neutrophils and eosinophils
- Macrophages
- Mechanism

Neutrophils and eosinophils

- Early responders to inflammation
- Neutrophils are primary components of pus
- Eosinophils are primary responders to parasitic infections

Macrophages

- Monocytes transform into macrophages
- Scavengers
  - Histiocytes – reside in one location (ex. Alveolar, Kupffer, Langerhans)
  - Drift throughout the RES
- Undergo phagocytosis,
- Interact with B and T cells

Stem cells differentiate into macrophages in the bone marrow and peripheral blood, and then either migrate or take residence in a specific location.

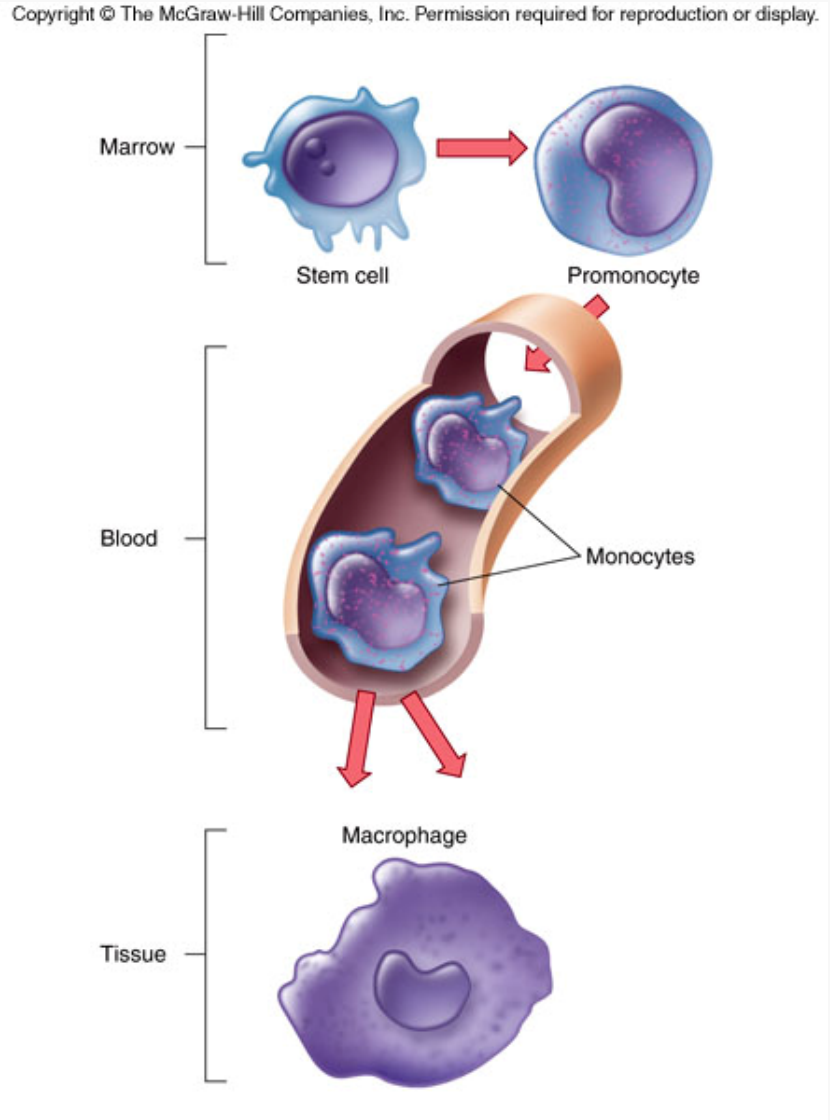


Fig. 14.17 The development stages of monocytes and macrophages.

Macrophages can take-up permanent residence in the lung (alveolar), liver (Kupffer) and skin (Langerhans).

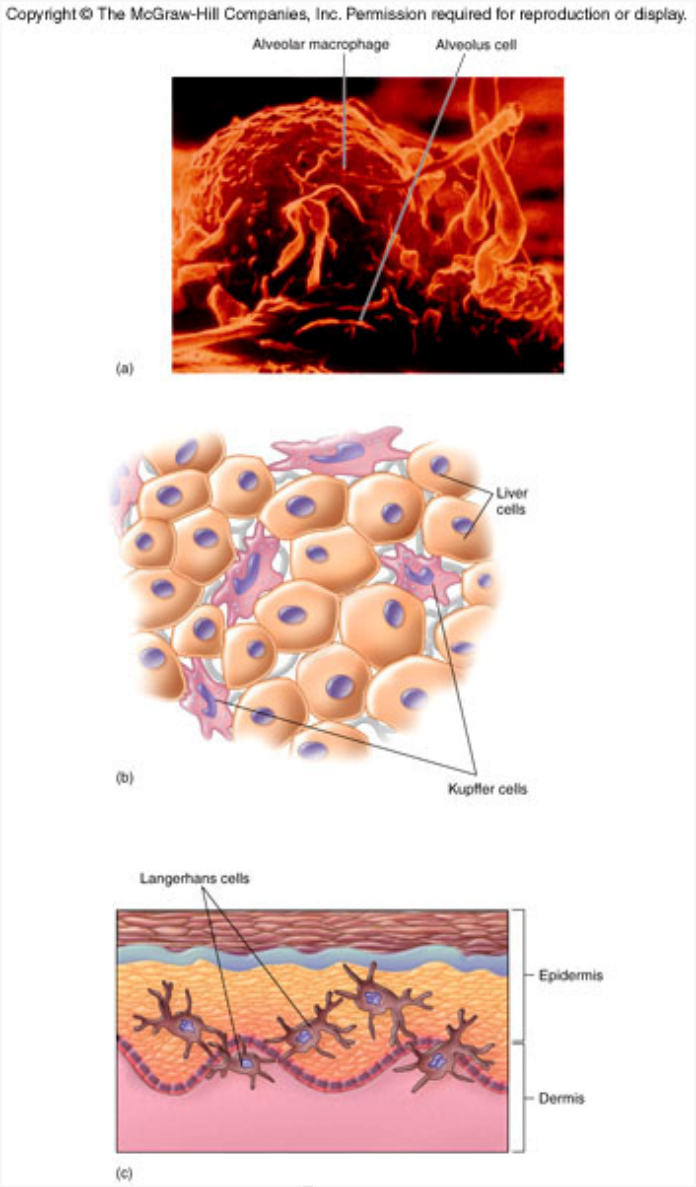


Fig. 14.18 Sites containing macrophages

Mechanism

- Chemotaxis
- Ingestion
- Phagolysosome
- Destruction

Chemotaxis

- Directed by
  - Pathogen-associated molecular patterns (PAMPs)
    - Peptidoglycan
    - LPS
  - Foreign debris

Ingestion

- Pseudopods enclose the pathogen or foreign material
- Form a phagosome

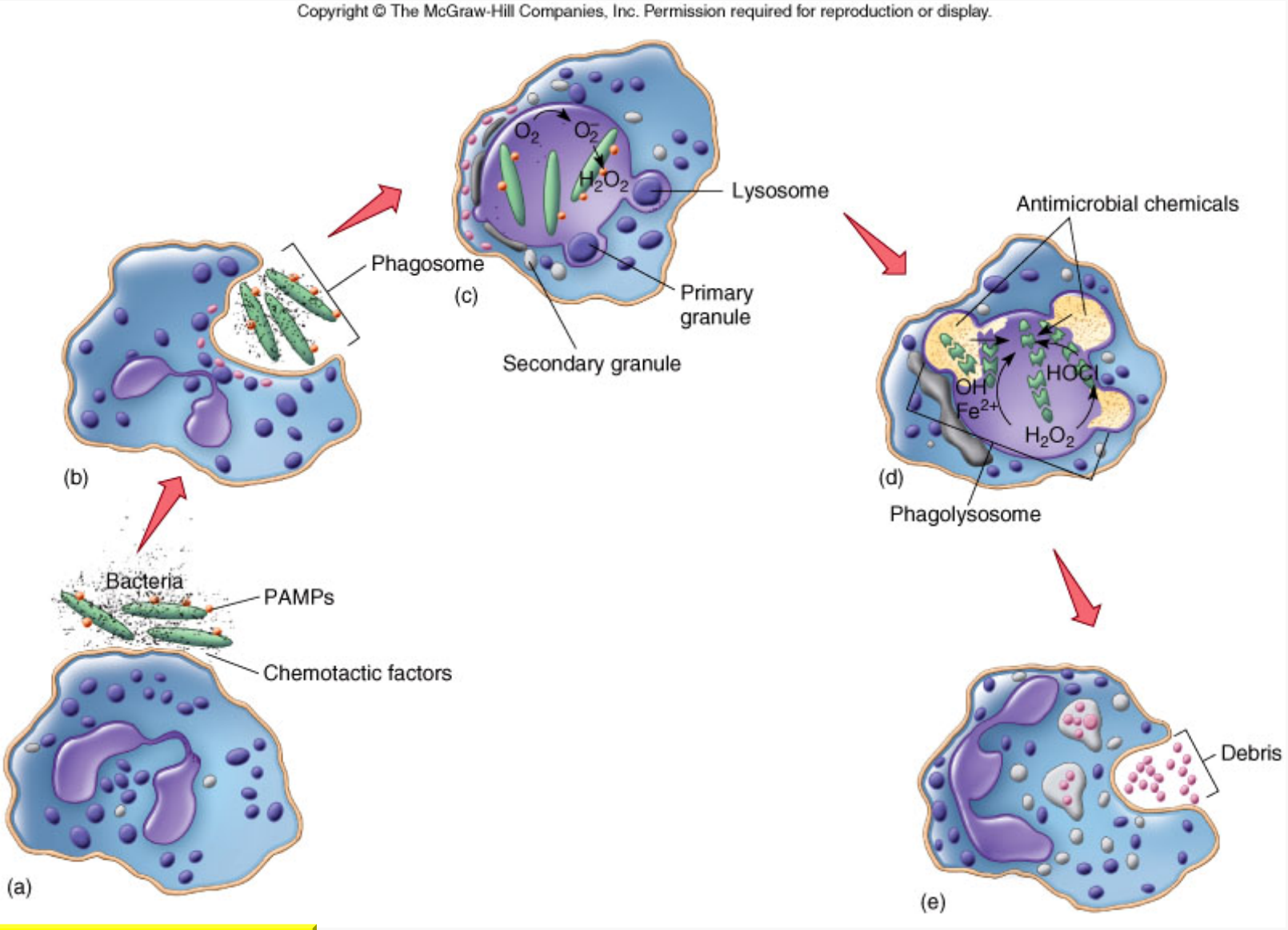
Phagolysosome

- Lysosomes fuse with the phagosome
- Other antimicrobials chemicals are released into the phagolysosome

Destruction

- Within the phagolysosome
  - Oxygen-dependent system
    - Oxidative burst (oxidizing agents)
  - Enzymes
  - Nitric oxide
- Undigestible debris are released

A summary of the mechanism of phagocytosis.



Run Animation: Phagocytosis

Fig. 14.19 The phases in phagocytosis

Interferon

- Produced due to viral infections, microbe infections, RNA, immune products, and antigens

Interferon

- Synthesis
- Classes
- Activity

Synthesis

- WBCs
- Tissue cells

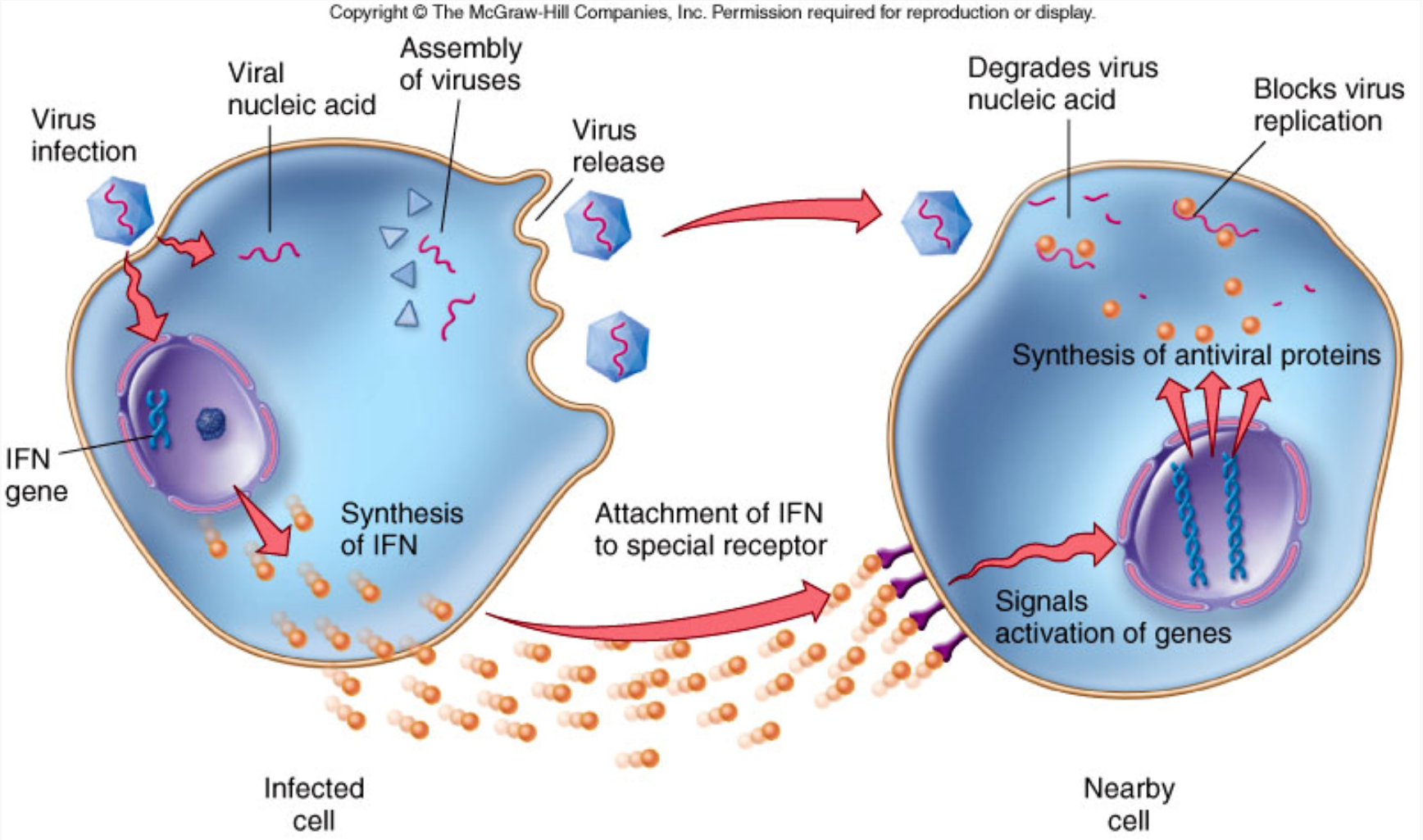
Classes

- Interferon alpha
  - Product of lymphocytes and macrophages
- Interferon beta
  - Product of fibroblasts and epithelial cells
- Interferon gamma
  - Product of T cells

Activity

- Ex. Virus - binds to host cell
- A signal is sent to the nucleus to synthesized (transcription and translation) interferon
- Interferon is secreted
- Binds to other host cells
- Host cells produce antiviral proteins
  - inhibit viral multiplication or translation
    - Not virus-specific

Interferon is produced, released, and taken-up by a near-by cell, where by original cell is not protected but the recipient cell is protected.



Run Animation: Antiviral activity of interferon

Fig. 14.20 The antiviral activity of interferon.

Other Roles of Interferon

- Activates and instructs T and B cell development
- Inhibits cancer cells
- Activates macrophages

Complement

- Consist of 26 blood proteins
- Produced by liver hepatocytes, lymphocytes, and monocytes
- Pathways
- Cascade reaction
- Stages

Pathways

- Classical
  - activated by the presence of antibody bound to microbes
- Lectin
  - activated when a host serum protein binds a sugar (mannan) in the wall of fungi and other microbes
- Alternative
  - activated when complement proteins bind to cell wall or surface components of microbes

The three complement pathways, their activators, and the complement proteins involved.

TABLE 14.1 Complement Pathways

Pathway	Activators	Host Components That Initially Bind	Complement Proteins Involved
Classical (Rapid, efficient)	Complement-fixing antibodies (IgG, IgM) (sometimes microbe surface components)	C1 complex	C1 complex C4 C2 C3
Lectin	Mannans	Mannose-binding lectin	
Alternative (Slower, less efficient)	Bacterial or fungal cell wall Viruses Parasite surfaces	C3	C3 Factor B Factor D Properdin

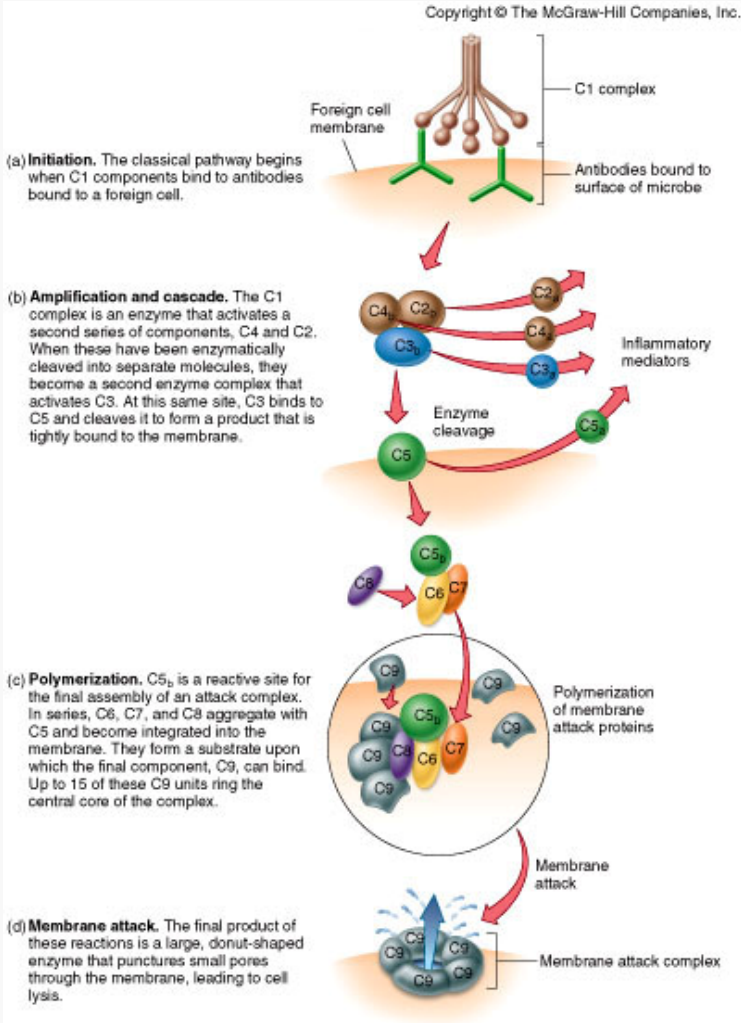
C5, C6, C7, C8, C9, Membrane Attack Complex

Table 14.1 Complement pathways

Stages

- Initiation
- Amplification and cascade
- Polymerization
- Membrane attack

The classical pathway begins with C1 components binding to antibodies, and ends by puncturing small pores through the membrane, leading to lysis.

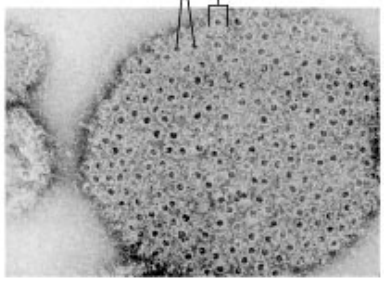


(a) **Initiation.** The classical pathway begins when C1 components bind to antibodies bound to a foreign cell.

(b) **Amplification and cascade.** The C1 complex is an enzyme that activates a second series of components, C4 and C2. When these have been enzymatically cleaved into separate molecules, they become a second enzyme complex that activates C3. At this same site, C3 binds to C5 and cleaves it to form a product that is tightly bound to the membrane.

(c) **Polymerization.** $C5_b$ is a reactive site for the final assembly of an attack complex. In series, C6, C7, and C8 aggregate with C5 and become integrated into the membrane. They form a substrate upon which the final component, C9, can bind. Up to 15 of these C9 units ring the central core of the complex.

(d) **Membrane attack.** The final product of these reactions is a large, donut-shaped enzyme that punctures small pores through the membrane, leading to cell lysis.



(e) An electron micrograph (187,000×) of a cell reveals multiple puncture sites over its surface. The lighter, ringlike structures are the actual enzyme complex.

Run Animation: Activation of complement

Fig. 14.21 Steps in the classical complement pathway at a single site.

The Complement System

- Serum proteins activated in a cascade.

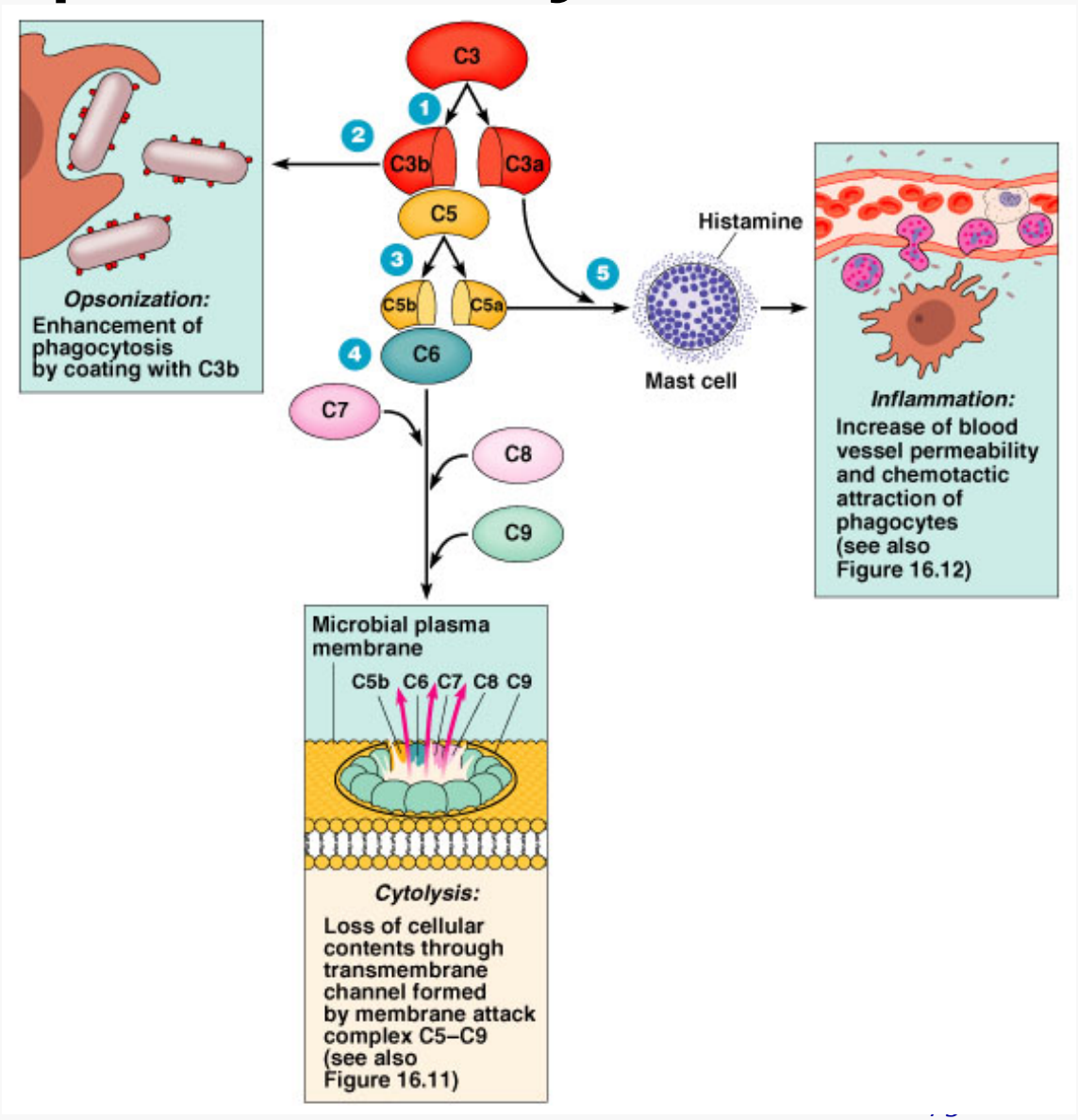


Figure 16.10

Effects of Complement Activation

- Opsonization or immune adherence: enhanced phagocytosis
- Membrane attack complex: cytolysis
- Attract phagocytes

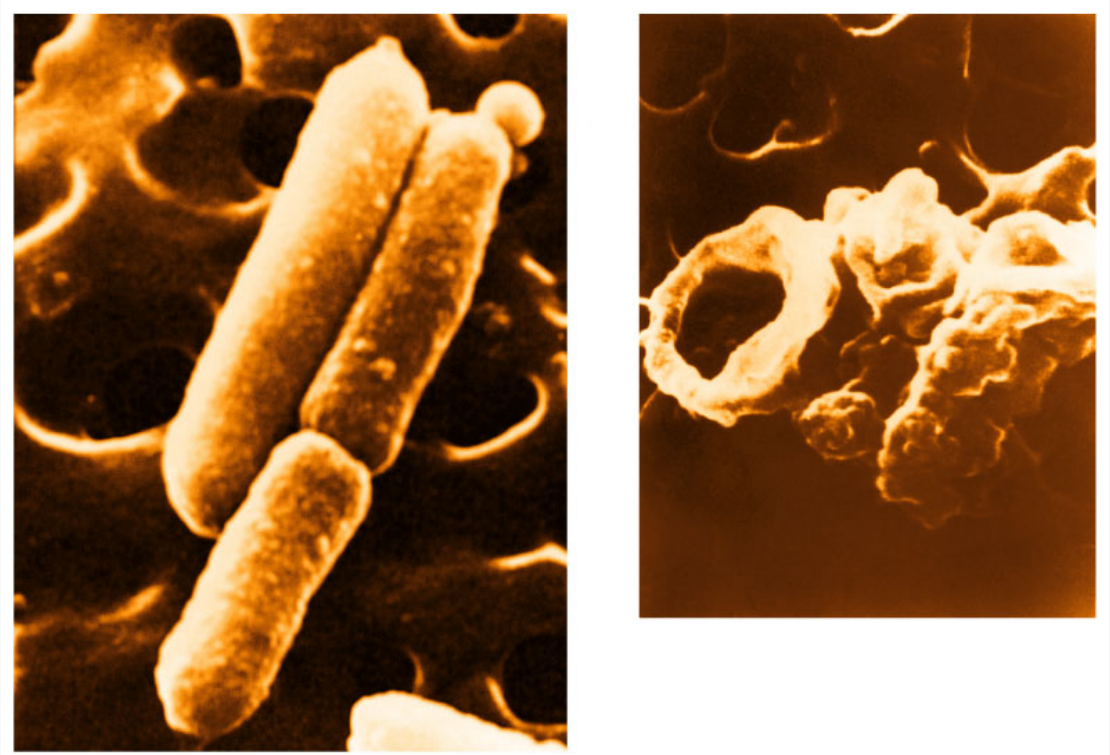
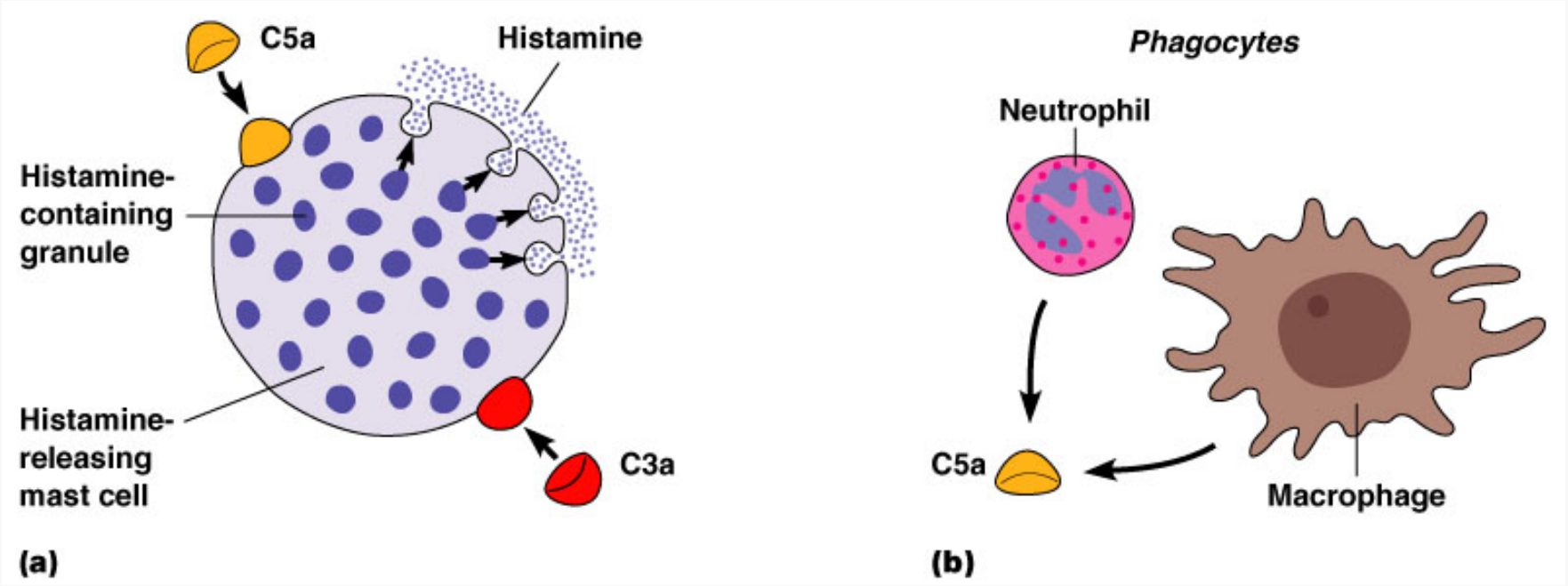


Figure 16.11

Effects of Complement Activation



Classical Pathway

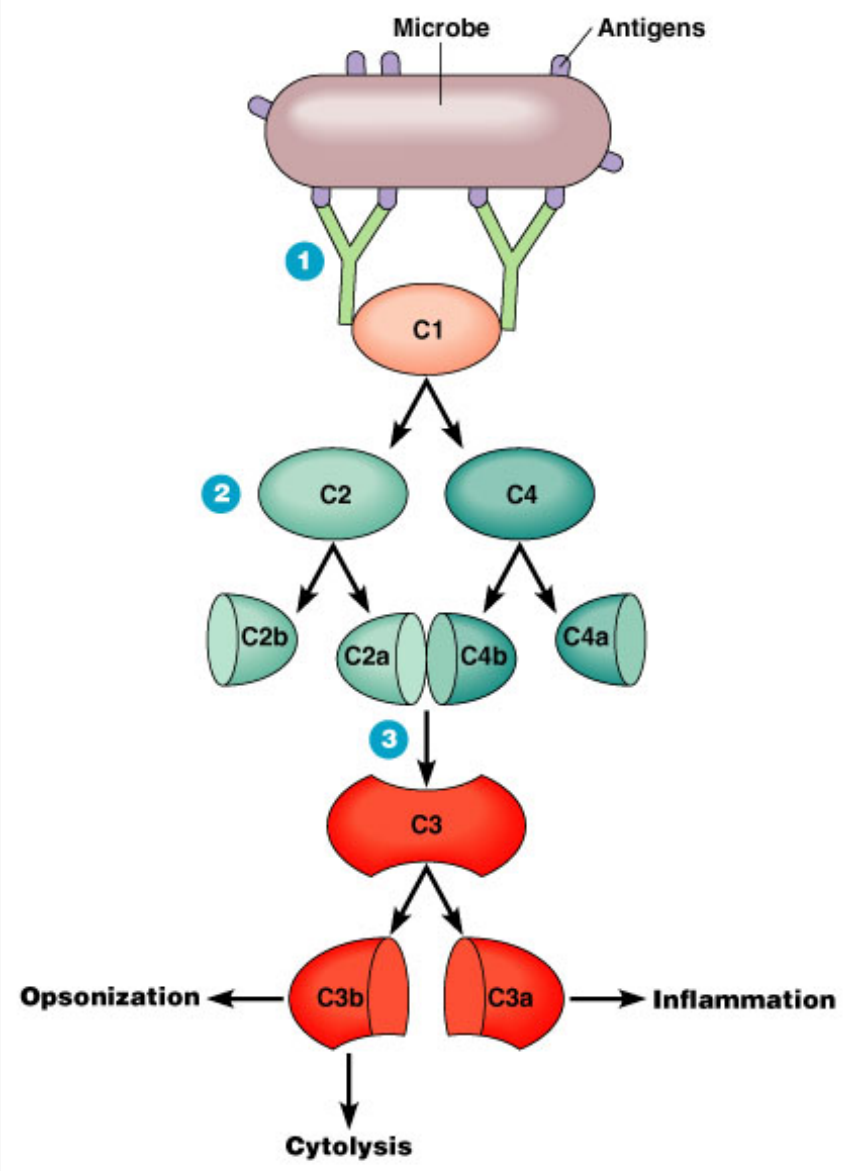


Figure 16.13

Alternative Pathway

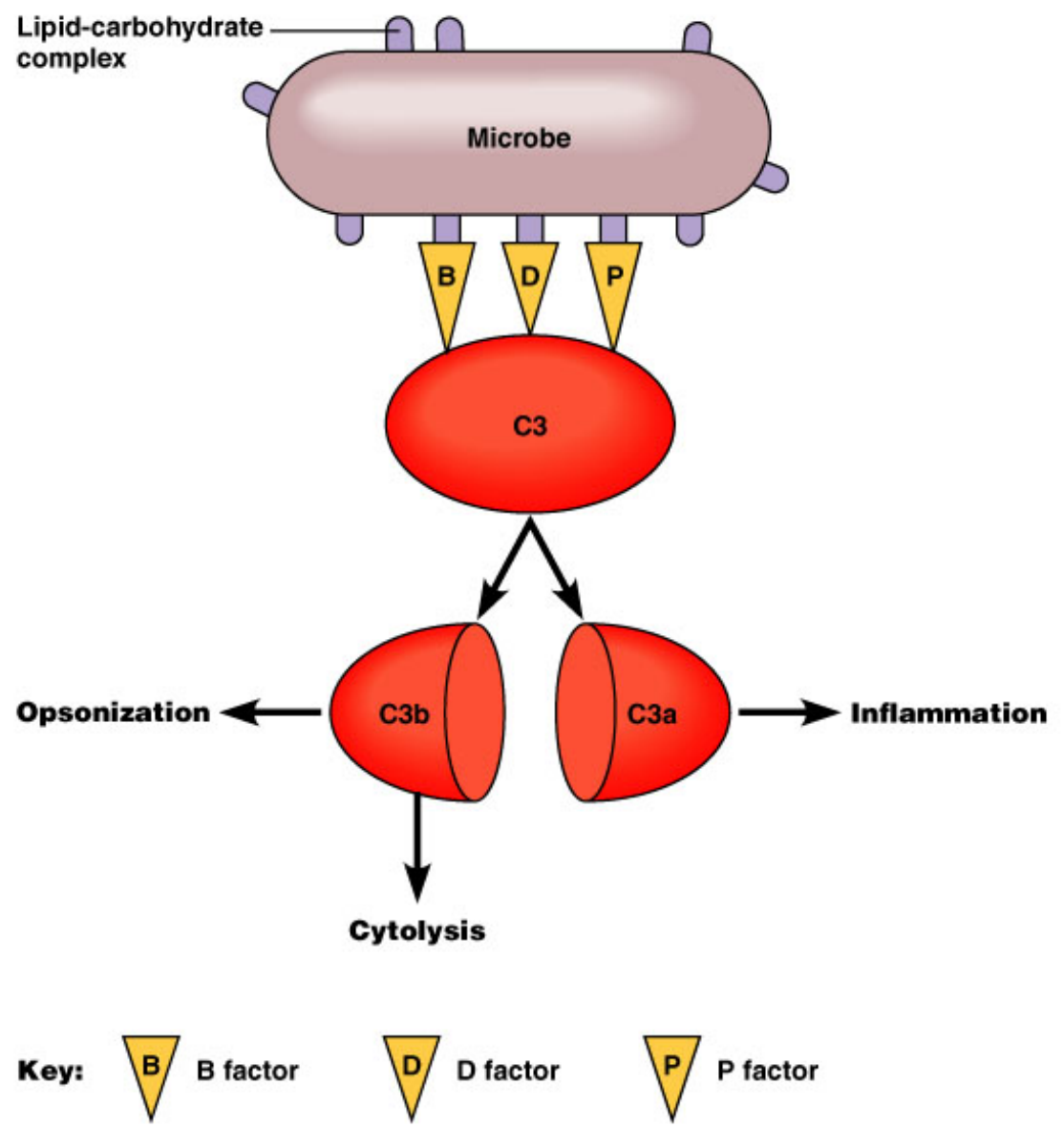


Figure 16.14

Lectin Pathway

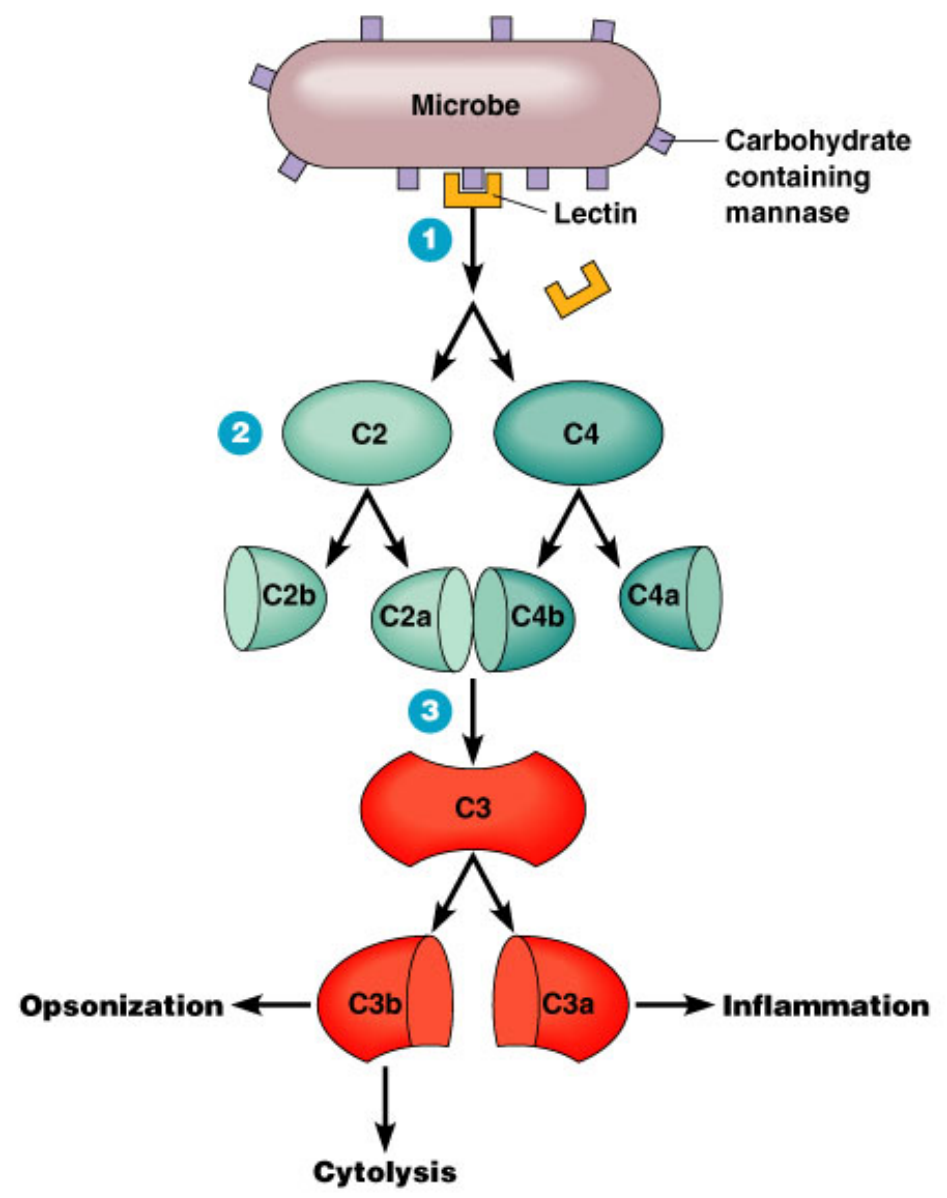


Figure 16.15

Some bacteria evade complement

- Capsules prevent C activation
- Surface lipid-carbohydrates prevent MAC formation
- Enzymatic digestion of C5a